Dynamics of TNF-α and IL-1β indices in patients with discogenic pain lumbar spine syndromes on the background of osteopathic treatment

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Dynamics of TNF-α and IL-1β Indicators in Patients with Discogenic Pain Syndromes of the Lumbar Spine in the Background of Osteopathic Treatment

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SUMMARY

The article presents the results of immunological studies in patients with discogenic pain syndrome of the lumbar spine, indicating the presence of a pronounced autoimmune inflammatory process. The dynamics of elimination of proinflammatory cytokines TNF-α and IL-1β was shown against the background of various methods of treatment.

Key words: pro-inflammatory cytokines TNF-α and IL-1β; osteopathic correction, discogenic pain syndrome, herniated lumbar intervertebral disc.

RESUME

The aim was to study the elimination dynamics of pro-inflammatory cytokines: tumor necrosis factor alpha (TNF--) and interleukin 1β (IL-1-) in patients with discogenic pain syndromes of the lumbar spine in the background of osteopathic treatment in comparison with other therapeutic techniques. The study involved 120 patients. Patients were divided into three experimental groups (EG) depending on the treatment, and control group (CG): EG 1 - with the use of manual therapy (osteopathy) (n = 30), EG 2 - with the use of homeopathy (n = 30), EG 3 - with the use of drug therapy (ksefokam) (n = 30); CG control group - placebo (n = 30). All patients undergo neurological examination, manual (osteopathic) diagnostics, magnetic resonance imaging of the lumbar spine, immunologic study of blood serum on the pro-inflammatory IL-1β and TNF-α cytokines. The mean values of TNF-- -in the onset of the disease did not exceed 10.70 pg / ml, while in the group with chronic relapsing disease course excess reached 17.10 pg / ml, ie it is more than 2 times. Acute discogenic pain syndrome was quickly arrested that is reflected in the TNF-
- -dynamics which decreased to normal in EG 1, EG 2 and EG 3. In the control group TNF-- -did not reach normal values (9.50 ± 5.23). The content of IL-1- -in the serum in all patients did not exceed normal values (5 pg / ml). This may be due to the fact that

patients consulted a doctor in 5 to 7 days from the onset of the disease, and IL-1-- is a predictor of inflammation in the acute period and starts the autoimmune process in the first hours and days (no later than 5-days) from the onset of the disease, that is confirmed by the results of our study. Clinical and MRI studies revealed the relationship between TNF --- increasing and degree of damage to the intervertebral disc. The more pronounced the destruction process of the disk, the higher is the level of TNF--. Thus, in groups of patients with frequent exacerbations and longer period of disease the TNF-- -level is significantly higher than normal and slowly returns to normal in all experimental groups. The study showed that manual (osteopathic) treatment of patients with discogenic pain syndromes of the lumbar spine actively affects not only on the clinical picture, but also on the elimination of pro-inflammatory cytokines. The same efficacy of osteopathic treatment and drug therapy of these patients was also shown significantly ($p < 0.001$). However, osteopathic treatment has no side effects as a group of non-steroidal pro-inflammatory drugs, and can be recommended as the most safe and effective treatment of discogenic pain syndromes.

Keywords: pro-inflammatory TNF-α and IL-1-β cytokines; osteopathic treatment, discogenic pain syndromes, herniated lumbar intervertebral disc.

Introduction

One of the most important problems of modern neurology is the problem of the effectiveness of the treatment of discogenic pain syndromes (DPS) [4–9]. However, the role of proinflammatory cytokines in the pathogenesis of discogenic pain syndromes has not been sufficiently studied [7]. There is very little data on the dynamics of their elimination during and after various types of treatment. In this regard, in the last two decades, scientific works have appeared on the role of interleukins as chemical carriers of pro-inflammatory signals [1, 2, 10, 14].

Despite the fact that to date some data have been accumulated on the involvement of proinflammatory cytokines TNF-α and IL-β in the pathogenesis of discogenic pain syndromes, a number of questions remain unanswered [1, 3, 11, 12, 13]. First, what is the correspondence between the level of cytokines and the phasing of clinical manifestations of discogenic pain syndromes? Second, how does the level of TNF-α and IL-β change in the blood serum of patients with herniated lumbar discs? There is also no information on the elimination of TNF-α and IL-β cytokines in patients with discogenic pain syndromes (lumbar spine) of EPP during manual (osteopathic) therapy [3].

In this regard, we examined 196 patients with discogenic pain syndromes of the lumbar spine (LBS) at the age from 15 to 72 years.

The purpose research It was the study speakers elimination proinflammatory cytokines: tumor necrosis factor α (TNF-α) and interleukin 1β (IL-1 β) in patients with this pathology during osteopathic treatment in comparison with other therapeutic methods. During the processing of clinical

Patients with the following diseases were excluded from consideration: DIC syndrome, sepsis, infectious diseases (especially infective endocarditis, recurrent herpes, chronic hepatitis C), traumatic and burn shock, allergic, autoimmune diseases, rheumatoid arthritis, cancer, graft rejection, cerebral ischemia, atherosclerotic dementia, chronic bronchitis, fungal mycosis, psoriasis, myeloma, collagenosis, type 1 diabetes mellitus, bacterial infections, pneumoconiosis, tuberculosis, sarcoidosis, AIDS, threatened abortion, myelogenous leukemia, multiple traumas, UV irradiation. The criteria for inclusion in the group were: age not less than 18 and not more than 60 years, discogenic radiculopathy, MRI-verified disc herniation. As a result of the selection of patients, a group of 120 patients with neurological manifestations of discogenic lesions of the lumbar spine was formed. All patients underwent neurological examination, manual (osteopathic) diagnostics, magnetic resonance imaging of the lumbosacral spine, immunological examination of blood serum for proinflammatory cytokines IL-1β and TNF-α.

The patients were divided into three experimental groups (EG) depending on the methods of treatment:

EG1 - with the use of manual therapy (osteopathy) (n = 30); EG2 - using homeopathy (n = 30);

EG3 - with the use of drug therapy (ksefokam) (n = 30); CG - control group - placebo (n = 30).

The groups were homogeneous by age and sex. 36 patients were 30–40 years old (30%), 78 patients were 40–60 years old (65%), 6 patients were 18–30 years old (5%).

Men made up 47.5% (57 patients) of all patients, women were 52.5% (63 patients).

When analyzing the anamnesis of the disease, it was revealed that in 52 patients (43.33%) with DBS, POP pathology was diagnosed for the first time (patients with rare exacerbations were also included here - once a year), and in the remaining 56.66% (68 patients) - repeatedly with exacerbations 2-3 times a year.

Before starting treatment for each patient was carried out grade craniosacral rhythm (CSR) in different parts of the body. In patients with radiculopathies, there was a significant decrease in the CVR parameter in the lower limb concerned, as well as a decrease in the frequency of the rhythm, especially with prolonged and severe discogenic lesions accompanied by mild depression. MRI data showed significant polymorphism. In most of the lumbar SMS, various MR signs of degenerative-dystrophic changes were observed (from flattening of the lumbar lordosis and a decrease in the height of the discs to herniation). Herniated lumbar discs were detected in all patients (100%). Often one patient had from 1 to 3 herniated discs. The most frequent localization of intervertebral hernias were levels: L5-S1 - in 64 patients (53.33%), L4 – L5 - in 48 patients (40%), L3 – L4 - in 8 patients (6.67%).

foraminal hernia.

Research methods

Before starting treatment, patients of all groups underwent a study of blood serum for proinflammatory cytokines IL-1β and TNF-α using an IMMULITE 2000 device. The content of IL-1β in the blood serum of all examined did not exceed normal values (5 pg / ml). This may be due to the fact that patients consulted a doctor on the 5-7th day from the onset of the disease, and IL-1β is a predictor of inflammation in the acute period and triggers the autoimmune process in the first hours and days (no later than 5 days) from the onset of the disease [1], which is confirmed by the results of our study. In contrast, TNF-α in all patients was significantly higher than normal values. Also, all patients underwent a neurological examination according to the classical scheme, an osteopathic examination and an MRI of the lumbar spine.

Treatment methods

Considering data history, neurological and osteopathic examinations, as well as MRI images, a treatment regimen was developed for EG1 patients, which included the following basic techniques:

1. Fascial correction of the posterior torsion of the sacrum.
2. Diagnostics and correction of pelvic bone dysfunctions.
3. Decompression L5-S1.
4. Correction of the ligamentous strain of the lumbar spine and pelvis.
5. Mobilization of the peripheral nerves of the lower extremities.
6. Soft tissue treatment of the lumbar region.
7. Correction of dysfunctions of the cervical spine with decompression C0-C1.
8. Balancing the meninges.
9. Occipito-sacral equilibration.
10. Compression of the 4th ventricle (CV4) (directional fluid option). Despite this treatment algorithm, in the treatment of patients with herniated discs of the lumbar spine, two stages of work were essentially distinguished:

The first stage - a local effect on the affected tissues, was used inacute period of the disease (5-7 days). The treatment was carried out at intervals of 3 days to avoid overloading the patient's body.

The second stage - global work with the patient's posture, was carried out in subacute period (2-3 weeks), in the early recovery period (from 4 to 6 weeks) and late recovery period (from 7 weeks to 6 months). At this stage, the gravitational lines and kinematic chains are balanced.

Patients EG2 were prescribed complex homeopathic treatment, the basis of which was the following drugs: Discum compositum, Traumeel C and Target T (injected 1 day s / c 2.2 ml each into the trigger zones of the lumbar spine). The following drugs were also used: Coenzyme compositum, Gepar compositum (s / c 2.2 ml in the liver area), Hepel (1 ton 3 times a day),

Osteochel S, Spigelon (1 ton 3 times a day - for muscle relaxation), Nux vomica Gomocord (to improve tissue trophism and detoxification - 10-15 drops per 100 ml of water 3 times a day) and Nervohel - 1 ton. 3 to 6 times a day. Injections were administered for 10–21 days every other day. Then, tablet forms of drugs were used. EG3 received drug treatment, which included the use of Xefocam 8-16 mg / day for 3-5 days.

In EG4, imitation of osteopathic treatment was carried out.

results

To assess the results of treatment of DBS EPP in the groups, we used a standard statistical method of analysis. The results were processed using the statistical software package STATISTICA 6.0 for Windows 2000 XP on a PC. Statistical analysis is carried out with the calculation of generally accepted indicators: arithmetic mean, standard deviation. The significance of the differences in the arithmetic mean was assessed using the Student's t-test for two samples with pairwise related options. It turned out that the mean values of TNF-α in patients with onset pain syndrome significantly differed from those in patients with chronic relapsing course. Average TNF-α values at the onset of the disease did not exceed 10.70 pg / ml, and in the group with chronic course of the disease, the excess reached 17.10 pg / ml. Thus, in patients with a chronic recurrent course of the disease, there is an excess of TNF-α by more than 2 times (the norm is 8.1 pg / ml). More detailed data are presented in table. 1 and 2.

Table 1

Dynamics of TNF-α values in patients with acute course of the disease

Группа	До лечения	После лечения
	M ± σ	M ± σ
ЭГ1	9,79 ± 2,31	6,16 ±0,84
ЭГ2	10,57 ± 7,01	8,13 ± 3,42
ЭГ3	10,70 ± 11,10	7,37 ± 7,68
КГ	10,54 ± 6,31	9,50 ± 5,23

Legend:
EG1 - osteopathic treatment EG2 - homeopathic treatment EG3 - drug treatment CG - control group (placebo)

Another important feature is the different dynamics of TNF-α during treatment in the groups with acute and chronic course of the disease (Tables 1 and 2). Acute discogenic pain syndrome stopped faster, which was reflected in the dynamics of TNF-α, which decreased to normal in EG1, EG2 and EG3. In the control group, TNF-α did not reach normal values (9.50 ± 5.23). In the group of patients with chronic recurrent course, TNF-α, although it decreased by

the background of treatment, but remained significantly above the norm (Table 2). Comparative dynamics of proinflammatory cytokines in groups with discogenic pain syndromes of the lumbar spine are presented in Table. 3 and 4.

table 2

Dynamics of TNF-α values in patients with chronic relapsing the course of the disease

Группа	До лечения	После лечения
	M ± σ	M ± σ
ЭГ1	17,10 ± 2,58	9,74 ± 1,72
ЭГ2	17,09 ± 2,73	11,34 ± 2,17
ЭГ3	15,94 ± 13,90	10,13 ± 9,02
КГ	16,37 ± 2,15	14,36 ± 2,35

Table 3

Significant differences in the mean values of TNF-α parameters before and after treatment

Группа	1 измерение TNF-α	2 измерение TNF-α	t	p
	M ± σ	M ± σ		
ЭГ1	14,66 ± 4,28	8,54 ± 2,26	12,29	0,001
ЭГ2	14,91 ± 3,90	10,27 ± 2,35	11,52	0,001
ЭГ3	13,14 ± 3,42	8,66 ± 2,51	10,26	0,001
КГ	14,80 ± 3,53	13,03 ± 3,14	10,27	0,001

Table 4

Significant differences in the mean values of TNF indicators in the studied groups after treatment

Группы	M	σ	M	σ	t	p
ЭГ1-ЭГ2	8,54	2,26	10,27	2,35	2,90	0,01
ЭГ1-ЭГ3	8,54	2,26	8,66	2,51	0,18	–
ЭГ1-КГ	8,54	2,26	13,03	3,14	6,36	0,001

A decrease in the standard deviation value indicates a decrease in the individual variability of TNF-α indices in EG 1.

From table. 4 that there were no significant differences in EG 1 and EG 3, since similar mean values of TNF-α were obtained. This means that osteopathic treatment and medication were equally effective (diag. 1).

Discussion and conclusions

The study showed that in patients with DBS of the lumbar spine, there is an increase in the level of the pro-inflammatory cytokine TNF-α, which does not contradict the data of foreign and domestic researchers.

However, the content of IL-1β in the blood serum of all examined did not exceed normal values (5 pg / ml) before and after treatment. In our opinion, this is due to the fact that IL-1β is a predictor of inflammation in the acute period and triggers the autoimmune process in the first hours and days from the onset of the disease. Therefore, at a later date, it is not possible to detect an increased content of IL-1β in the blood serum.

Clinical and MRI studies have revealed the relationship between the increase in TNF-α and the degree of damage to the intervertebral disc. The more pronounced the process of destruction of the disc, the higher the level of TNF-α. Thus, in the group of patients with frequent exacerbations and a longer period of illness, the level of TNF-α is significantly higher than normal and returns to normal more slowly in all experimental groups.

Often, MRI changes in discogenic pain syndromes of the lumbar spine are difficult to interpret unambiguously. This, of course, complicates the choice of treatment tactics (conservative treatment or surgery). In this situation, one of the possible solutions may be an immunological study of blood serum, in particular TNF-α. It can be assumed that an increase in the level of IL-1β in the blood of patients is observed in the acute phase of the disease (the first 5 days of the disease). However, we have not received data confirming this fact, since the patients examined by us sought help in the second week of the disease. Tumor necrosis factor is a local mediator of inflammation that is found in the intervertebral disc, indicating its damage. The value of TNF-α is different in different periods of the disease: a decrease in concentration occurs in the subacute phase, early and late recovery periods. Thus, the determination of the phase of the disease at the time of the patient's visit can be determined using the immunological markers IL-1β and TNF-α in conjunction with osteopathic examination and MRI diagnostics.

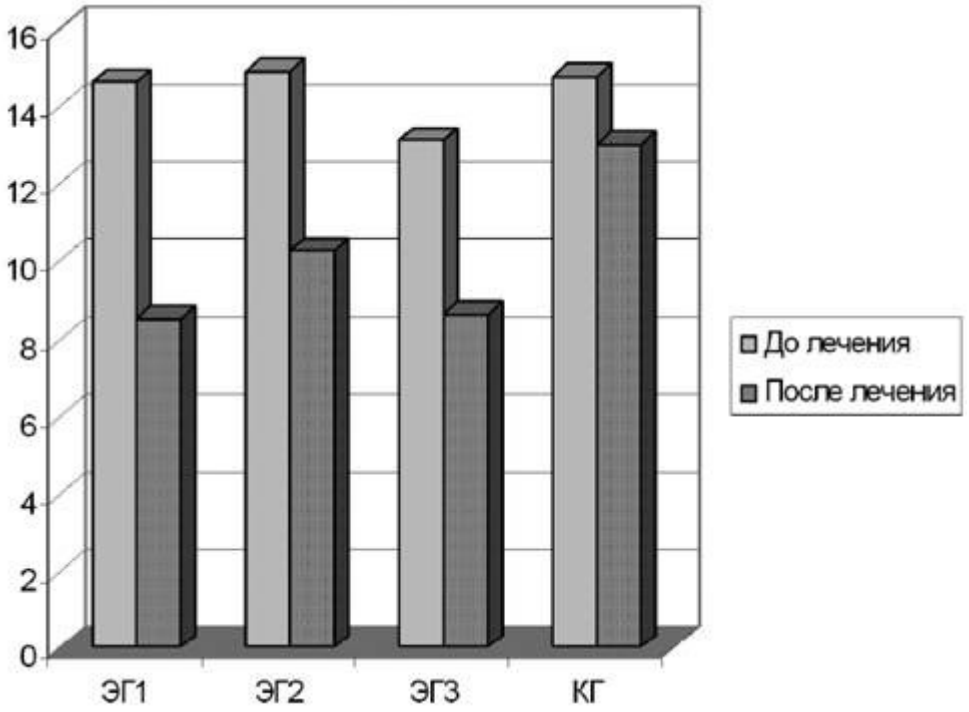

Diagram 1. Dynamics of elimination TNF-α in experimental groups after treatment

Modern diagnostic methods (clinical, osteopathic, MRI, immunological) make it possible to identify the factors of autoimmune inflammation in the pathogenesis of DBS POP, to assess the severity and prognosis of the disease. They make it possible to plan an algorithm of therapeutic measures and to clarify the choice of conservative and surgical treatment. This allows patients who are shown early surgical treatment to avoid the development of persistent neurological deficits, and patients with conservative treatment to avoid the traumatic consequences of surgery. The study showed that manual (osteopathic) treatment of patients with discogenic pain syndromes of the lumbar spine actively affects not only the clinical picture, but also the elimination of pro-inflammatory cytokines. The same effectiveness of osteopathic and drug treatment of this category of patients was also reliably shown. However, osteopathic treatment has no side effects, like a group of non-steroidal anti-inflammatory drugs, and can be recommended as the safest and most effective treatment for discogenic pain syndromes.

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