ORIGINAL ARTICLE

CONTENTS

Biomarkers of inflomation in the blood of patients with the degenerative lumbar spine disease and complications after transpedicular fixation

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ABSTRACT

Aim: To investigate the peculiarities of deviations of preoperative values of biochemical markers of inflammation in the blood serum of patients with degenerative diseases of the lumbar spine after transpedicular fixation, with a complicated postoperative course to predict the development of various postoperative complications.

Materials and Methods: The content of glycoproteins (GP), sialic acids (SA), C-reactive protein (CRP), seroglicoids (SG), haptoglobin (HG), Veltman`s test (VT) were investigated. The results are comparable by the Student-Fisher method.

Results: When compared to data of the control group, patients without complications showed 37.21% higher content of SA, by 67.36% – HG, by 56.70% – CRP, by 22.22% – VT; in patients with soft tissue inflammation – an increase of 136.84% of HG content, 86.00% – SA, 160.00% – CRP and a decrease in 51.11% of VT; in patients with hypercoagulation, the content of GP, SA, HG, CRP is higher by 109.30%, 82.00%, 131.57% and 133.33%, and VT – less by 48.48%; in patients with screw instability, the level of GP is higher by 48.83%, HG – by 78.94%, the SA – by 19.00%, the CRP – by 53.53% and lower VT – by 15.56%; with several complications GP more than 93.02%, SA – by 69.00%, HG – by 123.16%, CRP – by 111.33% of VT – lower by 40.00%.

Conclusions: According to our data, the indicators that are more suitable for predicting the development of complications are CRP, GH, and CA. However, none of the studied indicators is universal, and their prediction requires the use of diagnostic complexes.

KEY WORDS: complications, biochemistry, transpedicular fixation, prediction, degenerative diseases of the spine

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INTRODUCTION

Lumbar discectomy with transpedicular fixation of adjacent vertebrae is most often performed by a surgical procedure for the treatment of patients with a disk protrusion into the spinal canal [1]. The standard procedure is open discectomy (OD), which produces good results [2], which range from 75 % to 100 % [3]. However, transpedicular vertebral fixation is highly likely to develop complications that significantly worsen the patient's condition and quality of life. In particular, the OD can cause muscle damage and other complications [4]. In addition, the operation causes destabilization due to the required resection of the vertebral structures [5, 6]. The prevalence of infectious and specific complications is from 0.44 to 1.81 % [7].

Complications of decompression-stabilizing operations may be instability or fracture of one of the elements of the structure, the formation of pathology at adjacent levels, neurological disorders associated with a violation of the technique of installation of the transpedicular system [8].

Improper handling of transpedicular screws can lead to the development of a delayed infection [9, 10]. In this case, infection can lead to screwing and pain, which leads to the need to remove the screw [11].

A frequent complication in orthopedic interventions is the thrombosis of the deep veins of the lower extremities [12], which can lead to the development of pulmonary thromboembolism [13].

There is an interaction between inflammation and coagulation systems, in which inflammation leads to the activation of the coagulation system, and coagulation in turn increases inflammatory activity [14].

Due to the widespread spread of complications in transpedicular fixation of vertebrae in degenerative diseases of the lumbar spine, the development of a system of forecasting the development of various types of complications in the postoperative period is relevant on the basis of the results of preoperative biochemical examination. This may give a new opportunity to improve the quality of treatment by timely taking measures to prevent the complicated course of

the postoperative period and to improve the quality of treatment of patients with this pathology.

AIM

To investigate the peculiarities of deviations of preoperative values of biochemical markers of inflammation in the blood serum of patients with degenerative diseases of the lumbar spine after transpedicular fixation, with a complicated postoperative course to predict the development of various postoperative complications.

MATERIALS AND METHODS

The studies were conducted on the basis of the clinic of the Sytenko Institute of Spine and Joint Pathology Ukrainian National Academy of Medical Sciences (Accreditation Certificate (Higher Category) dated 19.04.2021 to 18.04.2024 M3 No 015211) in the department of laboratory diagnostics and immunology of the Institute (certificate of compliance with the system of measurement with the requirements of DSTU ISO 10012:2005 dated 14.03.2023 to 14.03.2026 No 01-0017/2023).

The research plan was considered and approved at a meeting of the Committee on Bioethics of the Institute of 19.04.2021, protocol No. 215.

The basis for the preparation of work was the data transferred from medical cards of inpatient patients (f. 003/o) department of pathology of the spine of the Institute, which are stored in the archive of the Institute.

Research design. The work is based on the results of retrospective analysis of the data of biochemical examination of 46 patients with degenerative diseases of the lumbar spine, which performed discectomy with transpedicular fixation of the vertebrae in the department of spine pathology in the period 2015-2023.

Observation groups. The biochemical parameters in patients of four groups were investigated, in which complications were observed in the postoperative period: I – inflammation of soft tissues around the instrument zone (10 patients); II – development of hypercoagulation conditions (6 patients); III – instability of transpedicular fixation (5 patients), IV – several complications at the same time (5 patients). The comparison group was the results of the preoperative examination of 20 people with uncomplicated postoperative period, and data of the control group, which included 20 donors (almost healthy people).

Criteria for patients in study or exclusion from the study – the presence of other lesions of the skeleton (injuries, osteporosis), as well as serious diseases that could affect the course of the disease (cancer, cardiac, liver and renal insufficiency of high degree, thrombotic diseases, autoimmune diseases (rheumatoid arthritis, lupus erythematosus, etc.; rheumatism, chronic infectious diseases (chlamydia, trichomonados, etc.; a severe course of Covid-19 in history, mental illness, including alcoholism, drug addiction), disruption Adding appropriate diseases in the process of diagnosis and treatment of the underlying disease.

Before surgery, inflammatory markers were determined in the blood serum of all patients: blood content of sialic acids (SA), C-reactive protein (CRP), seroglicoids (SG), haptoglobin (HG) according to the instructions to the sets [15]. The content of total glycoproteins (GP) in serum was determined by the modified method of O.P. Shtenberg and Ya.N. Dotsenko, the content of C-reactive protein (CRP) – a semi-quantitative latex test with fixed values of 6, 12, 24 and 48 mg/l, Weltman`s test (WT) – by modified method [16]. The results were processed using MS Windows software, № licensing package 439108-251. The normality of distribution was checked by Kolmogorov – Smirnova. The results are presented as the average square ± standard deviation (M±m). For comparison, the Fisher-Student Fisher method was used. The difference was considered statistically significant at $p<0.05$ [17].

To evaluate the diagnostic significance of these parameters in various types of complications, we calculated their diagnostic sensitivity (DS), which is the probability that the patient will have a positive test result. DS was evaluated by the chance (%) of positive analysis results in patients with appropriate disease by formula:

$$DS = \frac{RP}{RP + FN} \text{ x } 100\ \%,$$

where RP is really positive test results;
FN – false-negative test results [18].

RESULTS

Patients with uncomplicated post–operative period were shown by 37.21 % higher than 67.35 % – HG, as well as WT results by 22.22 % with respect to such in persons in the control group (Table 1).

The CRP concentration in serum <6 mg/l (an average of 3 mg/l) was recorded in 8 people, 6-12 mg/ml (an average of 9 mg/l) in two patients, 12-24 mg/l (an average of 18 mg/l) – in 1 patient of 20 in the group (as a whole in the group 7.05 ± 1.09 g/l), in that time, as in the control group of 30 people, the value of 6-12 mg/kg (an average of 9 mg/l) was determined in 7 people 12-24 mg/l (an average of 18 mg/l) – in one patient, the

Table 1. Biochemical markers of inflammation of patients with postoperative complications after transpedicular fixation of vertebrae

№ p/n	Indexes	Control group (n=20)	Patients without postoperative complications (n=20)	Patients followed by soft tissue inflammation (n=10)	Patients with the subsequent development of hypercoagulation (n=6)	Patients with subsequent instability of structures (n=5)	Patients with multiple complications at the same time (n=5)
1	2	3	4	5	6	7	8
1	the content of common glycoproteins, mmol/l	0,43±0,01	0,59±0,04 +37,21 %[1, 5)]	0,84±0,05 +95,57 %[1, 7)] +42,37 %[2, 6)]	0,90±0,06 +109,30 %[1, 7)] +52,54 %[2, 6)] +7,14 % [3, 4)]	0,64±0,04 +48,83 %[1, 7)] +8,47 %[2, 4)] -23,81 %[3, 5)]	0,83±0,09 +93,02 %[1, 7)] +40,68 %[2, 5)] -1,19 %[3, 4)]
2	the content of sialic acids, mmol/l	2,00±0,03	2,19±0,25 +9,50 %[1, 4)]	3,72±0,19 +86,00%[1, 7)] +69,86 %[1, 7)]	3,64±0,35 +82,00%[1, 7)] +66,20 %[1, 7)] -2,15 % [3, 4)]	2,38±0,45 +19,00 %[1, 5)] +8,68 %[1, 4)] -49,58 %[1, 6)]	3,38±0,45 +69,00 %[1, 7)] +54,34 %[1, 6)] -9,14 %[1, 4)]
3	gaptoglobin content of g/l	0,95±0,04	1,59±0,07 +67,36 %[1, 5)]	2,25±0,12 +136,84 %[1, 5)] +41,51%[2, 5)]	2,20±0,11 +131,57 %[1, 5)] +38,36%[2, 5)] -2,22 % [3, 4)]	1,70±0,10 +78,94%[1, 7)] +6,92 %[2, 4)] -24,44 %[2, 5)]	2,12±0,15 +123,16 %[1, 7)] +33,33 %[2, 5)] -5,78 %[2, 4)]
4	Weltman's test results, ml	0,45±0,01	0,35±0,02 -22,22 %[1, 5)]	0,22±0,02 -51,11 %[1, 7)] -37,14 %[2, 5)]	0,23±0,02 -48,48 %[1, 6)] -34,29 %[2, 5)] +4,55 % [3, 4)]	0,38±0,02 -15,56 %[1, 5)] +8,57 %[2, 4)] +72,72 %[3, 6)]	0,27±0,02 -40,06 %[1, 5)] -22,85 %[2, 5)] +22,73 %[3, 5)]
5	content of C-reactive proteins, mg/l	4,50±0,62	7,05±1,09 +56,70 % [1, 7)]	11,70±0,95 +160,00 %[1, 7)] +66,00 %[2, 7)]	10,50±1,01 +133,33 % [1, 7)] +48,94 % [2, 5)] -10,25 % [3, 4)]	6,90±0,66 +53,33 % [1, 7)] -2,13 % [2, 4)] -41,03 % [3, 5)]	9,60±2,40 +111,33 % [1, 7)] +36,17 % [2, 5)] -17,95 % [3, 4)]

[1)] in relation to the indicators of the control group (almost healthy people);
[2)] in relation to patients without postoperative complications;
[3)] with respect to patients with subsequent soft tissue inflammation;
[4)] $p > 0,05$;
[5)] $p < 0,05$;
[6)] $p < 0,01$;
[7)] $p < 0,001$.

other 22 people had a serum of CRP <6 mg/l, we took it as an average of 3 mg/l (as a whole in the group 4.50 ± 0.62). Based on the data, patients without postoperative complications, 56.70 % exceeded the data of the control group (table 1).

Analysis of the results of the examination of patients with postoperative inflammation of the soft tissue showed an increase of 136.84 % of HG content, by 86.00 % of the content of the SA and a decrease in 51.11 % of the results of WT. When measuring the CRP content in serum with latex test in the analyzed group of patients found out that of serum of 20 persons were 12-24 mg/l (an average of 18 mg/l) – in 6 patients and 6-12 mg/l (average 9 mg/l) – in 14 patients (as a whole in the group 11.70 ± 0.95 g/l). The comparison with such persons in the control group showed an exceeding by 160.00 % (table 1).

When comparing with the results of examination of patients without postoperative complications, it is stated that in patients who have been inflammation of the soft tissues in the postoperative period in serum were higher than in the comparison group by 41.51 %, SA – by 69.86 %, for 37.14 % lower WT results (table 1).

Serum CRP content was significantly higher by 66.00 % in a given group of patients than in patients who have been having complications (table 1).

In patients with postoperative development of hypercoagulation conditions, the content of GP, SA and HG were higher than those in the control group, respectively by 109.30 %, 82.00 %, 131.57 %. According to the results of WT, the analyzed group of patients was inferior to the persons of the control group by 48.48 %.

When measuring CRP concentrations in the blood of patients with the development of hypercoagulation conditions, it was recorded that 10 patients were CRP, 6-12 mg/l (an average of 9 mg/l), and in two patients was observed in the range of 12-24 mg/l (an average of 18 mg/l). After statistical treatment, the result in the group was 10.50 ± 1.01 mg/l, which exceeded 133.33 % of the level of indicator in persons of the control group.

Compared to patients without postoperative complications, higher values of 109.30 % were indicated by 82.00 %, HG by 131.57 % at 48.48 % lower results of WT.

Table 2. diagnostic sensitivity of the studied laboratory parameters of patients with degenerative spinal diseases and subsequent surgical treatment depending on the type of postoperative complications

№ n/p	Indexes	Diagnostic sensitivity, %			
		patients with the subsequent development of soft tissue inflammation	patients with the subsequent development of hypercoagulation	patients with subsequent development of instability of constructions	patients with subsequent development of several complications at the same time
1	the content of total glycoproteins	80	65	70	100
2	the content of gaptoglobin	90	70	60	75
3	results of Weltman`s tests	75	70	55	80
4	the content of C-reactive proteins	100	68	60	90
5	the content of sialic acids	90	65	40	80

The level of CRP in patients of the analyzed group was 48.94 % higher in relation to patients without complications, but 10.25 % less than in patients with postoperative inflammation of soft tissues.

In patients with the development of instability of metal structures compared to such persons of the control group, the level of 48.83 %was found in persons, HG – by 78.94 %, SA – by 19.00 % and lower results of WT – by 15.56 %.

Of the 20 patients with the development of instability of metal structures, the CRP concentration was in the range of 6-12 mg/ml (an average of 9 mg/l) in 13 patients, the value is less than 6 mg/l (an average of 3 mg /l) – in 7 patients. The average value in the group of 6.90 ± 0.66 mg/l, exceeding such in persons of the control group by 53.33 % (table 1).

Indicators of the analyzed group of patients did not have reliable differences with such patients without postoperative complications.

Comparison of inflammation markers of patients analyzed with patients with postoperative development of soft tissue inflammation showed that in patients with instability of metal structures in serum was 23.81 % less than GP, 24.44 % HG and 49,58 % SA. The result of WT and CRP in the group under consideration was 72.72 % and by 41.03 %, respectively, more than in patients with soft tissue inflammation (table 1).

Patients with simultaneous development of several complications were characterized by more significant abnormalities, since they developed several types of postoperative conditions at the same time. At the same time, they found at 93.02 % higher concentration of GP, by 69.00 % – SA, by 123.16 % – HG with at the same time by 40.00 % lower result of WT.

The serum content of the CRP in one patient of the analyzed group of 5 occurred in the range of 6-12 mg/l (an average of 9 mg/l), and in the one patient the concentration of CRP was within 12-24 mg/l (an average of 18 mg/l), that the group averaged 9.60 ± 2.40 mg/l, by 111.33 % exceeding such in persons in the control group (table 1).

When comparing the indicators of a group of patients with multiple complications with such patients with uncomplicated post-operative period, it was recorded that the exceeding of the serum of GP, SA, HG, respectively by 40.68 %, 54.34 % and 33.33 %. At the same time, lower of 22.85 % results of WT were observed (table 1).

The concentration of CRP in the analyzed group of patients was 36.17 % higher than in patients with uncomplicated postoperative period (table 1).

When comparing the indicators of a group of patients with the development of multiple complications with such in patients with the development of inflammatory complications of soft tissues, the results of WT exceeded the data of the comparison group by 22.73 % at 17.95 % of the CRP concentration (table 1).

The requirements of evidence-based medicine require the formalization of evaluative systems of diagnostic significance of the parameters under study.

Diagnostic sensitivity means the ability of the test to properly identify patients who really have this condition [18].

Based on the results obtained in this study, the DS of used tests were calculated. The results are given in table 2.

In patients who have postoperative inflammation of soft tissues around metal structures, the most informative are (in order of reduction of DS): CRP content (100 %), HG content (90 %), SA (90 %), total GP content (80 %), WT (70 %).

In patients with subsequent development of hypercoagulation in the study before the intervention, the largest DS in the content of HG (70 %), WT (70 %), CRP (68 %), content of total GP and SA (65 %) were required in the intervention.

In patients who have observed postoperative instability of metal structures, the most informative are (in

order of reduction DS): total GP content (70 %), CRP content (60 %) and HG (60 %).

In patients with several complications at the same time, the highest DS was observed in the content of total GP (100 %), the content of CRP (100 %), the results of the WT (80 %), and the content of SA (80 %), the content of HG (75 %) (table *2)*.

DISCUSSION

All patients before surgical treatment were characterized by moderate activation of inflammatory processes, which was reflected in the excess of the studied inflammatory markers. In the group with an uncomplicated postoperative period, the above may indicate the presence of chronic inflammatory processes in patients that accompanied the development of the underlying disease. This corresponds to the modern idea of the pathogenesis of osteochondrosis as a disease with degenerative and inflammatory bases of development [19].

In patients with postoperative soft tissue inflammation, there were greater differences with those in the control group than in patients without postoperative complications, indicating a higher baseline inflammatory activity. In degenerative diseases of the musculoskeletal system, but of a different localization – large joints – congenital activation of populations of systemic immune cells, especially macrophages, was recorded, which may lead to the conclusion that some people have a hereditary predisposition to these diseases of the musculoskeletal system [20].

In patients with postoperative development of hypercoagulable states, as in the previous group, biochemical signs of a higher inflammatory background were noted compared with those of both control subjects and patients without postoperative complications. The level of inflammatory markers in the analyzed group of patients generally corresponded to that in patients with postoperative soft tissue inflammation, which, in our opinion, can be explained by the pathogenetic relationship between inflammation and hypercoagulability [21].

When comparing the results of the examination of patients with the development of instability of metal structures with those of the control group, it was found that the markers of the inflammatory process in patients of the analyzed group were only slightly increased and corresponded to those of patients with an uncomplicated course of the postoperative period. Patients of the analyzed group were characterized by a lower level of baseline inflammation than patients with the development of soft tissue inflammation in the postoperative period, which was reflected in the lower values of the studied inflammatory markers. In general, patients with osteochondrosis have more frequent disorders of anatomical structures than healthy individuals [22]. In particular, deviations in the morphology of the upper articular process of the 5th sacral vertebra are quite common [23]. The angle of the sacrum and the type of pelvis are important, and under combined loading, the pelvis with a neutral type of tilt demonstrated the highest flexibility of the lumbar spine, on average by 2.46o, compared with that with a pelvis tilted forward or backward [24]. Probably, the presence of such features contributes to the development of instability of metal structures. In this case, the use of intraoperative navigation systems is highly advisable [25]. Perhaps greater deviations in preoperative laboratory parameters in this group of patients could be found among the parameters characterizing the processes of bone metabolism and mineralization [26]. In particular, deviations in visual indicators are reported by R. L. Witkam et al. (2022) [27]. This may be the rationale for the expediency of including the latter in the examination of patients before surgical treatment of spinal osteochondrosis.

Patients with the simultaneous development of several complications predictably exceeded the content of the studied inflammatory markers in the control group, as well as the group of patients with an uncomplicated course of the postoperative period by most indicators. Nevertheless, judging by the intensity of the manifestation of inflammatory markers, these patients did not have a simple summation of the intensity of inflammatory processes, but rather an expansion of the nomenclature of pathology with their mutual relationship and parallel course.

CONCLUSIONS

1. A comparative analysis of the results of preoperative laboratory examination of patients with transpedicular fixation of the vertebrae and the complicated course of the postoperative period showed that the development of complications in the postoperative period is preceded by changes in preoperative laboratory parameters.
2. In patients with uncomplicated course of the postoperative period before surgery, a moderate increase in serum content of total glycoproteins (<0.60 mmol/l), haptoglobin (<1.6 g/l), C-reactive protein (<12 mg/l).
3. In patients with soft tissue inflammation and with the development of hypercoagulation conditions, similar changes in preoperative markers of serum inflammation have been recorded: a significant increase in serum of total glycoproteins (<90 mmol/l), sialic acids (>3.5 mmol/l), haptoglobin (up to 2.1 g/l), C-reactive protein (>6-12 mg/l).

4. The development of instability of transpedicular structures was preceded by an increase in the serum of haptoglobin (<1.8 g/l) with a slight increase in the content of total glycoproteins (<0.70 mmol/l) and sialic acids (up to 2.5 mmol/l).
5. Before the development of multiple complications after transpedicular fixation of the vertebrae, there was a significant increase in serum haptoglobin (>2.0 g/l) and a moderate increase in the content of sialic acids (3.0-3,5 mmol/l), C-reactive protein (> 6-12 mg/l).
6. According to our data, indicators that are more suitable for predicting the development of complications, as well as its focus are the content of C-reactive protein, haptoglobin and sialic acids.
7. None of the studied indicators is universal for the differential diagnosis of possible complications, and to predict the latter, it is necessary to use diagnostic sets of indicators.

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CONFLICT OF INTEREST

The Authors declare no conflict of interest

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