

A faint, light-colored map of Germany is visible in the background of the cover. The map shows the outline of the country and is overlaid with a network of dots and lines, suggesting a scientific or technological theme.

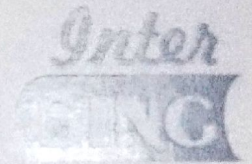
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COMPREHENSIVE TREATMENT OF OSTEOARTHRITIS PEFORMANS WITH CONCOMITANT METABOLIC SYNDROME

Abstract. Osteoarthritis peformans is the most common pathology of the musculoskeletal system. OAP, combined with metabolic syndrome (MS), leads to an overuse of the knee joints operation, and is one of the main causes of premature disability in people. Combined treatment using electrophoresis with neocaripasin in patients with OAP and concomitant MS reduces pain, the severity of inflammatory responses and improves quality of life.

Keywords: deforming osteoarthritis, metabolic syndrome, complex treatment.

Introduction. Osteoarthritis peformans (OAP) is the most common form of joint disease: 10-12% of the population suffer from it, and regarding a significant aging of the population, it is becoming an increasingly topical disease. Currently, osteoarthritis peformans is seen as a systemic metabolic disease, which is a part of metabolic syndrome (MS). Metabolic syndrome is a pathological condition which is characterized by the development of abdominal obesity, dyslipidemia, hypertension and carbohydrate metabolism disorders (insulin resistance phenomenon). The treatment of osteoarthritis peformans is a complex problem that does not always lead to positive results [1-5].

Objective: to evaluate the effectiveness of comprehensive treatment of patients suffering from osteoarthritis peformans of the knee with concomitant metabolic syndrome.

Materials and methods. Group of observations included 60 patients (38 women, and 22 men), aged between 50 and 70, suffering from OAP (the second and third radiologica stages) with concomitant metabolic syndrome. The patients were divided into 2 groups according to the method of treatment. The

patients from the first group (30 people) received nonsteroidal anti-inflammatory drug (NSAID) - meloxicam at a dose of 15 mg every day once a day and chondroprotector as a drug piaskledine 300 – 1 tablet a day for 3 months. All patients in Group II (30 people including 11 men and 19 women) were administered complex treatment, against the background of meloxicam and piaskledine electrophoresis with neocaripasin (using sinusoidal modulated currents (SMS) in a rectified mode 50% 50 Hz with current intensity 0,04-0,06 mA / cm², lasting 10-15 minutes daily with 14-16 procedures), repeating the course every 3 months for two years. All patients underwent assessment of pain on a Verbal Rating Scale, x-ray of the knee and biochemical blood tests (indicators of inflammation, lipid and carbohydrate metabolism) before and after the comprehensive treatment.

Results and discussion. Following the comprehensive treatment using electrophoresis with neocaripasin against the background of anti-inflammatory drugs and chondroprotectors there was a significant difference in the clinical course of OAP of the knee joints with concomitant metabolic syndrome in two groups

of observation receiving different treatments.

The patients of the first group compared with patients of the second group experienced more intense and prolonged pain according to the visual analogue scale VAS of pain (Figure 1).

Severity of inflammatory syndrome (according to biochemical findings of inflammation values) reduced in the experimental groups, namely in Group II, which

was subjected to complex treatment (Table 1).

Assessment of lipid metabolism according to lipidogram test and glucose, insulin and leptin values according to biochemical blood tests in different groups of patients before and after treatment. Reduction of lipid and carbohydrate metabolism was observed in the group of patients where combined therapy had been used. (Table 2).

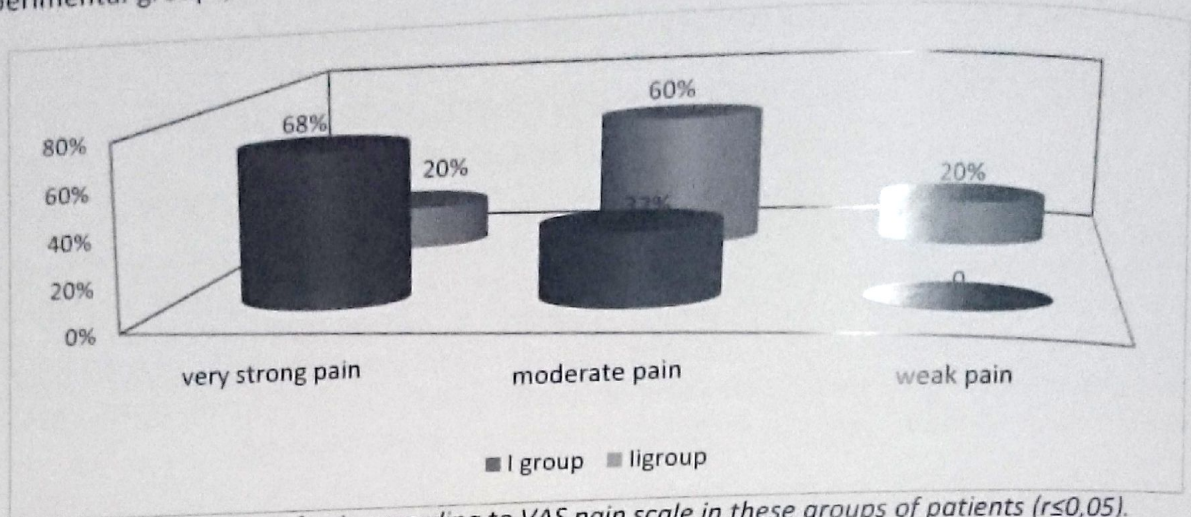


Fig. 1. The severity of pain according to VAS pain scale in these groups of patients ($r \leq 0,05$).

Table 1

Acute phase values of inflammation in patients, suffering from OAP with concomitant metabolic syndrome in various groups of treatment.

Value	I group, n= 30 M±m		II group, n= 30 M±m	
	Before treatment	After treatment	Before treatment	After treatment
CRP	+++	++	+++	++ or +
Fibrinogen, g/l	5,2 ± 0,7	4,3 ± 0,2	5,2 ± 0,4	3,7 ± 0,3
Seromucoid, unit	0,320 ± 0,002	0,260 ± 0,002	0,320 ± 0,003	0,230 ± 0,004
ESR, mm/g	34	20	35	15

Table 2

Values of lipid and carbohydrate metabolism in patients suffering from OAP with concomitant metabolic syndrome in groups with various treatment

Value	I group n= 30 M±m		II group n= 30 M±m	
	Before treatment	After treatment	Before treatment	After treatment
HDL cholesterol, mmol / L	1,19 ± 0,07	1,18 ± 0,07	1,19 ± 0,07	1,17 ± 0,07
TH mmol / l	1,8 ± 0,04	1,7 ± 0,03	1,9 ± 0,04	1,7 ± 0,03
Glucose, mmol / l	7,4 ± 0,3	6,2 ± 0,4	7,3 ± 0,3	5,4 ± 0,4
Insulin mcUn / l	15,2 ± 0,3	14,3 ± 0,2	15,3 ± 0,3	12,2 ± 0,2
Leptin, pg / ml	18,3 ± 0,2	16,5 ± 0,3	18,4 ± 0,2	13,5 ± 0,3

Conclusions: 1. After the comprehensive treatment of patients with osteoarthritis of the knee with concomitant metabolic syndrome all values of inflammation decreased by 3 times; lipid and carbohydrate metabolism – by 2 times and pain syndrome after VAS scale decreased by 3 times.

2. After the comprehensive treatment with neocaripasin electrophoresis against the background of anti-inflammatory and chondroprotective therapy, 54% (rs0,05) of patients with OAP of the knee with concomitant metabolic syndrome had a slowdown in affecting the knee joints, better efficiency and quality of life.

Prospects of further research. Based on the findings obtained, it is possible to use the comprehensive therapy in future for the treatment of patients suffering from osteoarthritis of the knee with concomitant metabolic syndrome.

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EXPERIENCE OF OPTIMIZING TREATMENT OF ACUTE INTESTINAL DISEASES IN BUKOVYNA

Abstract. The article dedicated to the study of efficiency application of contemporary probiotic «Probiz» as the component of the holiatry for patients with acute intestinal infection. Clinical and microbiological efficiency of probiz is well-proven as bacterial preparation, that could correct the abnormal intestine microbiocenosis from the first days of acute intestinal disease, caused by salmonella, shigella, citrobacter, proteus, pathogenic staphylococcus. «Probiz» could recommended in the holiatry of adult patients with different age and sexes in the case of acute diarrhea syndrome probably of infectious origin.

Key words: acute intestinal disease, probiz, treatment, microbiocenosis.

Introduction. Globally, the proportion of infections transmitted by fecal-oral mechanism is probably the largest. The problem of acute intestinal infections (All) and their treatment is closely connected with the microbiocenosis of intestines, which microflora is the primary target of the action of the exogenous flora and its factors of aggression. It is known that almost all patients with All have varying degrees of the intestinal dysbiosis in the first days. That means clinical and laboratory syndrome with changes of qualitative and/or quantitative composition of microflora of a biotope, translocation of various representatives in their unusual biotopes, the development of metabolic and immune disorders and possible clinical symptoms with amplification specific to the All digestive disorders with violation of water-electrolyte metabolism, the emergence enteral syndrome (diarrhea, bloating, rumbling) often the dysfunction of the colon, violation of the synthesis and absorption of essential vitamins, metabolic disorders and the development of All prolonged duration. However, many aspects of pathogenesis and treatment of bacterial diarrhea today is not investigated.

During the treatment of patients with All it is extremely important to protect the intestinal mucosa, and effective recovery of the normal intestinal biocenosis with the use of probiotics, which directly or indirectly affect the metabolic activity of relevant organs and tissues.

Currently the "gold standard" in the treatment and prevention of disorders of microbiocenosis, the use of bacterial medicine which regulates normal intestinal flora – probiotics are considered the best. In the correction of dysbiotic changes drugs on the basis of bifida and lactic bacteria obtained wide application. One of these drugs is "Probiz". It consists of Saccharomyces and complex of bifidobacteria and lactobacilli. Each 500 mg of hard gelatin capsule contains: Lactobacillus acidophilus 2 x10⁹ CFU, Lactobacillus rhamnosus 1,5 x10⁹ CFU, Lactobacillus plantarum 1,5 x10⁹ CFU, Lactobacillus reuteri 1 x10⁹ CFU, Lactobacillus casei 1 x10⁹ CFU, Bifidobacterium bifidum 1 x10⁹ CFU, Saccharomyces boulardii 2 x10⁹ CFU, in all 10 x10⁹ CFU live probiotic organisms. Today, the influence of Probiz components on the state of the microflora of the colon and clinical dynamics

of enteric infections has not been studied enough.

Objective: to study the effect of complex treatment including Probizon the state of the intestinal microbiota and clinical course of acute intestinal diseases.

Materials and methods. Under the supervision in infectious hospital MMI "Regional clinical hospital" Chernivtsi (Ukraine) there were 21 patients aged 18 to 54 years old (food poisoning was diagnosed in 7 people, salmonellosis – 9, gastroenterocolitis– in 5 patients). All patients were admitted to hospital primarily on the 2nd day of illness with an average degree of severity of the disease; there were 8 men and 13 women. the diagnosis was made on the basis of clinical and epidemiological data and with the help of coproculture verified the causative agent of all. Material for the study of species composition and populational level of microflora of cavity of the colon in the patients with acute intestinal infection were stool, which were taken from the median portions of faeces put in sterile bottles and transported to the microbiological laboratory of the regional clinical hospital, where a comprehensive microbiological study was carried out. The term since collection of material until the beginning of study did not exceed 2 hours.

All patients fulfilled clinical examination with the dynamics of a detailed study of the epidemiological history. It was found that the common factors of infection were meat, dairy products, confectionery; these epidemiological factors of transmission coincide with the data of other scientists. The clinical tests, capriform, bacteriological examination of faeces, gastric lavage, vomitus were taken into account.

Results and discussion. 7 patients with food poisoning caused by opportunistic flora (Tsytroubakter, Proteus, pathogenic Staphylococcus) were examined. The condition of all the patients was moderate, gastroenteritis version (acute onset of disease, short incubation period, short-term fever to subfebrile digits, nausea, vomiting, epigastric pain mainly in and around the navel, liquid stool without pathological impurities to 5-7 times a day). Clear dependence of clinical variant of the disease

from the etiological factor (bacteriologically confirmed) was not found. Observation of intestinal microbiota (4 patients) included the presence of pathogenic organisms, the total number of E. coli E. coli with reduced enzyme activity, opportunistic enterobacteria, staphylococci, fungi genus Candida, lactobacilli, bifidobacteria, hemolytic cocci. Changes in microbiocenosis of the colon was detected in all surveyed: the decrease in the number of lactobacilli, bifidobacteria, total number the E. coli. The content of lactobacilli < 10⁶ CFU /g of faeces was observed in 2 people, and B2 individuals was approaching to normal 10⁷ CFU /g (normal > 10⁶ CFU/g) of bifidobacteria was < 10⁷ CFU/g in 1 patient, in remaining patients to the normal range (> 10⁷ CFU / g). It was discovered a reduce of the total number of E. coli < 10⁶ CFU / g in 1 patient. 9 patients with salmonellosis caused by S. enteritidis were 3 examined. The condition of all the patients was moderate, 6 patients had gastroenteritis version, 3 – gastroenterocolitis. In all examined onset of disease was with symptoms of intoxication (fever, raising the temperature to febrile digits, headache, malaise), dyspeptic symptoms (nausea, recurrent vomiting, epigastric pain and preferably in the periumbilical area, frequent liquid stool to 8-10 times a day, which is greenish in color with an unpleasant odor, and in 3 patients with admixtures of mucus). Signs of dehydration I-II (6% weight loss) were observed in all patients.

Observation of intestinal microbiota (4 persons) included the presence of pathogenic organisms, the total number of E. coli E. coli with reduced enzyme activity, opportunistic enterobacteria, staphylococci, fungi genus Candida, lactobacilli, bifidobacteria, hemolytic cocci. Changes in colon microbiota, reduce the number of lactobacilli, bifidobacteria, the total number of E. coli was detected in all patients. The reduction of lactobacilli <10⁶ CFU / g of feces in 4 surveyed; the number of bifidobacteria was <10⁷ KYO / g 2 was found. Reduce of total number of E. coli below <10⁶ CFU / g to 2 people was discovered.

A clinical and laboratory study of 5 patients with gastroenteritis, gastroenterocolitis was

carried out. All the patients had gastroenteritis syndrome (acute onset, fever, nausea, vomiting, rumbling, abdominal pain predominantly in the periumbilical area, frequent watery stool character. The disease was of moderate severity.

The examination of intestinal microbiota (3 patients) included the presence of pathogenic organisms, the total number of *E. coli* with reduced enzyme activity, opportunistic enterobacteria, staphylococci, fungi genus *Candida*, lactobacilli, bifidobacteria, hemolytic cocci. Changes in colon microbiota was detected in all patients already in the first examination, reducing the number of lactobacilli, bifidobacteria, the total number of *E. coli*. The reduction of lactobacilli <106 CFU / g of feces in 3 patients, and 2 persons reached 106 CFU/g (normal > 106 CFU/g); the number of bifidobacteria was <107 KYO / g in 2 patients, and one reached in normal (>107CFU/g). Discovered reducing the total number of *E. coli* below <106 CFU/g was found in 2 people.

All patients received basic therapy, detoxification, rehydration with parenteral ("Trysil" rheosorbilact) and oral ("rehydron") the introduction of salt solutions, "Nifuroxazide" chelators ("Enterosgel"), enzymes (replacement therapy) and 11 patients were additionally administered probiotic "Probiz" 1 capsule 2 times a day for 5 days.

As a result of clinical and laboratory monitoring it was found that patients who received a treatment of "Probiz" improved their general condition and normalization of stool notified before (an average of one day) compared to the control group.

Conclusions. 1. Experience of the inclusion to traditional therapy for patients with food poisoning, salmonella, gastroenterocolitis combined probiotic "Probiz" showed that the application of the scheme accelerates regression of symptoms of intoxication and diarrhea syndrome, which generally leads to a reduction in the duration of the acute period of disease.

2. The results of the examination showed the efficacy and safety of the studied probiotic drug "Probs" in acute intestinal infections, primarily of bacterial origin.

3. Control examination of faeces for *Salmonella* group by the method of coprocultures after treatment were negative, indicating bacteriological efficiency of probiotic against the pathogens of intestinal diseases.

Prospective for further researches is the study of microbiological representatives of colon microflora in the dynamics of treatment by probiotics combined with various intestinal infectious diseases (viral and bacterial).

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REGRESSIVE MODEL FOR DETERMINING A RELATIVE NUMBER OF THYMOCYTES IN THE THYMIC CORTEX OF IMMATURE RATS BASED ON THE SERUM TRANSFORMING GROWTH FACTOR- β 1

Abstract. When the serum transforming growth factor- β 1 (TGF- β 1) rate increases, which is typical for liver damage, there is a suppression of the immune system and the quantitative morphometric changes in the thymus are morphological reflection of these abnormalities. This correlation between the serum growth factor and a relative number of thymocytes in the thymic cortex of immature rats is embodied in polynomial regression and allows an indirect and non-invasive method to determine the morphological indices of the thymus.

Key words: immature rats, thymus, transforming growth- β 1 factor, polynomial regression.

Introduction. TGF- β 1, transforming growth factor beta is a multifunctional cytokine involved in the regulation of proliferation, apoptosis and metabolic reactions in various target cells, it is a cytokine with systemic effect as the expression of its high-affinity receptor is widespread, the factor suppresses hematopoiesis and synthesis of pro-inflammatory cytokines, it also stimulates neoangiogenesis (J.A. Mengshol, L. Golden-Mason et al, 2010; J.P. Edwards, H. Fujii, 2013). The role of TGF- β 1 in the pathology of the liver is known - it is a profibrinogen factor that accelerates the pace of fibrosing through the activation of stellate cells, increased production of extracellular matrix proteins and collagen type I, besides TGF- β 1 is predictive of accidental thymic involution (M.Y. Kapitonov, 2006; A.A. Yarylin, 2003; J. P. Alekseeva, T.M. Bryzhina et al., 1991).

The issue of the role of TGF- β 1 in the development of secondary immunodeficiency is not clarified in an experiment adequately, the involvement of TGF- β 1 in the accidental involution of the thymus and the impact on cellular and humoral immunity has been proved (O.Y. Humynska, 2014; R.T. Robinson, J.D. Gorham 2007). However, quantitative characteristics of this relationship need further studying.

Objective: to establish a quantitative

relationship based on the qualitative relationship between the serum transforming growth factor- β 1 and a relative number of thymocytes of the thymic cortex of immature rats.

Materials and methods. The research involved 20 white nonlinear immature female rats aged 60 days. The animals were kept in vivarium conditions of M.I. Pyrohov VNMU with free access to water and food. All experiments were conducted in compliance with the "General ethical principles in experiments with animals" (Kyiv, 2001) and were consistent with the provisions of the "European Convention for the protection of vertebrate animals used for experimental and other scientific purposes." Sampling was performed under general thiopental anesthesia by cervical dislocation, fixation of morphological material was carried out by the conventional method. The study of histological structure of the thymic tissue was performed on the left lobe, the resulting material was fixed in 10% neutral formalin. After a standard procedure, it was embedded in paraffin, histological sections 5 microns thick were made in microtome HM-360 company "Zeiss". The sections were stained with hematoxylin-eosin. Obtained specimens were examined with a microscope Olympus BX 41 at different magnifications and photographed.

In addition to a qualitative descriptive assessment of histological structure of laboratory animals thymus, we also determined the following indices using Weibull's net [G.G. Avtandilov, 1990]: the relative area of the cortex and medulla, ratio of relative areas of cortex and medulla, the relative amount of thymocytes and epithelioretikulotsytiv cortex, the relative number of thymocytes and epithelioretikulocytes of the cortex, the relative number of thymocytes and epithelioretikulocytes of the medulla for morphological verification of the presence and assess of the extent of accidental thymus involution.

The serum transforming growth factor-β1 rate was determined by ELISA on a stripped immunosorbent analyzer StatFax 303+ (Awareness Technology), using reagents of a firm «DRG» (Germany).

Results and discussion. We have proved a clear link between qualitative characteristics of a relative number of thymocytes of the cortex and those of the serum transforming growth factor-β1, these characteristics can be transformed into quantitative ones by using regression analysis.

While studying the transforming growth factor in the serum of rats, we found that the content of TGF-β1 is $- 251,04 \pm 4,820$ pg / L, the relative number of thymocytes in the thymic cortex of immature rats is $51,20 \pm 0,49$.

In this case, the relationship between the number of thymocytes and the TGF-β1 rate as well as values of the population of lymphocytes in the peripheral blood in intact rats can be transformed into quantitative ones using regression analysis. In the simulation by means of step-by-step direct regression analysis of quantitative relationship between correlations, the regression model included the number of thymocytes of the cortex and TGF-β1 index with quite high levels of predictivity. Evaluation of prognostic contribution of an independent variable (TGF-β1) in a step by step procedure was determined by R², that is 0.9807 in this formula, i.e. in 98.07% a chance of matching the actual value (the number of thymocytes in the cortex of the thymus) calculated (for this model) at p < 0.001.

Table 1
Indices of regression model of the dependence of number of thymocytes in the thymic cortex on the index of transforming growth factor-β1 in the serum of intact rats

Results of regression for the dependent variable: number of thymocytes R=0,99; RI=0,98; adjusted RI=0,9807; F(2,17)=48,15; p<0,0001; Standard error: 0,25				
variable	B	Standard error B	t (34)	p-level
absolute term	31,29	0,64	48,71	0,000
TGF-β1 (i)	0,079	0,002	31,11	0,000

The coefficient of determination R², as a measure of the quality of forecasting approximates the estimated dependent variable for 98.07%. The standard error of the estimation in this case is 2.368, that in terms of the maximum and minimum value could reach approximately from 4.47% to 4.8% (i.e. theoretically, the maximum deviation can be up to 5%).

In carrying out serial analysis of residues of the dependent variable, none of the observations extends beyond two sigmas, besides, the average of the difference of the actual and calculated theoretically is "0". With this number of observations F critical is 2.17, in fact, in this formula it is 48.15, which is much more than the critical value. On this basis, we can state that the regression linear polynomial is significant at p < 0.001.

The graph of residue distribution (differences of theoretical and actual normal number of thymocytes in the cortex of the thymus) clearly shows their location on the line without deviation beyond the 95% confidence interval (Fig. 1). In the final version of this formula is as follows:

$$N = 31,29 + (0,079 \times \text{TGF } \beta - 1) \pm 0,25 \text{ (} a\sigma \pm 5\% \text{);}$$

Where: N – a relative number of thymocytes in the thymic cortex of immature rats; 31.29 is a free coefficient;

RI=0,9807 (an adjusted connected R) determines the predictivity of the model at 98,07 % at p<0,001; the value TGF-β1 for this

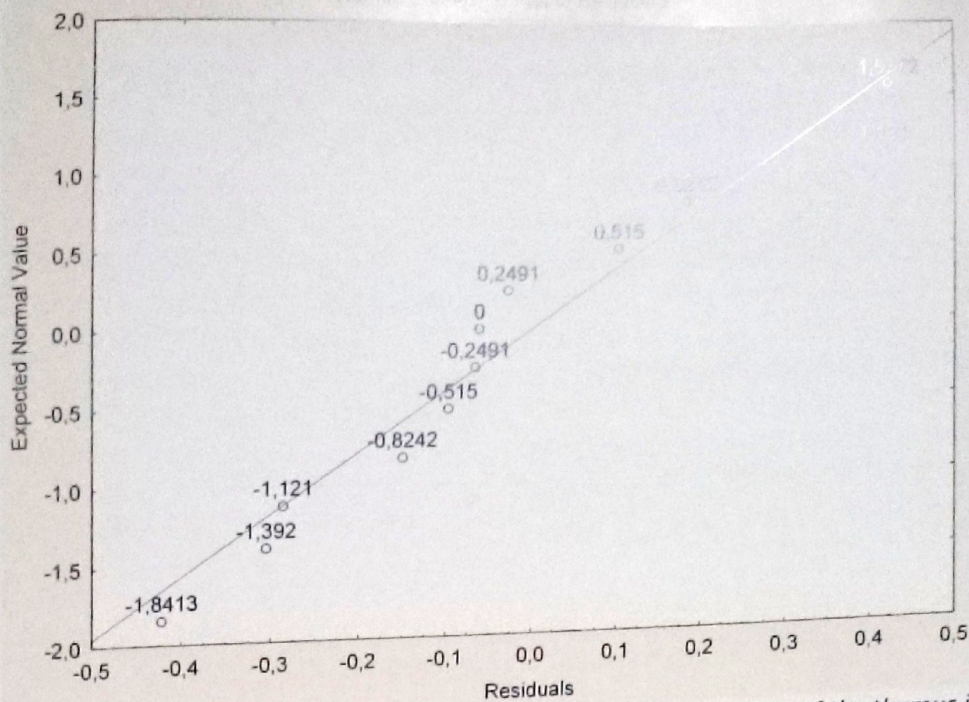


Fig. 1. Value of deviations in a modeled number of thymocytes in the cortex of the thymus in immature rats.

group of immature rats is $251,04 \pm 4,820$ pg/l; $\pm 0,25$ is a value of the standard deviation relatively the average value.

Conclusions. The above leads to the following conclusion that the number of thymocytes of thymic cortex is in a qualitative and quantitative dependence on the TGF- β 1 rate, which with high probability allows theoretically predict the number of thymocytes depending on the normal rate of the latter, polynomial is patented to the useful model number 100926.

Prospects of further research. The quality of the polynomial (formula) is high, which indicates its prospects of use to determine the relative number of thymocytes in the thymic cortex in terms of transforming growth factor- β 1 in the serum of immature rats as a method of indirect determination of morphological index with 95% probability this polynomial can be used in research activities.

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