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MECHANISMS OF AUTONOMIC DYSFUNCTION REALIZATION DURING COMORBID GASTROESOPHAGEAL REFLUX DISEASE AND NEUROCIRCULATORY DYSTONIA WITH INSOMNIA AMONG YOUNG PEOPLE

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Abstract

The aim of the study: to optimize diagnostics and treatment of comorbid gastroesophageal reflux disease (GERD) and concomitant neurocirculatory dystonia (NCD) with insomnia among young people by studying autonomic dysfunction and mechanisms of its realization.

Methods. The study was conducted in three groups of patients, homogeneous by gender and age. The first group included patients with GERD and insomnia, the second group counted those with NCD and insomnia, and the third group consisted of GERD with NCD and insomnia. We studied the quality of life (SF-36), quality of sleep (PSQI), the presence and severity of depression (PHQ-9), psychosomatic condition (Spielberger-Khanin scale), and determined the presence and severity of autonomic dysfunction syndrome (Wayne questionnaire), acidity of the stomach, ultrasound examination of the esophagus and stomach.

Results. The first group revealed sympathicotonia and increase of gastric juice aggression (in the stomach body 0.89 ± 0.05) and reactive (47.2 points) and personal anxiety (52.7 points), which suggests the advisability of use PPI (omeprazole 20 mg 2 times a day for 5 weeks), and melatonin 3 mg per night during 3 weeks. The second group showed parasympathicotonia predominant, a more pronounced decrease in vitality scale (31.5 ± 4.2), and a moderate increase in indicators of reactive (44.0 points) and personal anxiety (46.5 points), which suggests the advisability of use 3 mg of melatonin per night during 3 weeks. The third group demonstrated predominance of parasympathicotonia, motor disorders, a decrease in alkalizing function of antrum (5.4 ± 0.17), depression (81.8 %), and the greatest decrease in indicators of sleep quality (11.7) and quality of life, which suggests the advisability of use PPI (omeprazole 20 mg 2 times per day during 5 weeks), with prokinetics (domperidone 10 mg 3 times per day during 5 weeks), and melatonin 3 mg per night during 3 weeks.

Conclusions. Autonomic dysfunction has a key influence on the main pathogenetic factors in the formation of both GERD and NCD and insomnia, and the type of autonomic tone determines the features of the clinical course of both isolated and combined pathology.

Keywords: gastroesophageal reflux disease, neurocirculatory dystonia, autonomic dysfunction, insomnia.

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1. Introduction

Gastroesophageal reflux disease (GERD) is one of the most common diseases and it occurs among both out-patients and in-patients [1]. At the same time, reflux and heartburn are typical symptoms of GERD. They reduce daytime activity [2], performance efficiency, disrupt sleep and, as a result, significantly reduce the quality of life of the patient [3, 4]. In recent times, there has been a significant rejuvenation of this pathology and it is increasingly diagnosed in young and middle-aged people [5]. In its turn, it is in this age group that autonomic tone is most pronounced.

As far as it is known, autonomic nervous system (ANS), which consists of sympathetic and parasympathetic divisions, regulates the activity of internal organs, blood vessels and endocrine glands, as well as the activity of metabolic processes, ensuring homeostasis. Taking into account the above mentioned, the ANS is one of the leading systems that regulates processes of secretion and motility. Their mis-function leads to the formation of GERD [7].

Thus, the ANS is a kind of first “performer” in psychosomatic disorders, that is, when a person experiences a stressful impact, the central nervous system affects the ANS, activating the endocrine glands.

At the same time, it was noted that GERD usually has a comorbid course, and neurocirculatory dystonia (NCD) is one of the most frequent diseases that accompanies GERD [6]. More often this pathology affects young people who do not have an organic myocardial lesion, and therefore one of the leading places in pathogenesis also belongs to autonomic disorders.

Also nowadays insomnia [8, 9] is a frequent condition accompanying both GERD and NCD [10, 11]. Taking into account the fact that the vast majority of young patients do not have severe organic pathology, i.e. heart and lung diseases, therefore, violations of the ANS also have an important place in the formation of insomnia.

Taking into account that autonomic dysfunction syndrome (ADS) is a trigger for the development of these pathologies, its study in students suffering from GERD and concomitant NCD with sleep disorder is of great practical importance for providing timely treatment and prevention measures.

The aim of the study: to optimize diagnostics and treatment of comorbid GERD and concomitant NCD with insomnia among young people by studying autonomic dysfunction and mechanisms of its realization.

2. Materials and methods

There was a study conducted in 2017–2019 on the basis of the gastroenterological department of the Municipal Non-Commercial Enterprise “City Student Hospital”, Kharkiv, Ukraine, in which 81 patients and 20 practically healthy students took part.

Prior to the study, all sick and healthy students of the control group were informed of its aims. A voluntary consent for the study was obtained. All procedures performed in the study comply with the Declaration of Helsinki and current legislation of Ukraine in the field of bioethics of medical research (order of the Ministry of Health of Ukraine No. 281 of 01.11.2008 “On approval of instructions on clinical trials of drugs and examination of clinical research materials and model regulations on Ethics commissions”). It was approved by ethics committee at Kharkiv Medical Academy of Postgraduate Education (protocol No. 8 of 27.09.2017)

The criteria for inclusion of patients into this study group were: persons of both sexes from 18 to 35 years, the existence of a non-erosive form of GERD with concomitant NCD and insomnia. GERD was diagnosed according to ICD-10 and the recommendations of the 2006 Montreal Consensus. The diagnosis of NCD is made according to the standard protocol (Decree No. 436 of the Ministry of Health of Ukraine on 03.07.2006) and ICD-10. The duration of the history of both pathologies is from 1 to 5 years. Insomnia in these patients was diagnosed by the Pittsburgh Sleep Quality Index (PSQI) with an overall average score of more than 6.0.

The exclusion criteria were as follows: the combination of GERD with structural gastrointestinal disorders, in particular, peptic ulcer, neoplasms of the stomach and esophagus, Barrett’s esophagus, as well as the existence of concomitant pathology of other systems in these individuals and an increased average score of self-assessment of psychosomatic status on any of the scales of questionnaires, which is an indication for a psychotherapist advice.

The first group included 25 patients of 18–25 years old, 20.6 average (13 women and 12 men) with isolated GERD and insomnia, who received proton pump inhibitors (PPI) (omeprazole 20 mg 2 times per day for 5 weeks) and melatonin 3 mg per night for 3 weeks. The second group consisted of 25 patients of 18–25 years old, 21.5 average (13 women and 12 men) with isolated NCD and insomnia, who received melatonin 3 mg per night for 3 weeks. The third group comprised 31 patients of 18–25 years old, 21.1 average (16 women and 15 men) suffering from GERD with

concomitant NCD and insomnia, who received PPI (omeprazole 20 mg 2 times a day for 5 weeks) with prokinetics (domperidon 10 mg 3 times per day during 5 weeks) and melatonin 3 mg per night for 3 weeks. The control group included 20 almost healthy students of 18–25 years old, 20.2 average (10 women and 10 men).

Life quality was assessed using the unified SF-36 questionnaire, which includes assessment of the physical health scale and the mental health scale. The level of complete health corresponds to 100 points. The lower is the overall score, the worse is the quality of life.

The PHQ-9 (Patient Health Questionnaire) was used to determine the presence and severity of depression. According to the survey results, you can score from 0 to 27 points, which allows you to interpret the severity of depression from the absence of this violation to high-grade depression.

The psychosomatic condition of patients was assessed according to the Spielberger-Khanin scale to determine personal and reactive anxiety. When analyzing the results, the total indicator for each of the sub-scales can be in the range from 20 to 80 scores. When interpreting the indicators, the following anxiety assessments are used: up to 30 scores – low, 31–44 scores – moderate; 45 and more – high.

Based on the Wayne questionnaire the availability and severity of ADS was determined, as well as the type of autonomic status (sympathicotonia, vagotonia, and eutonia (vegetative tone)) was established. The questionnaire consists of 11 questions. As a result, a healthy person can score up to 15 points. If more than 15, then we can talk about the presence of VDS.

Patients were tested for the acidity of gastric juice by intragastric pH-meter method using IKZh-2 apparatus (produced in Ukraine). Motor function of the esophagus and stomach was identified using an ultrasound examination conducted on ALOKA SSD-650 machine (produced in Japan) and Ultima pro-30 machine (produced in Ukraine) – in the patient's left side and on the back; in epigastric region and projections at esophageal hiatus; fasted and 5, 10 and 15 minutes after drinking 0.5 l of liquid. The study measured the thickness of the esophagus wall, the esophagus width in the lower third, the diameter of esophageal hiatus, the presence of fluid regurgitation, and its duration. The organic and functional state of myocardium was studied with the help of pulse wave Doppler sonography with color mapping on the device ALOKA SSD-650 (manufactured in Japan) and ULTIMA pro-30 (manufactured in Ukraine).

To process statistical data, we used Microsoft Office Excel 2007 and the statistical data processing system Statistica 6.0. Under normal distribution, Student's t-test was used; in case of deviation from the normal distribution, nonparametric methods were used. The mean value (M), Student's t-test was assessed. The differences were considered significant at $p < 0.05$. The results were presented as $M \pm m$, where M is the median and m is the standard deviation.

3. Results

The study found that patients in groups 1 and 3 presented typical GERD complaints of heartburn, which bothered them more than twice a week, as well as at night, they often felt a sour taste in their mouth. Patients in groups 2 and 3 had typical NCD complaints: they were concerned about heart failure, sometimes pain in the lower third of the sternum, a decrease in blood pressure to 90/60 or an increase in it to 135/85. According to the results of pulse wave Doppler sonography with color mapping, no organic heart pathology was detected in patients of groups 2 and 3. On ECG, some of the patients in these groups showed a slight violation of the repolarization processes, while all the others showed no pathological changes.

When studying the sleep quality index in patients of the study and control groups according to the Pittsburgh questionnaire (PSQI), the following results were found (**Table 1**).

It was found that sleep disorders were observed in all groups under control, however, insomnia ($p < 0.05$) was more pronounced in patients of group 3 because all the indicators of this questionnaire were significantly higher in comparison not only with the control group, but also with patients of groups 1 and 2.

The quality of life indicators in accordance with the unified SF-36 questionnaire are shown in **Table 2**.

Table 1

Characteristics of sleep quality indicators in treatment and control groups

Indicators	Group 1 n=25	Group 2 n=26	Group 3 n=30	Control group n=20	p
Sleep duration	0.95	1.19	1.46	0.3	p<0.05
Sleep disturbance	1.16	1.0	1.52	0.25	p<0.05
Duration of falling asleep	50±10 min	45±14 min	60±15 min	13±3,5 min	
Sleep latency	2.4	1.95	2.7	0.32	p<0.05
Daytime dysfunction	1.27	1.53	2.01	0.15	p<0.05
Sleep efficiency	1.05	1.04	1.54	0.24	p<0.05
Subjective sleep quality	1.86	1.84	2.47	0.53	p<0.05
Use of sleep medication	0	0	0	0	
Average total score	7.74	7.55	11.7	1.8	p<0.05

Table 2

Characteristics of quality of life in treatment groups and control group individuals

Indicators	Group 1	Group 2	Group 3	Control group	p
Physical functioning	43.5±3.8	40.1±3.9	41.7±3.2	84.5±4.0	p>0.05
Role-physical functioning	27.0±3.3	34.9±3.9	36.7±4.0	71.4±3.0	p<0.001
Bodily pain	41.2±3.6	36.5±3.1	23.1±3.8	76.3±4.0	p<0.001
General health	35.5±3.9	34.3±3.6	32.2±3.9	74.9±4.1	p>0.05
Vitality scale	45.5±3.2	31.5±4.2	40.4±3.2	80.5±3.2	p<0.001
Social functioning	45.2±3.5	44.1±3.4	43.6±3.3	81.4±4.2	p>0.05
Role-emotional functioning	48.3±3.1	43.4±3.5	31.7±3.6	78.6±3.5	p<0.001
Mental health	44.5±3.3	38.4±3.9	30.5±2.7	75.4±3.7	p<0.001

Patients of all three groups compared to the control group showed a significant decrease in quality of life on all scales. At the same time, the lowest indicators are observed in patients with combined pathology, but on the role-physical functioning scale, the lowest indicator is observed in patients with GERD and insomnia, the vitality scale indicator is most reduced in patients with NCD and insomnia. On the other hand, unreliable differences ($p>0.05$) were found on the scales of physical, social functioning and general health.

Data from the PHQ-9 questionnaire is presented in **Table 3**.

Table 3

Characteristics of indicators in patients of treatment groups and control groups according to the PHQ-9 questionnaire

Indicators	Group 1	Group 2	Group 3	Control group	p
Absence of depression (1–4 points)	13.04 %	5.66 %	4.55 %	96.7 %	p<0.05
Mild depression (5–9 points)	21.74 %	20.11 %	13.65 %	3.3 %	p<0.05
Moderate depression (10–14 points)	65.22 %	74.23 %	81.8 %	0	p<0.05

Patients in all three follow-up groups were found to have moderate depression, but the highest percentage was observed in group 3 patients.

According to the results of the Spielberg-Hanin questionnaire, both personal and situational anxiety were higher in patients of groups 1, 2 and 3 than in the control group. Situational anxiety was higher in group 1 and averaged 47.2 points ($p<0.05$), in group 2 this indicator was 44.0 points ($p<0.05$), in group 3 – 41.5 points ($p<0.05$), in the control group – 22 points ($p<0.05$). Personal anxiety was higher in group 1 patients than in group 2 and 3 and was 52.7 points ($p<0.05$), 46.5 and 44.9 points, respectively ($p<0.05$), in the control group – 27 points ($p<0.05$).

During the study, it was found that according to the Wayne questionnaire, patients in groups 1, 2 and 3 have a syndrome of autonomic dysfunction. In students with GERD and insomnia, the results ranged from 19 to 37, with an average of 33. In patients with NCD and insomnia, the indicators ranged from 23 to 40, with an average of 35. In patients with combined pathology, the indicators were from 25 to 45, with an average of 39. Students in the control group had scores from 5 to 13, with an average of 8. Thus, ADS was most pronounced in patients with combined pathology. The type of autonomic tone is shown in **Table 4**.

Table 4

Type of tone autonomic nervous system in the treatment groups and the control group

Type of tone autonomic nervous system	Group 1	Group 2	Group 3	Control group	p
Eutonic	11.1 %	10.5 %	14.4 %	61.2 %	$p<0.05$
Vagotonic (parasympathicotonia)	12.5 %	48.5 %	45.5 %	13.7 %	$p<0.05$
Sympathicotonic	76.4 %	41.0 %	40.1 %	25.1 %	$p<0.05$

Thus, in patients with GERD with insomnia, sympathicotonia prevails, while in patients with NCD and insomnia and GERD with NCD and insomnia, parasympathotonia prevails, although it is not reliable.

When studying the secretory function of the stomach in the study groups, as well as in the control group, the following results were obtained (**Table 5**).

Table 5

Indicators of pH-metry in the treatment groups and the control group

Indicators of pH-metry	Group 1	Group 2	Group 3	Control group	p
The stomach body	0.89 ± 0.05	1.60 ± 0.1	1.32 ± 0.05	1.61 ± 0.1	$p<0.05$
The antrum	6.12 ± 0.15	7.22 ± 0.13	5.4 ± 0.17	7.21 ± 0.12	$p<0.05$

In the study of secretion in patients with isolated GERD and insomnia, indicators of increased aggression of gastric juice came to the fore, while in patients with GERD with concomitant NCD and insomnia, indicators of a decrease in the alkalizing function of the antrum came to the fore. In patients with NCD, the results are within the normal range.

When examining the motor function of the esophagus and stomach in patients of the study groups, as well as in the control group, the following results were found (**Table 6**).

In patients with combined pathology, changes in motility were most pronounced, compared not only with the control group, but also with patients with isolated GERD and insomnia. Patients with NCD and insomnia had results comparable to the control group.

Thus, for patients with GERD and insomnia given the prevalence of increased aggression of gastric juice, it is reasonable to use PPI (omeprazole 20 mg 2 times a day for 5 weeks), and melatonin 3 mg per night during 3 weeks. For patients with NDC and insomnia, given the noticeable decrease vitality scale, it is reasonable to use melatonin 3 mg per night during 3 weeks. For patients with comorbid GERD, NCD and insomnia, given the prevalence of motor-evacuation disorders in them, it is reasonable to use PPI (omeprazole 20 mg 2 times per day during 5 weeks), with prokinetics (domperidone 10 mg 3 times per day during 5 weeks), and melatonin 3 mg per night during 3 weeks.

Table 6

Indicators of ultrasound examination of the esophagus and stomach with water load in the treatment groups and the control group

Indicators	Group 1	Group 2	Group 3	Control group	p
The esophagus width in the lower third	2.57±2.1 cm	2.10±0.2 cm	2.63±2.8 cm	2.11±0.1 cm	p<0.05
The diameter of esophageal hiatus	1.83±0.25 cm	1.52±0.14 cm	1.93±0.27 cm	1.51±0.12 cm	p<0.05
The presence and duration of gastroesophageal reflux	7 minutes ± 1.3	5 minutes ± 1.5	9 minutes ± 1,3	5 minutes ± 1.1	p<0.05
The thickness of the esophagus wall	0.40±0.03 cm	0.30±0.07 cm	0.46±0.05 cm	0.31±0.07 cm	p<0.05

Analyzing the obtained data, it was found that in all study groups there is a autonomic dysfunction, which is directed towards sympathicotonia in patients of the first group, or parasympathicotonia in patients of the second and third groups. Autonomic dysfunction has a key influence on the main pathogenetic factors in the formation of both GERD and NCD and insomnia, and the type of autonomic tone determines the features of the clinical course of both isolated and combined pathology. Determination of autonomic tone opens up new opportunities for prevention and treatment of these groups of patients.

4. Discussion

Analyzing the obtained data, they are in close relationship with the main world trends in the study of this pathology [13, 14] and at the same time have a number of fundamental features. So, to date [15, 16] students studied the clinical picture of isolated GERD and GERD with combined pathology [17], however, we have studied the clinical features in the combination of GERD with NCD and insomnia.

At the same time, [18, 19] studied the role of autonomic dysfunction in various pathologies, however, the present study is devoted to the analysis of the role of autonomic dysfunction in the combination of GERD with NCD and insomnia, which have not yet been the subject of scientific consideration.

The relationship between GERD and psychosomatic disorders is shown in a number of works [21]. The level of depression and anxiety among students suffering from GERD was analyzed [7, 16]. The relationship between GERD, psychological stress and insomnia is shown in works [12, 22]. In its turn, this article studied and revealed the presence of a higher level of depression in patients with comorbid pathology compared to isolated one, and anxiety – in GERD with insomnia. In addition, the quality of life in patients with GERD was studied [2, 23]. At the same time, we have shown that the combination of GERD with NCD and insomnia significantly reduces the indicators of the SF-36 scale, in comparison with isolated pathology. At the same time, motor-secretory changes in students with GERD and GERD with concomitant obesity were studied [20]. We supplemented this study by reviewing these indicators in students with GERD in combination with NCD and insomnia.

Study limitations. The study was not conducted in case of identified concomitant pathology of other organs and in case of patients refuse to participate in the study.

Prospects for further research. Further study of the tone of the ANS in patients with both isolated GERD and GERD with combined pathology is important for the formation of treatment and prevention regimens for a particular patient, and at the same time it outlines new directions in approaches to both diagnosis and treatment of this pathology.

4. Conclusions

It is shown that patients with GERD and insomnia have more pronounced sympathicotonia and indicators of increased aggression of gastric juice (in the stomach body 0.89±0.05) and reactive (47.2 points) and personal anxiety (52.7 points) come to the fore, which suggests the advisability of use PPI (omeprazole 20 mg 2 times a day for 5 weeks), and melatonin 3 mg per night during 3 weeks.

It was found that in patients with NCD and insomnia, parasympathicotonia prevails, although it is unreliable, with a simultaneous more pronounced decrease in vitality scale (31.5 ± 4.2) compared to other treatment groups, with a moderate increase in the indicators of reactive (44.0 points) and personal anxiety (46.5 points), which suggests the advisability of use 3 mg of melatonin per night during 3 weeks.

In patients with GERD NDC and insomnia often prevails parasympathicotonia but it is unreliable and at the forefront compared to other therapeutic groups are to be released motor disorders, lower rates alkalizing function of the antrum (5.4 ± 0.17), the highest rates of depression (81.8 %), as well as the worst indicators of quality of sleep (11.7) and quality of life, which suggests the advisability of use PPI (omeprazole 20 mg 2 times per day during 5 weeks), with prokinetics (domperidone 10 mg 3 times per day during 5 weeks), and melatonin 3 mg per night during 3 weeks.

Autonomic dysfunction has a key influence on the main pathogenetic factors in the formation of both GERD and NCD and insomnia, and the type of autonomic tone determines the features of the clinical course of both isolated and combined pathology.

Conflict of interests

The authors declare that they have no conflicts of interest.

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THE IMPORTANCE OF NON-INVASIVE REGIONAL BRAIN OXIMETRY IN PREVENTING POSTOPERATIVE COGNITIVE DYSFUNCTION DURING LAPAROSCOPIC CHOLECYSTECTOMY IN ELDERLY AND SENILE PATIENTS

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Abstract

The adverse effect of general anesthesia in elderly patients during surgery requires monitoring of functions and processes to identify their dangerous abnormalities to prevent complications.

The aim of the study. To establish the effectiveness of non-invasive regional brain oximetry with rSO_2 determination during anesthetic support in laparoscopic cholecystectomy (LCE) to prevent postoperative cognitive dysfunction in elderly and senile patients.

Material and methods. 84 elderly and senile patients with diagnosed gallstone disease, acute cholecystitis, who underwent LCE with sevofluran inhalational anesthesia and total intravenous anesthesia with propofol were examined. rSO_2 was monitored. Cognitive functions were assessed using neuropsychological scales and the MMSE mental state examination scale.

Results. rSO_2 was found to be significantly decreased during the carbon dioxide insufflation as compared to before premedication: in LH (left hemisphere) – by 7.0 %, in RH (right hemisphere) – by 6.9 % (Group I); in LH – by 7.4 %, in RH – by 7.5 % (Group II). rSO_2 was significantly increased during the surgery, particularly in the middle of the operation, as compared to before premedication: in LH – by 14.66 %, in RH – by 13.94 % (Group I); in LH – by 11.60 %, in RH – by 11.53 % (Group II). The day following the surgery, cognitive functions significantly decreased by 8.7 % on the Luria's test, by 6.0 % on the MMSE test (Group I); in Group II – by 10.1 % and 6.3 %, respectively, as compared to before premedication. On Day 5 after the surgery, cognitive functions decreased by 2.7 % on the Luria's test, by 0.35 % on the MMSE test (Group I); in Group II – by 2.7 % and 0.35 %, respectively, as compared to before premedication.

Conclusions. A decrease in rSO_2 can occur during LCE in the Trendelenburg position, despite the fact that other intraoperative indicators remain stable, which allows it to remain unrecognized. rSO_2 monitoring in the perioperative period contributes to alertness and timely measures to prevent postoperative cognitive dysfunction.

Keywords: regional oximetry, cerebral hemoglobin oxygen saturation, rSO_2 , postoperative cognitive dysfunction, elderly and senile persons, laparoscopic cholecystectomy.

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1. Introduction

The modern concept of anesthetic support aims not only to provide adequate pain relief, but also to control all the patient's vital functions during the operation. It should be noted that in the last decade, the concern about the adverse effect of general anesthesia on the elderly patients' brain has been growing, since these surgical patients often have postoperative cognitive dysfunction, which in turn can cause an increase in morbidity and mortality [1]. Postoperative cognitive dysfunction (POCD) is a disorder that develops in the early postoperative period, persists for several days or weeks, more rarely – for months, and is clinically manifested by memory disorders, difficulties in concentration and long-term focus of attention, as well as higher cortical function impairment such as thinking, speech, etc. The patient has problems with learning, mental performance decreases, mood worsens, and depression occurs. All of this can lead to a decrease in the quality of life. Therefore, one of the most important tasks of modern anesthesiology is to objectify the general anesthesia monitoring, which provides for the control of functions and processes, identifying their dangerous abnormalities to prevent complications during anesthesia. Not only the cardiovascular and respiratory system functions should be monitored, but also the state of the central nervous system (CNS), in particular the functional state of the brain. According

to statistics, the most frequent complications in the process of anesthesia are various hypoxic conditions of the brain, which often cause POCD, especially in elderly and senile patients [2, 3].

Since the main tasks of neuromonitoring during anesthesia are to maintain and preserve the physiological body functions and provide optimal conditions for their improvement, the method of cerebral oximetry reflects the balance between the delivery and consumption of oxygen, which makes it possible to visualize the oxygen status of the brain and assess the oxygen saturation of tissues [4]. Today, the interest in cerebral oximetry has significantly increased due to non-invasiveness of the method, its highest level of safety, as well as technical achievements that have made this method more accurate and informative [5].

Now the problem of safety of anesthesia during surgical interventions in the elderly and senile patients does not lose its relevance. During general anesthesia, anesthetists have several tools to monitor the state of the brain. One of the methods to ensure the safety of anesthesia and prevent hypoxia episodes during anesthesia is to monitor the functional saturation of cerebral hemoglobin with oxygen (rSO_2). The main purpose of the non-invasive cerebral oximetry monitoring method is to measure regional cerebral oxygen saturation rSO_2 using near-infrared spectroscopy [6].

An important risk factor for POCD is considered to be elderly and senile age, which is associated with a natural decline in cognitive functions and various concomitant diseases – hypertension, atherosclerosis, ischemic disease, thrombosis, strokes, etc. [7].

Cerebral oximetry is widely used in neonatology, pediatrics, thoracic, vascular, cardiac surgery, and neurology [8, 9]. However, it remains unclear whether non-invasive regional brain oximetry is a reliable monitoring method for laparoscopic cholecystectomy to prevent POCD in elderly and senile population.

The aim of the work. To establish the effectiveness of non-invasive regional brain oximetry with rSO_2 determination during anesthetic support in laparoscopic cholecystectomy to prevent postoperative cognitive dysfunction in elderly and senile patients.

2. Materials and methods

The study was conducted from 2017 to 2020. During the study conducted in the Municipal Non-profit Company (MNC) “O. I. Meshchaninov Memorial City Clinical Emergency Hospital” of the Kharkiv City Council, 84 patients diagnosed with gallstone disease (GSD), acute cholecystitis who underwent laparoscopic cholecystectomy (LCE) were examined. The average age was 68.1 ± 0.63 years, and the average duration of the operation was 61.1 ± 2.7 minutes.

Before the beginning of the study, according to the Declaration of Helsinki, all patients were informed about the purpose, methods and design of the study. They personally agreed in writing to participate in the study: clinical examination, collection of material for laboratory tests, filling out questionnaires.

The study approved by the Commission on Ethics and Bioethics as part of the Scientific and Methodological Council of Kharkiv Medical Academy of Postgraduate Education, according to protocol No. 1 of February 18, 2020.

The study used the following inclusion criteria:

- 1) age of patients from 60 to 90 years;
- 2) confirmed diagnosis of GSD, acute cholecystitis;
- 3) physical status according to the American Society of Anesthesiologists (ASA) classification – I–III;
- 4) coronary heart disease (CHD);
- 5) cardiosclerosis;
- 6) hypertension grade I–II;
- 7) heart failure stage I–IIA, grade I, II;
- 8) no cardiovascular events in the history (myocardial infarction, cerebral vascular accident).

The criteria for exclusion from the study were:

- 1) patient's age less than 60 or more than 90 years;
- 2) patient's physical status according to the American Society of Anesthesiologists (ASA) classification – IV;

- 3) diabetes mellitus;
- 4) CNS diseases;
- 5) intracranial hypertension;
- 6) mental diseases;
- 7) the history of cardiovascular events (myocardial infarction, cerebral vascular accident);
- 8) patient's reluctance to participate in the study.

Based on the type of anesthesia, patients were randomized into 2 groups: Group I (n=42) – sevofluran (2–3 vol. %) inhalation anesthesia with AVL; Group II (n=42) – propofol (2 mg/kg/h) TIA with AVL. In both groups: analgesia – fentanyl (1 mcg/kg/h), relaxation – atracurium (**Table 1**).

Table 1

Patient randomization based on the type of anesthesia

Group I (n=42)	Group II (n=42)
sevofluran (2–3 vol. %) inhalation anesthesia with AVL	propofol (2 mg/kg/h) TIA with AVL
Analgesia – fentanyl (1 mcg/kg/h), Relaxation – atracurium	

Monitoring of hemodynamic parameters consisted of determining heart rate (HR), pulse rate (PR), systolic blood pressure (SBP), diastolic blood pressure (DBP), mean arterial pressure (MAP), and cardiac output (CO). These indicators were measured using the “Vismo PVM-2701” NIHON-KOHDEN monitor (Japan).

For continuous measurement and monitoring of functional oxygen saturation of cerebral hemoglobin (rSO₂), a non-invasive regional oximeter system Masimo O3 (USA) was used.

These indicators were continuously monitored throughout the entire period of anesthesia and surgery. However, for material processing the following stages were distinguished: stage 1 – before premedication; stage 2 – after premedication; stage 3 – intubation; stage 4 – beginning of the operation; stage 5 – carbon dioxide insufflation; stage 6 – middle of the operation; stage 7 – extubation; stage 8 – 20 min after the operation.

The patients' cognitive functions were assessed using neuropsychological scales: O.R. Luria's 10-word memory test and Mini-Mental State Examination (MMSE) scale. The memory evaluation according to O. R. Luria uses a quantitative 10-word memory test. The test is designed to diagnose auditory verbal memory.

The MMSE method is widely used in most modern epidemiological and clinical studies for screening and evaluating cognitive disorders, which confirms its validity and suitability. The MMSE scale consists of a number of sub-tests that allow to quickly and effectively evaluate time and spatial awareness, as well as short-term and long-term memory, speech function, gnosis, and praxis. The total score is calculated by adding up the scores for individual sub-tests.

The patients received cognitive evaluation three times: before the surgery, on the next day after the surgery, and on the fifth day after the surgery.

The obtained data were analyzed by statistical processing using SPSS19 software for Windows and descriptive statistics methods. Shapiro-Wilk test was used to determine the distribution of the obtained data. Provided the quantitative variables were in accordance with the normal distribution law, they were described as $M \pm m$. When studying the dynamics of indicators against the baseline levels in the case of normal distributions, Student's t-test was used for dependent samples, and for intergroup comparisons – Student's t-test was used for independent samples. The differences were considered statistically significant at $p < 0.05$.

3. Results

Patients did not differ significantly between the groups by hemodynamic parameters during LCE (**Table 2**).

It should be noted that patients in both groups showed an intraoperative decrease in hemodynamic parameters compared to the baseline, which is explained by the effect of general anes-

thetics and opioids during general anesthesia. However, these changes were moderate and did not require correction. After the operation, hemodynamic parameters tended to increase, but remained slightly lower than the baseline.

Table 2

Comparative evaluation of hemodynamic parameters in patients at different stages of the study

Stages of the study	Group	Hemodynamic parameters				
		HR, bpm	SBP, mm Hg	DBP, mm Hg	MAP, mm Hg	CO, l/min
Before premedication	I	78.02±1.8	157.98±2.1	94.05±1.4	114.95±1.4	8.16±0.1
	II	79.00±1.5	153.93±2.4	93.83±1.2	113.52±1.4	8.00±0.1
After premedication	I	83.95±1.6	143.81±1.7	88.45±1.4	106.55±1.4	7.34±0.1
	II	83.29±1.4	141.31±1.8	87.93±1.2	105.43±1.2	7.31±0.1
Intubation	I	81.88±1.2	135.83±1.5	87.14±1.4	103.24±1.3	6.66±0.1
	II	78.81±1.2	135.00±1.8	84.29±1.4	100.33±1.5	6.61±0.1
Beginning of the operation	I	79.24±1.4	127.38±1.8	81.31±1.4	96.60±1.5	5.97±0.1
	II	75.50±1.4	129.05±1.9	80.36±1.5	96.33±1.6	5.95±0.1
CD insufflation	I	79.12±1.4	124.64±1.7	78.88±1.4	94.26±1.4	5.48±0.1
	II	76.12±1.4	127.62±1.7	79.88±1.4	95.90±1.4	5.57±0.1
Middle of the operation	I	75.60±1.0	132.74±1.3	82.98±1.2	99.07±1.1	4.86±0.1
	II	74.07±1.8	135.60±1.5	84.17±1.2	101.10±1.2	4.92±0.1
End of the operation	I	75.33±1.3	128.45±1.5	82.02±2.2	95.33±1.4	6.73±0.04
	II	74.67±1.2	132.86±2.1	82.38±1.2	99.26±1.6*	6.59±0.1
20 min after the operation	I	79.33±0.9	137.62±1.4	84.17±1.1	101.98±1.1	7.72±0.1
	II	80.93±1.1	139.88±1.8	83.93±0.9	102.37±1.1	7.57±0.1

Note: * – statistically significant difference between the groups ($p < 0.05$)

Table 3 shows changes in rSO_2 during LCE in elderly and senile patients at various stages of the study.

Table 3

rSO_2 dynamics in elderly and senile patients during laparoscopic cholecystectomy (%)

Stages of the study	LH (left hemisphere of the brain)			RH (right hemisphere of the brain)		
	Group I	Group II	p	Group I	Group II	p
Before premedication	64.3±0.2	64.5±0.2	>0.05	64.7±0.2	64.8±0.2	>0.05
After premedication	64.8±0.2	64.4±0.2	>0.05	65.1±0.2	64.8±0.2	>0.05
Intubation	63.9±0.1	64.1±0.2	>0.05	64.0±0.2	64.2±0.2	>0.05
Beginning of the operation	67.1±0.2	66.1±0.2	<0.001	67.6±0.2	66.6±0.2	<0.001
CD insufflation	60.1±0.2	60.0±0.2	>0.05	60.5±0.2	60.3±0.2	>0.05
In the middle of the operation	75.4±0.3	72.9±0.3	<0.001	75.2±0.3	73.3±0.4	<0.001
Extubation	68.4±0.2	68.1±0.2	>0.05	68.4±0.1	67.9±0.2	<0.05
20 min after the operation	64.4±0.1	64.2±0.2	>0.05	64.7±0.2	64.6±0.1	>0.05

The study results showed that rSO_2 was significantly decreased during the CD insufflation as compared to before premedication: in LH – by 7.0 % ($p < 0.001$), in RH – by 6.9 % ($p < 0.001$) (Group I); in LH – by 7.4 % ($p < 0.001$), in RH – by 7.5 % ($p < 0.001$) (Group II). The difference in rSO_2 between the groups during the operation is also significant, which may evidence that sevoflu-

rane preserves rSO_2 somewhat better than propofol: in Group I, rSO_2 was significantly increased in the middle of the operation as compared to the period before premedication: in LH – by 14.66 % ($p<0.001$), in RH – by 13.94 % ($p<0.001$); in Group II, in LH – by 11.60 % ($p<0.001$), in RH – by 11.53 % ($p<0.001$).

In addition, the dynamic pattern of the results of the cognitive tests was studied.

In Group I, the results of Luria's test significantly decreased the day after the operation, as compared to before premedication, by 8.7 % ($p<0.001$), insignificantly decreased on the fifth day after the operation, as compared to before premedication, by 2.7 % ($p>0.05$). In Group II, the test results significantly decreased the day after the operation, as compared to before premedication, by 10.1 % ($p<0.001$), insignificantly decreased on the fifth day after the operation, as compared to before premedication, by 2.7 % ($p>0.05$).

In Group I, the results of MMSE test significantly decreased the day after the operation, as compared to before premedication, by 6.0 % ($p<0.001$), insignificantly decreased on the fifth day after the operation, as compared to before premedication, by 0.35 % ($p>0.05$). In Group II, the results significantly decreased the day after the operation, as compared to before premedication, by 6.3 % ($p<0.001$), insignificantly decreased on the fifth day after the operation, as compared to before premedication, by 0.35 % ($p>0.05$).

4. Discussion

At the moment, the assessment of postoperative cognitive dysfunction is not a standard component for assessing the quality of anesthesia, although, in our opinion, the quality of life of patients depends directly on the level of cognitive functioning of the patient [10].

Some researchers note that general anesthesia is associated with a more significant decrease in rSO_2 and point to a relationship between the occurrence of POCD and rSO_2 value, when an intraoperative decrease in rSO_2 is a predictor of POCD. X. Li et al. [11] showed this relationship in thoracic surgery, G. Papadopoulos et al. [12] – in operations for hip fractures in patients over 75 years of age. Some randomized studies have shown the use of oximetry to minimize brain destruction, based on the fact that a decrease in rSO_2 is associated with impaired cognitive function after surgery [13]. The use of cerebral oximetry is proposed not only to identify the risk of developing POCD, but also to determine the tactics of postoperative management of patients. Some researchers also report the relationship between cerebral oximetry values and the use of specific anesthetics [14] with the premorbid POCD background [15]. Thus, T. Ružman et al. [16] compared the effect on regional cerebral oxygenation (rSO_2) during inhalation anesthesia with sevoflurane and total intravenous anesthesia with propofol during LCE and concluded that sevoflurane anesthesia provides 4–11 % higher rSO_2 values compared to propofol and significantly fewer critical rSO_2 decreases in LCE. D. Salazar et al. [17] suggested that development of POCD was associated with a decrease in rSO_2 at a certain patient's position during the operation, and although a reliable relationship could not be identified, the authors concluded that protocols with rSO_2 measurement reduce the risk of POCD development. Other researchers have noted a decrease in rSO_2 when the patient is in the beach chair position [18]. In addition, the severity and frequency of POCD were reported to be decreased with a decrease in the level of rSO_2 when using a certain algorithm of actions, but the effect on the incidence of POCD is not the same in various studies [19]. This may be due either to the fact that measures aimed at preventing a decrease in rSO_2 levels in the brain are insufficient, or, conversely, the relationship between rSO_2 values and POCD is weak. F. Holmgaard et al. [20] found no differences in intraoperative rSO_2 values in patients with and without POCD either at discharge or 3 months after a cardiac surgery.

According to our study, the parameters of cerebral oxygenation rSO_2 decreased at carbon dioxide insufflation, but this decrease was short-term and lasted no more than 5 minutes. The decrease in rSO_2 could occur due to carbon dioxide insufflation, which is significantly associated with the potentiation of intracranial hypertension due to increased intra-abdominal pressure, delayed venous outflow from the brain and slow cerebral circulation. In its turn, the position of Trendelenburg can also cause an increase in intra-abdominal pressure and a decrease in rSO_2 . Intraoperative monitoring of cerebral oxygenation using regional cerebral oximetry allowed to reveal a

short-term decrease in rSO_2 and take timely measures to prevent further decrease in rSO_2 and development of stable POCD. A single-factor analysis of variance did not reveal any significant effect of episodic decrease in rSO_2 during the carbon dioxide insufflation on the decrease in cognitive functions in the postoperative period.

However, the issue of using regional cerebral oximetry in all elderly and senile patients during LCE remains relevant.

Research limitations. The study was not performed in case of neurological history or mental disorder of the patient, as well as in case of refusal of the patient to participate in the study.

Prospects for further researches. The study does not exhaust the entire depth of the problem of preventing the appearance of postoperative cognitive dysfunctions in elderly patients. In this regard, further work in this direction is possible. Also, the sample size was quite small, and statistical reliability was insufficient. Therefore, future studies require sampling with more patients.

5. Conclusions

During LCE, elderly and senile patients showed a short-term decrease in rSO_2 at the stage of carbon dioxide insufflation. rSO_2 was found to be significantly decreased during the carbon dioxide insufflation as compared to before premedication: in LH – by 7.0 %, in RH – by 6.9 % (Group I); in LH – by 7.4 %, in RH – by 7.5 % (Group II). But there was no significant effect on the temporary decrease in cognitive functions in the early postoperative period. The day following the surgery, cognitive functions significantly decreased by 8.7 % on the Luria's test, by 6.0 % on the MMSE test (Group I); in Group II – by 10.1 % and 6.3 %, respectively, as compared to before premedication. On Day 5 after the surgery, cognitive functions decreased by 2.7 % on the Luria's test, by 0.35 % on the MMSE test (Group I); in Group II – by 2.7 % and 0.35 %, respectively, as compared to before premedication.

A decrease in local brain tissue oxygenation (rSO_2) can occur during LCE in the Trendelenburg position, despite the fact that other intraoperative indicators remain stable, which allows it to remain unrecognized.

Non-invasive intraoperative regional cerebral oximetry makes it possible to quickly assess the rSO_2 value and identify possible episodes of its decline as early as possible.

The use of non-invasive intraoperative regional cerebral oximetry makes it possible to take timely measures to correct rSO_2 values and prevent brain hypoxia events.

Non-invasive regional cerebral oximetry may help reduce postoperative cognitive dysfunction.

Non-invasive rSO_2 monitoring in the perioperative period contributes to alertness and timely measures to prevent postoperative cognitive dysfunction.

Conflict of interests

The authors declare that they have no conflicts of interest.

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CLINICAL EVALUATION OF DIRECT PHOTOCOMPOSITIONAL DENTAL RESTORATION IN DIFFERENT CONDITIONS OF LIGHT POLYMERIZATION OF ADHESIVE SYSTEM

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Abstract

Photocomposite materials and adhesive systems are used for direct tooth restoration, among which 5th generation systems are most often used. To ensure curing, they are exposed to the light flux of the dental photopolymerizer, but the requirements and conditions of such exposure are insufficiently studied.

The aim – clinical evaluation of direct photocomposite restorations of teeth performed using an adhesive system, the curing of which was carried out in different light conditions.

Materials and methods. 185 people aged from 19 to 44 years were examined, in which 185 lateral teeth with carious cavities of the 1st class according to Black for medium and deep caries were restored by direct method from nanophotocomposite material. In patients of group 1 during the restoration of 62 teeth the polymerization of the adhesive system of the 5th generation was performed with a light flux of constant intensity 1500 mW/cm², in patients of group 2 were restored 60 teeth with polymerization of the same adhesive system with light flux by “soft start” with a final intensity of 1500 mW/cm², 63 teeth in persons of group 3 were restored with a gradual light effect of 1500 mW/cm² on the adhesive system at the bottom and each of the cavity walls using an additional device. The state of recovery was examined after 12 and 24 months.

Results. Within 12 months, the largest total number of disorders according to the clinical criteria “marginal adhesion”, “marginal staining”, “postoperative sensitivity” and “secondary caries” was found in patients of agroups 1 and 2, violations were found in 10 and 13 restorations, respectively (16.1±4.9 % and 21.7±5.8 % of the number of restorations in each group). In persons of group 3, disorders were identified in 3 restored teeth (4.8±2.6 %), which is statistically significant ($p<0.05$) better. After 24 months, statistically significant ($p<0.05$) the best indicators were again in patients of group 3, violations were found only in 4 restorations (6.7±3.2 % of them in this period). The worst was the state of recovery in persons of group 2, they had disorders in 20 restorations (42.6±10.4 %), in patients of group 1 – in 16 restorations (30.8±8.0 %).

Conclusions. Direct restoration of teeth from nanophotocomposite material, performed using the 5th generation adhesive system under the condition of its gradual polymerization at the bottom and each of the walls of the carious cavity of class 1 according to Black, showed high clinical efficiency, which in 12 and 24 months amounted to, respectively, 93.7±3.4 % and 88.9±3.5 %.

Keywords: dental caries, direct photocomposite restoration, adhesive system, light polymerization.

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1. Introduction

In modern restorative dentistry, photocomposite materials are used for direct restoration of teeth, which make it possible to significantly reproduce the anatomical-functional, optical and physical-mechanical characteristics of the hard tissues of natural teeth [1, 2]. However, these materials do not have independent adhesion to hard tissues, so the role of conditional mediator, which provides a strong adhesion of the photocomposite with enamel and dentin, take adhesive systems [3]. In the dental materials market there is a certain variety of adhesive systems that are used during the restoration work on teeth or orthopedic structures [4, 5]. Unmistakable choice of adhesive system and adherence to the technology of adhesive preparation minimizes the risk of marginal fit disorders, marginal discoloration, secondary caries and other complications [6, 7].

Adhesive systems are presented for eight generations, they have a wide range of indications, which allows you to work with most restoration materials, in particular, photocomposite materials, and can ensure their adhesion to the hard tissues of the teeth. Modern polymer-based adhesive systems are divided into total etching systems, which consist of two or three components, and self-etching adhesives, which are available in one- or two-stage version [8, 9]. Adhesives of all types not only create a unique joint between photocomposite materials and hard tissues of teeth, but also allow to comply with the requirements of minimally invasive preparation of cavities [10].

Regardless of the chemical composition and type of adhesive system, they all first etch and demineralize the hard tissues of the teeth to be restored [11, 12]. However, it should be noted that adhesives used after the total etching step showed longer-term stability of the enamel and dentin bond compared to self-etching adhesive systems, which showed higher adhesion to dentin and less adhesion to enamel. As a result, the connection of photocomposite material with enamel in the technique of total etching gives higher strength and significantly reduces the number of clinical disorders that may occur during the operation of such restorations [13]. Therefore, 5th generation adhesive systems in the total etching technique were used in this clinical study.

No less important is the task of ensuring the full curing of the adhesive systems used. The light exposure through which the curing process takes place must meet certain requirements. However, recommendations for the polymerization of adhesive systems contain quite general formulations, and the results of research on the intensity and direction of light flux from a light source with a certain wavelength, as well as the mode of light flux with constant intensity or increase is still insufficiently covered [14, 15]. In addition, there are few long-term clinical trials in this area, so their results and conclusions should be significant to minimize a number of clinical complications, which, unfortunately, often occur after dental restoration using any restorative materials and adhesive systems [16, 17].

The aim – clinical evaluation of direct photocomposite restorations of teeth performed using an adhesive system, the curing of which was carried out in different light conditions.

2. Materials and methods

In a clinical prospective randomized study conducted at the clinic of the Department of Dentistry No. 1 of Donetsk National Medical University during 2017–2019 were examined 185 people aged 19 to 44 years, in which were restored 185 lateral teeth with carious lesions of 1st class according to Black with about medium and deep caries. Among those surveyed were 95 men (51.4 %) and 90 women (48.6 %). All patients signed informed consent to participate in the study. The clinical trial was conducted in accordance with the principles of the Declaration of Helsinki, adopted by the General Assembly of the World Medical Association, and the Council of Europe Convention on Human Rights and Biomedicine, as well as the International Council of Medical Scientific Societies and the International Code of Medical Ethics (Minutes No. 13 of the meeting of the commission on bioethics of Donetsk National Medical University from 07.11.2016). Before the restoration, in patients were determined the level of oral hygiene according to the Fedorov-Volodkina hygienic index and the intensity of carious lesions of the teeth, as well as carried out professional hygiene measures.

Teeth to be restored were cleaned of plaque with brushes and pastes that did not contain fluoride compounds, and determined the color of the teeth to match future restoration. Carious cavities were prepared, forming them for restoration with photocomposite material according to generally accepted requirements [18]. Next, total etching of the hard tissues of the bottom and walls of the prepared cavity with orthophosphoric acid gel was performed, after which the adhesive system of the 5th generation Single Bond 2, 3M ESPE was applied and affected by the light flux of the LED photopolymerizer under certain conditions. Tooth restoration was performed with Filtek Z550 nanophotocomposite material, 3M ESPE, in a layered technique with polymerization of each layer by light flux in the “soft start” mode. Finally, the finishing and polishing of the restoration was performed.

All examined patients were randomly divided into three groups. In 62 patients of the 1st group, the restoration of 62 teeth was performed with the polymerization of the 5th generation adhesive

system applied to the bottom and walls of the prepared carious cavity, the light flux of the LED photopolymerizer with a constant intensity of 1500 mW/cm². In 60 patients of group 2, the same adhesive system was used in 60 dental restorations, which was polymerized using a light flux of LED photopolymerizer in the “soft start” mode with a final intensity of 1500 mW/cm². During the restoration of 63 lateral teeth in 63 patients of group 3, the adhesive system was applied to the bottom and walls of the cavity, then with the help of the proposed nozzle on the fiber gradually affected the adhesive system on the bottom and each wall of the cavity for 20 seconds at a minimum distance from the surface of solid tissues and perpendicular to them with a light flux of LED photopolymerizer of constant intensity 1500 mW/cm².

The condition of the restorations was assessed the next day, as well as after 12 and 24 months with the leading, according to the purpose of the study, clinical criteria “marginal fit”, “marginal staining”, “secondary caries”, “anatomical shape”, “hypersensitivity” and according to aesthetic criteria “colour matching” and “surface roughness of the restoration” [19]. In the presence of violations in the recovery according to the leading criteria, patients were excluded from the study, in the case of an acceptable state of recovery, with the appropriate consent of patients, corrected, in the case of unacceptable state of recovery was performed again. In the presence of violations of the aesthetic criteria of recovery, with the consent, corrected, patients continued to be observed. It should be noted that quite often several violations were detected in one recovery, so the number of violations and restorations with them was registered in each group, as well as the number of restorations without violations, the number of which determined the clinical effectiveness of recovery. The results of the initial and subsequent examinations were entered into the medical records of the dental patient (form 043/o, approved by the Ministry of Health of Ukraine)

Variation statistics were used for statistical processing using the computer program Microsoft Excel. Significance of differences between the indices of hygiene indices and the intensity of dental caries was determined by Student's test, the differences were considered statistically significant at $p < 0.05$. Indicators of qualitative characteristics are presented in the form of absolute and relative values.

3. Results

During the initial examination before dental restoration, the state of oral hygiene according to the Fedorov-Volodkina hygienic index in patients of the three groups did not differ ($p > 0.05$); Thus, in patients of group 1 the hygienic index was 1.35 ± 0.15 points, in persons of groups 2 and 3 – 1.23 ± 0.17 and 1.44 ± 0.14 points, respectively, that is, in all patients the hygienic condition of the oral cavity was good. Indicators of the index of the intensity of dental caries in patients of these groups also had no statistically significant differences ($p > 0.05$), they were equal to, respectively, 7.55 ± 0.89 ; 6.95 ± 0.74 and 8.34 ± 0.79 . The absence of statistically significant differences between the relevant indicators in patients of different groups indicates the identity of the study conditions.

The next day after the restoration in all restorations in patients of three groups of violations according to the studied clinical criteria were not detected, tooth restoration was in excellent condition, no complaints from patients were received.

After 12 months, all recoveries (100 %) in all patients (100 %) of the three groups were examined. It was found that patients of group 1 violated the marginal adhesion of the photocomposite material to the enamel of restored teeth in 7 restorations (11.3 ± 4.1 % of the number of restorations in patients of this group), marginal colour was also detected in 7 restorations (11.3 ± 4.1 %), while the depth of adhesion and colour penetration was only to the dentino-enamel limit, increased sensitivity of hard tissues was registered in 2 restored teeth (3.2 ± 2.3 %). It should be noted that secondary caries was found in about 2 restorations (3.2 ± 2.3 %), anatomical disorders were also found in 2 restorations (3.2 ± 2.3 %). In total, according to the above clinical criteria, which are leading in the study of the polymerization of the adhesive system, 20 violations were identified, relating to 10 restorations (16.1 ± 4.9 %). Other violations were identified by aesthetic criteria, in particular, the colour mismatch of the restoration material and hard tissues of the teeth within acceptable limits was found in 4 restorations (6.5 ± 3.2 %), increased surface roughness – in 6 restorations (9.7 ± 3 , 8 %).

In patients of group 2 at this time of the examination, the violation of the marginal adhesion of the material within the enamel was determined in 9 restorations (15.0 ± 4.7 % of the total number of restorations in this group), marginal staining at the border of photocomposite and hard tissues the border of enamel with dentin was established in 10 restorations (16.7 ± 4.9 %), increased sensitivity of hard tissues was found in 4 restored teeth (6.7 ± 3.3 %). It is important that secondary caries was diagnosed in 3 restored teeth (5.0 ± 2.7 %) next to the photocomposite material from which the restorations were made, and the anatomical violation was in 1 restoration (1.7 ± 1.7 %). Thus, according to the leading, from the point of view of the purpose of the study, clinical criteria, a total of 27 disorders were identified, which related to 13 restorations (21.7 ± 5.8 %). Regarding aesthetic characteristics, the colour discrepancy was found in 5 restorations (8.3 ± 3.6 %), and in 6 restorations (10.0 ± 3.9 %) increased roughness of the material was found.

In 63 patients of the 3rd group, violations of the marginal adhesion of the material to the enamel border of the restored teeth were found in 2 restorations (3.2 ± 2.2 % of the number of restorations in patients of this group), marginal staining with the depth of penetration also to the dentino-enamel border – in 3 restorations (4.8 ± 2.7 %). No cases of hypersensitivity of hard tissues and secondary caries in restored teeth were found, only in 1 restoration (1.6 ± 1.6 %) there was a violation of the anatomical shape. These indicators indicate that the total number of violations detected by the leading clinical criteria is 6, they were found in 3 restorations (4.8 ± 2.6 %). At the same time, aesthetic disorders are almost as many as in patients of other groups. Colour mismatch of the restoration within the allowable range was found in 5 restorations (7.9 ± 3.5 %), increased surface roughness of the material – also in 5 restorations (7.9 ± 3.5 %).

Restorations of teeth in which violations were found according to the leading clinical criteria were corrected with the consent of patients of all three groups, and patients with such restorations were excluded from the study. In the case of violations of aesthetic criteria, they were corrected, but patients with these restorations continued to participate in the study.

After 24 months, the number of examined patients was lower compared to the beginning of the study, in particular, 52 patients (82.5 % of the initial number) of 1 group with 52 restorations (82.5 % of baseline), 47 people (78.3 %) of group 2 were examined, in which there were 47 restorations (78.3 %), the number of patients in group 3 was 60 people (95.2 %), the same was the number of restorations – 60 (95.2 %).

Examination of tooth restorations after 24 months in patients of group 1 showed that for the first time in the study there was found absence of 1 restoration (1.9 ± 1.9 % of the number of restorations in this period in patients in this group). The number of restorations with disturbed marginal fit of the material increased to 11 (21.2 ± 5.8 %), with marginal staining on the border of photocomposite material and enamel, 10 restorations (19.2 ± 5.6 %) were detected, and the depth of these violations was within the enamel and partially entered the dentin. Secondary caries was diagnosed in 3 restored teeth (5.8 ± 3.3 %), it was found near or under restorations, in 2 restorations (3.8 ± 2.7 %) anatomical disorders were found. There were no cases of hypersensitivity of hard tissues in restored teeth. According to the leading criteria, a total of 27 violations were registered, taking into account the lack of recovery, relating to 16 restorations (30.8 ± 8.0 %). Regarding the inconsistency of the restoration in colour, it was within acceptable limits found in 7 restorations (13.5 ± 4.8 %), in terms of roughness, there were 8 such cases (15.4 ± 5.1 %).

In patients of group 2, the number of detected disorders was even greater. First of all, there were absence of 2 restorations (4.3 ± 3.0 % of the number of restorations in this group at this time). Violation of the marginal adhesion of the photocomposite material to the enamel and marginal staining at the restoration boundary was detected in 13 cases according to each of the criteria (27.7 ± 6.7 %), their depth reached the dentino-enamel boundary and beyond. Secondary caries was diagnosed in 6 restored teeth (12.8 ± 5.0 %), i.e. 2 times more than in the previous period, anatomical disorders – in 2 restorations (4.3 ± 3.0 %). Hypersensitivity of hard tissues was not detected. The total number of violations according to the leading clinical criteria, taking into account the lack of restorations, reached 36, violations concerned, in total, 20 restorations (42.6 ± 10.4 %). Colour discrepancy within the permissible limits was found in 7 restorations (14.9 ± 5.3 %), increased roughness – also in 7 restorations (14.9 ± 5.3 %), such were the indicators according to aesthetic criteria.

It should be noted that in patients of group 3 disorders were found significantly less frequently. Thus, there were only 3 cases of violation of the marginal fit of the material (5.0 ± 2.9 % of the number of restorations in the group during this period), all of them were within the enamel, the same was the number of restorations with marginal colour – 3 (5.0 ± 2.9 %). Hypersensitivity of hard tissues and secondary caries in the restored teeth did not occur, only in 1 restoration (1.7 ± 1.7 %) anatomical disorders were found. Regarding the total number of violations according to the leading criteria, the persons of group 3 had the least of them – only 7 in 4 restorations (6.7 ± 3.2 %). Colour mismatch and roughness of the material were found in the same amount, with such violations, in accordance with these aesthetic criteria, there were 6 (10.0 ± 3.9 %).

4. Discussion

A study conducted over two years showed significant differences in the results in individuals of different groups, which increased with increasing follow-up. However, even within 12 months, the number of recoveries with violations according to the leading clinical criteria in patients of group 3 was 3.3 and 4.3 times less than the same number in patients of groups 1 and 2, respectively ($p < 0.05$). Within 24 months, the number of restorations with disorders in persons 1 and 2 groups was, respectively, 4 and 5 times more than the number of restorations with defects in the examined patients of group 3 ($p < 0.05$). In total, for two years of observation of the leading clinical criteria in patients of group 1 were found 47 violations in 26 restorations (41.9 ± 2.3 % of the initial number of restorations in this group), in patients of group 2 – 63 violations in 33 restorations (55.0 ± 2.8 % of their original number), in persons of group 3 – only 13 violations in 7 restorations (11.1 ± 1.2 % of the initial number). If we analyse the number of restorations in excellent condition, i.e. without violations, then such, according to the ordinal numbering of groups, in two observation periods, in particular, within 12 months, there were 52 (83.9 ± 3.3 % of the initial number), 47 (78.3 ± 3.3 %) and 59 (93.7 ± 3.4 %), within 24 months – 36 (58.1 ± 2.8 % of the initial amount), 27 (45.0 ± 2.5 %) and 56 (88.9 ± 3.5 %). The obtained results in percent in each of the terms were taken as indicators of clinical efficiency of recovery, they indicate the advantages of the proposed step-by-step light polymerization of the adhesive system at the bottom and each of the walls of the prepared carious cavity.

The need to improve the technology of direct restoration of teeth with photocomposite materials is confirmed by the results of other clinical studies. Violations of the marginal fit of the material within two years had 63.0 % of the examined restorations, loss of fillings was registered in 19.2 % of cases, secondary caries - in 37.0 % of restored teeth [20]. In another study, after four years, marginal adhesion was found in 32 % of restorations using self-etching adhesive systems and in 13 % of restorations using pre-etched adhesive techniques, and marginal staining in 21 % and 11 % of restorations, respectively [21]. A significant number of disorders were detected according to these clinical criteria, the state of recovery of which depends in some way on the polymerization of the adhesive system that was used.

Study limitations. The study did not include persons under 18 years of age and over 44, due to the presence of certain age-related features of caries and the dynamics of caries-resistant hard tissues of the teeth, as well as patients, in the case of teeth of the lateral group to be restored, there were already fillings or carious cavities; if the teeth were previously covered with artificial crowns; if antagonist teeth were absent, occlusion pathology, increased tooth abrasion, or bruxism were identified; in the presence of periodontal pathology (periodontitis, periodontitis) and unsatisfactory oral hygiene. Patients with somatic diseases that contribute to the reduction of caries of dental hard tissues or the development of periodontal disease, persons with mental disorders, including due to alcohol or drug addiction, as well as when patients simultaneously participated in another study or planned during the study moving to another city.

Prospects for further research. In the future, it is planned to continue clinical monitoring of patients with dental restorations, which were made of nanophotocomposite material in different conditions of polymerization of the adhesive system of the 5th generation, in order to obtain long-term clinical results.

Research is also planned on the development and clinical testing of additional tools that would ensure full curing of the adhesive system by light flux of LED photopolymerizer during

direct restoration of teeth with photocomposite materials in different clinical situations, including carious cavities of different classes, and which would reduce time light exposure to the adhesive system at the bottom and each of the walls of the cavity in the restored teeth.

5. Conclusions

1. Carrying out direct restoration of teeth with carious cavities of 1 class according to Black from nanophotocomposite material using the 5th generation adhesive system with its gradual polymerization on the bottom and separately on each of the walls provides high efficiency, which according to leading clinical criteria is 12 months $93.7 \pm 3.4\%$, 24 months – $88.9 \pm 3.5\%$.

2. Light exposure to the adhesive system at the bottom and separately on each of the walls of the cavity should be carried out using the proposed nozzle on the light guide of the photopolymerizer, which directs the light perpendicular to the surface of hard tissues at a minimum distance from them.

3. The proposed conditions of light polymerization of the adhesive system ensure in the period of 12 and 24 months the absence of secondary caries in the restored teeth.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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DOES THE TERM OF DEFINITIVE OSTEOSYNTHESIS OF MULTIPLE LONG BONE FRACTURES OF LOWER EXTREMITIES IMPACT ON TREATMENT OUTCOMES IN POLYTRAUMA PATIENTS

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Abstract

The aim: to determine the timing impact of definitive multiple long bone fracture osteosynthesis of lower extremities on complications development, duration of Mechanical Ventilation (MV), Length of Stay in Intensive Care Unit (LOS-ICU), Hospital length of Stay (H-LOS) in patients with polytrauma treated according to Damage Control Orthopedics (DCO).

Materials and methods: a prospective controlled non-randomized trial in parallel groups conducted in polytrauma department of Kyiv City Clinical Hospital No. 17 from February 2016 to January 2020, which included 107 adult patients with polytrauma, multiple long bone fractures of lower extremities, one of which femur treated according to DCO.

The patients were divided into two groups: Group I included 51 patients who underwent definitive osteosynthesis of long bone fractures of lower extremities after patient condition stabilization ≥ 24 hours ≤ 5 days; Group II included 56 patients who underwent definitive osteosynthesis of long bone fractures of lower extremities during the period > 5 days after injury.

Results: there were no statistically significant differences between Group I and Group II patients in demographics, injury mechanism, trauma severity and general patient condition. Group I patients who underwent osteosynthesis from 2nd to 5th days after injury had lower pneumonia incidence, compared to Group II patients (17.6 % vs. 26.8 %, $p=0.047$), shorter MV duration (9.3 ± 6.9 vs. 14.9 ± 9.1 , $p=0.048$), ICU-LOS (13.5 ± 8.3 vs. 19.1 ± 11.0 , $p=0.037$), and H-LOS (30.3 ± 13.9 vs. 38.9 ± 15.5 , $p=0.046$).

Conclusion: performing definitive multiple fracture osteosynthesis of lower extremity long bones after polytrauma patient stabilization from 2nd to 5th days after injury allowed to reduce the frequency of pneumonia, shorten the duration of MV, LOS-ICU and H-LOS, compared with its implementation after 5th days.

Keywords: polytrauma, long bone fractures, definitive osteosynthesis, complication, outcomes.

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1. Introduction

Lower extremities injuries are common in patients with polytrauma [1, 2]. Long bone fractures, especially of femur, are associated with development of numerous complications, including Acute Respiratory Distress Syndrome (ARDS), fat embolism, pneumonia, sepsis, Multiple Organ Failure (MOF) and death [3, 4].

Patients with injuries of two or more segments, presented with bilateral, ipsilateral and contralateral fractures of femur and tibia, have increased risk of complications, compared with a fracture of one long bone and these patients need special care management [5, 6].

The choice of timing and method of lower extremity bone fracture fixation in patients with polytrauma is a controversial question [7, 8]. The literature presents many studies confirming the benefits of early definitive osteosynthesis within ≤ 24 hours in patients with polytrauma according to Early Total Care (ETC), but these patients are in stable clinical condition and have a fracture of one long bone of lower extremity [9, 10].

The use of ETC tactics is possible in patients with multiple long bone fractures of lower extremities, but most researchers prefer using Damage Control Orthopedics (DCO) [11, 12].

Taking into consideration that DCO involves temporary external fracture fixation, such a question arises – when does it necessary to converse the temporary fixation method on definitive osteosynthesis [13, 14]?

According to some researchers, the performance of definitive osteosynthesis from 2nd to 5th days after injury causes numerous complications and patient death. First of all, it is explained by a period of persistent immunological changes caused by trauma and performance of definitive osteosynthesis is the cause of development “Second-Hit” effect. Therefore, it is recommended to perform the definitive osteosynthesis during the “Window of Opportunity” from 5th to 10th days [15, 16].

Other scientists confirm that performing of osteosynthesis during the period from 2nd to 5th days is safe for the patient and it does not affect or even reduce the frequency of complications, especially pulmonary, and it does not shorten duration of Mechanical Ventilation (MV), Length of Stay in Intensive Care Unit (LOS-ICU) and Hospital Length of Stay (H-LOS) [17, 18].

Therefore, the choice of conversion timing of temporary fixation on definitive osteosynthesis of long bone fractures of lower extremities remains a relevant and controversial issue in patients with polytrauma, it requires further scientific research.

The aim of the research – to determine the timing impact of definitive multiple long bone fracture osteosynthesis of lower extremities on the complication development, duration of MV, LOS-ICU, H-LOS in patients with polytrauma treated according to DCO.

2. Materials and methods

Study design: a prospective controlled not randomized trial in parallel groups conducted in polytrauma department of Kyiv City Clinical Hospital No. 17 from February 2016 to January 2020.

Inclusion criteria: patient agreement or his/her legal representatives (in case of patient consciousness disorder) to participate in the study; age ≥ 18 years; polytrauma (associated injury of two or more anatomical regions, the severity of each one ≥ 3 points according to the Abbreviated Injury Scale (AIS); presence of at least one of the following parameters: hypotension (systolic blood pressure ≤ 90 mmHg), Glasgow Coma Scale (GCS) \leq points, acidosis (base excess ≤ -6.0), coagulopathy (activated partial thromboplastin time ≥ 40 s or international normalized ratio ≥ 1.4), or age ≥ 70 years) [19]; open/closed multiple (≥ 2 segments) long bone fractures of lower extremities, one of which is the femur fracture; Injury Severity Score (ISS) ≥ 18 points; patients who were treated according to DCO.

Exclusion criteria: the death of the patient within the first day before the definitive osteosynthesis; borderline patients who have stabilized within 24 hours of injury and treated according to the ETC; severe chronic comorbidity, which complicates patient's condition and impede stabilization needed for surgical treatment; III degree open fractures (Gustilo-Anderson); neoplasm; pregnancy.

The study design was approved by the Commission on Bioethical Expertise and Ethics of Scientific Research of Bogomolets National Medical University №120 from 23.03.2020. According to expert opinion on materials, the study did not contain an increased risk for subjects of the study and was performed taking into account bioethical norms and scientific standards in accordance with the "Ethical principles for medical research involving human subjects" of the Helsinki Declaration of the World Medical Association.

The study included 107 polytrauma patients with multiple long bone fractures of lower extremities who were treated according to DCO.

Depending on the timing of the definitive osteosynthesis all patients were divided into two groups:

- group I included 51 patients who underwent definitive osteosynthesis of long bone fractures of lower extremities after patient condition stabilization ≥ 24 hours ≤ 5 days;
- group II included 56 patients who underwent definitive osteosynthesis of long bone fractures of lower extremities during the period > 5 days after injury.

On admission to the hospital all patients, included in the study, were evaluated on ISS [20], AIS [21], GCS [22], monitoring of hemodynamic parameters, Focused Assessment Sonography for Trauma (FAST), Whole-body Computed Tomography (after emergency surgery).

All patients were monitored for general clinical and biochemical blood parameters, including coagulation tests, metabolic parameters, arterial blood gas.

According to the Clinical Grading System (CGS), patients were divided into "stable", "borderline", "unstable" and "in extremis" [23].

Bone fractures were classified according to the Arbeitsgemeinschaft für Osteosynthesefragen/Orthopaedic Trauma Association (AO/OTA) classification [24]. Open fractures were classified by Gustilo-Anderson [25].

Primary osteosynthesis of the long bones of lower extremities was performed by external fixation. Conversion of the temporary fixation on definitive one was performed depending on the localization and type of fracture in accordance with the recommendations of AO/OTA.

Criteria for the patient's readiness for the definitive fixation of long bone fractures of lower extremities were: relative stabilization of vital functions and patient clinical condition, stabilization of hemodynamics, without need for vasopressor support, metabolic parameters (venous blood lactate < 4 , bases excess ≥ -5.5 and pH ≥ 7.25) according to the Early Appropriate Care (EAC) protocol [26] and the Horowitz Index (PaO₂/FiO₂) ≥ 200 .

The control of the patient's condition at the post-hospital stage was carried out using telemedicine technologies. Counseling mode: synchronous and asynchronous "doctor-patient" consultations. Main method of evaluating treatment outcomes was counseling and completing the SF-36 scale. However, the results of telemedicine technologies usage in the treatment of patients with multiple fractures of the lower extremities will be demonstrated in our subsequent publications.

Endpoints: frequency of: pneumonia, ARDS, sepsis, MOF; duration of MV; LOS-ICU; H-LOS; mortality.

Pneumonia was defined on the basis of Clinical Pulmonary Infection Score (CPIS) ≥ 6 points [27]. ARDS was defined according to the “Berlin Definition” 2012 [28]. Sepsis was diagnosed according to the “Sepsis-3” criteria 2016 [29]. MOF was defined on the basis of the Sepsis-related Organ Failure Assessment (SOFA) [30].

Statistics

The normality distribution was verified using the Shapiro-Wilk test. Under normal distribution, the data is presented as mean, standard deviation \pm (SD). Qualitative comparative analysis was performed using Fisher’s exact test. The Student’s t-test was used to test the null hypothesis of no difference between groups. Statistically significant differences were considered at $p < 0.05$. The analysis was performed using the statistical software IBM SPSS Statistics 23.

3. Results

There were no statistically significant differences between the patients in the two study groups in demographics, mechanism of injury, severity of injury and general condition of the patient, localization and type of fractures $p > 0.05$ (Table 1).

Table 1

Cause and severity of trauma, demographic and clinical characteristics of study patients, localization and type of long bone fractures of lower extremities and methods of osteosynthesis

Indicators	Group I (n=51)	Group II (n=56)	P
Age (year)	42.4 \pm 17.2	40.2 \pm 15.8	0.243
Male (n/%)	38/74.5	39/69.6	0.194
Cause of trauma			
Traffic accident (n/%)	35/68.6	41/73.2	0.322
Fall (n/%)	12/23.5	12/21.4	0.219
Other (n/%)	4/7.9	3/5.4	0.368
Severity of trauma			
GCS (points)	9.3 \pm 3.4	9.1 \pm 3.8	0.517
ISS (points)	30.4 \pm 9.7	31.1 \pm 10.3	0.723
Severity of patient clinical condition			
Stable (n/%)	0	0	-
Borderline (n/%)	18/35.3	21/37.5	0.699
Unstable (n/%)	24/47.1	23/41.1	0.527
In extremis (n/%)	9/17.6	12/21.4	0.375
Characteristic of long bone fracture and method of definitive osteosynthesis			
Long bone fractures (n)	113	131	-
Closed fractures (n/%)	82/72.6	89/67.9	0.532
Open fractures (n/%)	31/27.4	42/32.1	0.276
Femur (n/%)	64/56.6	62/47.3	0.198
Tibia (n/%)	49/43.4	69/52.7	0.542
Diaphyseal fractures (n/%)	97/85.8	104/79.4	0.384
IMN (n/%)	92/81.4	99/75.6	0.495
Plate (n/%)	21/18.6	32/24.4	0.297
Simultaneously conversion (n/%)	33/64.7	42/75.0	0.128
Conversion in two stages (n/%)	18/35.3	14/25.0	0.549
IMN – Intramedullary Nailing			

Treatment outcomes including the incidence of pneumonia, ARDS, sepsis, MOF, death and treatment timing are shown in **Table 2**.

Table 2

Outcomes of patients treatment with multiple long bones fractures of the lower extremities

Outcomes	Group I (n=51)	Group II (n=56)	p
Pneumonia (n/%)	9/17.6	15/26.8	0.047*
ARDS (n/%)	8/15.7	12/21.4	0.069
Sepsis (n/%)	7/13.7	6/10.7	0.218
MOF (n/%)	6/11.8	10/17.9	0.489
Duration MV (days)	9.3±6.9	14.9±9.1	0.048*
LOS-ICU (days)	13.5±8.3	19.1±11.0	0.037*
H-LOS (days)	30.3±13.9	38.9±15.5	0.046*
Mortality (n/%)	5/9.8	7/12.5	0.089

Note: * – the difference between groups is significant, $p < 0.05$

4. Discussion

Polytrauma is an important medical and economic problem of modern health care system, as it is one of the leading causes of death of young person under 45 years of age [31, 32].

Males were dominated among patients included in the study in Group I and II (74.5 % vs 69.6 % respectively, $p=0.194$). The mean age of patients was 42.4 ± 17.2 in Group I vs. 40.2 ± 15.8 ($p=0.243$) in Group II. Traffic accident was the main cause for the injury in Group I and II (68.6 % vs 73.2 % respectively, $p=0.322$) (**Table 1**).

An early accurate assessment of injury severity and patient clinical condition is important for the choice of further management in polytrauma patients [31]. Nowadays more than 50 scales have been proposed to evaluate the severity of injury and patient's condition, assessing anatomical lesions, physiological parameters, and combinations thereof.

We used the ISS to assess the severity of trauma, which points were 30.4 ± 9.7 in Group I and 31.1 ± 10.3 in Group II ($p=0.723$) (**Table 1**).

In our study we used the CGS to determine the severity of patient's condition. Although this scale is difficult to apply because it includes a large number of instrumental, laboratory, and clinical indicators, characterized four parameters (shock, acidosis, coagulation and soft tissue injury), it allows accurate assessment of the patient's condition [23, 31].

At admission to hospital, most patients were in unstable and borderline conditions (**Table 1**). Further management was based on the Pape H. C. algorithm (2005) [23].

The conversion of fixation method from temporary to definitive was performed in 100 % of cases. IMN was performed in 81.4 % of these cases in Group I and in 75.6 % in Group II (**Table 1**). The priority direction was the definitive osteosynthesis of femur fracture. After the definitive stabilization of one segment, the decision to perform the definitive osteosynthesis of the other injured segment was made, providing low risk assessed by the EAC and $\text{PaO}_2/\text{FiO}_2 \geq 200$.

The conversion of temporary fixation on definitive one was performed simultaneously in 64.7 % of cases in Group I and in 75.0 % in Group II. In other cases the conversion was performed in two stages. The time from trauma to definitive osteosynthesis of lower extremity long bones was 3.8 ± 1.1 days in Group I and 9.5 ± 3.8 days in Group II.

One third of all fractures were open (27.4 % vs. 32.1 % $p=0.276$) (**Table 1**). However, these fractures did not affect the timing of definitive surgery, as patients with Gustilo-Anderson type III fractures had been excluded from the study; and type I and II fracture osteosynthesis was performed the same as closed fractures with adequate antibacterial therapy.

As noted above, patients with multiple long bone fractures of lower extremities are characterized by general complications, among which pulmonary ones occupy a leading position.

In the literature the incidence of pneumonia in this category of patients ranges from 18.1 % to 50.0 % [3–5].

According to the results of the study, the most common complication was pneumonia, its incidence was higher in Group II patients compared to Group I (26.8 %, vs. 17.6 %, respectively), and it had a statistically significant difference ($p=0.047$) (**Table 2**).

Another common pulmonary complication was ARDS with incidence of 15.7 % in Group I and 21.4 % in Group II. There was no statistically significant difference between the groups, but there was a trend towards a significant difference ($p=0.069$) (**Table 2**).

There was also no statistically significant difference in sepsis rate ($p=0.218$) and MOF ($p=0.489$) between patients in compared groups (**Table 2**).

According to the literature, in this category of patients sepsis is diagnosed from 14.6 % to 21.6 % of cases [3, 5, 11], MOF from 12,0 % to 40,2 % [3, 5, 11].

Polytrauma is an important social problem as it is characterized by high morbidity and mortality rates. According to the literature, mortality ranges from 16.9 % to 35.5 % among patients with polytrauma and multiple long bone fractures of lower extremities [3, 5, 8, 11].

In our study, mortality among Group I and Group II patients was 9.8 % vs 12.5 %, respectively ($p=0.089$) (**Table 2**), and it had no statistically significant difference. However, it should be noted that, according to the study, 13 patients who had died within the first 24 hours before the definitive surgery were excluded. Mortality rate with excluded patients from the study was 20.8 %.

Also it should be noted that the majority of studies have demonstrated the incidence of complications and mortality during patient's stay in a hospital. Few studies describe these characteristics after patient discharge at outpatient stage of treatment. Therefore, in order to register complications and death of a patient within 1 year after polytrauma, we use the telemedicine technologies in our practice, designed by us. This method allows to monitor and correct the patient's rehabilitation process, to diagnose the development of the disease in time and to prescribe treatment.

In addition to social problems, polytrauma is a major economic expense cause because patients require long-term MV, longer LOS-ICU and H-LOS, which increases direct and alternatives costs, as other patients' access to this medical institution is limited [26].

According to various scientific sources, MV lasts from 7.8 to 13.3 days [3, 5, 7, 11], LOS-ICU is 8.8–19.4 days [5, 7, 8, 11], H-LOS ranges from 32.2 to 44.3 days in patients with multiple long bone fractures of lower extremities [5, 8, 11].

The results of our study, presented in **Table 2**, indicated that Group I patients who underwent definitive osteosynthesis from 2 to 5 days after injury had a shorter duration of MV ($p=0.048$), shorter LOS-ICU ($p=0.037$) and H-LOS ($p=0.046$), with statistically significant difference.

Study limitations. In our study we did not evaluate patients treated according to ETC tactics and who were underwent definitive multiple fractures osteosynthesis of long bones of lower extremities during the first day. In addition, patients with open Gustilo-Anderson type III fractures were not included because of delaying definitive osteosynthesis.

Prospects for further research. Further studies should be randomized to include more patients with multiple closed and open fractures of long bones of lower extremities treated according to ETC and DCO tactics.

5. Conclusions

Polytrauma patients with multiple long bone fractures of lower extremities are characterized by severe combined injuries that lead to numerous general and local complications.

Performing definitive osteosynthesis in case of multiple long bone fractures of lower extremities from the 2nd to the 5th day after the injury can significantly reduce the frequency of pneumonia, reduce the duration of mechanical ventilation, the length of stay in the intensive care unit and the length of hospital stay.

This study was not random for a number of reasons, but the question of the timing of definitive osteosynthesis is relevant and requires further study.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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THE INFLUENCE OF NANO-SILVER ON FORMATION OF MICROBIAL BIOFILMS IN CASES OF TRAUMATIC LESION OF THE AUXILIARY APPARATUS OF THE EYE

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Abstract

Pyoinflammatory complications remain an acute problem in the post-operative period of traumatic lesions of the auxiliary apparatus of the eye (AAE). Silver both in the ionic form and in composition of chemical compounds is highly toxic for microorganisms, and as a result, it shows bactericidal effect to many bacterial strains, including gram-negative microorganisms. The peculiarity of AgNPs is efficiency of influence on the wide array of microorganisms, significant anti-biofilm effect and absence of resistance reaction.

The aim of the research. To study the influence of the colloidal nano silver on formation of biofilms by microorganisms discharged from the wounds of patients with traumatic lesions of the auxiliary apparatus of the eye.

Materials and methods. During 2018–2019, we examined 60 patients with traumatic lesions of the auxiliary apparatus of the eye. For evaluation of the influence of colloid nano silver solution on the processes of formation of the biofilm, we selected microorganisms which were cultured most frequently (*Staphylococcus aureus*, *Acinetobacter* spp., *Klebsiella ozenae*) from the patients.

Results. The obtained data suggest that colloid nano silver inhibits efficiently formation of biofilms at the early stages (initiation, the 0 day of incubation) of their formation by all the three microorganisms, and the degree of inhibition of the biofilm formation did not depend on the silver concentration.

The effect of colloid silver in the concentrations used by us at later stages of biofilm formation (the 3rd and the 7th day) with respect to *K. ozenae* is less efficient – the growth of cell biomass was observed ($p \leq 0.05$), and it did not depend on the silver concentration. At the same time, the effect of the colloid nano silver on *S. aureus* and *Acinetobacter* spp. on the 3rd and the 7th days was more efficient than at the early stage ($p \leq 0.05$).

Conclusions. Nanoparticles of colloid silver are an efficient means to combat biofilms, as well as to prevent their formation.

Keywords: colloidal nano silver, biofilms, minimum inhibitory concentration (MIC), trauma of the auxiliary apparatus of the eye, infection.

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1. Introduction

Pyoinflammatory complications remain an acute problem in the post-operative period of traumatic lesions of the auxiliary apparatus of the eye (AAE), since they cause delayed wound healing and provoke formation of adverse vicious cicatrices [1, 2]. For prevention of pyoinflammatory

complications and chronization of processes of wound healing it is important to carry out monitoring of the species composition and sensitivity of microorganisms which are discharged from the traumatic lesions of the patients to the most common antibiotics [3,4].

At the present stage of the development of medicine and pharmacology, a quite acute problem is the development of chemotherapeutic agents, which are an alternative to antibiotics, since in the clinical practice in the whole world a steep increase of the number of resistant microorganism strains [5,6]. Antibacterial properties of silver are known from a long time. Silver both in the ionic form and in composition of chemical compounds is highly toxic for microorganisms, and as a result, it shows bactericidal effect to many bacterial strains, including gram-negative microorganisms [7, 8]. Antimicrobial efficiency of silver depends on the size of the particles, antibacterial activity of the nanoparticles surpasses activity of the common silver solutions [9, 10]. It is proved that nanoparticles of silver (AgNPs) affect penetrability of bacterial membranes and adhesion of bacteria to the cell membrane [11, 12]. AgNPs also affects membrane and intracellular proteins of bacteria, remnants of phosphoric acid and DNA, distorts cell division, causing their death [13, 14]. So, the peculiarity of AgNPs is efficiency of influence on the wide array of microorganisms, significant anti-biofilm effect and absence of resistance reaction [15, 16].

Methods of treatment of wounds with biofilms must include wound cleansing with application of antiseptic and antimicrobial medicines for prevention of wound re-infection and inhibition of the repeated formation of biofilms [17, 18].

The aim of the research. To investigate the influence of the colloidal nano silver on formation of biofilms by microorganisms discharged from the wounds of patients with traumatic lesions of the auxiliary apparatus of the eye.

2. Materials and methods

During 2018–2019, we examined 60 patients with traumatic lesions of the auxiliary apparatus of the eye, who sought help at the emergency room at the Eye Microsurgery Department of the Municipal Non-commercial Enterprise of Sumy Regional Council Sumy Regional Clinical Hospital. Examination and treatment of the patients were carried out according to the standards of provision of the medical assistance. The procedure of examination of those persons met the regulations of the ethics committee. At the preliminary stage bacteriologic examination of smears from the wounds was carried out, with identification of the species composition and population level of microorganisms based on the bacteriologic laboratory of the Centre of the Collective Use of Scientific Equipment of the Medical Institute of Sumy State University. For evaluation of the influence of colloid nano silver solution on the processes of formation of the biofilm, we selected microorganisms which were cultured from the patients most frequently (*Staphylococcus aureus*, *Acinetobacter spp.*, *Klebsiella ozenae*).

This clinical research is met Ukrainian legislation, modern ethical standards and principles of scientific clinical research and was approved at the meeting of the Commission on Ethics of the Shupyk National Medical Academy of Postgraduate Education (protocol No. 1 of January 9, 2020). All patients provided informed written consent to participate in the study.

Two groups were formed: the control one (microorganisms without influence of the colloid nano silver solution) and the main one (microorganisms were exposed to the colloid nano silver solution). The colloid nano silver solution (Nanomaterialy i Nanotekhnologii (Nanomaterials and Nanotechnologies) LLC, Ukraine, registration number 05.03.02-04/66400 as of 16.09.2010) was added to the microorganisms for 0, 1, 3 and 7 days of incubation in the amount equal to 2.5, 5, 10 minimum inhibitory concentrations for every species of microorganisms.

Evaluation of the influence of silver nanoparticles on the formation of biofilms was carried out by the definition of the volume of the formed biofilm, with gentian violet staining [19, 20]. The optical density of microbial biomass was defined by the Thermo Scientific Multiscan FC microplate photometer ESW 1.01.16 (wavelength 595 nm). The coefficient of the microbial biomass reduction was calculated as a proportion of the optical density of the tested sample to the optical density of control in the percentage equivalent.

The results of the performed investigations underwent statistical processing. The Graph-PadQuickCalcs program with the definition of t-Student criterion was used for carrying out the calculation.

3. Results

Sixty patients with traumatic lesions of the auxiliary apparatus of the eye were examined. Seventy-five strains of microorganisms were isolated and identified from them. Considering the frequency of microorganisms isolated from the patients with lesions of the AAE, we selected *Staphylococcus aureus*, *Acinetobacter spp.*, *Klebsiella ozenae* for study the influence of colloid nanosilver on the formation of biofilm.

We tested antimicrobial and antibiofilm properties at different concentrations of the colloidal nanosilver. We found the MIC for planktonic cultures of clinical isolates of *S. aureus*, *Acinetobacter spp.*, *K. ozenae* was equal to 12.5 $\mu\text{g/ml}$.

The adhesion of bacterial cells to the surface is considered the first step for biofilm formation. Consequently, in the beginning, we examined the influence of silver nanoparticles on bacteria adhesion. The obtained data (**Fig. 1**) suggest that colloid nanosilver inhibits the formation of biofilms at the beginning stage efficiently. The degree of the biofilm formation inhibition for *Klebsiella* and *Staphylococcus* was dependent on the silver concentration and was not dependent on the quantity of the silver for *Acinetobacter spp.*

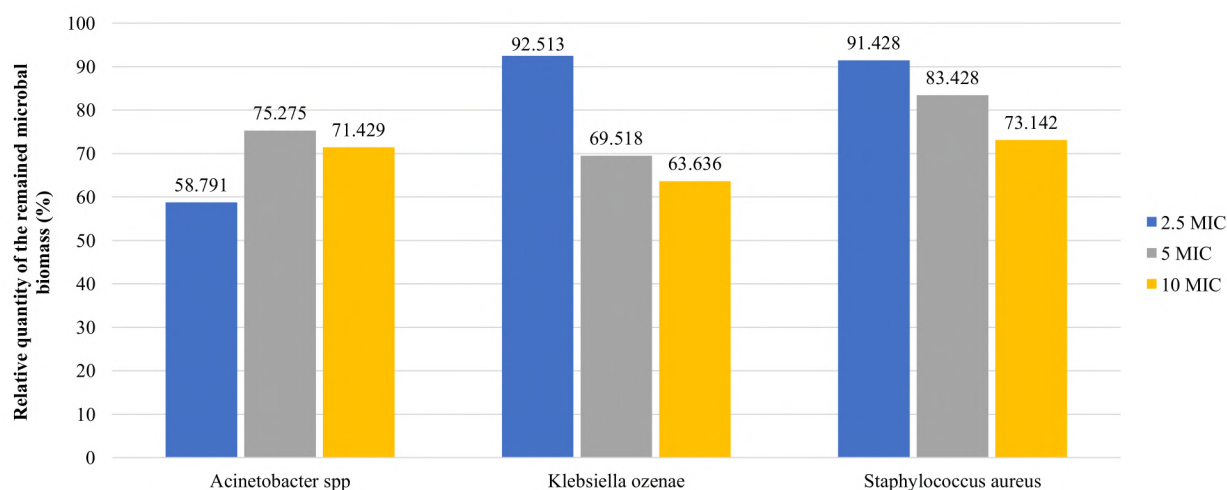
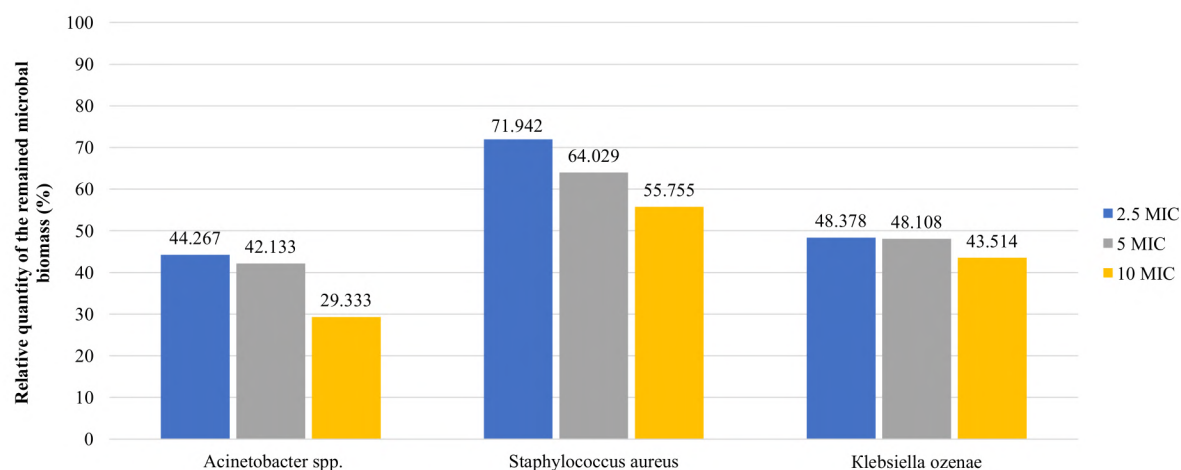
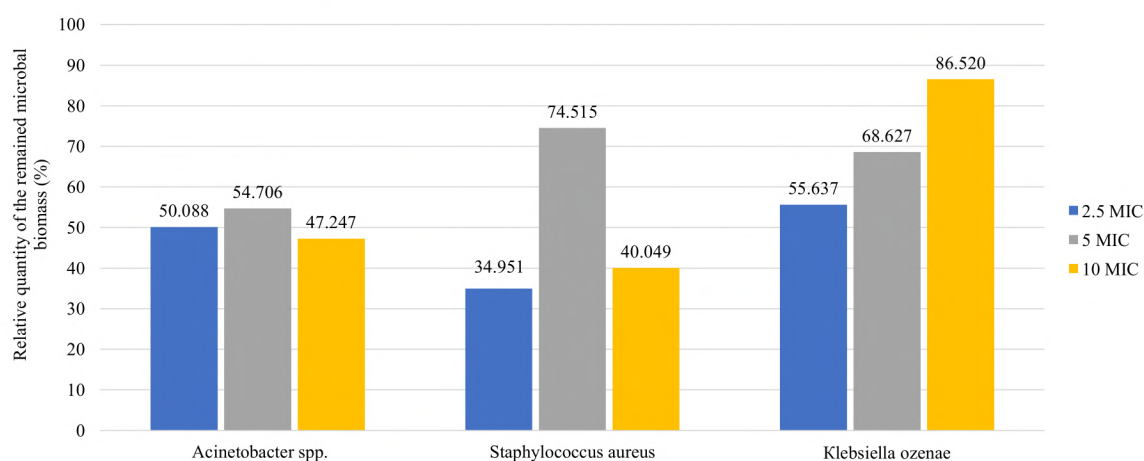
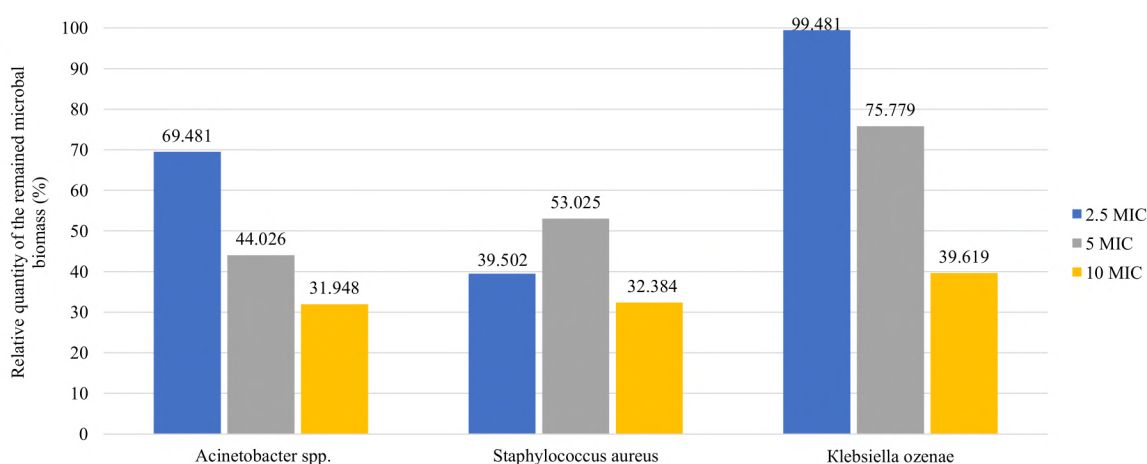


Fig. 1. Influence of nanosilver on the immature biofilms (initiation)

As it is shown in **Fig. 2–4**, we have revealed the intense activity in colloidal nanosilver against mature biofilms formed by all types of tested microorganisms. The efficiency of silver increased directly with the growth of the silver amount in the culture medium. Moreover, the silver acts differently on biofilms with various stages of maturation. It was especially noticeable on the one-day films. The biofilms formed by *Acinetobacter spp.* was the most susceptible to the influence of nanosilver. The relative quantity of the remaining bacteria cells in the biofilm was the least after treatment among all species. *S. aureus* formed the most stable composition of the biofilm since the remained biofilm mass varied from 71.9 to 55.8 (44.3 %) after silver processing.

The effect of colloid silver at later stages of biofilm formation (the 3rd and the 7th day) against *K. ozenae* and *Acinetobacter spp.* is less efficient (**Fig. 3, 4**) than at an early stage. The volume of the cell biomass after silver action was more significant ($p \leq 0.05$) comparing to the 1-day biofilm. There was not also a correlation between the silver concentration and remained biomass. At the same time, the effect of the colloid nanosilver on *S. aureus* biofilm on the 3rd and the 7th days was more efficient than at the early stage ($p \leq 0.05$).

**Fig. 2.** Influence of nanosilver on the mature biofilms (1day)**Fig. 3.** Influence of nanosilver on the mature biofilm (3 days)**Fig. 4.** Influence of nanosilver on the mature biofilm (7 days)

5. Discussion

Attention to wound infection is critical for quick repair with no side effects. It gains exceptional value due to the rapid growth of antibiotic resistance and insufficient needs to search for new medicine with antimicrobial activity. Nanomaterials have become a promising alternative to

conventional antibiotics. It was shown in several studies that AgNPs possesses broad-spectrum antibacterial activities [7, 21]. The increasing number of studies have demonstrated the presence of biofilm in wounds of varied etiology [22]. The wound is inevitably created under aseptic surgical conditions. The prevention of bacteria entering the wound is based on the interruption of microbial attachment to the tissue on an initial step [22]. In this study, we report the capabilities of colloidal nanosilver to prevent the formation of biofilms by *Acinetobacter spp.*, *Klebsiella ozenae*, and *S. aureus*. According to other scientist data, the minimum biofilm eradication concentration for antiseptics exceed MIC for planktonic bacteria more than 10–1000 times [3, 4]. We revealed that colloidal nanosilver effectively destroys the biofilms formed by microorganisms isolated from patients with traumatic lesions of the auxiliary apparatus of the eye even at a concentration equal to 2.5 MIC. The effect of the nanosilver varied in different terms and was the highest on 1-day films. Probably the reason for such variation was the difference in biofilm composition. The immature biofilm consists mostly of cells that are more sensitive to the silver influence than exopolysaccharide matrix. It is known that ionic silver may be inactivated by extracellular polymeric substances (EPS) and other organic matter within the biofilm [23].

Study limitations. Our research is limited by studying the effect of nanosilver on the formation of biofilms by microorganisms isolated from traumatic wounds of the auxiliary apparatus of the eye.

Prospects for further research. The further investigation of other nanometals effect on the biofilms formed by microorganisms isolated from patients with lesions of the eyes will provide us new knowledge.

6. Conclusions

1. As a result of the clinical-experimental research, we received a positive effect of colloidal nanosilver at the concentration 31.5–125.0 µg/ml on the biofilms formed by *S. aureus*, *Acinetobacter spp.*, *Klebsiella ozenae*.

2. Nanosilver inhibits the formation of biofilms at the beginning stage efficiently. The degree of the biofilm formation inhibition for *Klebsiella* and *Staphylococcus* was dependent on the silver concentration and was not dependent on the quantity of the silver for *Acinetobacter spp.*.

3. The intense activity in colloidal nanosilver against mature biofilms formed by all types of tested microorganisms. The efficiency of silver increased directly with the growth of the silver amount in the culture medium.

4. The silver acts differently on biofilms with various stages of maturation.

Colloidal nanosilver could be used for the prevention of complicated wound infection in patients with traumatic lesions of the auxiliary apparatus of the eye. Use of colloidal silver could reduce the risk of post-traumatic deformations of the periorbital region, decrease the duration and cost of treatment as well as period of rehabilitation.

Acknowledgments

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Conflict of interest

The authors declare that they have no conflicts of interest.

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FEATURES OF SURGICAL ACCESS DURING VIDEOTHORACOSCOPY OPERATIONS IN THE WOUNDED WITH CHEST TRAUMA

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Abstract

The aim. To improve the treatment of wounded with combat chest injury by optimizing low-traumatic surgical access using video thoracoscopy.

Materials and methods. In the period from 2014 to 2019, 103 injured were treated with video-assisted thoracoscopic surgical interventions in case of chest trauma. According to the objectives of the study, two clinical groups of victims were formed. The comparison group included 54 (52.4 %) victims, the main group – 49 (47.6 %). The wounded accounted for 72 persons (69.9 %), injured – 31 (30.1 %). In case of wounds to the chest, the selection of victims for VTS surgical interventions and the timing of their implementation was carried out taking into account the location, type of injury and trauma, the severity of the condition of the patients, the presence of a combined wound, the possibility of two or one-lung ventilation during the intervention, the timing of admission to a medical institution with the moment of injury, the technical capabilities of military-technical operations. In staging trocars during combat chest injury, we adhere to the general rules for video-assisted thoracoscopic interventions on the chest – the rules of the “triangle”. When a chest injury is involved, the port setting has its variability, which is based on the type of injury and the purpose of the surgical intervention. You can use both standard points of installation of thoracoports, and non-standard individual ones that will correspond to the set clinical goals.

Research results and discussion. High efficiency in visualization of the operating area and the technical convenience of surgical techniques have been established. This allows a rational and consistent audit of the anatomical zone of the wound. With a chest injury, the most rational sequence for conducting a pleural cavity audit is on the principle of paramount importance.

Conclusions. Features of online access – port setting for injuries to the chest depends on the area of the inlet of the gunshot. When setting ports, it is not necessary to adhere to standard points, the introduction of a thoracoport is possible at any point on the chest wall, but with the obligatory observance of the triangulation rule. The number of input ports for combat trauma to the chest depends on the technical need for a full operation. In the vast majority of military-technical operations, 3 thoracoports are enough.

Keywords: combat injuries of the chest, video thoracoscopy, thoracoport, revision of the pleural cavity.

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1. Introduction

The incidence of wounds and chest injuries in peacetime reaches 7 %, in modern military conflicts – 7.5–11.7 % [1, 2]. Surgical tactics for chest trauma is varied and depends on the type of injury, the time of the first medical and specialized care, the severity of the injured, the presence of complications, the technical capacity of the medical institution [3, 4].

Five years of experience of the armed conflict in eastern Ukraine showed that the fire arms weapons caused the injury of special gravity (non-nuclear weapons of mass destruction – jet system of salvo fire, cassette bombs, explosive devices of high-precision action etc.). At the same time, the majority of affected chest injuries appeared to be sufficient drainage of the pleural cavity by wide-band tubes, and the thoracotomy frequency reaches only 15–20 % [5]. The search for new effective methods of diagnosis and surgical treatment of the injured and traumatic chest trauma leads to an increasing use of videothorascopical technologies at all levels of medical care in the area of ATO and JFO (Joint Forces Operatoin).

The aim. Improvement of treatment of the wounded with chest trauma by optimizing the low traumatic surgical access when using videothoracoscopy.

2. Materials and methods

In order to provide surgical assistance to skill with elements of specialized care, there are deployed military-mobile hospitals in the zone of the ATO and JFO in the east of Ukraine. Since July 2014 the application of endovideosurgery in the field for the treatment of trauma of the abdomen and chest was started in Ukraine for the first time. Minimally invasive operative interventions were performed using the endovideosurgical complex ECONT (manufacturer of Ukraine).

Specialists of the surgical department of the mobile hospitals have been led by both traditional and videothoracoscopy equipment, which allowed to use minimally invasive technologies as close as possible to the combat zone.

All patients were informed of their participation in the study. Each patient signed an informed consent to participate in the study. All materials were provided at a meeting of the bioethics commission at the Odessa National Medical University. Minutes of the meeting number 15 attached, data 12.03.2020

In the period 2014 to 2019 the treatment of 103 wounded were used videothorascopical surgical intervention in the combat trauma of the chest. Two clinical groups of victims were formed according to task research. The comparison group was 54 (52.4 %) injured, the main – 49 (47.6 %). The main group included victims who underwent minimally invasive surgery. To the group of companions – victims who underwent surgical interventions through classical thoracotomy approaches. The wounded were 72 (69.9 %), injured - 31 (30.1 %). By the nature of combat damage to the thorax prevailed cases of gunshot wounds – 68 (66.0 %). Among them more often happen non-penetrating breast wounds – 40 (38.9 %) cases, including 17 (34.7 %) in the comparison group of wounded and 23 (42.6 %) primary group patients ($\chi^2=0.30$; $p>0.05$, p.e. 7 %). Gunshot wounds penetrating injuries of the thorax were in 28 (27.2 %) injured. Blast chest trauma detected in 31 (30.1 %) injured: at 13 (24.1 %) men of comparison groups and 18 (36.7 %) of wounded from main group ($\chi^2=0.74$; $p>0.05$, p.e. 5 %). As a type of injury in patients of both clinical groups prevailed fragmentation wounded – 26 (48.2 %) cases in the comparison group and 19 (38.8 %) – the main. In 23 (22.7 %) cases, there were bullet wounded.

The nature of the chest injuries was dominated by combined injuries prevailed – 42 (40.3 %) cases: 24 (44.5 %) damaged in the comparison group and 18 (36.7 %) in the main line ($\chi^2=2,18$; $p>0,05$, p.e. 3 %). Almost the same number amounted to isolated damage – 40 (38.9 %) cases: 18 (33.3 %) damaged in the comparison group and 22 (44.9 %) of wounded in the main group, respectively.

In case of wounds in the thorax, the selection of operative interventions and terms of their performance were carried out taking into account the localization and type of injury and injuries, the severity of patients and the presence of the combined injury, the possibility of during the intervention, duration of admission to the medical facility after injury or injury, technical capabilities of the VTS. VTS operations were conducted in the following clinical cases: 7 (13.5 %) of lung sealing operations for pneumothorax and 6 (11.5 %) of lung sealing operations in unstable aerostasis; 6 (11.5 %) operations to stop pleural bleeding continuing; 5 (9.6 %) stabilization of the rib frame; 15 (28.8 %) operations for coiled hemothorax; 1 (1.9 %) operation with atypical resection of the damaged lungs; 3 (5.8 %) operations regarding drained pleurisy; 9 (17.4 %) removal of foreign bodies threatening complications ($\chi^2=19,2$; $p<0.001$, p.e. 1 %). Single-lung ventilation with video-

thoracoscopy operative interventions at combat injuries and injuries was performed without complications in 36 (69.2 %) cases.

Among the complications of the early postoperative period were impaired tightness of the lung parenchyma, which showed incomplete the straightening of the lungs and maintaining a small or medium pneumothorax for 3–5 days after being injured. In the comparison group, such complications were observed in 4 (7.4 %) the wounded, which required an additional surgical intervention from thoracotomy access to final sealing of the lungs.

In the primary group, these complications were observed in 2 (4.1 %) wounded patients, who managed to neutralize using conservative measures. There were no fatalities after the VTS. The period of stay in the hospital after the VTS operations was 16 ± 1.2 bed-days and depended on the severity of thoracic wounds and the presence of combined wounds. At this, the average duration of stay on treatment by the wounded in the group of comparisons was 24 ± 1.4 bed-day. The results indicate high efficiency of videothoracoscopy interventions in the wounded with combat (fire) injury.

At the same time, in the course of videothoracoscopy intervention in the wounded with chest trauma, there were no defined features of operational access – the location of the thoracoports, depending on the area of the firearm injury. Taking into account our experience, surgical features in minimally invasive surgical treatment of gunshot wounds, we have proposed a method of selecting the thoracoports during videothoracoscopy treatment of the chest trauma.

3. Results

In staging trocars for combat trauma of the chest, we adhere to the general rules for videothoracoscopy interventions on the chest – the rules of the “triangle”, where the trocars are introduced at the points on the tops of a conditional triangle designed to the thorax in relation to the area of alleged operative intervention. The place of introduction of endoscopic camcorder is most often chosen in 5–6 intercostal space on the middle axillary line. This videothoracoscopy location allows to conduct a full inspection of almost all divisions of the pleural cavity and its organs, to keep under the control “working” instruments in all operative intervention. Sometimes the location of the videothoracoscop is chosen at the point, which is the most suited for the introduction of pleural drainage – 7–9 intercostal space on the middle or posterior axillary line. This position of the video camera has almost the same advantages as with the introduction of a videothoracoscopy in 5–6 intercostal space on the middle axillary line (under the conditions of use of optics with 30 degree view angle), but also allows not to make a separate incision for pleural drainage.

After the revision of the pleural cavity, it was determined the place to enter the “working” tools according to the principles of the “triangle”. The trocars were introduced under the visual control of the videothoracoscop. In all cases of VTS for the intervention it was enough three thoracoports (taking into account the thoracoports for the camera) to hold the planned volume of operation. It is one 10 mm trocar and two 5mm trocars, or two 10 mm trocars, one of which has an adapter for 5 mm endoscopic instruments. The use of two 10 mm trocars allows to rearrange the camera during operative intervention in order to change the viewing angle of the chest and change the placement of the “working” instruments.

We consider inappropriate, in most cases, the introduction of thoracoports because of the existing post-traumatic wounds, as the location of such wounds does not always meet the requirements for a full examination of the pleural cavity, limits the inspection and manipulation of the wound with side of the pleural cavity, as well as does not comply with the rules of aseptics, as all penetrating wounds in the combat conditions are initially contaminated. However, if during the operative intervention the introduction of the video camera or one of the “working” tools provides the most advantageous position that will allow to perform the basic stage of the operation, we consider the permissible installation of a thoracoport through the wounded canal. However, we are convinced that such manipulations should be performed only after thorough surgical treatment of the selected wounded canal.

One of the significant disadvantages of videothoracoscopy is the inability to direct palpation of anatomical structures and palpation detection of pathological changes in them, revealing and clarifying the location of the foreign bodies in the organs of the chest. The use of endoscopic ultrasound devices or endoscopic tactile mechanoreceptor apparatus is currently possible only in

scientific and research medical institutions due to the high-cost data of devices. Therefore, in order to assess the possibility of videothoracoscopy removal of foreign bodies, it is necessary to use the obligatory procedure at the stage of preoperative training in the case of Spiral computer imaging of the chest and conduct a thorough analysis of obtained photographs using 3D reconstruction, with a clear representation of topographic-anatomical features of the zone of alleged operative intervention and assessment of real technical possibilities of the task execution.

In cases where the pleural cavity is conducted on a videothoracoscopy and instrumental palpation of lungs, we have not managed to confidently establish the exact location of a foreign body by using a method of direct palpation lungs: the nearest to foreign body thoracport move in the chest was introduced by a finger of the operating surgeon, and with the help of endoscopic atraumatic clamp the lung was recorded in order to prevent its displacement during palpation. Thus we were able to detect foreign bodies that could not be detected at visual inspection through the video camera.

Thus, the staging of the thorax's combat trauma has a variability that is based on the type of injury and the purpose of surgery. It can be used both the standard points of installation of thoracoports and custom-made individual, which will correspond to the supplied clinical purposes.

In the implementation of proposed methods of setting ports during thoracoscopy established high efficiency in the visualization of the operating area (area of the wounded organ) and technical convenience of surgical receptions. It is allowed to rationally and consistently conduct an audit of the anatomical zone of injury.

In the chest trauma of the most rational sequence of the pleural cavity revision we consider the principle of primary importance. First inspect pericardium, then mediastinal and lung root. If the audit detect signs of cardiac damage or trunk vessels with the correct tactic is to continue operation traditional open method. In the second place the audit of the diaphragm is carried out, in detecting its damage it is necessary to resolve the issue of the need for further videothoracoscopy, thoracoscopy or laparoscopy. And, finally, the revision of the lungs and chest wall. This revision sequence avoids common errors, when the surgeon quickly finds the output hole of the wounded canal on the parietal pleura with a wounded area of the lungs, which is subject to inner wound opening and begins its sewing, without the possibility of other heavier damage.

Lung collapse is required for full revision of the pleural cavity. It is achieved by the use of selective pulmonary ventilation or the creation of additional pressure in the pleural cavity by introducing gas. In the absence of emphysema and lung changes, its collaboration passes without leaving air into the lung tissue, which leads to full atelectasis of the lungs, which allows without significant difficulties to carry out operative manipulations in the pleural cavity and on the lungs. However, in the case of emphysema changes in the lungs, the collaboration may not be complete, which makes it difficult to conduct revision and operation in the pleural cavity. In these cases it is necessary to enter the carbon dioxide into the pleural space and shrink the lungs using the "working" tools to remove the air from the lungs.

4. Discussion

In modern thoracic surgery, surgical interventions are undergoing changes to reduce their trauma. The desire for minimally invasive interventions is explained by their advantages, first of all, in the form of reduction of pain in the postoperative period, early activation of patients, earlier return to normal physical activity [6]. This direction of improvement of surgical interventions is carried out at many pathologies of thoracic surgery. In modern medical publications much attention is paid to the features of technical support of minimally invasive interventions, types of surgical access to the chest in various pathological conditions, the peculiarities of surgical maneuvers during surgery [7].

These publications cover both diseases and injuries of the chest. The advantage of our study is that we have not only conducted a theoretical justification for the feasibility of using surgical approaches in videothoracoscopy, but also conducted a practical test [8]. The second advantage of our study was the use of various minimally invasive interventions in combat, because in the surgical experience of military field surgery, data on the use of videothoracoscopic technologies are very limited. Therefore, our experience disseminates knowledge in the section of minimally invasive surgical procedures [9].

The disadvantages of our work are the limited minimally invasive interventions in combat pathology of the chest, in connection with which the small amount of data obtained can not be used as a guide [10].

The number and location of thoracoports in case of combined combat wounds of the thorax remain debatable, as it is impossible to give a full assessment of the extent of damage to the internal organs of the thorax, to determine the course of the wound canal before surgery.

Promising development of endosurgery in combat pathology of the chest is the further study of the wound process in the wounded, improving the technical equipment of surgical teams of military hospitals, in-depth study of the postoperative course in the wounded with combat chest injury.

5. Conclusions

Features of operative access are the setting of the ports at wounds in the thorax depends on the area of the inlet fire-fuel opening. When staging ports do not necessarily adhere to standard points, the introduction of thoracoports is possible at any points of the chest wall, but with the mandatory observance of triangulation rules.

The number of the transferred ports in the chest trauma depends on the technical need for a full operation. In the vast majority of videothoracoscopy operations 3 thoracoports are enough.

Installation of thoracoports though to the wound, obtained by wounds, is not advisable, because it does not always meet the requirements for a full examination of the pleural cavity, limits the inspection and manipulation of the wound on its inner side, and does not comply with the rules of aseptic.

One of the thoracoport passages can be used for direct palpation the closest to it areas of the lungs in order to establish the exact location of the foreign bodies, which are impossible to identify visually.

Conflict of interest

The authors declare that they have no conflicts of interest.

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EVALUATION OF THE MINERALIZING POTENTIAL OF ORAL FLUID IN CHILDREN WITH DOWN SYNDROME DEPENDING ON THE LEVEL OF THE CARIOGENIC PROCESS

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Abstract

Early diagnosis of dental caries in children is difficult. This fact is applied to children with Down syndrome. In order to identify predictors of dental diseases, a crystallographic method is widely used for studying oral fluid.

The aim of the work is to evaluate the mineralizing potential of oral fluid in children with Down syndrome before and after the course of preventive measures.

Material and methods. We examined oral fluid in children with Down syndrome. Children and adolescents at the age of 8 months to 17 years (n=21) were divided into groups depending on the age and the level of caries intensity. The results were compared with the data of 55 children without chromosomal pathology.

Results. The group of children with Down syndrome (MG), during the initial examination includes type II – 11 people (53 %) and type III – 7 people (33 %) microcrystallization of saliva, which generally corresponds to the situation in the group of children without chromosomal pathology (CG), where type II included 62 % (34 people) and type III – 22 % (12 people). The average value of the mineralizing potential of saliva in the main group was 2.78 ± 0.22 , and in the control group – 2.89 ± 0.17 .

Conclusions. After preventive measures during the re-examination of children with Down syndrome, there was a tendency to an increase in the level of parameters of the mineralizing potential of saliva while maintaining this level after 6 months.

Keywords: dental caries, children, Down syndrome, mineralizing potential, preventive measures.

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1. Introduction

Dental caries in children is one of the most common infectious diseases [1]. It is difficult to diagnose caries in children at an early stage [2]. This fact is applied to children with Down syndrome. Working with children in this category is significantly complicated for the dentist due to the peculiarities of mental development and emotional instability of the child in a dental clinic [3].

In order to identify predictors of dental diseases, oral fluid is widely studied as a biological substrate [4]. One of the methods widely used in dentistry is a crystallographic method for studying biological substrates. The method is based on the evaluation of the micromorphological picture of dried biological fluids, which reflects the processes in the human body. In case of pathological conditions, the crystal-forming properties of the body fluid are changed [5].

As a diagnostic criterion for dental diseases, structural changes in crystals of mixed saliva are examined [6]. One of the main functions of mixed saliva is its mineralizing potential – providing mechanisms maintaining the dynamic balance of mineral components in the oral fluid [7].

Highly informative crystallographic research methods, the relative availability of diagnostic material, non-invasiveness, as well as their cost-effectiveness, allow to use these research methods in paediatric dentistry for rapid and early diagnosis of dental diseases [8].

The aim of the study is to evaluate the mineralizing potential of oral fluid in children with Down syndrome before and after the course of preventive measures.

2. Materials and methods

The study was conducted on the base of the University Dental Center of Kharkiv National Medical University during 2017–2018.

We examined oral fluid of 76 patients at the age of 8 months to 17 years. The main group consisted of patients with Down syndrome (n=21, MG). The control group (n=55, CG) consisted of conditionally healthy children without chromosomal pathology. Children and adolescents were divided into groups depending on the level of caries intensity (UIC, P.A. Leus, 1996).

All the examined children and their parents have been informed of the aim of the study and the methods to be applied. Parents have given written consent to participate in the study.

The study project was approved by the Ethics and Bioethics Commission (protocol No. 4 – 2017 of 07/06/2017) and was carried out in accordance with the Declaration of Helsinki specifying the procedure of biomedical human research.

Microcrystallization of saliva (MCS) was determined according to P. A. Leus [9]. The oral fluid was taken in two hours after food intake. Using a sterile plastic spoon, unstimulated saliva was collected from the sublingual area of the oral cavity. Three drops of oral fluid were applied to a glass slide, which had previously been degreased and numbered, and dried at 18–25 °C in a horizontal position. The obtained results were studied in the light of the monocular microscope “BIOLAM C1”. Pictures of the crystals were obtained through the photomicrographic attachment (PMA-9). Microscopy of the dried drops determined the type of micro-installation of saliva and evaluated the mineralizing potential of saliva (MPS) expressed in points.

In order to increase the resistance of teeth hard tissues, a set of preventive measures was assigned for each child with Down syndrome (according to the scheme), namely the use of a combination of toothpastes and foams for oral care containing calcium, fluorine and milk enzymes (lactoperoxidase, lactoferrin, glucose oxidase), a remineralization gel for home use, which is a source of easily digestible calcium, phosphorus and magnesium compounds, and a gel containing amine fluoride, sodium fluoride, chlorhexidine and betaine.

The accumulation, correction, systematization of the initial information and visualization of the obtained results were carried out in Microsoft Office Excel 2007 spreadsheets. Statistical analysis was performed using STATISTICA 6.1 (developed by StatSoft.Inc).

Nominal data were described with absolute values and percentages. The average and standard deviation of the variables were calculated. For related samples, Student's t-test was used for paired cases.

3. Results

In the main group, among children with intact teeth, type II microcrystallization prevails in 8 people (38 %). The higher the activity of the carious process, the greater the proportion of children with type III microcrystallization of saliva (**Fig. 1**).

Among children of the control group, type I microcrystallization is found only in children with intact teeth in 5 people (9 %) and children with low caries activity in 4 people (7 %). In the group with a very high carious process activity, type III microcrystallization significantly prevails in 7 people (13 %) (**Fig. 2**).

According to the results of the microcrystallization test of saliva, it was found that in the group of children with Down syndrome (MG), during the initial examination, type II in 11 people (53 %) and type III in 7 people (33 %) microcrystallization of saliva prevail, which generally

corresponds to the situation in the group of children without chromosomal pathology (CG), where type II was 62 % (34 people), and type III – 22 % (12 people).

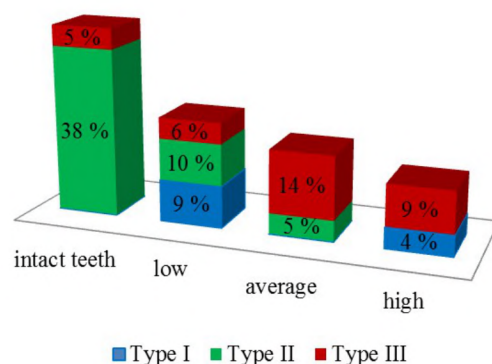


Fig. 1. Distribution by types of microcrystallization of saliva at different levels of the carious process activity among children with Down syndrome (MG)

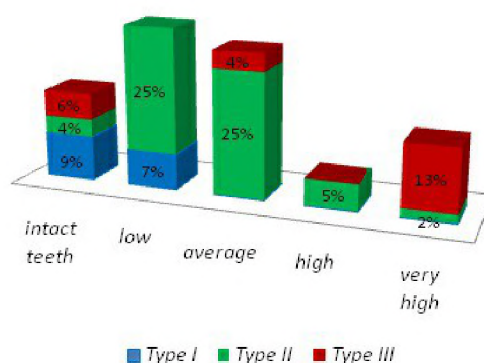


Fig. 2. Distribution by types of microcrystallization of saliva at different levels of the carious process activity among children in the control group

Mineralizing potential of saliva was evaluated as very low with an average value 0 to 1.0 points; low – with 1.1 to 2.0 points; satisfactory – with 2.1 to 3.0 points; high – with 3.1 to 4.0 points; very high – with 4.1 to 5.0 points.

In the patients of the main group (MG), the MPS values are as follows: a very low level was detected in 2 people (10 %); low – in 4 people (19 %); satisfactory – in 7 people (33 %); high – in 8 people (38 %) (**Fig. 3**).

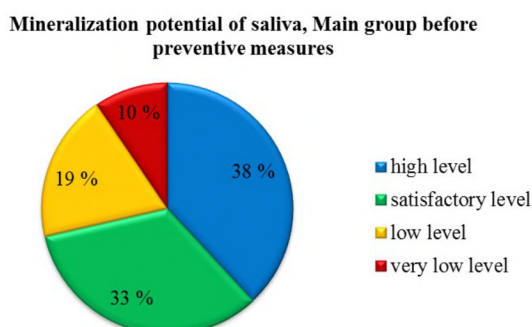


Fig. 3. Mineralization potential of saliva in the main group (MG) before preventive measures

In the patients of the control group (CG), a very low mineralizing potential of saliva was detected in 1 person (2 %); low – in 3 people (5 %); satisfactory MPS – in 40 people (73 %); high – in 9 people (16 %); very high – in 2 people (4 %) (**Fig. 4**).

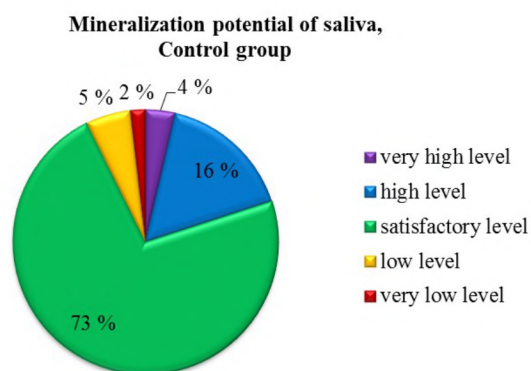


Fig. 4. Mineralization potential of saliva in the control group (CG)

The average value of the mineralizing potential of saliva in the main group was 2.78 ± 0.22 , and in the control group – 2.89 ± 0.17 .

Before preventive measures in the group of children with Down syndrome (MG), the following results were obtained: type I of the microcrystallization test of saliva consists of 14 % (3 people), type II – 53 % (11 people) and type III – 33 % (7 people) (**Fig. 5**).

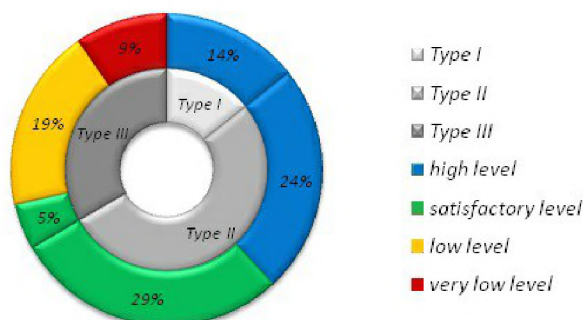


Fig. 5. Distribution by MCS types and MPS categories in a group of children with Down syndrome (MG) before caries preventive measures

After preventive measures (re-examination) we can see increasing of type I level of microcrystallization of saliva and was 38 % (8 people). MCS type III was not detected **Fig. 6**.

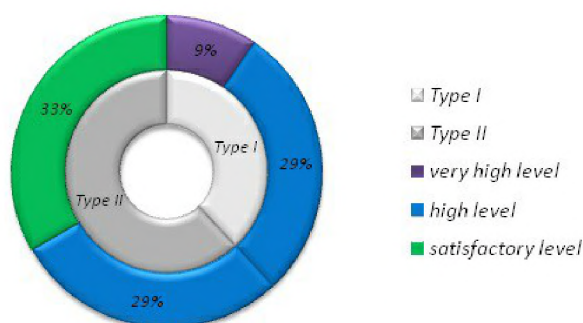


Fig. 6. Distribution by MCS types and MPS categories MPS in a group of children with Down syndrome after preventive measures

According to the results 6 months after – it was found that type I consists of 29 % (6 people), type II – 71 % (15 people) (**Fig. 7**).

After preventive measures, the examination of children of the main group (re-examination), the percentage of type I microcrystallization of saliva increased by more than 2.5 times and was 38 % (8 people), and MCS type III was not detected. During the examination of children with Down

syndrome (MG), 6 months after the course of preventive measures, there was a decrease in the component of type I microcrystallization of saliva (up to 29 % (6 people)) and an increase in the level of the component of MCS type II (up to 71 % (15 people)), MCS type III was not detected (**Fig. 8**).

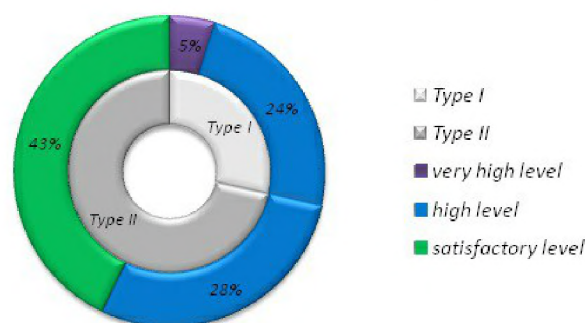


Fig. 7. Distribution by MCS types and MPS categories in a group of children with Down syndrome (MG) 6 months after caries preventive measures

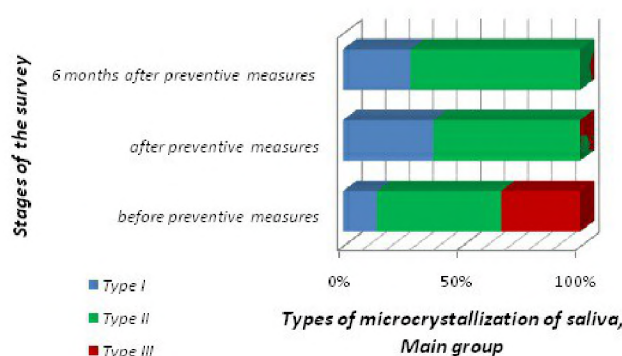


Fig. 8. Distribution by type of microcrystallization of saliva in a group of children with Down syndrome (MG) at different stages of the examination

Changes in the oral fluid in children with Down syndrome (MG) at the examination stages (before the course of prevention, after the course of preventive measures and 6 months after the caries preventive measures) are presented in **Table 1**.

Table 1

Distribution by MCS types and mineralizing potential of saliva ($M \pm m$)

Parameter	Main group, n=21			Control group, n=55
	Before preventive measures	After preventive measures	6 months after preventive measures	
MCS, %	I – 14 %	I – 38 %	I – 29 %	I – 16 %
	II – 53 %	II – 62 %	II – 71 %	II – 62 %
	III – 33 %	III – 0 %	III – 0 %	III – 22 %
MPS, points	2.78 ± 0.22	$3.48 \pm 0.2^*$	$3.35 \pm 0.17^*$	2.89 ± 0.17

Note: * – $p < 0.05$ is statistically reliable compared with parameters of caries preventive measures

The level of parameters of the mineralizing potential of saliva after preventive measures increased (2.78 ± 0.22 to 3.48 ± 0.2). These results indicated the maintenance of this level (3.35 ± 0.17).

4. Discussion

Unfortunately, in our study, due to the small sample size (this is due to a number of ethical obstacles), we did not always succeed in analyzing the statistical significance of the obtained re-

sults, as well as assessing the prognostic significance of this study parameter to evaluate the effectiveness of the proposed complex of preventive measures.

However, the problem of early childhood caries exists and various approaches to its solution are needed.

The subject of our study is relevant in pediatric dentistry and meets the requirements of modern scientific research. Further study of the pathogenetic mechanisms of dental caries in children with Down syndrome, by identifying disease predictors, will expand the range of preventive measures used to prevent dental diseases.

Our study requires further analysis of the results with an increase in the number of study participants and the observation period. It would also be interesting to investigate the effectiveness of the proposed complex of preventive measures adapted to the behaviour of children with Down syndrome and extrapolate the study data to young children without chromosomal pathology.

The studies reflecting the relationship between the body state and the oral fluid properties are widely represented in the literature. Therefore, the assessment of oral fluid, as a non-invasive research method, is a promising direction in the prevention of dental diseases for young children with and without chromosomal pathology.

Properties of saliva are extremely important for general oral cavity conditions especially in children [10, 11]. According to the literature, different factors could be important for development of pathological conditions: individual anatomy [12], environment [13], infectious disease [14, 15], habits [16], immune processes [17, 18] and other.

The recent studies have proved the influence of internal factors and environmental factors on the mineralizing potential of human saliva etc [19, 20]. The structural properties of mixed saliva are directly affected by general somatic diseases [21, 22], such as gastrointestinal diseases, bronchopulmonary pathology, diabetes mellitus, blood diseases, immune disturbance, etc [23, 24].

Adverse factors include acidification or alkalisation of saliva, the addition of electrolytes, carbohydrate intake etc [25]. Thus, fluctuations in the pH and concentration of electrolyte components of saliva above or below the physiological norm can change the physical and chemical composition of saliva, shift the ratio of structures and, consequently, decrease the resistance of micelles or disruption of micelle formation processes [26], even anatomical peculiarities [27].

It is proved that such changes in the physical and chemical properties of the oral fluid can lead to a cariogenic situation or to a situation that will contribute to the formation of mineralized dental deposits in the oral cavity [28].

Considering the above mentioned, we can assume that the biophysical and chemical properties of the oral fluid of children and adolescents with Down syndrome also undergo changes.

After examining children with Down syndrome, studying the medical history, collecting anamnestic data from parents, we defined that in addition to chromosomal changes every child with Down syndrome has any concomitant pathology.

In addition, nutritional characteristics, bad habits, difficulties in hygienic procedures (sometimes a total absence of oral hygiene) are additional factors that affect the composition and properties of the oral fluid.

An individual prevention program was developed for each child, including parental hygienic education. The choice of the proposed combinations of prevention means is due to the peculiarities of the mental development of children with Down syndrome, their emotional instability when interacting not only with the dentist, but also with their parents when performing hygienic manipulations in the oral cavity. The proposed combinations of prevention measures are aimed at optimizing the work of the dentist, as well as contribute to a more qualitative procedure of oral hygiene at home.

The implementation of the proposed preventive measures, which were carried out by the dentist in the clinic and at home, revealed an improvement in the oral hygiene of the child, an increase in the mineralizing potential of saliva which is consistent with the data of other authors [29, 30].

5. Conclusions

After preventive measures, the examination of children with Down syndrome (re-examination), the percentage of type I microcrystallization of saliva increased by more than 2.5 times, and

MCS type III was not detected. During the examination of children with Down syndrome (MG), 6 months after the course of preventive measures, there was a decrease in the component of type I microcrystallization of saliva and an increase in the level of the component of MCS type II, MCS type III was not detected.

In addition, there is a tendency to increase the level of parameters of the mineralizing potential of saliva after preventive measures while maintaining this level after 6 months.

Early detection of risk factors for caries in children using non-invasive diagnostic methods, timely prevention of dental diseases, and hygienic awareness of parents raising a child with Down syndrome can prevent the development of dental diseases in a child.

Conflict of interest

The authors declare that they have no conflicts of interest.

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DYNAMICS OF STRESS LABORATORY FINDINGS AND THEIR RELATION TO PSYCHOEMOTIONAL STATE DURING REGIONAL ANESTHESIA IN PATIENTS WITH LOWER LIMBS INJURIES

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Abstract

The choice of an adequate method of anesthesia for surgical treatment of lower limbs injuries remains a critical task today. Each method applied in this treatment has its advantages and disadvantages. In recent years, regional anesthesia has been the preferential method.

The aim of the study. To study the stress laboratory findings and their relation to the patients' psychoemotional state in perioperative period while performing regional and combined anesthesia.

Material and methods. It was studied 60 patients aged 18–59 years, who underwent metal osteosynthesis operations due to lower limbs injuries. Surgical treatment was performed under regional anesthesia and regional anesthesia followed by sedation. The patients of both groups were conducted hemodynamics monitoring and determined the intensity of pain in accordance with visual analogue scale and stress indicators with a laboratory method. The psychoemotional state was assessed with the Spielberger-Hanin anxiety scale.

Results. According to the study it was determined, that in patients, who were planned to have surgery, significant psychoemotional stress and stress concentration of hormones in the blood and their interrelation was discovered. Patients about before surgery had a relationship between situational anxiety and cortisol $r=0.7$; $p=0.00006$ in group I; $r=0.6$; $p=0.002$ in the second group. The relationship between VAS and cortisol $r=0.5$; $p=0.04$ in groups I and II. After surgery, the connection was in group I patients between situational anxiety and cortisol $r=0.4$; $p=0.02$; the relationship between insulin and the HOMA index $r=0.5$; $p=0.01$.

Conclusions. Before the operation, all patients revealed significant psychoemotional stress and stressful changes in the concentration of hormones in the blood. Reliably pronounced dynamics of the indicators was with the use of combined conduction anaesthesia. Thus, the performed study allows to recommend combined regional anesthesia as the method of anesthesia choice, particularly in patients with high anxiety.

Keywords: regional anesthesia, lower limbs injury, pain intensity, psychoemotional state, biochemical markers of stress.

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1. Introduction

A large number of surgeries for lower limbs injuries are performed all over the world and in our country, therefore their adequate anesthetic support remains a critical task. A lot of works have been dedicated to the issue of choice of the anesthesia method during these surgeries, the advantages and disadvantages of both general and regional anesthesia are described [1, 2]. In recent years, the methods of regional anesthesia are preferred due to their sufficient level of pain control as well as economic efficiency [3, 4].

From the perspective of practical anesthesiology, an important factor when selecting the anesthesia method is probability of complications developing both during, and after surgery [5, 6]. Unfortunately, none of the anesthesia methods is deprived of adverse effects and events, however, most researchers indicate the relative safety of regional anesthesia while meeting the requirements of their implementation, adequate monitoring and consideration of counterindications [7, 8].

The analyses of the perioperative complications of anesthesia has been the subject of many works [9]. Most part of them is dedicated to the problems of organ dysfunctions, such as respiratory and heart failure, renal failure, intrainestinal dysfunction, etc. [10, 11]. This is due to the fact that any arising organ failure leads to the worsening of the postoperative period, while the time spent by the patients in the intensive therapy unit and in the hospital increases, the mortality rate increases,

the quality of life decreases [12, 13]. At the same time, much smaller number of publications is dedicated to the problems of the patients' psychological state [14, 15]. The question arises, if psychoemotional stress, depression can be a complication of the perioperative period or if they are just patient's individual characteristics? This question can be unambiguously answered, that all significant deviations in the patient's psychological status, arising in the perioperative period, certainly, are complications and should not only be noted in the medical documentation, but also adequately evaluated and corrected. In the Standards of the European Society of Anesthesiologists the following sections are dedicated to the patients' psychological state: the indicators of psychometric assessment of quality of the postoperative recovery and scale of life quality, related to health [16, 17].

Thus, the large-scale implementation of the assessment methods of the patients' psychological state in perioperative period for different types of surgeries is a critical task of the modern anesthesiology. It will allow to carry out a differentiated choice of anesthesia method taking into account the patient's individual psychological characteristics and, thus, improve the course of the postoperative period.

The aim of the work. To study the stress laboratory findings and their relation to the patient's psychoemotional state in perioperative period while performing regional and combined anesthesia during surgeries for lower limbs injuries.

2. Materials and methods

60 patients, who underwent metal osteosynthesis operations due to lower limbs injuries, were included into the study on the base of Anesthesiology and Intensive Therapy Department of MNE of KhRC "Regional Clinical Traumatological Hospital" in 2017–2020 years.

The criteria for inclusion to the study were age 18–59 years; planned lower limbs surgery related to injuries; the duration of surgery more than 60 minutes, the type of anesthesia: regional anesthesia, regional anesthesia followed by sedation; anesthetic risk according to ASA – I–II; informed consent to participate in the study and understanding of the contents of psychometric techniques and VAS.

The criteria for exclusion from the study were diabetes mellitus, myocardial infarction, neurological disorders, respiratory diseases, visual and aural disorders, repeated surgery; the use of tranquilizers, antidepressants, nootropics; alcoholism, drug abuse; pain syndrome not related to the injury and surgery.

The study was conducted in accordance with the requirements of good clinical practice, the Council of Europe Convention on Human Rights and Biomedicine, the Helsinki Declaration of the World Medical Association and approved by the local ethics committee of the Kharkiv Medical Academy of Postgraduate Education (protocol No. 2, from 26.06.2020). All patients signed informed consent for participating in the clinical trial.

Depending on the anesthesia method the patients were divided into 2 groups: group I (n=33) included the patients, who were operated on under conditions of regional anesthesia (the average age 40.4 ± 1.8 years); group II (n=27) included the patients, who were operated on under conditions of regional anesthesia followed by sedation with 1 % propofol at target concentration 2 mg/kg/h (the average age 40.0 ± 2.1 years).

Body mass ratio (BMR) in patients of group I was 26.3 ± 0.8 kg/m² and in patients of group II – 26.4 ± 0.7 kg/m². The patients of both groups did not differ from each other in anthropometric indexes ($p > 0.05$).

All the patients underwent complex clinical laboratory examination and preoperative preparation.

Before surgery, patients received standard preventive premedication at the bedtime: per os Sibazon 10 mg.

When performing surgeries in patients of both groups, distal block of sciatic nerve with the posterior approach in popliteal space was applied. The sciatic nerve block was performed in combination with a "three-in-one" femoral nerve block. For identification of nerve trunks the «Stimuplex» electrostimulator was used. Puncturing was performed with a specific electrically secured needle «Stimuplex A», which allows to increase the accuracy of determining the localization of the

nerve. As the needle approached the nerve trunk, the contraction of the associated muscle group was obtained in response to irritation by an electrical impulse. An adequate motor response was considered a plantar foot flexion. The nerve block in patients of both groups was carried out with 1 % solution of lidocaine 800 mg with an addition of epinephrine (1:200000), as an adjuvant.

The postoperative anesthesia was performed with non-steroidal anti-inflammatory drugs (dexametopfen, at the patients' request).

BMR was determined according to the formula: m/h^2 , where m is for mass of the body (kg), h is for height (m)

The monitoring was carried out, which included control of the systolic blood pressure (SBP), diastolic pressure (DIA), cardiac rate (CR), electrocardiography and arterial oxygen percent saturation (SpO_2) with the help of monitor G3L («Heaco», United Kingdom), mean arterial pressure (MAP) was determined according to the formula: $(2 (SBP)+DIA)/3$, the indicators were recorded before surgery, at the traumatic stage and on the first day after surgery.

The intensity of pain was evaluated according to the visual analogue scale (VAS) before the surgery (stage 1) and in the first 24-hour period after the surgery (stage 3). The visual analogue scale represents a continuous scale in the form of a horizontal or vertical line 10 cm long and two extreme points "no pain" and "severe pain that you can only imagine" located on it.

In our study we used a specific ruler with a slider, in which we suggested the patient to indicate the intensity of the pain syndrome. The distance between the marks "No pain" and "Unbearable pain" was drawn on a coloured scale and is 10 cm long on one side and on the other side coloured symbols from blue to red according to the intensity of the pain syndrome were drawn. Based on the allocation of points the following classification is recommended: no pain (0 points), weak pain (1–4 points), moderate pain (4–6 points), severe pain (7–9 points), very severe pain (10 points).

The study of psychoemotional state included determining of the level of personal anxiety, which characterizes a stable tendency to perceive a wide range of situations as threatening, to respond to such situations with the anxiety state and a situational anxiety, which is characterized by tension, psychic tension, nervousness. The situational anxiety causes attention failure, sometimes it causes violation of fine coordination. These data were evaluated at three stages of the study: before the surgery (stage 1) and on the first day after surgery (stage 3) according to the Spielberger-Hanin scale, which was developed by an American psychologist Charles Spielberger in 1970 and adapted by Russian psychologist Yuriy Hanin in 1976.

The assessment methodology of the situational and personal anxiety determines the anxiety level based on the self-assessment scale (high, medium and low anxiety), it is carried out with two cards: one is for situational anxiety, the second one is for personal anxiety measuring.

The interpretation of indicators was determined by points:

- up to 30 points – low;
- 31–44 points – moderate;
- more than 45 points – high.

All laboratory tests were also recorded at three stages of the study: stage 1 – before surgery; stage 2 – at the traumatic stage and stage 3 on the first day after surgery.

Blood glucose measurement was evaluated with the glucose oxidase test by means of the "GLUCOSE SpineLab", Ukraine reagent kit.

Indicators of cortisol and insulin levels were determined with the immunoenzyme method by means of "Vector-Best-Ukraine" reagent kit.

Index HOMA (The Homeostatic Model Assessment), which displays the degree of insulin resistance, that depends on the stress reactions degree, was calculated by the formula:

$$HOMA=(Glucose\ (mmol/l))\times Insulin\ (umol/ml))/22,5.$$

Cortisol-insulin correlation (C/I) was calculated by the formula:

$$C/I=Cortisol\ (nmol/l)/Insulin\ (umol/ml).$$

For statistical processing of the obtained data, the «SPSS Statistics 19.0» program was used. Parametric and nonparametric methods of statistics were used with the usage of Student's and Mann-Whitney criterion. To evaluate the relations between the indicators a correlation analyses was carried out with the usage of Spearman criterion.

3. Results

All surgical interferences were performed to young and middle-aged patients without significant concomitant pathology and with moderate risk of anesthesia (I–II in accordance with ASA). Therefore, the course of intra- and postoperative periods in patients passed without significant disturbances of vital organs. In patients of both groups, the normodynamic type of blood circulation with an average blood pressure within the range of 90–110 mm Hg, normal hemoglobin oxygen saturation ($SpO_2 \geq 95\%$) and sufficient diuresis were noted intraoperatively. None of the examined patients needed additional measures of hemodynamic and respiratory support during surgery and in the early postoperative period.

The main differences that we discovered between the patients' groups, dealt with their psychoemotional state and laboratory stress markers. So, before surgery, the patients of both groups showed significant psychoemotional tension according to the Spielberger-Hanin scale, which can be explained both by the expectation of surgery and the damage associated with it, and by the presence of post-traumatic pain syndrome (**Table 1**).

Table 1

Anxiety indicators in patients of groups I–II at the stages of the study (Me [Q1; Q3]), points

Measurement	Group I (n=33)	Group II (n=27)
Situational anxiety before surgery	49.5 [48.0; 50.0]	46.0 [44.0; 50.0]
Personal anxiety before surgery	54.0 [51.0; 55.0]	49.0 [44.0; 56.0]
Situational anxiety after surgery	41.0 [40.0; 42.0]	34.0* [30.0; 38.0]
Personal anxiety after surgery	45.0 [44.0; 48.0]	34.5* [30.0; 42.0]

Note: * – significant difference between groups: $p < 0.01$

In the early postoperative period, the indicators of situational and personal anxiety in the group of patients who underwent additional sedation were significantly lower ($p < 0.01$).

Pain intensity indicators according to VAS in the patients before surgery were 5.2 ± 0.1 points in group I and 5.1 ± 0.2 points in group II ($p > 0.05$). In 24 hours after the surgery a decrease of the pain syndrome intensity was observed 3.7 ± 0.1 points in group I and 3.1 ± 0.1 points in group II ($p < 0.05$). It supports the fact that the mechanisms of nociception are implemented in numerous ways, thus deprivation of central routes of perception can be significant. Moreover, the emotional colouring of the situation during the survey plays a certain role, as the anxiety in general and the emotional tension accordingly in the patients of group II were lower.

Through laboratory studies of hormonal indicators of the stress response in patients of both groups, some well-known patterns were discovered and confirmed, which were evident as an increase of cortisol concentration in the blood plasma, cortisol/insulin correlation and the insulin resistance index HOMA (**Table 2**).

In the process of surgical interference under regional anesthesia the cortisol level was decreasing in both groups. This dynamics was more significant in group II compared to group I ($p < 0.01$). Thus, there was a tendency to decreasing in the dynamics of cortisol/insulin index to normal and subnormal values in both groups.

Table 2

Hormonal reactions in perioperative period in patients of groups I–II (Me [Q1;Q3])

Stage of the Study	Groups	Measurement			
		Cortisol, nmol/l	Insulin, umol/ml	C/I	HOMA
1	I (n=33)	630.3 [589.3; 655.6]	10.3 [8.6; 12.2]	59.8 [52.7; 68.2]	2.1 [1.9; 2.7]
	II (n=27)	657.7 [598.2; 691.9]	9.8 [8.3; 11.7]	67.0 [55.9; 85.1]	2.0 [1.9; 2.5]
2	I (n=33)	508.4 [498.8; 575.4]	8.5 [7.9; 10.6]	59.9 [53.2; 69.9]	2.2 [2.1; 2.5]
	II (n=27)	445.7** [399.5; 504.2]	7.3 [6.1; 10.4]	57.3 [45.5; 74.8]	1.6** [1.3; 2.2]
3	I (n=33)	478.3 [453.5; 500.5]	9.2 [8.5; 10.5]	51.6 [41.4; 56.1]	2.5 [2.2; 2.8]
	II (n=27)	368.6** [338.0; 400.3]	8.4* [6.6; 10.0]	49.7 [35.9; 58.7]	1.6** [1.3; 2.2]

Note: * – $p < 0.05$ by comparison to the group I at the third stage of the study; ** – accuracy of difference between groups $p < 0.01$

The insulin resistance index HOMA in the patients of group I did not change significantly (**Table 2**), while in group II its decrease was noted (**Table 2**), which was significant compared to group I ($p < 0.01$).

The glycemia level in patients of both groups was at the upper limit of normal which also indirectly characterizes the stress response in the patients without concomitant diabetes mellitus. In the initial state, the glucose concentration in the patients of group I was 5.1 ± 0.1 mmol/l, during the surgical interference it was 5.8 ± 0.1 mmol/l, the next 24 hours after surgery it was 5.9 ± 0.1 mmol/l, there were no differences at all stages of surgical treatment ($p > 0.05$). In patients of group II similar results were obtained at all stages of the study – 5.1 ± 0.1 mmol/l; 5.2 ± 0.1 mmol/l and 4.9 ± 0.1 mmol/l, respectively ($p > 0.05$).

Thus, in patients of both groups in the perioperative period a significant psychoemotional reaction was discovered with the increase of situational and personal anxiety, an intense pain syndrome and specific “stress” reaction. While studying the relation between these indicators, some patterns were discovered.

In preoperative period in the patients of both groups a strong connection between the indicators of situational anxiety and the cortisol level in the blood plasma ($r = 0.7$; $p = 0.00006$ in group I and $r = 0.6$; $p = 0.002$ in group II) was discovered. Moderate relation was discovered between the indicators of pain intensity according to VAS and the cortisol concentration before the surgery in both groups ($r = 0.5$; $p = 0.004$).

In the postoperative period in patients of group II there were no significant relations of the studied indicators. At the same time in patients of group I remained a moderate relation between the indicator of situational anxiety and the cortisol concentration in the blood ($r = 0.5$; $p = 0.01$), insulin in the blood ($r = 0.4$; $p = 0.02$) and the insulin resistant index HOMA ($r = 0.5$; $p = 0.01$).

4. Discussion

Some researchers note that it is the patient’s psychoemotional state that is one of the key in the implementation of many stressful reactions of the body, and also significantly affects the intensity of the pain syndrome and the associated treatment effectiveness. V. M. Zagurovsky [18]. Also, some authors claim in their studies that the psycho-emotional state before surgery is intense and requires psychological and pharmacological support. V. I. Strashnov et al. [19]. At the same time, the authors argue that the anesthetic risk in these conditions increases, due to the negative impact of emotional stress on the state of vital functions. A. Pinto et al. [20]. According to the results of the assessment of the hormonal profile, it was found that with a high and medium level of anxiety, the

indicators of anxiety were higher. V. G. Syusyuk [21]. In the conducted studies, it was found that after surgery, the level of triviality was significantly lower and had a correlation with biochemical markers of stress. V. I. Kolomachenko [22].

Thus, our study demonstrated the importance of investigation of the patients' psychological state in the perioperative period since the significant emotional tension and the pain syndrome are related to a negative course of stress reaction that can affect the course of the perioperative period and the results of the treatment to a certain extent. In our opinion, the regional anesthesia combined with sedation can significantly minimize these effects and, therefore, it is the method of anesthesia choice for these surgeries, especially in patients with significant psychoemotional tension.

Study limitations. The studies were not conducted as a result of the identification of concomitant pathology of other organs and systems and as a result of patients refusing to study.

Prospects for further research. In the future, this study is possible with a larger sample of patients to more accurately obtain data. It is possible to expand the research phase with the expansion of the range of laboratory tests.

5. Conclusions

In patients who are planned to have surgeries on lower limbs, a significant psychoemotional tension and stress changes in the concentration of hormones in the blood, which are closely inter-related, were discovered in the perioperative period.

All patients showed a positive dynamics of the studied parameters, significantly more apparent when using combined regional anesthesia with sedation, so the indicator of the concentration of cortisol in the blood at the first stage in patients of group I was 630.3 nmol/l and 657.7 nmol/l in patients of group II, respectively, insulin indicators in group I were 10.3 umol/ml in group II this indicator was 9.8 umol/ml. In the postoperative period, in patients of group I, cortisol was 478.3 nmol/l and 368.6 nmol/l in patients of group II, insulin indicators in group I were 9.2 umol/ml in group II and 8.4 umol/ml.

When using isolated regional anesthesia, a significant relation between the indicator of situational anxiety, cortisol concentration this indicator amounted to $r=0.7$; $p=0.00006$ in group I and in group II $r=0.6$; $p=0.002$, insulin concentration and the insulin resistance index remained in patients this indicator was $r=0.5$; $p=0.001$ in patients of group I. The study allows us to recommend combined regional anesthesia as a method of anesthesia choice, especially in patients with increased anxiety.

Conflict of interests

The authors declare that they have no conflicts of interest.

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RETROSPECTIVE ANALYSIS OF THE STATE OF DIRECT DENTAL RESTORATIONS AFTER ENDODONTIC TREATMENT

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Abstract

Endodontic treatment is accompanied by the loss of a significant amount of tooth crowns, which leads to a significant decrease in their strength characteristics. The restoration of endodontically treated teeth, as a rule, is carried out by the direct method, however, a unified approach regarding direct or indirect restoration has not yet been determined.

The aim – retrospective analysis of the clinical condition of direct restorations of endodontically treated teeth.

Materials and methods. 284 patients aged 25 to 60 years were examined; they studied the state of 888 previously performed direct restorations of the anterior and posterior teeth after endodontic treatment in a period of 2 to 10 years. Restorations were evaluated according to the adapted clinical criteria “integrity of the restoration”, “marginal fit of the material”, “marginal staining”, “anatomical shape”, “colour correspondence for the restoration”, “roughness of the surface of the material”, as well as the criterion “condition of the contact point” for located on the contact surfaces of the teeth of the restorations.

Results. Of the 888 examined direct restorations, 760 restorations (85.6±1.18 %) were located in the posterior teeth, with 562 restorations in the molars (63.3±1.62 % of the total) and 198 in the premolars (22.3±1.40 %), and 128 restorations (14.4±1.18 %) were detected in the anterior teeth, while in the incisors – 80 restorations (9.0±0.96 %), in the fangs – 48 (3.5±0.76 %). 720 restorations (81.1±1.31 %) were made from photocomposite materials, 97 restorations (10.9±1.05 %) from chemical curing composites, 71 (8.0±0.91 %) from glass-ionomer cements. The most common violations were colour mismatch – in 511 restorations (57.5±1.66 %), marginal staining – in 470 restorations (52.9±1.68 %), surface roughness – in 357 restorations (40.2±1.0, 65 %). More often than others, in the reconstructions of their photocomposites and glass ionomers there was a colour mismatch, and surface roughness for chemical composites.

Conclusions. For direct tooth restoration after endodontic treatment in 81.1±1.31 % of cases, photocomposite materials are used, less often chemical curing composites and glass ionomers. Of the violations of such restorations, the most frequent are colour mismatch, surface roughness and edge staining.

Keywords: endodontically treated teeth, direct restorations, photocomposites, chemocomposites, glass ionomers, retrospective assessment.

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1. Introduction

Untimely or poor-quality treatment of dental caries, as you know, leads to the development of complications, as a result of which endodontic intervention or tooth extraction becomes necessary. Innovative technologies of endodontic treatment, including the use of an endomotor, heavy-duty and flexible instruments with shape memory, optical zoom, providing the possibility of instrumental processing of curved and obliterated, additional and rudimentary root canals, as well as systems and materials ensuring their reliable and durable obstruction, allow you to save teeth, the removal of which, it would seem, is almost inevitable [1, 2].

After successful endodontic treatment, the inevitable task of adequately restoring the crown of the teeth arises. In most cases, the treatment of caries complications, be it pulpitis or periodontitis, is accompanied by the loss of a significant part of the volume of the tooth crown, regardless of whether it is an anterior tooth or a lateral one. Removal of hard tissues pathologically altered due to the carious process and creation of free access to the root canal mouths for their full instrumental

processing and obturation, often the search for additional canals or removal of the material of the previous restoration, if necessary, repeated endodontic intervention leads to a significant decrease in the strength characteristics of such teeth [3, 4]. The weakened and thinned walls of the cavities after endodontic manipulations, especially in the teeth of the lateral group, need hardening in order to withstand high chewing pressure.

Regarding the restoration of tooth crowns after endodontic treatment, a single approach has not yet been determined. Of course, the leading role in the selection must be assigned to the factor of the degree of destruction of the crown [5]. However, quite often in clinical practice, direct restoration of such teeth is carried out without taking into account the volume of lost hard tissues, localization and cavity configuration, and different designs are used for hardening, including intracanal pins, stump inserts and so on [6, 7]. The choice of materials for direct restoration, of course, is very wide, but often clinical feasibility fades into the background, giving way to financial motivation, which, in terms of the durability of the functioning of such recovery, cannot be dominant [8]. The use of indirect restorations from innovative materials using digital technologies, as a certain alternative, seems more promising in terms of the duration of their operation, but very costly [9].

The discussion on the use of a direct or indirect method of restoration should be based, first of all, on an evidence-based clinical factual base regarding the state and duration of the operation of direct tooth restorations after endodontic interventions.

The aim – retrospective analysis of the clinical condition of direct restorations of endodontically treated teeth.

2. Materials and methods

A survey of 284 patients aged 25 to 60 years was carried out in 2018–2019 in the clinic of the Department of Dentistry No. 1 of the Donetsk National Medical University and in a private dental clinic (Kharkov). Patients, among whom were 120 men (42.3 ± 2.9 % of the total number examined) and 164 women (57.7 ± 2.9 %), turned to clinics for dental care; they examined the state of 888 previously performed direct restoration of teeth of the lateral and frontal groups after endodontic treatment in a period of 2 to 10 years. All patients gave informed consent to participate in the study, which was carried out in accordance with the principles of the Helsinki Declaration adopted by the General Assembly of the World Medical Association, the Council of Europe Convention on Human Rights and Biomedicine (1997), relevant standards of WHO, the International Council of Medical scientific communities, International Code of Medical Ethics (1983), which is confirmed by the bioethics commission of the Donetsk National Medical University No. 21, 09.11.2017.

In patients, the intensity index of carious lesions of the teeth and the hygienic condition of the oral cavity were determined by the Fedorov-Volodkina index [10]. In the course of assessing the state of direct restorations, their localization, as well as their belonging to a particular class of cavities according to Black, was studied, then restorations were assessed using the adapted clinical criteria “restoration integrity”, “marginal fit of the material”, “marginal staining”, “anatomical shape”, “color correspondence of the restoration”, “surface roughness of the material”, as well as according to the additional criterion “state of the contact point”, which was used in case of restoration of the contact surfaces of the teeth [11]. The presence or absence of violations was determined by each of the criteria.

Statistical processing of the results of the index estimation was carried out using variation statistics and the software product MS Excel XP. The differences between the indicators at $p < 0.05$ were considered statistically significant, in accordance with Student's criterion. The results obtained during the assessment of restorations according to clinical criteria were presented in the form of absolute and relative indicators.

3. Results

During the dental examination, it was found that the index of intensity of carious lesions of the teeth in all patients participating in the study was 9.78 ± 0.85 , the state of oral hygiene in them was satisfactory, the hygiene index was 1.92 ± 0.25 points.

In total, in the course of the study, 888 patients restored after endodontic treatment of teeth were identified, in men there were 328 such teeth (37.0 ± 1.62 % of the total), in women – 560 (63.0 ± 1.62 %) (difference is reliable, $p < 0.05$). Most of the restorations were in the teeth of the upper jaw – 516 (58.1 ± 1.66 %), in the teeth of the lower jaw there were 372 restorations (41.9 ± 1.66 %) ($p < 0.05$). Similar ratios were also established during the analysis of indicators depending on the gender of the examined, in men 180 restorations were found (54.9 ± 2.75 % of the total number in males) in the teeth of the upper jaw and 148 restorations (45.1 ± 2.75 %) in the teeth of the lower jaw, in women – 336 (60.0 ± 2.07 % of the number of recoveries in females) and 224 (40.0 ± 2.07 %), respectively.

Of the total number of teeth after endodontic treatment, the absolute majority ($p < 0.05$) were lateral – 760 out of 888 (85.6 ± 1.18 %), frontal teeth only 128 (14.4 ± 1.18 %), this, women revealed significantly ($p < 0.05$) more restored lateral teeth, there were 474 (53.4 ± 1.67 % of the total number), and the front teeth, which were 86 (9.7 ± 0.99 %), in men these indicators amounted to 286 (32.2 ± 1.57 %) and 42 (4.7 ± 0.71 %).

The distribution of restored lateral and frontal teeth depending on belonging to a particular jaw was as follows: the lateral teeth of the upper jaw were 426 (48.0 ± 1.68 %), the lateral teeth of the mandible – 334 (37.6 ± 1.63 %), anterior teeth – 90 (10.1 ± 1.01 %) and 38 (4.3 ± 0.68 %), respectively.

As for the number of restored lateral teeth of the upper and lower jaw in men and women, in males there were slightly more such teeth on the upper jaw – 153 (17.2 ± 1.15 % of the total number of examined teeth) than on the lower, – 133 (15.0 ± 1.09 %), the ratio of these indicators was approximately the same for females – 273 (30.7 ± 1.38 %) and 201 (22.6 ± 1.27 %). The number of restored upper frontal teeth in women was more than 2 times higher than that in men – 63 (7.1 ± 4.83 %) and 27 (3.0 ± 4.83 %), respectively, significantly less was restored lower anterior teeth – 23 (2.6 ± 2.18 %) and 15 (1.7 ± 2.18 %).

Most of all ($p < 0.05$) restorations were in molars – 562 (63.3 ± 1.62 % of the total), while molars of the upper jaw prevailed, there were 308 (34.7 ± 1.06 %), restored molars of the lower jaw were 254 (28.6 ± 1.06 %). Further, in decreasing order of the number of restorations, premolars are located, their total number was almost three times less ($p < 0.05$) than molars, that is, the total number of restored premolars was 198 (22.3 ± 1.40 %), premolars of the upper jaw – 118 (13.3 ± 0.37 %), lower jaw – 80 (9.0 ± 0.37 %). Even fewer ($p < 0.05$) restorations were detected in the incisors – only 80 (9.0 ± 0.96 %), 59 restorations in the maxillary incisors were revealed (6.6 ± 0.13 %), which is almost three times more than in the incisors of the lower jaw, these teeth had 21 restoration (2.4 ± 0.13 %). The fangs were the least frequently ($p < 0.05$) fangs endodontically treated, as the teeth most resistant to caries, 48 restored fangs (3.5 ± 0.76 %) were found after this intervention, and if there were 31 such fangs on the upper jaw (3.5 ± 0.09 %), then on the bottom – only 17 (1.9 ± 0.09 %), that is, almost two times less.

Analysis of the restoration structure depending on the localization of the carious cavities in the teeth showed that their greatest number was reliably ($p < 0.05$) class 2 according to Black, that is, with contact and chewing surfaces of molars and premolars, such restoration was revealed in the examined patients 623 (70.2 ± 1.54 %), and more of them were in the teeth of the lateral group of the upper jaw than the lower – 349 (39.3 ± 1.17 %) and 274 (30.9 ± 1.17 %), respectively. More than four times less ($p < 0.05$) teeth were found with restorations due to Black class 1 carious cavities; there were 137 restorations of such localization (15.4 ± 1.21 %) in the teeth of the upper and lower jaw they were almost equally divided – 75 (8.4 ± 0.26 %) and 62 (7.0 ± 0.26 %). Restorations with localization of class 4 according to Black were slightly less revealed – only 113 (12.7 ± 1.12 %), of which 77 (8.7 ± 0.2 %) – in the front teeth of the upper jaw, 36 (4.1 ± 0.2 %) – in the teeth of the lower jaw, which is half as much. Fifteen restorations were also located in the cavities of class 3 according to Black (1.7 ± 0.43 %), this minimum number ($p < 0.05$) of restorations was distributed as follows: in the front teeth of the upper jaw – 10 (1.1 ± 0.03 %), the lower jaw – only 5 (0.6 ± 0.03 %). Not a single case of localization of cavities and restorations of the 5th and, especially, 6th class according to Black in the examined teeth has not been established.

The most interesting fragment of the study is devoted to the analysis of the structure of the entire array of tooth restorations after endodontic treatment and violations in them, depending on

the materials used. Of all 888 examined restorations, 720 restorations (81.1 ± 1.31 %) were made from photocomposite materials ($p < 0.05$), 97 (10.9 ± 1.05 %) were made from chemical curing composites, in 71 restorations (8.0 ± 0.91 %) used glass ionomer cements, these materials were the least popular.

Photocomposite materials for direct restoration were used for localization of carious cavities in class 1, according to Black's classification, in 97 teeth (13.5 ± 1.27 % of the total number of restorations from photocomposites), in class 4 – in 89 teeth (12.4 ± 1.23 %), in class 3 – only in 8 teeth (1.1 ± 0.39 %), but most often ($p < 0.05$) photocomposite restorations were performed for carious cavities of class 2, there were 526 (73.1 ± 1.65 %).

Chemical curing composites were used to restore 66 teeth with class 2 cavities (68.0 ± 4.73 % of the number of restorations from these materials) ($p < 0.05$), 24 teeth (24.7 ± 4.38 %) – with cavities of class 4, 7 teeth (7.2 ± 2.63 %) – with cavities of class 3.

Restorations in 40 teeth (56.3 ± 5.89 % of the number of restorations from glass ionomers) with localization of carious cavities of class 1 and in 31 teeth (43.7 ± 5.89 %) with cavities of class 2 were made of glass ionomer cements.

As for the violations revealed during the examination of the state of restorations from all restoration materials, the most frequent ($p < 0.05$) discrepancy was observed between the colour of the restoration and hard tissues of the restored teeth, such violations were found in 511 restorations (57.5 ± 1.66 % of their total number). The number of cases of marginal staining at the border of the material and tooth enamel was slightly less, although there were more than half of all examined patients with restorations with these disorders – 470 (52.9 ± 1.68 %). The increased surface roughness of the material was found in 357 restorations (40.2 ± 1.65 %) ($p < 0.05$). Almost the same number of restorations had violations of the marginal fit of the material and the anatomical shape, in particular, there were, respectively, 277 (31.2 ± 1.55 %) and 275 (31.0 ± 1.55 %). Violation of the integrity was found in 105 restorations (11.8 ± 1.08 %), it is the least number of such violations ($p < 0.05$).

The clinical criterion regarding the condition of the contact point was used to evaluate only those restorations that covered the contact surfaces; there were 751 such restorations (84.6 ± 1.21 % of the total). Contact point violations were detected in 260 restorations (34.6 ± 1.53 % of the number of restorations of the specified location).

Most often, photocomposite materials are used in clinical practice for direct restoration of teeth after endodontic treatment. This is also evidenced by the results of a retrospective analysis. However, a significant number of violations in direct photocomposite reconstructions identified during this study should be noted. Half of all restorations from photocomposites do not correspond to the hard tissues of teeth by colour; there were 365 of them (50.7 ± 1.86 % of the number of all photocomposite restorations). A little less ($p > 0.05$) was restoration with regional staining along the perimeter – 340 restorations (47.2 ± 1.86 %). Disorders in the following three clinical criteria differed slightly from each other ($p > 0.05$): 208 restorations (28.9 ± 1.69 %) were found with increased roughness of the surface of the material, 193 restorations were found with a broken edge of the photocomposite (26.8 ± 1.65 %), with violation of the anatomical form – 179 restorations (24.7 ± 1.61 %). The integrity was completely or partially violated in 68 restorations (9.4 ± 1.09 %) ($p < 0.05$). Of all the photocomposite restorations, 623 restorations (86.5 ± 1.27 %) covered, along with others, contact surfaces; therefore, they were examined with respect to the contact point, while it was insolvent in 165 cases (26.5 ± 1.54 % of the number of restorations of a given location).

In the recoveries from chemical curing composites, the structure of the disturbances was somewhat different. The highest values were according to three clinical criteria: increased roughness of the material was found in 88 restorations out of 97 (90.7 ± 2.95 % of the number of restorations from these materials), edge staining at the border with enamel was found in 84 restorations (86.6 ± 3.46 %), and only 1 less restoration with colour mismatch – 83 (85.6 ± 3.57 %) ($p > 0.05$). Almost two times less ($p < 0.05$) there were restorations with a broken marginal fit of the composite – 43 restorations (44.3 ± 5.04 %). Violation of the anatomical form was detected in 62 restorations (63.9 ± 4.88 %), integrity was broken in 18 restorations (18.6 ± 3.95 %) ($p < 0.05$). All 97 restorations from chemical curing composites were located on the contact and other surfaces of the teeth, of which the contact point was broken in 69 restorations (71.1 ± 4.6 %).

Glass ionomer cements were most used to restore teeth after endodontic treatment, and these restorations were only in the posterior teeth. Almost all the restorations had a colour mismatch and high roughness, in particular, there were 63 such restorations (88.7 ± 3.75 % of their total number) and 61 (85.9 ± 4.13 %) ($p > 0.05$). Broken marginal fit and marginal staining were detected, respectively, in 46 (64.8 ± 5.67 %) and 41 restorations (57.7 ± 5.86 %) ($p > 0.05$). A little less ($p > 0.05$) was anatomical disorders; they were found in 34 restorations (47.9 ± 5.93 %). The integrity was completely or partially violated in 19 recoveries (26.8 ± 5.25 %) ($p < 0.05$). Defects of the contact point were found in 26 out of 31 restorations located on the contact surfaces, this amounted to 83.9 ± 6.61 % of the number of restorations of this localization.

4. Discussion

A retrospective analysis, first of all, showed that the vast majority of direct restorations were located on the chewing and contact surfaces of endodontically treated lateral teeth, while direct restoration of teeth with such localization of cavities is a complex and not always feasible clinical task. Nevertheless, direct restorations were used more often than indirect ones, and this is connected with photocomposite materials, the use of which allows to recreate the lost anatomical shape and aesthetic characteristics of teeth in one visit. This can explain such a large proportion of photocomposite restorations, especially since they demonstrate a fairly high “survival rate”. So, after 3 years, on average, 90.7 % of restorations maintained their integrity, after 5 years – 89.5 % of restorations, however, these results are given without differentiating the restorations performed in teeth with viable pulp or after endodontic treatment [12]. When localization on the chewing and contact surfaces of the teeth of the lateral group, the safety of the restorations after 3 years was fixed at 93 % and 95 % [13, 14], and after 7–8 years – at 85 % [15], which, in general, is consistent with the data obtained in our study, in particular, the integrity was established in 95.6 ± 1.09 % of photocomposite restorations, but this indicator did not take into account the terms of their functioning.

In photocomposite restorations of the lateral teeth after their endodontic treatment with localization in grade 2 after 12 months, marginal staining was found in 11.6 % of cases, impaired marginal adaptation – in 10 %, increased roughness – in 18.3 % of cases [16]. Given the short observation period, these indicators are quite comparable with the results obtained in our study. In another study, within 24 months, the number of restorations from the photocomposite in unsatisfactory condition was significantly lower – only 2.3 ± 0.16 %, but these data relate only to the anterior teeth after endodontic treatment [17].

High strength parameters of photocomposites ensure the preservation of restorations, but the frequency of color mismatch of restorations from a photocomposite and restored teeth is noteworthy. Photocomposite materials are color stable enough, probably the discrepancy is due to the color change of the endodontically treated teeth, which progresses over time. Nearly half of the restorations from photocomposites recorded edge staining, however, in restorations from other materials, this violation, as well as color mismatch, was much more common. It should also be noted that more than 70 % of the restorations from chemical curing composites and almost 84 % of glass ionomer restorations localized on the contact surfaces had contact point defects, and photocomposition restorations with contact point violations were only a quarter, despite the fact that in other studies contact failure of the item was registered within 24 months in 78.3 ± 1.5 % of restoration of posterior teeth from photocomposites, in the period of 36 months – in 80.3 ± 1.25 % of restorations [18].

Nevertheless, the advantages of direct restorations of endodontically treated teeth from photocomposites over restorations from other materials are obvious. However, it would be correct to compare them with indirect restorations from the same photocomposites, ceramic or other innovative materials.

Study limitations. The study did not include patients whose age was less than 25 years and more than 60 years, as well as patients with terms of tooth restoration after endodontic treatment of less than 2 years and more than 10 years. Patients were not included in the study if there were two or more fillings in the teeth restored after endodontic treatment; if these teeth were previously coated or prepared for covering with artificial crowns; if the restored tooth was abnormally located in the

dentition or did not have antagonist teeth; if periodontal or bite pathology was diagnosed, increased tooth abrasion, bruxism; if the level of oral hygiene was unsatisfactory. Persons suffering from mental illness were not admitted to the study, including in the case of alcohol or mental dependence.

Prospects for further research. The results of a retrospective assessment of the state of direct restoration of teeth after endodontic treatment revealed their most frequent violations. In the course of further long-term comparative clinical research, it seems appropriate to study the effectiveness of direct photocomposite tooth restoration and indirect restoration using digital technologies and innovative materials. The results of the study will form the basis of recommendations for practical implementation.

5. Conclusions

Direct restorations after endodontic treatment are most often performed in the posterior teeth, of which 760 were reconstructed from 888 examined (85.6±1.18 %), 128 restorations were revealed in the frontal teeth (14.4±1.18 %).

Of all the examined restorations, 720 restorations (81.1±1.31 %) were made from photocomposite materials, 97 restorations (10.9±1.05 %) were made from chemical curing composites, 71 (8.0±0, 91 %) – from glass ionomers.

Among the violations in direct restorations, the most frequent were the colour mismatch found in 511 restorations (57.5±1.66 % of the total), marginal staining revealed in 470 restorations (52.9±1.68 %), and roughness surface found in 357 restorations (40.2±1.65 %).

Conflicts of interest

The authors declare that they have no conflicts of interest.

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CHANGES IN THE MORPHOLOGIC STATE OF RED BLOOD CELLS IN PATIENTS WITH POLYTRAUMA

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Abstract

The measurement of RBC indices is of particular importance as an indirect intermediate component of the recovery process after exposure to hypoxia, ischemia, hypothermia in patients with traumatic disease due to polytrauma.

The aim of this study was to evaluate the parameters of the morphologic state of red blood cells as a reaction of patients with traumatic disease.

Materials and methods. A prospective study was carried out evaluation of 120 patients suffering from polytrauma. The patients were divided into 3 groups according to the principle of using additional substances as a part of IC. The parameters of morphologic state of red blood cells were studied.

Results. The course of acute and early periods of traumatic disease has accompanied variability morphological forms of red blood cells, as evidenced by a decrease in MCV and RDW increased levels of the 3rd to 5th day. The optimized therapy used in the treatment of patients, has a positive effect on the parameters of red blood cells, contributes to a better recovery of red blood cells after hypoxia resulting multiple trauma.

Conclusion. The study has demonstrated variations in the morphologic properties of red blood cells in the acute and early period of traumatic disease, as confirmed by pathological changes of the erythrocyte indices. The administration of the proposed

therapy with the use of D-fructose-1.6-diphosphate sodium salt of hydrate has a positive effect on the parameters of red blood cells, contributes to a better recovery after hypoxia resulting multiple trauma. Given this, the calculations of the red blood cell indices may carry additional diagnostic information, which allows identify trends for not obvious pathological changes and quality of treatment.

Keywords: traumatic disease, red blood cells indices, D-fructose-1.6-diphosphate sodium hydrate.

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1. Introduction

The massive bleeding, violation of microreological properties of the blood, hypoperfusion are key factors in the pathogenesis of traumatic diseases. These pathological changes lead to a decrease in the availability of oxygen to the tissues, disturbances in the hemostasis system, stimulation of the inflammatory response, which ultimately leads to the development of hypoxia [1, 2]. The probability of septic complications, multiple organ failure and mortality depends on its duration and severity [2, 3].

Red blood cells (RBC) are the most important cells that, on the one hand, perform the oxygen transport, and on the other hand, they are subject to changes when exposed to hypoxia [4–6]. The RBC's structure is optimal for its main function: efficient oxygen delivery and CO₂ removal. It lacks organelles and a nucleus, thereby providing more space for the oxygen-carrying protein hemoglobin. Furthermore, its typical biconcave, flexible shape does not only maximize the surface/volume ratio for gas exchange, but also makes it capable of withstanding the mechanical stress it experiences during the many times it travels the circulatory system. Often, RBCs have been oversimplified as a 'bag of hemoglobin', while in reality they are much more complex. Their membrane-cytoskeleton build-up enables the cell to resist fragmentation while undergoing extensive deformation in the microcapillaries and the spleen. Furthermore, RBCs contain important enzymes and substrates for several metabolic pathways and antioxidant defense mechanisms [7].

Blood viscosity is determined by red blood cells flow properties that include adhesion, aggregation and deformability, i. e., ability to change shape under a given stress without hemolysis. Erythrocyte deformability affects blood flow in large blood vessels, due to the increased frictional resistance between fluid layers under laminar flow conditions. It also affects the microcirculatory blood flow significantly where erythrocytes are forced to pass through blood vessels with diameters smaller than their size. Numerous pathologies are associated with a decrease of RBC deformability [8–10].

Progressing changes in RBC shapes are accompanied by impairment of the cytoskeleton and plasma membrane, decreased intracellular adenosine triphosphate (ATP) concentration, as well as changes in the functional characteristics of RBC: reduced transport function and increased membrane deformability [4].

Recent literature supports the notion that the condition of the membrane and the ability of erythrocytes to deform largely depend on the intracellular content of ATP. If ATP level will decrease, the deformity decreases and if it will increase, the deformity increases [10, 11]. The glycolysis is the single source of ATP in erythrocytes. Energy is important for ensuring the integrity of the membrane and the biconcave shape of erythrocytes, the ability to perform oxygen transport function and energy production for ion pumps [12, 13]. Oxidation of glucose in the erythrocyte has two goals: energy and antioxidant. Inhibition of glycolysis leads to a violation of these functions and, accordingly, hemolysis. When the level of ATP falls below 10 % of the normal value the erythrocytes lose potassium ions, their spherulation occurs and eventually undergo osmotic lysis [9, 11, 13].

Today, many different erythrocyte indices are important diagnostic indicators. These parameters characterize morphological characteristics and allow to estimate the size of RBCs and hemoglobin content in them. The deviations from normal values of these indicators point the nature of anemia and the function of forming hemoglobin in RBCs [9–11].

Thus, the measurement of RBC indices is of particular importance as an indirect intermediate component of the recovery process after exposure to hypoxia, ischemia, hypothermia in patients with traumatic disease due to polytrauma.

The aim of this study was to evaluate the parameters of the morphologic state of RBCs as a reaction of patients with traumatic disease (TD). In case, they were operated according to multi-stage surgical correction strategy and use different variants of intensive care (IC).

2. Materials and methods

The study was conducted in anesthesiology and intensive care unit for patients with combined trauma on the basis of prof. A. I. Meshchaninov Kharkiv City Clinical Hospital of Emergency Medicine. We carried out evaluation of 120 patients suffering from polytrauma in the period from 2015 to 2017.

All studies were conducted in accordance with the Council of Europe Convention on the Protection of Human Rights and Human Dignity in Connection with the Application of Biology and Medicine: Convention on Human Rights and Biomedicine (ETS No. 164) of 04.04.1997, and the Helsinki Declaration of World Health Association (2008). All of patients or their legal representatives signed an informed consent to participate in the study, and all measures were taken to ensure patient anonymity (the ethics committee of V. N. Karazin Kharkiv National University School of Medicine, protocol No. 3, from 11.03.2020)

The conditions for including patients into the study were multiple trauma, ISS>15 points, class III–IV blood loss according to the classification of the American College of Surgeons, body temperature 34–36 °C, age 18 to 60 years (average age 37.9±12.8 years), absence of severe traumatic brain injury.

The patients were divided into 3 groups according to the principle of using additional substances as a part of IC. The Control group consisted of 32 patients and had not composed additional substances destination for intensive care. 32 patients were included in CP group, and in addition to the IC algorithm Ceruloplasmin (5 mg/kg 1 time per day intravenously at a rate of 30 drops per minute for 10 days) was prescribed. FDP group included 56 patients who additionally the intensive care algorithm was assigned a solution of D-fructose-1,6-diphosphate sodium hydrate (150 mg/kg per day administered intravenously at a rate of 10 ml per minute over 10 days from the time of admission to the operating room).

All of patients were comparable by severity of trauma and condition at the time of admission.

To achieve this goal, we conducted a study of the parameters of morphologic state of erythrocytes. Actually, an important diagnostic indicators are some RBC indices. Mean Cell Volume (MCV), Mean cell hemoglobin (MCH), Mean cell hemoglobin concentration (MCHC), Red cell distribution of width (RDW) were analyzed in patients all of groups. The erythrocyte morphofunctional state parameters were determined on a hematology analyzer ABX Micros 60 by HORIBA ABX Diagnostics (France).

The following control points were used: at the time of admission, 24 hours later, on the 3rd, 5th and 14th days of intensive care during the strategy of multi-stage surgery. Statistical processing of the obtained results was performed using the software «Microsoft Office 2010», «Microsoft Excel 2010». Statistical analysis was done using the Student's t-test.

3. Results

Statistical analysis has revealed that the MCV was within normal range in patients groups C, CP and FDP, and averaged 88.4±3.9 mkm. The dynamic of MCV figures are presented in **Table 1**.

Too large a size of RBCs will cause difficulty in the passage of blood cells through the smallest capillaries, a small size will lead to insufficient hemoglobin inside. In both cases, the risk of hypoxia increases – oxygen starvation with corresponding consequences for the whole body [7].

Thus, in the control group, whose patients were given IC according to the local protocol, without additional means to counteract hypoxia, after 24 hours, the MCV was 74.2±3.6 μm³, that is 16 % likely (p<0.05) lower for the starting level (MCV_{start}). In groups CP and FDP, after 24 hours, MCV was reduced to 78.1±3.8 μm³ and 83.2±4.3 μm³, which is 11.7 % and 5.9 % lower than the starting value. On the 3rd day of hospital stay, there was a relative decrease in MCV in all studied patients. In the Control and CP groups it were by 15.8 % and 14.5 % significantly (p<0.05) lower than the starting level, while in group FDP by 4.3 %, which is likely no different from the MCV_{start}.

Table 1

The dynamic of morphometric and functional properties of red blood cells, M±m

Group	At admission	After 24 hours	On 3 day	On 5 day	On 14 day
MCV, μm^3 ($88.4 \pm 3.9 - \text{MCV}_{\text{start}}$)					
Control	88.6±3.9	74.2±3.6*	74.4±2.8*	75.1±4.4*	80.6±5.4
CP	88.4±3.6	78.1±3.8*	75.6±5.8*	79.8±5.4	82.8±5.1
FDP	88.2±4.2	83.2±4.3	84.6±4.1	86.6±5.2	88.4±4.3
MCH, pg ($30.1 \pm 1.4 - \text{MCH}_{\text{start}}$)					
Control	31.2±1.3	25.9±1.6*	25.4±2.2*	27.1±1.2	28.6±1.1
CP	29.8±1.6	26.4±1.3*	25.7±2.8	28.2±1.2	30.8±2.2
FDP	28.9±1.2	28.1±1.6	27.4±2.3	28.6±1.3	31.4±1.8
MCHC, g/l ($327 \pm 17 - \text{MCHC}_{\text{start}}$)					
Control	319±18	296±18	298±24	302±18	302±14
CP	324±14	303±22	302±20	308±18	314±16
FDP	339±16	308±25	306±18	312±15	325±12
RDW, % ($13.1 \pm 0.9 - \text{RDW}_{\text{start}}$)					
Control	13.4±1.2	17.6±1.8*	16.2±1.3*	14.7±1.2	13.8±1.1
CP	13.2±1.2	16.7±1.5*	15.1±1.3	14.0±0.8	13.4±0.9
FDP	12.8±0.9	14.7±1.2	14.1±1.1	12.9±0.7	12.8±1.1

Note: * – significance of differences in the Student's t-test relative to baseline $p < 0.05$

MCV relative decline may be due to high content of fragments of red blood cells (acute traumatic coagulopathy, mechanical hemolysis etc) [6, 14]. Further, on the 5th day, the index of mean cell volume has slightly increased in all of groups and amounted to $75.1 \pm 4.4 \mu\text{m}^3$, $79.8 \pm 5.4 \mu\text{m}^3$, $86.6 \pm 5.2 \mu\text{m}^3$ in Control, CP and FDP groups, i. e. 15 %, 9.7 % and 2 % below $\text{MCV}_{\text{start}}$, respectively. On day 14, the upward trend has continued MCV and did not differ significantly from baseline in all of groups.

4. Discussion

This shows the unconditional benefit of prescribing additional compounds that affects the metabolism of oxygen in the body. In addition, despite the similar dynamics of recovery of MCV numbers in the blood of patients in groups CP and FDP, their maximum deviations from baseline were observed in group CP. In our opinion, this is due to the increased content of fragments of RBCs in the blood, as a result of acute traumatic coagulopathy. Therefore, the additional appointment of D-fructose-1.6-diphosphate sodium salt of the hydrate has a positive effect on the functional state of RBCs.

Also, the analysis of the data indicators of MCH have shown no significant difference in the control points in patients of control, CP and FDP groups and demonstrated the following dynamics (Table 1). 24 hours after the start of the IC index of MCH has decreased by 14 %, 12.3 % and 6.6 %, on the 3rd day – by 15.6 %, 14.6 % and 9 % relative to starting level ($\text{MCH}_{\text{start}}$), respectively in patients of control, CP and FDP groups. From the 5th to the 14th day, this indicator had a tendency to recovery and was authentically no different from starting level in all of groups.

Thus, it could be noted that, in general, on the 3rd day of treatment, were observed significant ($p < 0.05$) and maximum deviations MCH from $\text{MCH}_{\text{start}}$ in Control and FDP groups. It was despite the similar dynamic of MCH numbers in the blood for all investigated groups. The obtained data have evidenced of the unconditional benefit of prescribing D-fructose-1.6-diphosphate sodium salt hydrate. This is due to the affect the metabolism of oxygen in the body, which is likely pathogenetically significant in the restoration of MCH.

The study has not revealed significant differences between the groups of the mean cell hemoglobin concentration in the RBCs. Control, CP and FDP groups have shown reduction of MCHC

indices relative to starting level ($MCHC_{start}$) by 9.5 %, 7.3 % and 5.8 % in 24 hours after admission to the operation room, and by 8.7 %, 7.6 % and 6.4 % – in the 3th day. On the 14th day it was characteristic to restore the indicators of MCHC almost to baseline in all groups.

There is a less deep fall and faster recovery of MCHC numbers in the FDP group compared to the control and CP groups, despite the lack of significant differences between the groups at all control points. The administration of the proposed therapy with the use of D-fructose-1.6-diphosphate sodium salt of hydrate has a positive pharmacologic effect relative to the state of MCHC in the blood of the patients with TD. This is based on the fact that patients in the FDP group differed in the appointment of an additional substance to the main treatment protocol.

In addition, the analysis of the dynamics of RDW in the blood of patients showed the absence of any significant differences between Control, CP and FDP groups. However, it is noteworthy that 24 hours after admission to the operative the RDW levels in the blood were 17.6 ± 1.8 %, 16.7 ± 1.5 % and 14.7 ± 1.2 %, which were 34.5 %, 27.5 % and 12.2 % higher than the starting level (RDW_{start}) in patients of Control, CP and FDP groups. So, that means this indicator significantly ($p > 0.05$) has not been changing in the acute period of TD only in group FDP. On the 3rd day of observation RDW figures were increased by 23.7 %, 15.3 % and 7.6 % in Control, CP and FDP groups. The tendency to normalization of this indicator has persisted both on the 5th day and on the 15th day (**Table 1**).

RDW characterizes the degree of anisocytosis, i.e. fluctuations in the volume (size) of RBCs, indicates the presence of a heterogeneous population of cells [12].

The value of the RDW index more than 14.5 % could be considered an indicator of tissue hypoxia [15]. So in our study, the increase in the value of the RDW index may be result of tissue hypoxia and blood transfusions [12, 16].

Isik T et al. have shown RDW levels as an independent correlate predictor index of adverse outcomes also associated with both presence and severity of isolated ischemia than baseline RDW levels measured at ischemic patients and controls [17].

Bujak K et al. noted the negative prognostic effects of elevated RDW levels may be attributed to the adverse effects of independent risk factors such as inflammation, oxidative stress, and vitamin D₃ and iron deficiency on bone marrow function (erythropoiesis). Elevated RDW values may reflect the intensity of these phenomena and their unfavourable impacts on bone marrow erythropoiesis. Furthermore, decreased red blood cell deformability among patients with higher RDW values impairs blood flow through the microcirculation, resulting in the diminution of oxygen supply at the tissue level [18].

The FDP group showed a faster recovery of the RDW indicator, despite the absence of statistically significant differences between the groups at all control points. The administration of the proposed therapy with the use of D-fructose-1.6-diphosphate sodium salt of hydrate has a positive effect on the state of extensibility of erythrocyte membranes, their elasticity and hemolytic stability.

Previous studies on this topic demonstrated the notion that increased RDW and decreased RBC, MCHC, MCV, hemoglobin, hematocrit were significantly associated with hospital mortality [19, 20].

In summary, in this study, we demonstrated variations in the morphologic properties of RBCs in the acute and early period of TD, as confirmed by pathological changes of the erythrocyte indices. The important thing is that all of patients were comparable by severity of trauma and condition at the time of admission, but differed in treatment protocol. So, the changes in the laboratory parameters are objective indexes of the presence of significant differences in patients of compared groups. The optimized therapy used in the treatment of patients in group III, has a positive effect on the parameters of RBCs, contributes to a better recovery of RBCs after hypoxia resulting multiple trauma.

Study limitations. The study was not conducted in case of identified comorbidities, and in case of patients refuse to participate in the study.

Perspective of further research of this problem are presented in the further study of relationship morphologic changes of RBCs and indicators of cellular metabolism.

5. Conclusion

This study confirms that for multiply injured patients morphological changes of RBCs are characteristic, manifested by changes in erythrocyte indices (MCV, MCH, MCHC, RDW). The course of acute and early periods TD has accompanied variability morphological forms of red blood cells, as evidenced by a decrease in MCV and RDW increased levels of the 3rd to 5th day.

The administration of the proposed therapy with the use of D-fructose-1,6-diphosphate sodium salt of hydrate has a positive effect on the parameters of RBCs, especially contributes to a better recovery of MCV, RDW indices after hypoxia resulting multiple trauma.

Given this, the calculations of the red blood cell indices may carry additional diagnostic information, which allows identify trends for not obvious pathological changes and quality of treatment.

Conflict of interests

The authors declare that they have no conflicts of interest.

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BASIC FIBROBLAST GROWTH FACTOR AND ADIPONECTIN IN ADOLESCENCE WITH JUVENILE IDIOPATHIC ARTHRITIS TREATED WITH METHOTREXATE

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Abstract

Methotrexate has been applied clinically for juvenile idiopathic arthritis (JIA) treatment for decades. It is recommended for use globally, according all modern guidelines. Despite the fact that fibrosis molecular mechanisms as well as methotrexate (MTX) elimination and fibrosis indexes were studied a lot there is still not enough information for adolescence. Adiponectin, fibroblast growth factor and fibrosis indexes in adolescents with JIA treated with methotrexate were studied in this work.

The aim was to study dynamics of molecular-cellular mechanisms activation of fibrotic processes development in the liver in adolescents with juvenile idiopathic arthritis treated with methotrexate.

Materials and methods: A total of 68 children with juvenile idiopathic arthritis, were enrolled in the study. 25 boys (36.8 %) and 43 girls (63.2 %) were examined. Children were divided into three groups in accordance with the methotrexate dose. The following data were analyzed: ESR (mm/hour), C-reactive protein (mg/l), Hemolytic activity (CU), circulating immune complexes, (g/l), ALT (U/l), AST (U/l), Adiponectin (mcg/ml), BFGF (pg/ml), APRI index, FIB-4 Score.

Results: According to our results when patients start using MTX they have significantly positive effect. Therefore, when analyzing all parameters liver pathologies may occur before MTX use. When MTX used, its proinflammation and antifibrotic effects lead to normalization of all organs and systems, as well as joints and liver. Also, long-term MTX use can lead to adverse effects.

Conclusions: So, it is important to control possible liver disorders in adolescence treated with MTX. According to our study results we find out that there are decreasing of liver damage parameters in patients which started using MTX.

Keywords: Juvenile idiopathic arthritis, methotrexate, basic fibroblast growth factor, adiponectin.

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1. Introduction

Juvenile idiopathic arthritis (JIA) is the most common chronic disease of childhood. One in 1,000 children is affected by the various subtypes of JIA. Methotrexate (MTX) is a cornerstone of therapy worldwide for JIA, yet there remains vast variability in drug dosing and administration, as well as unpredictable outcomes on the drug [1]. Methotrexate (4-amino-10-methylpholic acid) is commonly administered orally as a single weekly dose. MTX dosage is clearly regulated by modern treatment guidelines. After oral administration, MTX is absorbed in the proximal jejunum by the proton-coupled folate transporter, which transports reduced folates and MTX [2]. MTX maximum plasma concentrations are between 0,3 and 1,6 $\mu\text{mol/L}$, and occur at up to two hours after administration [3]. Also MTX can distribute to the synovial fluid with comparable levels to those found in plasma [4]. MTX side effects on the gastrointestinal tract are associated precisely with the antagonism of MTX and folate. Adding folic or folinic acid to therapy almost eliminates such side effects as nausea, vomiting, diarrhea, or stomatitis [3]. Manifestations of nausea and diarrhea are more often observed with oral administration of MTX [5]. Major elimination route of MTX is renal excretion constitutes. MTX is subject to first-pass metabolism in the liver and is converted to 7-hydroxymethotrexate, which is a major metabolite of MTX [6]. MTX in small proportion is excreted in the bile and some enterohepatic recycling also happens [3, 6, 7]. The plasma half-life of low dose MTX varies from 4.5 hours to 10 hours [4]. Hepatotoxicity is one of the main side effects of MTX in the JIA treatment. Slight increase in aminotransferases level, less commonly hepatic steatosis, fibrosis and cirrhosis are most common manifestations [8].

The precise mechanisms of MTX toxicity are still not clear. It was suggested that MTX hepatotoxicity may result from a depletion of hepatic folate stores and the accumulation of MTX polyglutamates in the liver [9]. However, folate supplementation has been associated with a reduced incidence of hepatic adverse effects (elevated transaminases) induced by MTX treatment [10].

MTX-related hepatic fibrosis may be mediated through an adenosine pathway. MTX was shown to enhance the release of adenosine from cultured hepatoma cells. Adenosine binds to the adenosine A2A receptor on hepatic stellate cells which is the principal fibrogenic cell type in the liver, and promotes collagen production [11, 12].

Moreover, MTX is known to interfere with the generation of methionine from homocysteine. Excess homocysteine can induce endoplasmic reticulum stress and promote fat accumulation in the liver. Homocysteine can also activate proinflammatory cytokines and hepatic stellate cells, leading to liver fibrosis [13]. MTX-induced hepatic damage may be related to reactive oxygen species generation. MTX was shown to cause oxidative tissue damage by increasing lipid peroxidation in the liver tissue and decreasing the level of antioxidant enzymes [14].

Fibrosis can cause impaired liver function due to changes in the tissue microenvironment, various growth factors synthesis, inflammatory cytokines functioning, a violation of the liver normal structure as a result of changes in the distribution and proportions of febrile collagen.

Despite the significant compensatory liver potential in childhood, it is important to prevent of steatosis and fibrosis development in the future. Adiponectin is the most common protein secreted by white adipose tissue. It circulates in the blood, and its concentration in serum is inversely proportional to fat mass. The wide distribution of adiponectin receptors in peripheral tissues and organs allows adiponectin to exert a pleiotropic effect on the general body metabolism. In addition to the well-known anti-diabetic, anti-atherogenic and anti-inflammatory properties, have been obtained data on the direct effect of adiponectin on non-alcoholic fatty liver disease development.

The study of the risk of developing fibrosis is possible including use of trigger factors for the development of fibrosis. Fibroblast growth factor (FGF) showed a potential effect on tissue repair and regeneration [15, 16]. It was first identified as a protein capable of stimulating fibroblast proliferation, and it is now known that the group of these factors includes 22 members. FGFs perform multiple functions by binding and activating fibroblast growth factor receptors (FGFRs), and the main signalling pathway is FGFR stimulation leading tissue repair and regeneration [17, 18]. Fibroblast growth factor receptors 1, 2, and 4 are expressed in the liver, with FGFR4 exclusively in hepatocytes [19, 20]. FGF1 and FGF2 are produced during hepatocyte replication and are mitogens for both endothelial and stellate liver cells [21].

Despite the fact that treatment with methotrexate JIA is the key, it makes sense to study the balance between its positive and negative effects, including finding out the risk of fibrosis.

The aim was to study dynamics of molecular-cellular mechanisms activation of fibrotic processes development in the liver in adolescents with juvenile idiopathic arthritis treated with MTX.

2. Materials and methods

The study group included JIA patients, a total of 68 children 25 boys (36.8 %) and 43 girls (63.2 %). The average age of patients was 13.3 ± 0.3 years. This study was carried out from 2017 to 2019.

Children were treated at the Cardiac-Rheumatology Department, State Institution “Institute for the Protection of Children and Adolescents’ Health”, Academy of Medical Sciences of Ukraine with Juvenile idiopathic arthritis. The diagnosis juvenile idiopathic arthritis was established in accordance with EULAR recommendations relevant at the time of the study. Treatment was carried out according to the same recommendations for all children. Informed consents’ from all patients were obtained.

This work complies with ethical standards and it was approved by ethical committee of Kharkiv medical academy of postgraduate education from the 18th of February 2020, protocol No. 1. This work was carried out according to the Helsinki Declaration.

Inclusion criteria’s were boys and girls from 10 till 18 years old with JIA (with oligoarthritis and polyarthritis) treated with MTX or patients whom MTX were prescribed, but they did not received it yet on the moment of the study start.

Exclusion criteria’s: children with chronic liver pathology, gastrointestinal, genetic and endocrinal disorders which occurred before JIA were diagnosed, children with uveitis. All examined patients had no viral hepatitis.

All adolescents underwent laboratory tests: clinical blood count, liver tests (AST (U/L), ALT (U/L)), acute phase indicator (C-reactive protein (mg/l)), Hemolytic activity (CU), circulating immune complexes, (g/l), Adiponectin (mcg/ml), BFGF (pg/ml). Abdominal organs ultrasound examination, joints ultrasound, and joints X-Ray were provided.

Level of adiponectin in the blood was determined by an enzyme-linked immunosorbent assay using the Human Adiponectin ELISA reagent kit, manufactured by BioVendor.

Determining the level of BFGF in the blood was carried out by an enzyme-linked immunosorbent assay using the Human bFGF ELISA reagent kit, manufactured by Elabscience.

Fibrosis indexes were calculated with Microsoft Excel program using standard formulas:

APRI index (AST to Platelet Ratio Index) was calculating using formula:

$$[(AST/ULN\ AST) \times 100] / \text{Platelets } (109/L)].$$

FIB-4 score index (Fibrosis 4 Score) was calculated using following formula:

$$(\text{Age} \times \text{AST}) / (\text{Platelets} \times (\text{sqr}(\text{ALT})).$$

Adiponectin was studied to assess the risk of liver steatosis. Adiponectin was measured according to the instructions by ELISA. To assess the risk of liver fibrosis, the basic fibroblast growth factor (BFGF) was studied. We measured it according to the instructions by ELISA.

Children were divided into three groups according to the dose of methotrexate per 1 m². The first group (0 (n=18)) included children with JIA who had just been appointed MTX and they had not received it yet. In the second (1 (n=21)) were children who receive MTX less than 12.5 mg, third (2 (n=25)) included ones who had dose more than 12.5 mg. The distribution of indicators was carried out in accordance with an average value of 12.5.

Statistical analysis was carried out with software package Statistica 6.0. Before statistical processing, all data was checked for normal distribution. Normal distribution data were analyzed with a Pearson correlation method, a Spearman correlation was used for not

normally distributed data relationships. One-way ANOVA was used to analyze differences between groups. LSD test was used to calculate the statistical significance. Differences were considered significant at $p < 0.05$.

3. Results

The proportions of gastrointestinal tract disorders associated in the study groups treated with MTX were as follows: nausea – 42.1 %, belching – 3.2 %, epigastric pain – 51.0 % pain in the pyloroduodenal zone – 41.4 %, pain in the right hypochondrium – 37.7 %, abdominal pain – 21.7 %. Liver size increase during palpation was found in 73.8 % of adolescents. The presented data cannot be the criteria for the diagnosis of fibrosis and steatosis. It seems to be of particular importance to be able to differentiate, based on biomarker analysis, between risk of steatosis and fibrosis development. Thus we analyzed biochemical parameters (**Table 1**) and their correlations.

Table 1

Laboratory parameters value in adolescents with JIA, taking into account the dose of MTX per 1 m²

Grouping	0	1 (<12,5)	2 (>12,5)
Indicator	n=18	n=21	n=25
ESR mm/hour	5.33±1.45	3.67±0.46	6.04±1.26
Hemolytic activity, CU	0.99±0.04	0.94±0.1	1±0.04
Circulating immune complexes, g/L	1.17±0.062	1.33±0.099	1.21±0.045
ALT U/L	20.9±1.97* ^{0,1}	31.1±2.37	25.8±1.79
AST U/L	25.1±2.25* ^{0,1}	32.4±2.39	29.9±2.09
APRI index	0.29±0.031	0.36±0.04	0.37±0.03
FIB-4 Score	0.24±0.028	0.30±0.023	0.29±0.017
Adiponectin(mcg/ml)	1.53±0.144	1.51±0.08	1.47±0.12
BFGF(pg/ml)	6876.4±338.05	7517.3±209.7	7134.9±228.4

Note: *^{0,1} – the presence of a statistically significant difference between groups and figures is indicated; it is noted between which particular groups this difference is present $p < 0,05$

In the same group correlation of BFGF with the degree of functional disorders of the joints ($r=0.496$, $p=0.036$) were found. Thus, the more disorders in the joints, the more active are the processes associated with collagen metabolism as a result of JIA. An increase in the level of BFGF in the central bloodstream can lead to the activation of fibrotic processes in various organs and tissues, and especially in the liver. This may be a reflection of the increased risk of sclerotic processes in the liver.

Positive correlation between BFGF level and hepatomegaly according to ultrasound data ($r=0.752$, $p=0.014$) may indicate both the spread of autoimmune inflammatory process to the liver and fibrosis.

Alterative processes in the liver associated with autoimmune inflammation are confirmed by the presence of a positive correlation between ALT and BFGF ($r=0.512$, $p=0.029$). It is possible to assume that, on the one hand, hepatocyte necrosis takes place in the liver and at the same time proliferative processes occur in the vascular component of the organ stroma, which can enhance the acceleration of the fibrosis process. This is confirmed by the revealed positive correlation between the content of BFGF and the FIB-4 Score index ($r=0.546$, $p=0.019$).

In this study, no correlation was found between platelets level, AST and BFGF, which indicates that their action is different, although not detected with statistics methods, which directed towards to fibrotic processes development, since the combination of these indicators in fibrosis index gives a positive correlation with BFGF. Inflammatory process activity also presented in this study with decrease hemolytic activity level ($r=-0.878$, $p=0.021$) and an increase in BFGF level in the central bloodstream, which is typical for autoimmune disorders.

A positive correlation of adiponectin and BFGF ($r=0.577$, $p=0.019$) may reflect an increase in its anti-inflammatory effect upon activation of collagen synthesis, in addition, adiponectin inhibits the adhesion of monocytes to vascular endothelial cells.

On the other hand, an increase in adiponectin levels with increased fibrotic activity may be associated with a steatosis risk due to visceral adipose tissue development.

BFGF correlations in group 1 were presented with statistically significant dependence with CIC ($r=0.476$, $p=0.039$) which is associated with an increase of autoimmune process characteristic activity of the inflammation phase. In this group also, there were no statistically significant correlations with BFGF, which was noted in the previous group and negative correlations were found with AST ($r=-0.568$, $p=0.011$) and the APRI index ($r=-0.647$, $p=0.002$), which may indicate a rather low risk of fibrosis in this group. This may be due to the antifibrotic effect of MTX, both on the joints and on the liver.

Group 2 did not show statistically significant correlations. That is, the lack of correlations defined in the previous groups, possibly indicates effective treatment, a decrease in the activity of inflammation and fibrosing.

4. Discussion

Our findings showed that although a relatively large proportion of patients with JIA reported symptoms of nausea and epigastric pain, relatively few of these patients could in fact be diagnosed with steatosis or fibrosis. A large proportion of patients with JIA failed to achieve predicted values for the parameters of abnormal liver tests values. These findings are consistent with those of large population studies which suggest that taking folic acid reduces the negative effects of MTX when taken orally. These findings are consistent with those of large population studies [3].

Despite the fact that fibrosis molecular mechanisms as well as MTX elimination and fibrosis indexes were studied a lot there is still not enough information for adolescence. According to our results when patients start using MTX they have significantly positive effect. Therefore, when analyzing all parameters liver pathologies may occur before MTX use. When MTX started its proinflammation and antifibrotic effects lead to normalization of all organs and systems, as well as joints and liver. Also, long-term MTX using can lead to MTX hepatotoxicity caused by MTX polyglutamates accumulation in the liver [9] or folate supplementation [10] which was reported by others.

So, it is important to control possible liver disorders in adolescence treated with MTX. According to our study results we find out that there are decreasing of liver damage parameters in patients which started using MTX.

The coexistence of antifibrotic effects of MTX, its gastric side effects and risk of liver steatosis and fibrosis development in patients with JIA requires further studies aiming to determine the mutual relationship of these phenomena and their association with liver risk. MTX-related hepatic fibrosis through an adenosine pathway was reported [11]. Homocysteine can also activate proinflammatory cytokines and hepatic stellate cells, leading to liver fibrosis [13]. MTX-induced hepatic damage may be related to reactive oxygen species generation [14].

To apply this knowledge in the daily practice of a doctor further studies are necessary. BFGF may be a valuable complement to liver tests. Additionally, it can help identify abnormal liver functioning, which may be associated with the reported symptoms.

Study limitations

We are aware that the small sample size is a limitation of the study. Despite the fact that liver biopsy remains diagnostic standard it is invasive method and cannot be used to perform population screening and assess the course of the disease in patients with diagnosed steatosis or fibrosis. Therefore, liver biopsy was not performed, and we cannot definitively exclude liver fibrosis and steatosis. However, morphological study cannot be provided in pediatrics as a screening method. Our study comprised mostly adolescence with JIA treated with MTX without any other serious comorbidities and our results should not be extrapolated to the general population. On the other hand, the strength of our results is that we recruited adolescences with JIA without other serious chronic diseases, with different dose of MTX.

Prospects for further research

In the future, it is planned to analyze the dependence of BFGF in patients with JIA with other parameters. It is also planned to study the correlation of the degree of differentiation of BFGF with hepatocyte growth factor. BFGF data analyzing with routine laboratory and instrumental studies is appropriate for the timely determination of the risks of developing irreversible pathological changes in the liver during JIA treatment with MTX.

5. Conclusions

In patients with JIA, the activity of systemic inflammation increases even before the start of treatment, as evidenced by a statistically significant correlation of BFGF level in group of patients who did not receive MTX. This indicates a close relationship between the intensity of the inflammatory process and collagen synthesis activation, which can further provoke liver fibrosis.

In patients who started receive MTX alternative processes in the liver associated with autoimmune inflammation can be reduced firstly according to obtained data. Adequate treatment of MTX in accordance with modern guidelines reduces the risk of fibrosis and the activity of the inflammatory process.

Conflict of interests

The authors declare that they have no conflicts of interest.

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AN IMPROVED TRANSABDOMINAL PREPERITONEAL ALLOPLASTY FOR RECURRENT INGUINAL HERNIAS AFTER LICHTENSTEIN'S SURGERY

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Abstract

The aim. Improve results of the surgical treatment of recurrent inguinal hernias after Lichtenstein's surgery by using an advanced TAPP technique.

Materials and methods. An analysis of the surgical treatment of patients with recurrent inguinal hernias after Lichtenstein's surgery using traditional and improved preperitoneal transabdominal alloplasty (TAPP), for the period of 2012–2019, was performed. The traditional TAPP technique was performed for 52 patients who made up the 1st group. An improved TAPP technique was implemented for 53 patients who composed the 2nd group.

The features of the improved TAPP technique, which was different from the traditional one, were by additional mobilization of the parietal peritoneum by 3–4 cm along the upper edge of the defect, the mesh implant was used with a larger size in comparison to the classical one – 15×15 cm and fixed, besides the traditional points, additionally on the lower and lateral edges with medical glue Sulfacrylate.

Results. The results of surgical treatment in the early postoperative period were not significantly different and were comparable. During the long-term period, 51 patients from the 1st group, and 50 patients from the 2nd group were examined. Thus, in the first group in 4 (7.9 %) cases during 6 months period after the application of the traditional TAPP technique, chronic pain was observed on the site of the implanted mesh; among the 2nd group of patients chronic inguinal pain was not observed. In 5 (9.8 %) patients of the 1st group, the recurrence of inguinal hernia was diagnosed, instead of the 2nd group, where relapse was observed in 1 (2 %) case.

Conclusions. Thereby, the results of the traditional and improved TAPP techniques confirm the higher efficiency of the improved technique, due to the absence of the chronic inguinal pain and a lower rate of relapses, which is achieved by wider mobilization of the parietal peritoneum along the upper edge of the defect, and usage of the larger mesh and its additional fixation by gluing it at the lower lateral edge.

Keywords: recurrent inguinal hernia, TAPP, optimization of alloplasty of recurrent hernias.

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1. Introduction

Most surgical interventions for inguinal hernias are performed using Lichtenstein's surgery [1, 2]. However, the Lichtenstein's operation is the most common, accessible by most surgeons, and relatively technically simple – the recurrence rate of inguinal hernias remains at the level of 3.1–10 % [3–5]. The treatment of recurrent inguinal hernias after Lichtenstein's surgery with Lichtenstein's reoperation is technically difficult [6], due to scarring changes in the tissues of the inguinal region and altered anatomy of the inguinal canal, accompanied with an even higher frequency of repeated recurrences of 9.3–12 % [7, 8]. Thereby, in the surgical treatment of inguinal hernias, posterior preperitoneal access is more appropriate [9]. Among the opened and laparoscopic preperitoneal techniques, according to the EHS recommendation [1], the transabdominal preperito-

neal approach alloplasty (TAPP) is more relevant. At the same time, the traditional TAPP technique in the treatment of recurrent inguinal hernias is accompanied by repeated recurrences, which make 6–8 % [10]. The main reasons for repeated recurrences of inguinal hernias after traditional TAPP approach are insufficient coverage of the hernial defect with mesh, the absence of mesh fixation along its lower edge in the projection of the iliac vessels, and trauma to the femoral nerve branches during mechanical mesh fixation [11, 12].

In our opinion, improvements in the traditional TAPP approach will facilitate the amelioration of the treatment outcomes for recurrent inguinal hernias after Lichtenstein's surgery.

The aim of the work. Improve results of the surgical treatment of recurrent inguinal hernias after Lichtenstein's surgery by using an advanced TAPP technique.

2. Materials and methods

The analysis of the surgical treatment of 105 patients with recurrent inguinal hernias after Lichtenstein's surgery was held in the clinic of the Department of Surgery and Proctology, P. L. Shupyk National Medical Academy of Postgraduate Education. All patients were male. The age of patients is from 24 to 76 years old (average age 53.4 ± 1.2). Concomitant pathology was diagnosed in 41 (39.1 %) cases with a predominance of chronic cardiovascular diseases in the stage of compensation.

The Ethics Commission of the Shupyk National Medical Academy of Postgraduate Education approved and authorized the study on January 10, 2012 No. 2, and confirmed that the study complies with the Helsinki Declaration of the World Medical Association. All patients who participated in the study agreed to conduct this study.

According to the classification of G. Campanelli [13], patients were distributed as follows: R1 recurrent high lateral hernias with a slight defect were observed in 36 (34.3 %) patients, R2 was low medial hernias with a slight defect in 55 (52.4 %) cases, R3 recurrent hernias with a large defect – in 14 (13.3 %) patients. In concern to the occurrence of relapse, in particular, 3 months after surgery, hernia recurrence occurred in 26 (24.8 %) cases, after 6 months in 63 (60.0 %) cases, and after 12 months in 16 (15.2 %) patients.

The traditional TAPP technique was performed during the period of 2012–2016 yrs for 52 patients with recurrent inguinal hernias after Lichtenstein's surgery, which made up the 1st group. An improved TAPP technique was performed during the period of 2017–2019 yrs for 53 patients, with recurrent inguinal hernias after Lichtenstein's surgery, which made up the 2nd group. Patient groups were comparable in patients' age and size of recurrent inguinal hernias. Antibiotic prophylaxis in patients of both groups was performed by administering a daily dose of Third generation cephalosporins (ceftriaxone 2.0) before surgery.

The traditional TAPP technique, which was performed in patients of the first group, consisted in the fact that under the general anaesthesia after application of the carboxyperitoneum, three trocars were placed using a Veress needle: 10 mm below the belly button, two 5 mm trocars at the same level along the edges of the rectus abdominis muscles. After diagnostic laparoscopy, the parietal peritoneum from the iliopubic tract to the medial umbilical fold was arcuately cut along the upper edge of the hernial defect. The mobilization of the parietal peritoneum with distinguishing of the hernial sac was performed. After that, a 12x15 cm polypropylene hernia mesh was placed preperitoneally and fixed with a hernia stapler Protac, along the upper lateral edge, to the Cooper's ligament and abdominal muscles. The peritoneum was sutured with continuous running sutures with Vicryl 2-0.

In the second group of patients, improved TAPP technique was performed [14], which was different from the traditional one by additional mobilization of the parietal peritoneum by 3–4 cm along the upper edge of the defect, the mesh implant was used with a larger size in comparison to the classical one – 15X15 cm and fixed, besides the traditional points, additionally on the lower and lateral edges with medical glue Sulfacrylate [15, 16].

Evaluation of the results of traditional TAPP technique in the 1st group of patients and improved TAPP technique was carried out by taking into consideration complications in the early postoperative period (seroma, infection of trocar wounds, the period of recovery of the physical

activity). In the remote postoperative period after 6, 24, 36 months results were assessed by questioning, re-examination, evaluation of the presence or absence of the chronic inguinal pain [17, 18], and repeated hernia recurrence.

Descriptive statistics were generated for the baseline, immediate postoperative and long-term periods. Comparison groups were carried by T test (timing recovery of physical activity, the normal approximation by Shapiro-Wilk test) and the chi-square test (cases complications). Significance was set at $p < 0.05$.

3. Results

The immediate results of the performed traditional TAPP method in the 1st group of patients showed that scrotal hematoma was diagnosed in 4 (7.7 %) patients, seromas at the site of mesh implantation in 5 (9.6 %) cases, there were no infections of trocar wounds. Recovery of the physical activity was after 10+2.1 days. Similar immediate results were observed among 2nd group of patients, to whom performed an improved TAPP technique. Seromas occurred in 6 (11.3 %) patients ($p2-1=0.775$), the scrotal hematoma was observed in 3 (5.7 %) patients ($p2-1=0.676$), infected trocar wounds was not observed, and the physical activity was restored after 10+1.6 days. Scrotal hematomas that were observed in patients of both groups with inguinal-scrotal hernias were associated with distinguishing of the hernial sac and were eliminated with conservative treatment. Seromas were also eliminated by conservative treatment (nonsteroidal anti-inflammatory drugs), which was confirmed by ultrasound diagnostics of the abdominal wall.

The long-term results, among 51 patients of group 1 in 4 (7.9 %) cases, during the 6 months period after the application of the traditional TAPP technique, chronic pain was observed on the site of the implanted mesh, which was periodically relieved by analgesics and nonsteroidal anti-inflammatory drugs. Among the 2nd group of patients, chronic inguinal pain was not observed.

Among 51 patients of the 1st group who were examined by questionnaire, control examinations, and ultrasound diagnostics of the abdominal wall after 6, 12, 24, 36 months after surgery. In 5 (9.8 %) cases, the recurrence of inguinal hernia was diagnosed. In 2 patients, recurrence of inguinal hernia occurred 7 months after surgery, in 3 patients after 9–11 months, respectively. During the observation of 50 patients of group 2 within 6–36 months, to whom were performed improved TAPP technique, recurrence of inguinal hernia was observed in 1 (2 %) patient ($p2-1=0.097$, $OR=0.188$ (0.004–1.79), 2 months after surgery, as a result of excessive physical exertion 2 weeks after surgery. Evaluation of immediate and long-term results indicates a reduction in the risk of all complications in Group 2 – 1 (2.0 %) compared with Group 1–9 (17.7 %) by 90.5 % – $OR=0.095$ (0.002–0.75), $p=0.009$.

4. Discussion

As you can see, the immediate results of patients from groups 1 and group 2 were not significantly different and were comparable.

Long-term results in patients of groups 1 and 2 were different. In particular, in patients of group 1 chronic inguinal pain was in 4 (7.9 %), compared with the absence of chronic pain in patients of group 2, i. e. there was a tendency to significantly improve the clinical outcome. The best results in the long-term postoperative period of 6-36 months were obtained in patients of the 2nd group, to whom were provided the improved TAPP technique, in comparison with the 1st group, to whom were performed the traditional TAPP technique. The absence of chronic postoperative pain in patients of the 2nd group, after the improved TAPP technique, is explained by the fact, that with this technique, the fixation of the mesh along the lateral edges, where the branches of the femoral nerve pass, was performed with glue, what excluded its damage. The mechanical stapler fixation of the mesh with the traditional TAPP technique is most likely caused trauma to the branches of the femoral nerve, which leads to chronic postoperative pain.

Regarding repeated recurrences of inguinal hernias, there is a difference among patients of groups 1 and 2 (1 – 5 (9.8 %), 2 – 1 (2 %)), with a tendency to improve the clinical effect of improved TAPP. In observation of 5 patients with recurrent inguinal hernias that arose after the traditional TAPP technique in the 1st group of patients, with ultrasound diagnostics was found that in 4 cases

a hernial defect was found along the upper edge of the mesh, which indicates the insufficiency of its overlap with the mesh and that it caused relapses. The improved TAPP technique, which was performed in the 2nd group, significantly reduced the probability of recurrent inguinal hernia, as long as it involves wider overlapping with a mesh of a larger size (15×15 cm), of the upper edge of the hernia defect.

In 1 patient with a recurrent inguinal hernia after the traditional TAPP technique, the ultrasound diagnostics revealed a defect along the lower edge of the mesh, confirming the likelihood of flexion of the mesh because it does not fix on the lower edge. During the performance of the improved TAPP technique, the probability of relapse decreases, as far as the mesh on the lower edge is fixed with glue.

In 1 patient with a recurrent inguinal hernia after improved TAPP technique, an ultrasound scan revealed a recurrence along the upper edge of the mesh; the mesh was, most likely, migrated as a result of excessive physical exertion during the early postoperative period.

Thus, the results of the traditional and improved TAPP techniques confirm the higher efficiency of the improved technique. The frequency of the chronic inguinal pain after using the traditional TAPP technique is 7.9 % and was absent after the performed improved TAPP technique. The frequency of the re-recurrence of inguinal hernia decreased to 2 % when performed an improved TAPP technique, versus 9.8 % with a traditional TAPP technique.

Study limitations. The study did not include patients with multiple recurrences of hernia, with inguinal-cellular recurrences of large hernias, intractable recurrent inguinal hernias, recurrences of inguinal hernias with concomitant decompensated cardiovascular and respiratory diseases, in portal hypertension cases.

Further research prospects. The prospect of the study is to study the laparoscopic IPOM and open method Stoppa effectiveness [19] in recurrent inguinal hernias and the study of the use of laparoscopic IPOM in recurrences of inguinal hernias after TAP with adhesive cover composite mesh using a [20].

5. Conclusion

Improved TAPP for recurrent inguinal hernias after Liechtenstein's surgery due to wider mobilization of parietal peritoneum on the upper edge of the defect, the use of mesh size and additional fixation with glue on the lower lateral edge, which does not cause trauma to the axillary nerves closes defects in the area of medial and lateral inguinal fossae, and reduces the probability of chronic inguinal pain from 7.9 % in traditional TAPP to its absence in advanced TAPP, and reduces the recurrence of inguinal hernia from 9.8 % in traditional to 2 % in the advanced method TAPP.

Conflict of interest

The authors declare that they have no conflicts of interest.

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JUSTIFICATION OF SELECTION OF MEANS AND METHODS OF THE ORAL CAVITY HYGIENE IN CHILDREN WITH CYSTIC FIBROSIS

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Abstract

Cystic fibrosis (CF) promotes the development of gingivitis in children.

The high prevalence and early manifestation of gingivitis is due to a combination of many factors. The pathogenic mechanisms of cystic fibrosis lead to disruption of normal physiological processes in the oral cavity, in particular, to a decrease in the level of salivation, to an increase in the viscosity of saliva, to a suppression of local immunity. Therefore, poor oral hygiene contributes to oral diseases.

The aim of the study was to determine the level of oral hygiene in children with CF as one of the reasons for the development of gingivitis, and to select dental hygiene products that active towards factors that affect plaque.

Material and methods. A total of 24 children with CF in the Ukrainian population participated in the study. The hygienic index OHI-S (J. C. Green, J. R. Wermillion, 1964) was calculated. The data were analyzed using Student's criterions. The analysis was performed with a confidence level of 95 %.

Results. The level of hygiene of the oral cavity was unsatisfactory among patients (OHI-S=2.19±0.11). Hygiene methods and dental hygiene products, to taking into account the manifestation of the pathogenesis of somatic disease, were selected. A follow-up study after 3 months revealed a significant positive trend in indicators of oral hygiene.

Conclusions. This study has shown the low level of oral hygiene in children with CF. Hygienic education and motivation of these patients could help them achieve a higher level of oral health knowledge and are important starting points for the treatment and prevention of gingivitis. There was a significant improvement of the oral hygiene level after training children and after the proper selection of hygiene products. The dentists should use means and methods that have not contraindicate in patients of this category. It is recommended to monitor the hygiene indices to establish the effectiveness of the measures and necessity for individually therapy correction.

Keywords: children, cystic fibrosis, dental plaque, oral hygiene.

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1. Introduction

To date, the impact of CF on the development of gingivitis in children has been known. It was proved that microbial colonization of the oral cavity and dental plaque are the main factors of caries and periodontal disease. Peculiarities of the pathogenesis of CF probably contribute to the implementation by microorganisms of their pathogenic potential. It heretofore was investigated that microbiocinosis of plaque in children with CF is characterized by active colonization of enamel of teeth by α -hemolytic streptococci, which form associations with gram-positive or gram-negative bacteria and fungi *C. albicans*. Wherein the age of the child and the composition of the microbiota of the respiratory system affect the characteristics of the microflora of the plaque [1].

The volume of plaque increases and biofilm forms change in conditions of insufficient oral hygiene. The replacement of microorganisms and the emergence of similar species with strong pathogenic properties occur. Microorganisms produce acids, endotoxins, lysosomal enzymes, that destroy the enamel and cells of periodontal tissues [2, 3]. Inflammatory processes of gums in patients with CF begin in conditions of low salivation, changes in rheological properties of the oral fluid, with a decrease of the factors of local immunity [4, 5].

Different factors could affect the formation and quality of the plaque in children with CF [6]. Usually it is a chronic colonization of pathogenic microflora among these patients. Anatomically determined a transition of microflora from the lungs to the oral cavity, in particular, *Ps. Aeruginosa*, that quickly attaches to the surfaces and proliferates [2, 7].

The content of the immune defence factors in the oral fluid decreases with insufficient secretion of saliva. The amount of immunoglobulins, lysozyme and proteins that have adhesive properties and have involved in antimicrobial protection, is not sufficient to evacuate bacteria. At the same time, conditions for bacterial adhesion and the association of microorganisms disimprove the microbiocenosis and the properties of the biotope of the oral cavity [8, 9].

An increase of the concentration of electrolytes in mixed saliva is present at CF. The formation of dental pellicle and protein depletion accelerate if low values of the pH of the oral liquid and in the presence of calcium and phosphorus ions. These microelements also reinforce the adhesion of proteins to hydroxyapatite of enamel [10, 11].

Patients receive regularly inhalations with corticosteroids and other medicaments as a treatment of CF that leads to violations of normal physiological processes in the oral cavity, including immunosuppressive action. Moreover, this increases the frequency of colonization of bacteria. In addition, the part of the hormonal drug deposits in the organism and oral cavity and on the dental plaque [12–14].

A diet with high-energy value is necessary for patients with CF. They must compensate energy necessity with carbohydrates, protein and fats [15, 16]. At the same time, an excess of carbohydrates in the diet leads to an increase in the activity of enzymes of the microflora and to the producing of organic acids. These are cariogenic and periodontopathogenic factors in the context of unsatisfactory oral hygiene and immune disturbance [17, 18].

Since microflora of the oral cavity is the main initiator of pathogenicity factors, removal of the dental plaque should be the first stage of dental rehabilitation [19, 20].

The formation of general knowledge and skills of oral hygiene in children is a very important initial measure. The next step will be the individual selection of hygiene products.

Given the manifestation of the pathogenic factors of CF, it is necessary to prescribe toothpastes and mouthwashes with certain active substances. Products contains fluoride, enzymes, antiseptics have the opportunity to remove biofilms. It is also necessary to use bioactive additives on condition of inflammation of periodontal tissues. It is correct to prescribe means contain mineral salts and enzymes for stimulation of salivation in these patients [21, 22].

It is known that fluorides exhibit bacteriostatic and bactericidal effects, reduce the viscosity of saliva due to exposure at oral mucins. The known facts about the direct connection of the level of fluoride and the level of sIgA in the oral liquid [21, 23].

Enzymes in hygienic products (lysozyme, lactoperoxidase, lactoferrin) actively dissolve the organic matrix of microbial biofilm, have antimicrobial, antiviral, bactericidal effects. Numerous studies have shown a decrease of amount of plaque and reduced inflammation of periodontal tissues from the influence of these enzymes [24].

Complex mineral salts in hygiene products provide normalization of metabolic processes and stimulate salivation. Bioactive additives exhibit anti-inflammatory, keratoplastic effects. They stimulate metabolic processes in periodontal tissues and reduce bleeding gums. These are medicinal plant extracts, vitamins and microelements in the composition of dental hygiene products [24].

During professional hygiene it is necessary to use such means and tools that can provide a qualitative cleansing effect and, at the same time, could not damage the enamel of the tooth. There are contraindications to the use of some methods, instruments or apparatus in children with concomitant pathology. The use of air-abrasive systems in professional oral hygiene has a contraindica-

tion in these patients. Also limited use of professional pastes with a high degree of abrasiveness due to the tendency to osteoporosis in these children [10]. The same reason could limit the appointment of an electric toothbrush for patients with CF.

The aim of the study was to determine the initial level of oral hygiene in children with CF and after 3 months of professional and home-based hygiene measures and to select dental hygiene products that active towards factors that affect plaque in CF patients.

2. Materials and methods

To achieve this goal a clinical dental examination of 24 children aged 3–17 years with a confirmed diagnosis of CF were conducted in Kharkiv Regional Children's Clinical Hospital №1, Kharkiv, Ukraine, during 2016-2018. Oral care education and individual selection of hygiene products and methods and professional oral hygiene were carried out in this group.

Children were not divided by age groups. An assessment of initial oral hygiene and after 3 months was carried out.

The hygienic index OHI-S (J. C. Green, J. R. Wermillion, 1964) was used to determine the state of hygiene of the oral cavity. The criteria for interpreting the index were “good”, “satisfactory”, “unsatisfactory” and “bad” hygiene.

The study was conducted in accordance with the requirements of the Council of Europe Convention on Human Rights and Biomedicine, the Helsinki Declaration of the World Medical Association and approved by the local ethics committee of the Kharkiv National Medical University (protocol No. 6, from 01.06.2016). All patients signed informed consent for participating in the clinical study.

The data were analyzed using Student's criterions. Statistical analysis of the results was performed using generally accepted statistical methods the calculation of the arithmetic mean (M) and average error (m).

3. Results

During the clinical observing, we found a significant prevalence of dense biofilm with enhanced adhesive properties. Children and their parents said that they could not remove all the plaque themselves while was cleaning their teeth (**Fig. 1**).



Fig. 1. Dental plaque in children with cystic fibrosis at the first examination

The level of hygiene of the oral cavity was unsatisfactory among patients ($OHI-S=2.19\pm0.11$). The index in 4 children (16.7 %) was estimated as “satisfactory” hygiene, in 13 children (54.2 %) as “unsatisfactory” and as “bad” hygiene in 7 (29.1 %) children. “Good” hygiene of the oral cavity was not defined in the group.

The training of hygienic care of the oral cavity and individual selection of hygiene products had been carrying out. We prescribed toothpastes containing xylitol, plant enzymes, phosphorus, magnesium and lysozyme for daily care. In addition, the using of mouthwash, containing calcium lactate, lactoperoxidase, lactoferrin was prescribed.

In the dental office, circular brushes that have little friction and rubber cups were used to remove the plaque. We used abrasive low-dispersion fluoride paste (RDA 27) to clean and to polish the surfaces of the teeth. Then a gel with chlorhexidine and betaine to prevent the formation

of biofilm on the enamel of teeth and to ensure the water balance of the mucous membrane was prescribed for 7–10 days.

An oral hygiene assessment was performed after 3 months. Hygienic habits and skills obtained after training were tested. The analysis showed the value of the index OHI-S=1.27±0.46 had a significant difference ($p<0.01$) in relation to the initial data. Interpretation of the index: in 6 children (25 %) was “good” hygiene, in 16 children (66.7 %) – as “satisfactory” and “unsatisfactory” hygiene in 2 (8.3 %) children, mostly younger. “Bad” oral hygiene was not registered.

4. Discussion

The obtained data are clearly showing that cystic fibrosis patients have different factors that affect caries, gingivitis or another oral pathology. According to known data, it is believed that somatic disease and caused by it secondary pathology affects the health of the oral cavity. Similar trend was found at the presence of enamel defects, dental caries, dental hygiene and plaque in children with CF [25, 26].

With insufficient hygiene, the secretion of saliva decreases, the protective mechanisms weaken, the evacuation of bacteria is impaired [27]. Frequent intake of high-calorie carbohydrate food contributes to the formation of an exopolysaccharide matrix on the teeth surfaces. This promotes microbial biofilm formation. In conditions of poor hygiene, the critical mass of microorganisms increases, which is the starting point of pathological processes in the oral cavity [28].

We have found up that individual selection of hygiene products and methods should have performed taking into account the certain changes in the oral cavity's status. The presence of a dense microbial dental biofilm – an important hygiene level factor – requires the use of fluoride-containing agents, enzymes, antiseptics, chlorhexidine and betaine. Inflammation of periodontal tissues requires the inclusion of bioactive additives in this list. It is advisable to use agents containing mineral salts and enzymes to stimulate salivation.

So, CF patients need training and correction of oral hygiene skills, the right pathogenically sound choice of oral hygiene products.

Study limitations. Such studies are not invasive and could be limited by the reluctance of patient-physician collaboration. In addition, the limitations of our study were related to the age of children and their ability to adopt hygiene skills. It is known that some oral hygiene indices cannot be applied in young children. Also, the composition of oral hygiene products for young and older children is different. Thus, we excluded children under 3 years old from the study in order to unify the research design. However, the issue of oral hygiene in the youngest children with cystic fibrosis has not yet been investigated and has a certain scientific interest.

Prospects for further research. Teaching children to brush their teeth can reduce tooth plaque in the short term. Thanks to the data obtained, it becomes necessary to develop individual schemes of prevention of the oral cavity diseases in children with cystic fibrosis, taking into account the age, concomitant pathology, etc.

5. Conclusions

This study has shown the low level of oral hygiene in children with CF. These patients rarely pay attention to oral hygiene due to the complicated treatment of CF.

Hygienic education and motivation in CF patients are important starting points for the treatment and prevention of dental diseases and could help them achieve a higher level of oral health knowledge.

Hygiene products for daily care for CF patients should be selected to taking into account the manifestation of the pathogenesis of somatic disease and should consist xylitol, plant enzymes, microelements, immunomodulating and saliva enhancing components. The dentists should use means and methods that are not contraindicate in patients of this category.

It is recommended to monitor the hygiene indices to establish the effectiveness of the measures and necessity for individually therapy correction.

Conflict of interests

The authors declare that they have no conflicts of interest.

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MODERN ASPECTS OF THE PROBLEM OF FRACTURES OF THE PROXIMAL FEMUR

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Abstract

The purpose of the study is to study the current global clinical and epidemiological features of proximal hip fractures and the risks of their development and spread. The paper identifies the main aspects of the spread and treatment of fractures of the proximal femur; main world modern epidemiological characteristics of hip fractures and levels of risks of their development and spread. The relationship between comorbidities in patients with proximal hip fractures and the risk of various treatment complications is shown. The main types of treatment tactics are identified, the groups of the most common comorbidities in such patients are given. As a result of the work it was established: the percentage of fractures of the proximal thigh is 9.00–45.00 % among all skeletal fractures in the older age group and among all age categories – 17.00–24.00 %; global annual morbidity is 1.7 million people, and mortality – 11.00–23.00 % in 6 months and 22.00–29.00 % in a year; increase in the frequency of these fractures with age with doubling after 50 years every ten years; average age of patients – 75–79 years; predominance of women over men in 2–3 times; the lowest annual age-standardized cases among women are in Nigeria, South Africa, Tunisia and Ecuador, and the highest are in Denmark, Norway, Sweden and Austria, which is also typical for men; significant economic burden of treatment and high levels of fractures with osteoporosis, cardiovascular disease, diabetes, chronic obstructive pulmonary disease and more; the advantage of surgical treatment over conservative.

Keywords: comorbidities, proximal hip fractures, hip fractures, mortality, prevalence, risks of the development of fractures.

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1. Introduction

Recently, among the adult and child population of the entire world community, there has been a stable negative dynamics of high levels of injuries without any tendency to reduce them. In addition, there is a steady increase in the incidence of musculoskeletal system, which, along with high levels of injuries, causes their significant medical, social and economic consequences. Medico-social significance of high levels of injuries and diseases of the musculoskeletal system is determined by their high prevalence, negative trends in primary morbidity and disability, large direct and indirect economic losses, high rates of decline in quality of life, increase in the DALY index and other reasons which are considered one of the main structural components of the so-called «burden of disease». The medical and social significance of this pathology is also confirmed by the fact that injuries and diseases of the musculoskeletal system cause the greatest socio-economic losses, as people with high employment potential (young and middle age) have a leading level of disability due to trauma.

According to most world researchers, despite significant advances in modern science and practical health care, injuries and diseases of the musculoskeletal system still remain one of the main causes of high levels of both temporary and permanent disability and mortality throughout the world community. These diseases consistently occupy leading positions among the main causes of primary disability of the population, leaving only cardiovascular pathology and oncological nosology and annually account for about 7.00–8.00 % of the total number of persons first recognized as disabled.

Therefore, the aim of our study was to study the world's current clinical and epidemiological characteristics of fractures of the proximal femur and the risks of their development and spread.

2. Clinical and epidemiological characteristics of fractures of the proximal femur

Fractures of the proximal femur are currently one of the most common types of fractures [1, 2] and are in third place among the most common types of fractures [3]. According to epidemiological data, fractures of the femur have higher levels of prevalence in Northern Europe and the United States and lower – in Africa and South America, and Asian countries have average levels [4]. In recent decades, there has been a stabilization of the prevalence of femoral fractures in economically developed countries [5] and an increase in Asian countries [6].

According to various data, such fractures currently make from 9.00 to 45.00 % [7] in the structure of all skeletal fractures among patients of older age groups [8], and among all persons are 17.00–24.00 % of all fractures. The global annual incidence is about 1.7 million people, and by 2050 their number is projected to reach 6 million 260 thousand per year [6]. Given that the average age of the world's population is increasing significantly, the number of hip fractures is projected to triple over the next 50 years. Other projections suggest an increase in the burden of femoral fractures due to the steady increase in life expectancy [9] to 319 million global fractures by 2040 [10].

These fractures are reported to be associated with significant mortality and disability rates. Mortality due to them reaches 11.00–23.00 % in 6 months and up to 22.00–29.00 % in the first year, and disability is estimated at 5964 DALI per 1000 people [10]. Caring for such patients is a serious global economic burden [11].

Numerous epidemiological studies have confirmed that the incidence of proximal femoral fractures increases significantly with age [12] and doubles every ten years after the age of 50. It has been found that the average age of patients with hip fractures increases by one year every five years [13]. More than 50.00 % with damage to this localization are over 60 years old [14]. It is noted that among females of older age groups the frequency of these fractures is 2–3 times higher compared to men (about 60.00–70.00 %) [15]. According to other studies, at the age of 70–80 years, the frequency of these fractures reaches 1000–1200 cases per 100 thousand women and 300–400 per 100 thousand men. It is indicated that the majority of these patients are elderly and senile – the average age of treated patients with this type of fracture is 75–79 years. Fractures of the proximal thigh are three times more common at the age of 80–89 years compared with 65–69 years. Among people of this age group, fractures of the femoral neck are third after fractures of the radial and humerus. It is noted that the increase in age characteristics entails an increase in the frequency of these fractures: at the age of 50 the risk of fracture of the proximal thigh is 1.80 %; in 60 years – 4.00 %, in 70 – 18.00 %, and in 90 – already 24.00 %. At the same time, the risk of developing fractures of the proximal femur throughout life among men is about 6.00 %, and among women twice as high – 18.00 %; and from the age of 50 the risks for men are about 11.00 % and for women – 23.00 %.

Among all fractures of the proximal femur, spinal and cervical fractures account for almost 90.00 % [16]. The fracture of the femoral neck is much more common: 75.30–80.20 % against 19.80–24.70 % of spinal fractures.

It has been proven that the most common cause of hip fractures is osteoporotic bone changes [17]. The prevalence of osteoporotic femoral fractures worldwide is about 1.66 million cases each year [18]. Among European countries, their number reaches 400 thousand annually, and Asian countries account for about 30.00 % of fractures. World prevalence of osteoporotic hip fractures is recorded at 20.00 % of all osteoporotic fractures [19]. According to many WHO studies, osteoporotic fractures of the proximal femur are the leading causes of premature death in women, along with coronary heart disease, endometrial and breast cancer. Studies have shown a link between the share of health care spending in many countries around the world on osteoporosis (from 0.7 % in Luxembourg to 5.2 % in Cyprus) and the incidence of osteoporotic fractures [20]. It is stated that the levels of fractures of the femur are defined by many scientists as an international burden of osteoporosis, as they account for a significant amount of financial costs associated with fractures of most countries in the health sector due to high levels of disability and mortality among men and women aged 50 years and older [21].

2. 1. Risk levels of fractures of the proximal thigh

According to studies conducted using the Medline OVID study among 63 countries, there was a significant heterogeneity in the risk of femoral fracture [22]. For the purpose of mapping, the frequency of hip fractures was determined using color coding according to the risk categories marked as significant level of risk, medium level or low level (marked in red, orange or green, respectively) (Table 1) [22].

Among women, the lowest annual standardized age cases were found in Nigeria (only two cases per 100,000), South Africa (only 20 cases), Tunisia (58 in total) and Ecuador (73 cases). The highest levels were recorded in Denmark (574 cases per 100,000), Norway (563 cases), Sweden (539 cases)

and Austria (501) (**Fig. 1**) [22]. The low estimates obtained from Nigeria and South Africa were due to the poor quality and antiquity of the study.

Table 1

Color coding

Color category	Risk	Incidence per 100,000			FRAX risk of occurrence (%)	
		women	men	women and men	men	women
Red	high	more than 300	150 and more	more than 250	more than 15	more than 15
Orange	medium	from 200 to 300	from 100 to 150	from 150 to 250	from 10 to 15	from 10 to 15
Green	low	less than 200	less than 100	less than 150	less than 10	less than 10

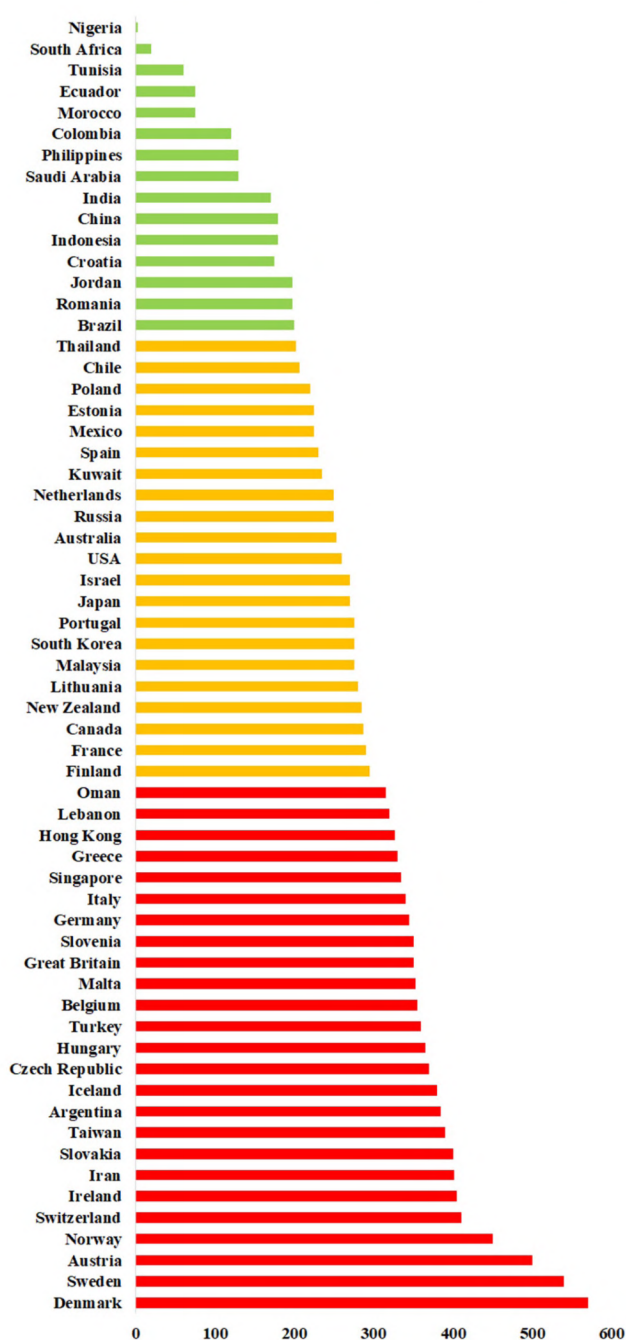


Fig. 1. Age-standardized annual level of hip fractures in women (per 100,000) depending on color coding

For men the standardized age of hip fractures in world countries was about twice lower than for women (**Fig. 2**) [22]. It is noted that in countries where higher values were noted among the female population, higher rates were observed among the male population and vice versa. Not taking into account the results obtained from Africa, the highest annual levels of this disease among the male population were found in Denmark (290 cases per 100,000 population) and the lowest in Ecuador (only 35 cases per 100,000 population).

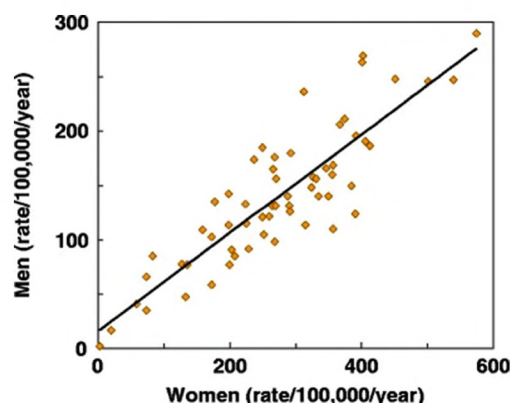


Fig. 2. World standardized rates of hip fractures (per 100,000/year) in men compared to women

As for the risk of fracture of the femur, these studies have identified many high-risk regions mapped from North-Western Europe (Finland, Denmark, Sweden, Ireland, Iceland and Norway) east to Russia and down to borders of Central Europe (Austria, Germany, Belgium and Switzerland) and then in the southwest (Czech Republic, Hungary, Greece and Slovakia) and further to Kuwait, Oman, Iran. Other countries with high levels of risk for men were Japan, Singapore, Korea, Malta and Taiwan. Regions with moderate levels of risk for the male population included India and China, Oceania and Argentina, and North America. Countries with a low risk of hip fractures in men included Latin America (with the exception of Saudi Arabia, Argentina, the Iberian Peninsula and Africa, and two Southeast Asian countries (Thailand and Indonesia)) (**Table 2**) [22].

For the female cohort, a similar men picture of the distribution of the risk of fractures of the femur was recorded. A significant difference was observed only for the Russian Federation, where the risk for women was moderate. In addition, a number of countries with high levels of risk of developing the disease among European countries were more cohesive and ranged from North-Western Europe (UK, Denmark, Iceland, Ireland, Norway and Sweden) to Central Europe (Austria, Belgium, Switzerland, Germany and Italy) and later to the south-west (Slovenia, the Czech Republic, Slovakia, Hungary and Greece) and extended to Iran, Oman and Lebanon. Other countries with high levels of risk for women included Taiwan, Singapore, Malta and Hong Kong. Regions with a moderate risk of developing the disease included the Russian Federation, Oceania, North America and southern Latin America. Low-risk regions included northern Africa and Saudi Arabia, Jordan and Latin America, China, Indonesia, India and the Philippines. It is noteworthy that among European countries, most were classified as high-risk or moderate. Low levels of risk were noted only in Romania and Croatia (**Table 2**) [22].

Table 2

World standardized by age indicators of hip fracture (per 100,000) and its risk categories

Country	Level	Women	Risk	Men	Risk	Women+Men	Risk
1	2	3	4	5	6	7	8
Australia	N	252	M	105	M	183	M
Austria	N	501	H	246	H	380	H
Argentina	R	390	H	124	M	264	H
Belgium	N	356	H	169	H	268	H

Continuation of Table 2

1	2	3	4	5	6	7	8
Brazil	R	199	L	77	L	141	L
The UK	R	349	H	140	M	250	M
Venezuela	R	150	L	45	L	100	L
Hong Kong	N	324	H	148	M	240	M
Greece	R	326	H	158	H	247	M
Denmark	N	574	H	290	H	439	H
Ecuador	N	73	L	35	L	55	L
Estonia	R	225	M	-		-	-
Israel	R	265	M	131	M	201	M
India	R	159	L	109	M	135	L
Indonesia	R	173	L	59	L	119	L
Iran	R	402	H	269	H	339	H
Ireland	N	406	H	191	H	304	H
Iceland	N	385	H	150	H	273	H
Spain	R	228	M	92	L	164	M
Italy	N	334	H	140	M	242	M
Jordan	N	198	L	114	M	158	M
Canada	N	290	M	131	M	215	H
China	R	173	L	103	M	140	L
Columbia	R	127	L	78	L	104	L
Kuwait	R	236	M	174	H	207	M
Lithuania	N	270	M	156	H	216	M
Lebanon	N	310	H	114	M	196	M
Malaysia	R	269	M	114	M	205	M
Malta	N	355	H	160	H	263	H
Morocco	R	73	L	66	L	69	L
Mexico	N	225	M	115	M	173	M
Nigeria	R	2	L	2	L	2	L
the Netherlands	N	249	M	121	M	188	M
Germany	N	346	H	166	H	261	H
New Zealand	N	288	M	140	M	218	M
Norway	R	563	H	262	H	420	H
Oman	R	312	H	236	H	276	H
South Africa	R	20	L	17	L	19	L
South Korea	N	268	M	176	H	224	M
Poland	R	224	M	133	M	181	M
Portugal	N	268	M	98	L	188	M
Russia	R	249	M	185	H	219	M
Romania	N	198	L	142	M	172	M
Saudi Arabia	R	135	L	77	L	107	L
Serbia	R	184	L	88	L	139	L
Singapore	N	331	H	156	H	248	M

Continuation of Table 2

1	2	3	4	5	6	7	8
Slovakia	N	401	H	263	H	335	H
Slovenia	N	349	H	-	-	-	-
The USA	N	260	M	122	M	195	M
Thailand	R	203	M	91	L	150	M
Taiwan	N	392	H	196	H	299	H
Tunisia	N	58	L	41	L	50	L
Turkey	N	357	H	110	M	240	M
Hungary	N	367	H	206	H	291	H
The Philippines	N	133	L	48	L	93	L
Finland	N	293	M	180	H	239	M
France	N	291	M	126	M	212	M
Croatia	R	177	L	135	M	157	M
Czech Republic	N	374	H	211	H	297	H
Chile	N	207	M	85	L	149	L
Switzerland	N	413	H	186	H	306	H
Sweden	R	539	H	247	H	401	H
Japan	N	266	M	165	H	218	M

Note: risks – H – high; M – medium; L – low; levels – N – national; R – regional

Mapping the risks of hip fractures is given in Fig. 3–5 [22].

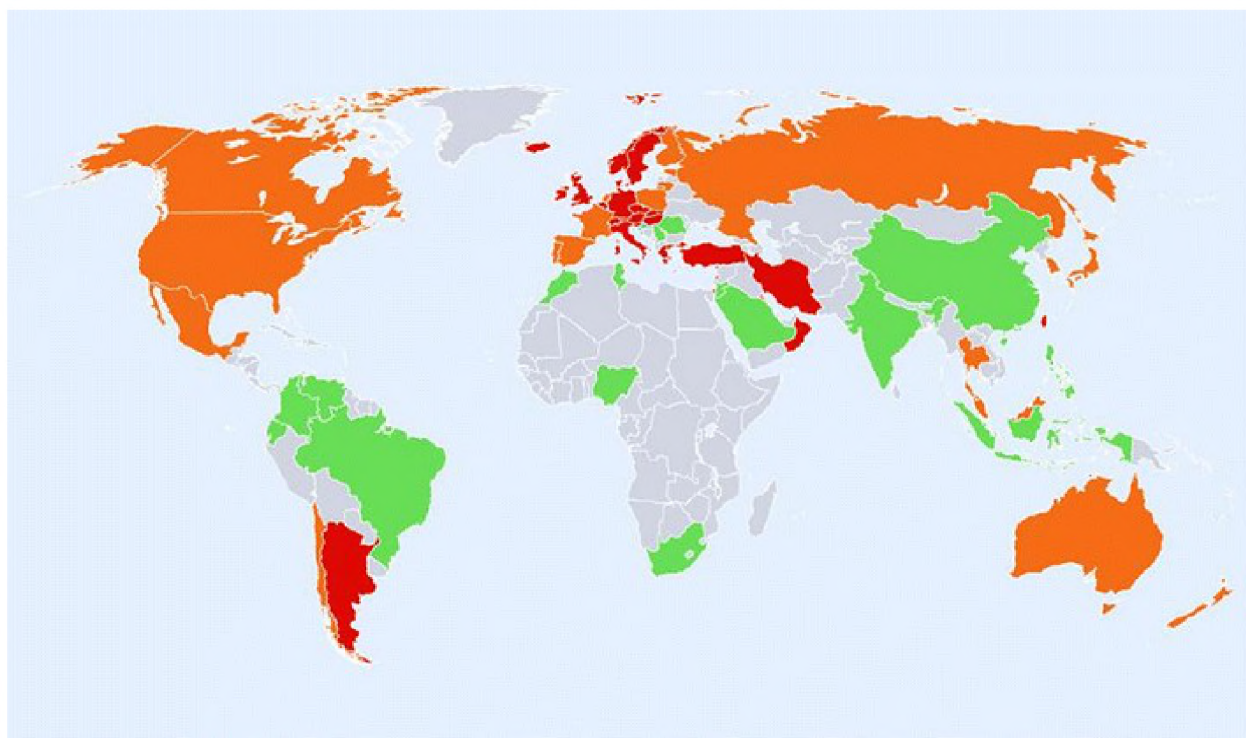


Fig. 3. Frequency of fractures of the femur in women in different countries of the world with a breakdown by risk (red – annual incidence >300/100000, orange – 200–300/100000, green – <200/100000).

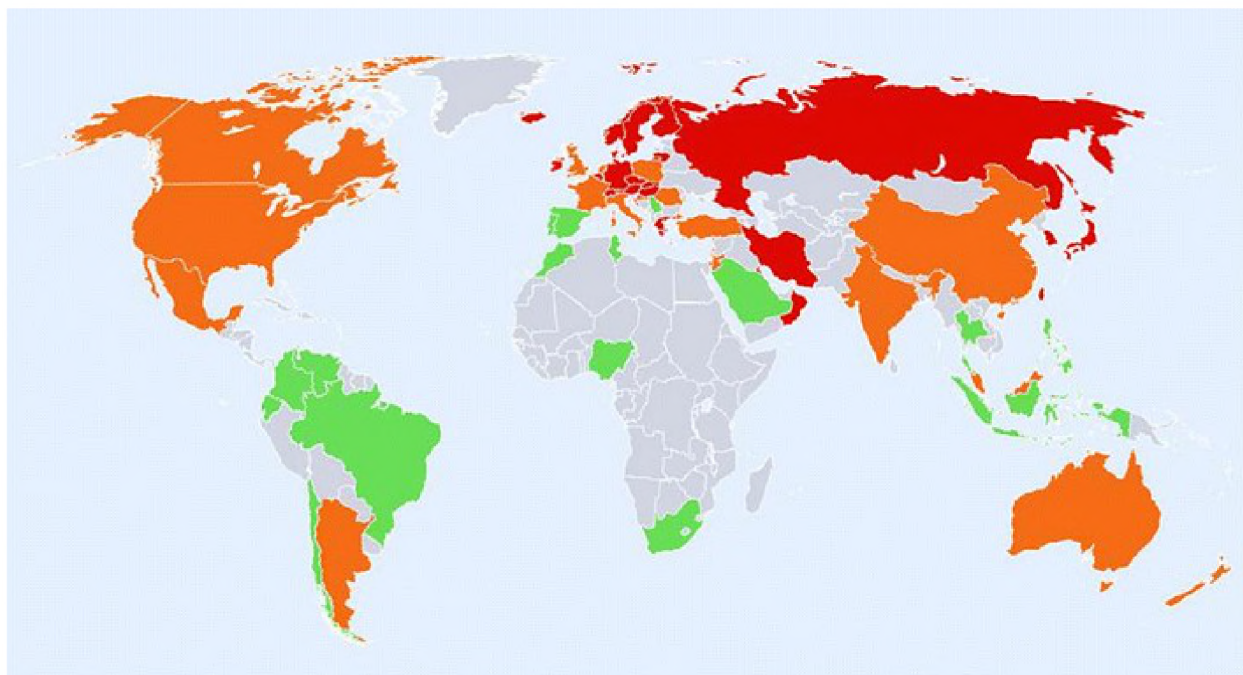


Fig. 4. Frequency of fractures of the femur in men in different countries of the world with a breakdown by risk (red – annual incidence $>150/100000$, orange – $100-150/100000$, green – $<100/100000$)

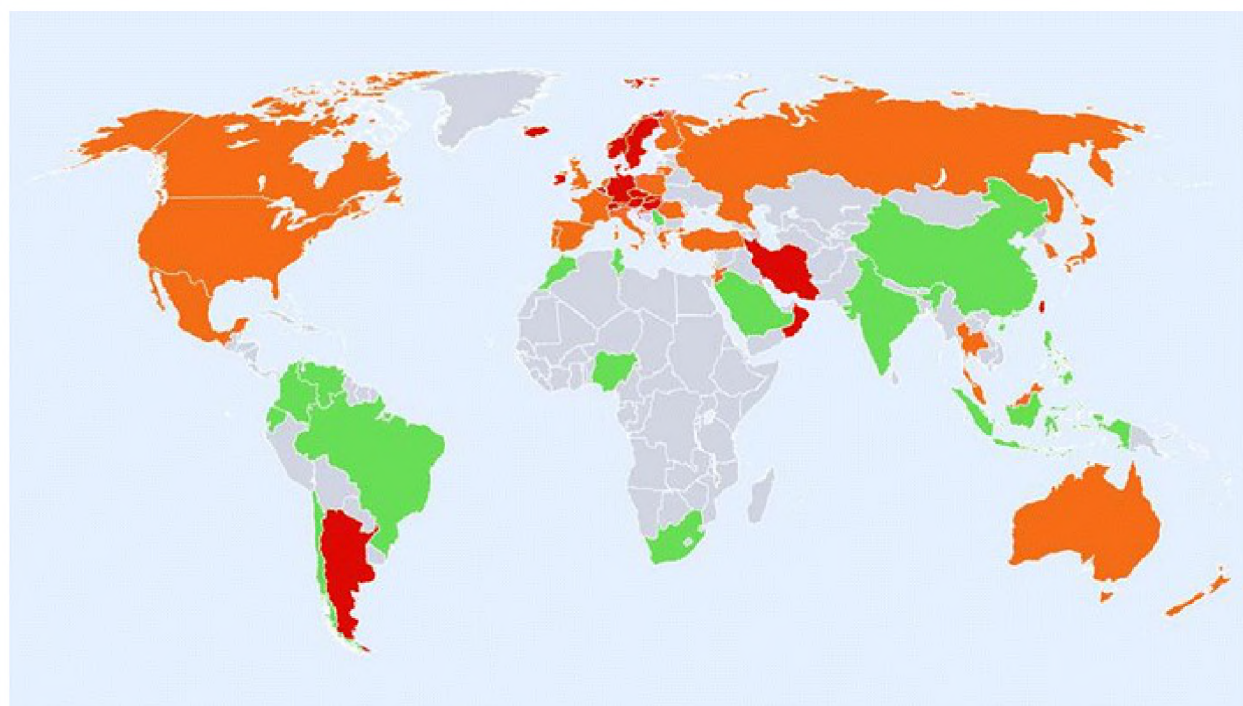


Fig. 5. Frequency of fractures of the femur in women and men in different countries of the world with a breakdown by risk (red – annual incidence $>250/100000$, orange – $150-250/100000$, green – $<150/100000$)

2. 2. The economic burden of treating fractures of the proximal thigh

In addition, many studies indicate a significant financial cost for the treatment of fractures of the proximal femur [23] due to the predominance of patients with reduced functional status and the presence of a significant number of comorbidities [12], so the treatment of such patients in most

cases require a long stay in hospital, a significant rehabilitation period and a complex individual comprehensive treatment program [24]. The presence of concomitant pathology significantly increases the risk of adverse treatment outcomes [25]. Because of this, many world clinics involve an interdisciplinary team in the treatment of such patients [26], which includes specialists in several medical fields (orthopedics, surgery, therapy, anesthesiology, rehabilitation, geriatrics, psychiatry and psychotherapy, neurology, social medicine, etc.). [27].

Thus, according to studies in the UK, about 70.00 % of such patients are admitted to the hospital with indicators of physical condition ASA 3–4; 35.00 % of them have one concomitant pathology, 17.00 % – two, and 7.00 % three or more [28]. Among the most common comorbidities were cardiovascular (35.00 %), respiratory (14.00 %), cerebrovascular (13.00 %), diabetes (9.00 %), malignant neoplasms (8.00 %) and renal insufficiency (3.00 %). Indicators of existing concomitant pathology of varying severity of most patients with such fractures in Ukraine reach 60.00–100.00 % and include in most cases cardiovascular (90.00 %) and bronchopulmonary (20.00–26.00 %) diseases. The vast majority of patients have two or more comorbidities.

The treatment of such patients according to research is quite high: in the UK from 9429 pounds (about 10896 euros) to 14435 (16681 euros) [29]; and in the United States, about \$ 40,000 in the first year after the fracture (direct medical expenses) and almost \$ 5,000 in subsequent years (rehabilitation, etc.) [30]. In total, the United Kingdom spends about £ 2 billion annually on proximal hip fractures (including medical and social care) at a stationary cost of £ 0.785 billion [26], and the United States spends more than \$ 10 billion [31].

2. 3. Relationship between functional status and treatment results of proximal hip fractures

The choice of the necessary tactics of surgical intervention in the treatment of fractures of the proximal femur is made taking into account the age of the patient and the presence of concomitant pathology, which is exacerbated by injury and long-term treatment and rehabilitation. Many authors point to a significant risk of developing a wide range of postoperative complications in patients with concomitant severe somatic diseases. At the same time practicing traumatologists state that the necessary correction of concomitant pathology during surgery in patients with fractures of the proximal femur is associated with a forced significant period of immobilization (prolonged bed rest, skeletal traction, derotation immobilization may be another), even more dangerous complications (especially against the background of existing comorbidities) in the form of circulatory disorders in the femoral head with the development of aseptic necrosis, bedsores, hypostatic pneumonia, various thromboembolic complications and other disorders. In this regard, the set of existing comorbidities in general determines the choice of a mechanism of surgery (osteosynthesis and endoprosthesis).

At the moment, clear data have already been collected on the impact of comorbidities on the development of fractures and the risks of adverse treatment outcomes. Thus, high correlations between the general mechanisms of osteoporosis (which is a factor in the increased risk of fracture) and cardiovascular disease have been identified. Other studies have found an increased risk of femoral fractures in patients with diabetes mellitus and its complications that contribute to bone damage; as the interaction of bone tissue and insulin are key factors in the development of osteoporotic bone lesions. A high incidence of osteopenia and osteoporosis in patients with chronic obstructive pulmonary disease has been established. Comorbidity of osteoporosis and Alzheimer's disease, scleroderma and other diseases has also been established.

Studies of the structure of comorbidity in patients with fractures of the femoral neck on the background of osteoporosis indicate the predominance of cardiovascular diseases: coronary heart disease, hypertension, arrhythmias (which lead to chronic heart failure), and vascular diseases of the central nervous system. It is noted that comorbidities can be significantly exacerbated by traumatic injuries and stress, thereby significantly increasing the risk of surgical treatment. Congestive heart failure, chronic obstructive pulmonary disease, diabetes, malignancies and other comorbidities significantly increase the risk of death after fracture of the femoral neck.

According to many systematic reviews and meta-analyzes, the presence of comorbidities along with age, type of injury, sex, preoperative activity, physical status, cognitive impairment is a predictor associated with high rates of postoperative mortality in the treatment of proximal fractures. In this regard, a significant (and in most cases the main) influence on the choice of treatment tactics for this type of fracture has the presence of concomitant injuries and somatic pathology, the general somatic and mental status of the patient (as fractures of the femoral neck are most common in elderly patients and old age, and most people (65.00 % to 100.00 %) 60 years and older suffer from at least one (or more) concomitant chronic diseases, ie almost all elderly and senile patients with fractures of the femoral neck have a significant burdened somatic status).

Many authors indicate that the presence of concomitant somatic pathology plays a significant role in determining the timing of surgery and the period of rehabilitation postoperative recovery of such patients. Yes, Michel J. P. et al. (2002) identified the possibility of predicting the development of fatalities after surgery in the treatment of fractures of the femoral neck on the basis of the ASA classification. It was found that in operated patients of elderly and senile age (mean age 82.4 years) with trauma of the proximal femur with significant concomitant somatic disorders (ASA III and ASA IV) mortality rates in the first year were 9 times higher in compared with operated patients with less severe comorbidities (ASA I and ASA II). A retrospective analysis of other studies of surgical treatment of femoral neck fractures (Sexson SR and Lehner J. (1987)) revealed that in more physically «healthy» (had 1 or 2 concomitant somatic diseases) patients annual survival rates were significantly higher when fixing the fracture within 24 hours after injury in comparison with those patients in whom surgery was performed without the necessary stabilization of concomitant 3 or more somatic diseases. Moran C. G. et al. (2005) in the treatment of patients 60 years and older with fractures of the femoral neck established the following levels of overall postoperative mortality: 9.00 % – within 30 days, 19.00 % – 90 days and 30.00 % – 1 year and indicated that patients in the presence of significant concomitant somatic disorders (due to which surgery was postponed) stated an increase in the risk of death by 2.5 times within 30 days.

2. 4. Treatment of patients with fractures of the proximal thigh

The selection of tactics for the treatment of patients with fractures of the proximal thigh in recent years is a very serious issue [3]. Previously, the main method of treatment was conservative, which was determined by the use of skeletal traction. The results of such treatment were not considered satisfactory due to significantly high levels of burden. Most patients became significantly weaker due to prolonged skeletal traction, their condition was aggravated by muscular malnutrition and joint contracture and the intensification of comorbidities. The majority of authors at conservative treatment note development at 65.00 % of bedsores, at 23.00 % – hypostatic pneumonia, and at 18.00 % – a thrombosis of deep veins with statement of mortality rates during the first year from 33.70 % to 71.00 %.

Therefore, world practice has long recognized the advantage and significant effectiveness of the surgical method of treatment of such fractures over conservative. The use of conservative treatment is possible only in unplaced fractures or in the presence of severe comorbidities (acute myocardial infarction, acute cerebrovascular accident, acute pneumonia, acute surgical disease, severe mental disorders, etc.).

The choice of one or another surgical tactic for the treatment of femoral neck fractures has also caused considerable controversy among the medical community in recent decades [32]. Thus, osteosynthesis with internal fixation of a screw or pin is used for fractures without displacement or with minimal displacement [32], while primary arthroplasty is proposed for displaced fractures [18]. Meta-analyzes of existing world studies indicate that arthroplasty shows slightly better results compared to internal screw fixation [18]. Different methods of fixation also show different results: for example, the dynamic hip screw (DHS) has found slightly better treatment rates over many years; although the use of intramedullary osteosynthesis with blocked nails (IMN) [12] (including the mini-invasive technique of osteosynthesis with the PFN nail) also

noted quite good treatment results [3]. The choice of one or another tactic of surgical treatment has been developed by scientists for many years [33] and noted the advantages of slanted metal osteosynthesis by dynamic femoral system DHS or intramedullary fixation of PFN in different types of fractures, although research in this area is still conducted today.

It should be noted that despite the significant list of surgical techniques used and available modern implants [34], the frequency of complications and unsatisfactory results of surgical treatment is still quite high [35] and according to various data up to 30.00 %. Mortality after surgical treatment during the first year after fracture in different regions ranges from 30.80% to 35.10% [36], and among those patients who survived 78.00 % after a year and 65.00 % through two need outside care. Other studies indicate that only 40.00 % of patients fully recover their preoperative functional level, and 20.00 % of operated patients require long-term care [37]. Studies also confirm the presence of negative long-term consequences (mortality 10 years after fracture) [38], although other studies have shown a moderate increase in mortality over the long term [39]. Of particular importance is the inpatient mortality of victims, which according to various estimates ranges from 0.00 to 14.00 %, due to different diagnostic and therapeutic approaches [28].

Thus, it should be noted that fractures of the proximal femur is a very common disease (especially among the elderly and senile), which has high levels of adverse effects and is characterized by the need for significant costs for treatment and rehabilitation, which leads to significant medical and social significance. A significant proportion of patients with these types of fractures are characterized by the presence of many comorbidities and low functional levels. The presence of significant comorbidities in patients with fractures of the proximal femur is a major factor in the choice of surgical treatment and a significant predictor of increased risk of adverse events. Surgical treatment of this type of fracture must be performed with the necessary correction of the patient's somatic status and taking into account a multidisciplinary approach and the involvement of additional specialists (general practitioners – family medicine, therapists, cardiologists, pool monologues, urologists, psychiatrists and others).

Study limitations. Excessive identification of such fractures (double counting), inaccurate reporting or other coding of fractures, and population-level errors are possible, especially in regional rather than national studies. These constraints at the population level have little effect in explaining global heterogeneity. Another limitation is the possible differences in different countries due to ethnic differences and the fact that in some regions of the world not all cases of hip fractures fall under medical attention.

Prospects for further research. Subsequent clinical studies will be conducted to establish the possibility of predicting the consequences of treatment of hip fractures depending on the medical-epidemiological and anamnestic characteristics of patients. The results of this trial will inform clinical practice.

3. Conclusions

1. According to the results of many studies, it was determined that the percentage of fractures of the proximal thigh is 9.00–45.00 % in the structure of all skeletal fractures in patients of older age groups and among all age groups – 17.00–24.00 % of all fractures. It is stated that the global annual incidence is 1.7 million people, and mortality due to them reaches 11.00–23.00 % in 6 months and 22.00–29.00 % in the first year.

2. According to the literature, the incidence of fractures of the proximal femur increases significantly with age and after the age of 50 doubles every ten years with an increase in the average age of patients by one year every five years. It was determined that the average age of treated patients with this type of fractures is 75–79 years. The predominance of women of older age groups with such fractures over men in 2–3 times was established.

3. Research has shown that among women, the lowest annual standardized age cases are recorded in Nigeria (two cases per 100,000), South Africa (20 cases), Tunisia (58) and Ecuador (73 cases); and the highest – in Denmark (574 cases per 100,000), Norway (563 cases), Sweden (539 cases) and Austria (501). For men, the age-standardized level of hip fractures was twice

lower than for women, and the global prevalence levels in the countries almost corresponded to the female population.

4. According to the literature, a significant economic burden of treatment of fractures of the proximal thigh has been revealed: Great Britain – from 9429 pounds to 14435; US \$ 40,000 (direct medical expenses) and \$ 5,000 (rehabilitation, etc.). It is estimated that the United Kingdom spends about £ 2 billion a year at a stationary cost of \$ 0.785 billion and the United States more than \$ 10 billion a year.

5. High levels of the relationship between proximal hip fracture and osteoporosis, cardiovascular disease, diabetes, chronic obstructive pulmonary disease, Alzheimer's disease, scleroderma and other diseases have been identified.

6. The advantage and significant efficiency of the operative method of treatment of fractures of the proximal thigh over the conservative one was stated. It is determined that the use of conservative treatment is possible only in unplaced fractures or in the presence of severe comorbidities.

Conflicts of interest

The authors declare that they have no conflicts of interest.

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