

Modernization of education in institutions offering vocational education and training at the moment, is connected with the implementation of the competence-based approach. Competence-based approach is focused on a such result of the formation where the determining factor is a combination of knowledge, skills and ability to apply the knowledge in professional practice.

The objectives of the improvement program include the improvement of the knowledge, acquisition of skills, new competencies in this specialty.

The retraining of the specialist begins with methodologically consistent studying of the theoretical foundations of physiotherapy, clinical and physiological justification for the use of methods, systematization of the exercises, drawing physiotherapy techniques, biomechanics of movement, biochemistry of muscle activity and their clinical implementation. The doctors are taught on training medical monitoring methods in sport, rehabilitation, training athletes for the competitions. Lectures cover topical issues of using the new technologies, information and training programs in the rehabilitation process for the acquisition of professional competences.

In the pedagogical process, as a visual material, we use multimedia equipment, electronic control training tests, online resources, methodical textbooks, simulators, training videos, movies, working in the simulation center. At the practical classes, students work out on functional samples in order to obtain the most complete and comprehensive information about the physical development, health assessment, indicators of its physical performance. Then, their learned techniques are put into practice of treating patients at various stages of their rehabilitation.

Based on the theoretical and practical knowledge specialist can provide qualified preventive and rehabilitative care to maintain the health of healthy people and the patients with reduced functional reserves of the body.

The important task is to develop the best methods of independent work. It is carried out in the process of developing and testing the methods of physiotherapy, writing term papers, essays, speeches at physiotherapists, balneologists, physical therapists and sports medicine doctors' Association, devoted the introduction of new technologies into practice; new techniques of using the equipment.

After the familiarization of each section of the program, some kind of control is carried out: a set-off test or a test of practical skills in the specialty.

Thus, as a result of learning, using andragogic learning model, people who have successfully mastered the educational program, acquire professional competence, knowledge, abilities, skills. Students are motivated to achieve the goal of learning and formation of common cultural and professional competence and readiness to work in modern conditions.

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HUMAN ENDOGENOUS RETROVIRUS HERV-E λ 4-1 EXPRESSION IN COXAE ARTHROPLASTIC

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Considering the ability of some retroviruses to activate in result of stress impact and produce proteins that possess immunotrophic characteristics, the objective of this research is to study the possibility of activating human endogenous retrovirus *HERV-E* λ 4-1 as a result of surgery with massive damage of tissue at the example of total replacement of coxae with endoprosthesis, and also study its part in emergence of post-surgical infectious complications among patients with coxae arthrosis during early post-surgical period of coxae endoprosthesis care. As a result of the study, an increase in expression frequency of *HERV-E* λ 4-1 has been revealed during the following 21 days after surgery in mononuclear blood cells among patients with complicated flow of post-surgical period depending on expression of system inflammatory reaction. Correlation dependence between development of infectious post-surgical complications and expression of *HERV-E* λ 4-1 during post-surgical period.

Introduction. An increase in number of patients with pathologies of coxae (CP) is an urgent problem of modern medicine that is defines by an increase in part of aged population [22]. Arthroplasty of CP is an efficient method of treating this pathology that provides an improvement in life quality of patients, so, decrease in number of post-surgical complications after arthroplasty is important for efficient reproduction of the joint function.

Prosthetics of CP is a major surgery that goes along with local and system alterations in immunologic state in early post-surgical period, specifically

increase in production of IL-1 β , IL-6, IL-8, TNF- α , C3a component of compliment, decrease in production of LI-10 [6, 17]. Infectious complications are one of major causes of a prosthesis' incompleteness, according to our data [21], they emerge in 1–3 % of all cases of total coxae replacement surgery, therefore, prevention and early diagnosis of them are significant factors of restoring the function of joint. In order to predict possibility of emergence of infectious complications, level of C-reactive protein and erythrocytes' sedimentation speed are used as well as study of anamnesis, physical and roentgenologic inspection, study of joint liquid, and a number of serological tests are used nowadays [24]. However, these indexes are not specific enough, and they correspond to reference values in case of presence of paraprosthesis infection in 3 % of cases. On the other hand, increased level of C-reactive protein and erythrocyte sedimentation speed correlates with presence paraprosthesis infection only in 87 % of cases [11]. Therefore, development of minimally-invasive, informative, and specific method of predicting risk post-surgical infectious complications is an urgent problem of arthroplasty.

Endogenous retroviruses (ER) emerged in genome of the spinal as a result of infecting embryonic cells at early stages of development with exogenous retroviruses, and they represent their provirus form that is always present in genome [2, 15]. ER inherit according to laws of Mendel, and form about 8 % of human genome [12]. Expression of ER is regulated at different levels – at the level of various stress signals (damage of tissue, superinfection, factors of the environment, hormonal alterations), epigenetic state of genome, intracellular factors of transcription, splicing mechanism [4, 14, 16]. Regular elements, localized in U3 region of 5'LTR, carry out key part in control of ER expression [7]. Intracellular factors of transcription are modulated by stress factors that cause ER expression and, sometimes, synthesis of virus proteins that possess immunomodulating characteristics [9, 14, 20].

According to bibliographic data and also the received results, human ER of class I *HERV-E* λ 4-1 associates with a number of autoimmune diseases – system butterfly disease, expand sclerosis, rheumatoid arthritis, and frequency and level of its expression in mononuclear blood cells of patients correlates with a disease activity [8, 10, 20, 25]. This ER is replicably-competent and able to produce proteins, its amino-acid sequence (8,8 kb) contains open frames of read in regions *gag* and *env*. Antibodies to *HERV-E* λ 4-1 in blood serum of healthy individuals are not located [23].

Considering the ability of certain ER to activate in result of stress impacts, and also produce proteins that possess immunotrophic characteristics, the objective of this research is to study the possibility of activating ER λ 4-1 as a result of stress impact, represented by surgery with a massive damage of tissue at the example of total replacement of coxae

with endoprosthesis [6], and also the part of ER λ 4-1 in emergence of infectious complications among patients with coxae arthrosis in early post-surgical period of coxae endoprosthetics.

Materials and methods of research. *Donors and patients:* The study included patients with diagnosis «coxae arthrosis», 3 – of displastic genesis, 3 – post-traumatic, and 26 – idiopathic, 16 men and 16 women in age of 34 to 74 years old, all patients of clinic «Federal state budget institution Novosibirsk scientific-research institute of traumatology and orthopedy of J.L. Tsivian». All patients were delivered to the clinic to carry out surgery of initial endoprosthetic of coxae. Peripheral venous blood of dependently-healthy persons of the number of staff donors (20 men and 12 women in age of 34–56 years old) has been provided by the department of blood transition of the institution. According to modern diagnosis criterions, all patients had initially low level of post-surgical complications' risk [18]. Retrospectively, according to indicator of presence or absence of infectious paraprosthesis complications, patients have been divided into 2 groups: patients with non-complicated flow of post-surgical period, 9 men and 9 women, formed control group; patients, whose post-surgical period was complicated by infectious paraprosthesis maturation, 7 men and 7 women, formed the experimental group. Protocol of research corresponded to ethical standards and was regulated by ethical committee of Federal state budget institution Scientific-research institute of traumatology and orthopedy of J.L. Tsivian in accordance with Helsinki Declaration of Universal association «Ethical principles of carrying out scientific medical researches with participation of human» and its addendums of 2000 and «Ethical principles of carrying out scientific medical researches with participation of human» according to the order of Ministry of healthcare of Russian Federation № 266 (Rules of clinical practice in Russian Federation) dd. 19/06/2003.

Definition of body temperature. Body temperature of the patients has been evaluated in axillary cavity twice a day, at 7 a.m. And 4 p.m. during the whole period of research.

Expression of env gene of human ER HERV-E λ 4-1 has been defined 48 hours before carrying out the surgery and also after day 1, 7, 14, 21 of post-surgical period.

Introduction of mononuclear cells. MNC have been discharged by centrifugation of heparinized venous blood on gradient of ficoll of 1,078 g/cm³ (Lymphocyte separation medium, MP Biomedicals, LLC, Eschwege, Germany).

Revelation of RNA has been carried out via method of phenol extraction [5] with facilitation of test-system VectorsRNA – extraction (Vector-best, Novosibirsk).

Amplification of the received DNA has been carried out on programmed amplifier «Tercik» (DNA – technologies, Moscow) with facilitation of couples

of oligonuclear primers to gene *env ER λ 4-1* [23]. The received cDNA fragments have been analyzed in 2% gel of agarose with addition of 0,00001% of bromide etidium (VectoDNA-EF, Vector-Best, Novosibirsk). Samples with presence of cDNA line in gel that corresponded to the expected size of the amlicon have been considered positive. Products of amplification have been standardized according to β-actine and visualized on densitometer Pharmacia-LKB.

Research design: diagnostic, retrospective, prospective.

Statistical procession of the received data has been carried out with facilitation of application pack STATISTICA v.10.0 (StatSoft Inc, USA). The results are provided as Me (25%; 75%). To estimate statistical significance of differences between qualitative variables, we have used two-side variant of accurate criterion of Fisher, and U-criterion of Mann-Whitney has been used to estimate qualitative variables. Analysis between researches in different terms of post-surgical period has been carried out with facilitation of non-parametrical type of criterion of Newman Keuls for qualitative values, and

Q-criterion of Cochran for qualitative. Differences have been considered reliable if $p < 0,05$.

Results of research and their discussion. Clinically, indicators of deforming arthrosis of coxae have been revealed among patients, included into the research. They displayed in an expressed pain syndrome, limited mobility, limping, shortening of limbs.

Roentgenologically, among all patients we have registered signs of hyperplasia of coxae bone tissue with para-articular ossificates and central wedge-shaped osteophyte that led to external shift of femoral bone head. During the surgery signs of inflammatory alterations such as synovitis, injection of vessels, hyperplasia of joint capsule, synovia, bone tissue. No growth of pathogenic microorganisms has been revealed under bacteriological study of material, taken from the area of surgical wound.

According to the received data of general-clinic laboratory research, no signs of local or system inflammatory process have been revealed among patients by the beginning of the study among all patients (Table 1).

Table 1

Parameters of general-clinic laboratory signs during pre-surgical period (Me(25;75))

Studied parameter	Reference indexes	Control group	Experimental group
Erythrocytes	male 4,5 – 5,0·10 ¹² /l, female 3,9 – 4,7·10 ¹² /l	4,3(4,0; 4,7)	3,9(3,7;4,2)
Hemoglobin	male 130–160 g/l, female 120–140 g/l	139(125; 150)	124,5(118,0;133,0)
Thrombocytes	180–320·10 ⁹ /l	234 (201; 296)	230,0 (196,0; 288,0)
Leukocytes	4,0–9,0·10 ⁹ /l	5,8 (4,8; 6,8)	5,4 (4,6; 7,1)
Stab neutrophils	1–6 %	4,5 (3,0; 7,0)	3,0 (2,0; 5,0)
Segmented neutrophils	47–72 %	57,5 (52,0; 62,0)	56,0 (45,0; 64,0)
Eosinophils	0,5–5 %	3,0 (1,0; 5,0)	3,0 (2,0; 6,0)
Lymphocytes	19–37 %	30,0 (28,0; 37,0)	29,5 (18,0; 34,0)
Monocytes	3–11 %	2,0 (2,0; 4,0)	5,5 (3,0; 6,0)
ESR	male 2–10 mm/hr, female 2–15 mm/hr	13,0 (9,0; 21,0)	19,0 (14; 22,0)
Fibrinogen	2–4 g/l	3,1 (2,6; 3,6)	3,25 (2,9; 4,0)
Leucosytic index of intoxication	0,3–1,5	0,97 (0,35; 1,5)	0,39 (0,3; 0,54)

Note. * – $p < 0,05$, Mann-Whitney U-test for two independent groups; control group $n = 18$; experimental group $n = 14$.

In the group of patients with complicated flow of post-surgical period early complications such as infection of haematoma have been registered among 3 patients on days 4–7. Early deep paraprothestic infectious complications emerged among 11 patients after 14 days of research. Average period of hospitalization for patients with complicated flow of post-surgical period equaled (23 (17; 40) days) and exceeded the corresponding index of the control group (17 (15; 21) days), $p < 0,05$.

Results of studying dynamics of blood temperature in armpit of patients during pre-surgical and post-surgical period are presented in Table 2.

It has been established that patients of the studied groups did not differ according to body temperature. During day 1 of post-surgical period an increase in body temperature took place in control group of patients, and it decreased by the seventh day of the observation and normalized completely by day 14. Among group of patients, whose post-

surgical period was complicated by infectious paraprosthetic aftereffects, increase in body temperature also took place on day 1 after the surgery, and it did not exceed the corresponding value of the control group, but by day 7–14 body temperature of these patients exceeded that of the control group. An increased body temperature preserved up to 21 day of the observation in a number of cases. The

received data of body temperature dynamics as a marker of non-specific system inflammation during post-surgical period correspond to opinions of authors [1, 13] that prove the presence of hyperthermia ($> 38,5^{\circ}\text{C}$) is observed among 15 % of patients during early post-surgical period (day 1–3) of total replacement of coxae and is not linked with emergence of local or system infectious complications.

Table 2

Values of body temperature in armpit, $^{\circ}\text{C}$, Me (25; 75)

Observation period, days	Control group	Experimental group
Before surgery	36,6 (36,6; 36,7)	36,6 (36,5; 36,6)
1	37,4 (37,4; 37,8)**	37,8 (37,5; 38,0)*, **
7	36,7 (36,6; 37,3)**	37,2 (37,1; 37,9)*, **
14	36,6 (36,6; 36,7)	37,4 (37,1; 38,0)*, **
21	–	37,4 (36,7; 37,9)*, **

Note. * – $p < 0,05$, Mann-Whitney U-test for two independent groups; ** – $p < 0,05$, non-parametrical variant of Newman-Keuls Range test; control group $n = 18$; experimental group $n = 14$.

During evaluation of *env ER λ 4-I* expression of the group of conditionally-healthy donors, frequency of this parameter equaled 1/32 (3,1%). The receive data corresponds to results [19] that also testify for revelation of gene *gag ER λ 4-I* in

MNC of donors in certain cases. It is possible that this phenomenon is linked to presence of persistent forms of infections among them. The following data has been received during revelation of *env ER λ 4-I* expression among patients (Table 3):

Table 3

Expression of *env ER λ 4-I* MNC of patients with coxae arthrosis (n , %)

Observation period, days	Control group	Experimental group
До операции	1 (6%)	0 (0%)
1	7 (41%)*, **	14 (100%)*, **
7	2 (12%)*, **	3 (21%)**
14	0 (0%)	7 (50%)*, **
21	–	5 (45%)*, **

Note. * – n (%), comparison of groups – Fisher exact test, two-tailed; ** – dynamics – Cochran Q Test; control group $n = 18$; experimental group $n = 14$.

It has been revealed that expression of *env ER λ 4-I* equals 1/32 (3,1%) before the surgery, and it corresponds to frequency of this value among donors ($p > 0,05$); an increase in frequency of *env ER λ 4-I* expression takes place in control and experimental group of patients during day 1 of post-surgical period. This parameter decreased with a high degree of reliability by the seventh day of research in control group. For the group of patients with high complicated flow of post-surgical period expression of *env ER λ 4-I* exceeds the similar parameter of patients of the control group; by day 7 expression frequency decreases, but then it raises

again by day 14 and preserves up to the 21st day of observation. While estimating dependence between *env ER λ 4-I* and body temperature, we have established a direct correlation between these parameters on day 1 ($R = 0,52$; $p \leq 0,002$), 7 ($R = 0,56$; $p < 0,001$), and 14 ($R = 0,73$; $p < 0,001$ of observation).

During evaluation of dependence of *env ER λ 4-I* expression and emergence of infectious post-surgical complications via correlative analysis using coefficient of ranging correlation of Spearman, relation between these two parameters has been established on the 14th day of observation ($R_s = 0,58$; $p = 0,001$).

Thus, *env ER λ 4-1* expresses among all patients with coxae arthritis who have been exposed to surgery of coxae endoprosthetics on day 1 of post-surgical period; this parameter returns to normal by the 14th day of observation among patients with non-complicated flow of post-surgical period; body temperature and frequency of *env ER λ 4-1* expression of patients with complicated flow of post-surgical period exceed these indicators of patients with non-complicated flow of post-surgical period; expression of *env ER λ 4-1* preserves after day 14 of observation and correlates with frequency of development of post-surgical infectious complications.

It is known that surgical intrusion is followed by system inflammatory reaction with increase in production of pro-inflammatory cytokines – IL-1α, IL-1β, IL-12, IL-2, γ-IFN [3], and this process is described by an increase in body temperature. We suppose that this reaction, one of components of which is hyperproduction of cytokines, activates expression of *env ER λ 4-1* that, in its turn, is followed by production of virus proteins that possess immune-modelling features and thus provide for formation of post-surgical infectious complications. The received results correspond to the data [16] that revealed stimulation of ER expression in lymphocytes in case of extreme burn among mice. The revealed activation of *ER λ 4-1* during post-surgical period requires further investigation of its possible mechanisms.

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