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Biochemical and immunological blood parameters in patients with inflammatory complications after spine screw fixation

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As a result of screw fixation at the surgical treatment of patients with spinal diseases, certain complications may occur, of which soft tissues inflammation is frequent. Therefore, it is especially important to study the metabolic status of patients before surgery to determine the increased possibility of complications. Objective. To study the biochemical and immunological blood serum parameters and determine their diagnostic sensitivity in patients with the thoracic and lumbar spine diseases after screw fixation with postoperative inflammatory response. Methods. Comparisons of blood parameters were carried out in two groups of 20 patients in each group: the first one — patients at whom the postoperative period passed without complications, the second group — a soft tissues inflammation around the metal structure was observed in the postoperative period. Blood for the study was taken before the surgery on an empty stomach for determination of: C-reactive protein (CRP), sialic acid, alkaline phosphatase (ALP) activity, haptoglobin, content of total chondroitin sulfate (ChS), glycoproteins, circulating immune complexes (CIC), the rate of spontaneous lymphocyte migration, the level of lymphocyte migration with antibodies to bone and cartilage antigens. For quantitative characterization of diagnostic reliability of laboratory test was used the criterion of diagnostic sensitivity. Results. In patients with postoperative soft tissue inflammation around the metal device before surgery, the following indicators were the most informative: the content of ChS (95 %), CRP (80 %), glycoproteins (95 %), haptoglobin (92 %), ALP activity (80 %), sialic acid content (90 %), CIC concentration (70 %), the rate of spontaneous lymphocyte migration (65 %). Conclusions. The laboratory parameters complex with the highest diagnostic sensitivity can be recommended for the selection of preventive measures in the preoperative period, which will improve the results of surgical treatment, reduce its duration and costs. Key words. Surgical treatment, spinal disease, complications, inflammation, screw fixation, laboratory parameters.

У результаті використання транспедикулярної фіксації в хірургічному лікуванні пацієнтів зі захворюваннями хребта можуть виникнути певні ускладнення, з яких частим є запалення м'яких тканин навколо конструкції. У зв'язку з цим особливу актуальність набуває дослідження метаболічного статусу пацієнтів до початку хірургічного лікування для визначення підвищеної вірогідності ускладнень. Мета. Дослідити біохімічні й імунологічні показники крові та визначити їхню діагностичну чутливість у пацієнтів зі захворюваннями грудного та поперекового відділів хребта після транспедикулярної фіксації зі запальними ускладненнями в післяопераційному періоді. Методи. Порівняння проводили у двох групах по 20 хворих у кожній: I — особи, в яких післяопераційний період перебігав без ускладнень, II — у післяопераційному періоді спостерігали запалення м'яких тканин навколо металоконструкції. Кров для дослідження відбирали до операції натщесерце та визначали: С-реактивний білок (СРБ), сіалові кислоти, активність лужної фосфатази (ЛФ), гаптоглобін, вміст загальних хондроїтинсульфатів (ХС), глікопротеїни, циркулюючі імунні комплекси (ЦІК), коефіцієнт спонтанної міграції лімфоцитів, рівень міграції лімфоцитів із антитілами на кістковий і хрящовий антигени. Для кількісної характеристики діагностичної надійності лабораторного тесту використаний критерій діагностичної чутливості. Результати. У пацієнтів із післяопераційним запаленням м'яких тканин навколо конструкцій до операції найінформативнішими виявилися: вміст ХС (95 %), СРБ (80 %), глікопротеїнів (95 %), гаптоглобіну (92 %), активність ЛФ (80 %), вміст сіалових кислот (90 %), концентрація ЦІК (70 %), коефіцієнт спонтанної міграції лімфоцитів (65 %). Висновки. Комплекс лабораторних показників із найбільшою діагностичною чутливістю може бути рекомендований для вибору профілактичних заходів у передопераційному періоді, що дозволить покращити результати хірургічного лікування, зменшити його тривалість та вартість.

Key words. Surgical treatment, spinal disease, complications, inflammation, screw fixation, laboratory parameters

Introduction

From 60 to 70% of people in the general population suffer from spinal diseases [1, 2]. Increased duration and demand for a better quality of life in the aging process have resulted in a significant increase in the number of candidates for correction and stabilization of the spine among adult patients. Because of this, in recent decades a step has been taken towards expanding knowledge in the field of vertebrology. It has been shown that major operations disturbing the balance of the spine, result in an unacceptably high percentage of unsatisfactory results and audit interventions [3].

In modern conditions surgical treatment of patients with back pain increasingly requires the use of high-quality instruments with the installation of a transpedicular structure. The introduction of new developments has significantly expanded the possibilities of care for patients with spine abnormalities. At the same time, the widespread use of transpedicular fixation has revealed a number of possible complications, one of which is peri-structural soft tissue inflammation [4]. In this regard, the study of the metabolic status of patients before surgery to determine the risk of complications is especially relevant [5]. The requirements of evidence-based medicine require the formalization of systems for assessing the diagnostic significance of the studied parameters. Assessment of diagnostic sensitivity of the test offered for use is based on exact establishment of the diagnosis and division of patients according to certain signs [6, 7].

The aim of the study: to assess the biochemical and immunological parameters of blood and determine their diagnostic sensitivity in patients with diseases of the thoracic and lumbar spine after transpedicular fixation with inflammatory complications in the postoperative period.

Material and methods

The study of the effectiveness of the proposed method was carried out within the research work of the Sytenko Institute of Spine and Joint Pathology National Academy of Medical Sciences of Ukraine. «To study the main errors and complications of transpedicular fixation in spinal surgery and develop measures for their prevention and treatment», discussed and approved at a meeting of the local Committee on Bioethics (Minutes No. 179 of 14.05.2018).

The patients were examined before surgery. Comparisons were performed in two groups. Group I included 20 subjects aged (38 ± 12) years, in which the postoperative period was without complications. The second group consisted of 20 individuals aged (36 ± 14) years, who during the postoperative period had inflammation of the soft tissues around the metal structure. Also, the values of patients in both groups was compared with the control, which included 20 healthy subjects (10 men and 10 women) aged (42 ± 15) years.

Blood for the study was taken from patients before surgery on an empty stomach from the ulnar vein. After centrifugation at 3,000 rpm for 15 min, serum was separated and the C-reactive protein content was determined by latex test, sialic acid by Hess method, alkaline phosphatase activity by kinetic method, and haptoglobin by hemoglobin method [8]. The content of total chondroitin sulfates was evaluated by the reaction with rivanol by the Nemeth-Csoka method in the modification of L. I. Slutsky, glycoproteins by the modified method of O. P. Steinberg and Ya. N. Dotsenko [9]. Markers of cellular and humoral immunity were also determined: circulating immune complexes by precipitation in 3.5 % solution of polyethylene glycol (6,000 Da) on a SF-46 spectrophotometer, the rate of spontaneous lymphocyte migration, the level of lymphocyte migration with antibodies to bone marrow and cartilage antigens according to capillary modification by Yu. P. Delevsky, T. M. Krymkina and L. V. Kovalchuk method [10–12].

The diagnostic sensitivity criterion (DS) was used to quantify the diagnostic reliability of the laboratory test. It is calculated as the probability that the patient will get a positive test result in the presence of disease or complications. DS was evaluated by the proportion (%) of positive test results in patients with the corresponding disease by the formula [13]:

$$MS = (m/M) \times 100\%,$$

where m is the number of patients who have deviations from the reference values; M is the total number of patients.

Semi-automatic biochemical analyzers «GBG STAT FAX 1904 plus» and Stardust FC were used during biochemical studies.

Statistical analysis of the data was performed using Microsoft Excel XP software packages (license number 00218-04981-27336-AA152) according to the Student-Fisher parametric criterion with the determination of the arithmetic mean and standard deviation. After that, the series was analyzed for uniformity and the presence of statistical significance of the difference between the comparison series with $p < 0.05$ [14].

Results and discussion

Patients without postoperative complications before treatment showed moderate deviations of the studied

laboratory parameters, namely: 37.21 % higher content of glycoproteins in the serum than in the control group, and significantly 67.36 % increased concentration of haptoglobin (Table 1).

Serum C-reactive protein concentration above 6 mg/ml but less than 12 mg/ml was recorded in 4 patients out of 20 (norm is less than 6 mg/ml), while in the group of almost healthy subjects the threshold was exceeded in only one person.

There was also a significant increase by 38.37 % in the content of total chondroitin sulfates in the serum of patients in whom the postoperative period was without complications, compared with that in almost healthy subjects. These changes in biochemical parameters indicate the presence of inflammatory and dystrophic processes in connective tissue.

Assessment of the value of markers of cellular and humoral immunity in individuals with spinal diseases, in whom the postoperative period was without complications, detected a significant increase of 25.32 % in the content of circulating immune complexes compared with the control group. This was accompanied by a significant increase in the coefficient of spontaneous lymphocyte migration by 21.70 %. Such changes reflect the physiological activation of the body's defense mechanisms aimed at removing antigens formed due to degradation of connective tissue in the presence of dystrophic processes in the spine.

The level of lymphocyte migration with antibodies to bone antigen in group I patients was significantly increased by 10.58 %, with antibodies to cartilage antigen by 12.50 %. The results indicate the activation of the immune system against the tissues of its own connective tissue.

Assessment of the indicators of laboratory examination of group II patients with postoperative soft tissue inflammation identified more pronounced deviations from control. In particular, it showed increased alkaline phosphatase activity (by 54.96 %), reflecting the restructuring of bone tissue with a predominance of anabolic processes. This is confirmed by the level of total chondroitin sulfates, which increased by 60.47 % (Table 1).

Biochemical markers of the inflammatory process have changed significantly: the content of haptoglobin has increased by 2.4 times, sialic acid by 2.3 times. C-reactive protein content was higher than 18 mg/ ml but less than 24 mg/ml in 5 patients; more than 12 mg/kg, but less than 18 mg/ml in 7; more than 6 mg/kg, but less than 12 mg/ml in 8.

Assessment of the values of markers of cellular and humoral immunity in patients of group II detected more significant changes in immune status than in group I. They indicated a 2.2-fold increase in circulating immune complexes compared with controls, as well as the rate of spontaneous lymphocyte migration by 64.15 %.

The level of migration of lymphocytes with antibodies to various connective tissue antigens has increased significantly compared with almost healthy people. Accordingly, to bone antigen, this excess was 60.58 %, to cartilage 64.77 %, to synovial membrane 39.19 %.

Table 1

Laboratory parameters in patients with diseases of the thoracic or lumbar spine, determined before surgical treatment with introduction of transpedicular metal structures

Indicator	Unit of measurement	Group		
		control group (n=20)	Group I without complications (n = 20)	Group II with inflammation of soft tissues (n = 20)
Alkaline phosphatase activity	Units/l	195.2 ± 1.9	215.2 ± 12.8	284.9 ± 13.8 [1, 2)]
Glycoproteins	mmol/l	0.43 ± 0.01	0.59 ± 0.04 [1)]	0.84 ± 0.05 [1, 2)]
Sialic acids	mmol/l	2.00 ± 0.03	2.19 ± 0.05	4.72 ± 0.01 [1, 2)]
Haptoglobin	g/l	0.95 ± 0.04	1.59 ± 0.07 [1)]	2.25 ± 0.12 [1, 2)]
Chondroitin sulfates	g/l	0.086 ± 0.004	0.119 ± 0.008 [1)]	0.138 ± 0.013 [1)]
Circulating immune complexes	Units	53.88 ± 6.22	67.52 ± 6.60 [1)]	115.90 ± 7.15 [1, 2)]
Spontaneous lymphocyte migration rate (LIF)	—	1.06 ± 0.12	1.29 ± 0.14 [1)]	1.74 ± 0.17 [1, 2)]
Lymphocyte with antibodies to bone antigen migration rate	Units	1.04 ± 0.11	1.15 ± 0.12 [1)]	1.67 ± 0.15 [1)]
Lymphocyte with antibodies to cartilage antigen migration rate	Units	0.88 ± 0.07	0.99 ± 0.08 [1)]	1.45 ± 0.06 [1, 2)]

[1)] $p < 0,05$ in comparison with control group;
[2)] $p < 0,05$ in comparison with Groups I and II

If we compare the results of the examination of group II patients with persons without postoperative complications (group I), it should be noted that the activity of alkaline phosphatase in them was 31.96 % higher. Markers of inflammation in patients who had soft tissue inflammation in the postoperative period were also elevated compared with the uncomplicated group: haptoglobin levels 41.51 %, sialic acids 2.1 times. At the same time, there was an increase of 15.97 % in the level of total chondroitin sulfates (Table 1).

The obtained results indicate the development of an active inflammatory process in group II patients even before surgery, which after the manipulations was significantly activated and manifested by local exacerbation.

In the process of comparing the values of markers of cellular and humoral immunity, a significantly higher level of circulating immune complexes (by 71.65 %) was recorded in the serum of group II patients compared to group I (Table 1).

The value of the rate of spontaneous lymphocyte migration in the group of patients with postoperative soft tissue inflammation was higher than in those without complications by 34.88 %.

The level of migration of lymphocytes with antibodies to various connective tissue antigens in group II patients significantly exceeded those in patients without postoperative complications: bone antigen by 45.22 %, cartilage antigen by 46.46 %. These changes are characterized by excessive activation of the immune system before treatment in patients who have postoperative soft tissue inflammation. Presumably, there is a significant autoimmune component in the development of inflammation, which should be taken into account during preoperative preparation of patients in order to normalize the immune status.

Based on the obtained results, the diagnostic sensitivity of the used tests was calculated (Table 2).

Table 2

Diagnostic sensitivity of the studied indicators in patients with spinal diseases and subsequent surgical treatment

Indicator	Diagnostic sensitivity (%)
Glycoproteins	95
Alkaline phosphatase activity	80
Haptoglobin	92
C-reactive protein	80
Chondroitin sulfates	95
Sialic acids	90
Circulating immune complexes	70
Spontaneous lymphocyte migration rate	65
Lymphocyte with antibodies to bone antigen migration rate	60
Lymphocyte with antibodies to cartilage antigen migration rate	65

In patients with postoperative inflammation of soft tissues around metal structures before surgery, the most informative were the content of total chondroitin sulfates (95 %), glycoproteins (95 %), C-reactive protein (80 %), haptoglobin (92 %), sialic acids (90 %), alkaline phosphatase activity (80 %), concentration of circulating immune complexes (70 %), spontaneous lymphocyte migration rate (65 %), lymphocyte migration rate with antibodies to cartilage antigen (65 %) and synovial membrane antigen (60 %) .

An experimental study in animals after transpedicular dynamic fixation under conditions of lumbar spine injury 14 days after the intervention revealed a decrease in ESR, white blood cell count and C-reactive protein, as well as a tendency to decrease the concentration of glycosaminoglycans, glucuronic and sialic acid inflammatory process in the tissues of the spine [15]. Other authors talk about the possibility and nature of complications after transpedicular fixation, without citing important laboratory markers for diagnosis and prediction [16, 17].

Conclusions

Laboratory parameters of patients with diseases of the thoracic or lumbar spine, who developed inflammatory complications after surgery, differed before surgery from persons with similar diagnoses and treatment without complications.

When planning surgery, special attention should be paid to patients with high levels of indicators, the diagnostic sensitivity of which is from 60 to 95 %: total chondroitin sulfate, the content of C-reactive protein, glycoproteins, haptoglobin, sialic acids; alkaline phosphatase activity, concentration of circulating immune complexes, coefficient of spontaneous lymphocyte migration, level of lymphocyte migration with antibodies to cartilage antigen and synovial membrane antigen.

The set of laboratory parameters with the highest diagnostic sensitivity can be recommended for the selection of preventive measures in the preoperative period, which will improve the results of surgical treatment, reduce its duration and cost.

Conflict of interest. The authors declare no conflict of interest.

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BIOCHEMICAL AND IMMUNOLOGICAL BLOOD PARAMETERS IN PATIENTS WITH INFLAMMATORY COMPLICATIONS AFTER SPINE SCREW FIXATION

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