EFFECACY OF COMPLEX TREATMENT OF VERTEBRAL PAIN SYNDROME USING ELECTROPHORESIS WITH KARIPAIN IN PATIENTS WITH LUMBOSACRAL OSTEOCHONDROSIS

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Relevance Pain in the lower back for many years remains one of the most frequent causes for a medical consultation all over the world (V. V. Povoroznyuk, 2003). According to different sources, from 60 to 80 % of patients are persons of working age from 30 to 59 years [1, 3]. Among the causes of pain syndrome development, damage of intervertebral discs takes one of the important positions. Fibrosis ring protrusion can lead to disk-radicular conflict with the emergence of pronounced pain syndrome, motor, sensitive and reflex disorders. Nowadays there are no specific recommendations regarding the management of patients with intervertebral disc damage. Among the multiple treatments for this condition, none has a sufficient number of studies conducted with long, statistically reliable results.

Consequently, the current medicine simultaneously offers different methods of treatment of diseases caused by injuries of intervertebral discs: they are surgical and conservative, pharmacological and physiotherapeutic, but it is the successful combination of individual methods that is the key to the success of treatment. In case of back pain caused by spinal osteochondrosis, nonsteroidal anti-inflammatory drugs, muscle relaxants, physiotherapeutic techniques are traditionally used, but all these drugs do not affect the immediate cause of pain – damage to the intervertebral disc. The disc consists of a nucleus pulposus tightly surrounded by a fibrous ring formed from fibrous cartilage tissue. Due to the high water content, the core does not shrink and provides shock absorption functions. By the age of 10, almost all cells of the nucleus pulposus die and degenerative changes develop [4]. In the disc tissues there is degradation of the proteoglycan matrix due to the activation of metalloproteinase, interleukin-1 and other factors, the content of chondroitin sulfate-4 decreases, dehydration and partial loss of nucleus pulposus function occur. As a result of reducing of the disc height the load on the fibrous ring is increased and there are prerequisites for its dissociation. During a sharp increase in pressure in this segment, cracks are formed in the fibrous ring, the elements of the nucleus pulposus are shifted forming protrusion, and when the fibrous ring breaks, forming hernia (prolapse) of the intervertebral disc (MPD) with possible formation of relative instability of the spine, osteophytosis of the vertebral bodies (spondylosis), compression of the spinal cord (radiculopathy), spinal cord brain (myelopathy) or vessels of the relevant basin [3] (Fig. 1). As a result of repeated trauma, as well as age-induced involutive changes, degradation of proteoglycans of the IVD matrix is progressing through the activation of metalloproteinase, interleukin-1 and other factors, as well as decreased content of chondroitin sulfate-4, dehydration and partial loss of the nucleus pulposus function.

Back pain caused by the pathology of IVD is still an unresolved problem. Motor disorders, pelvic organ control disorders and the rapid growth of

neurological deficiency require surgical treatment, at least an immediate consultation of a neurosurgeon. Open microsurgical decompression is the gold standard for treatment of lumbar hernia of intervertebral discs with a sagital size greater than 5 mm that cause compression of the spinal cord or stenosis of the spinal canal [6]. According to literature, the efficacy of such intervention is 90 %, complication is less than 2 %, but with smaller prolapses the efficacy is much lower [7].

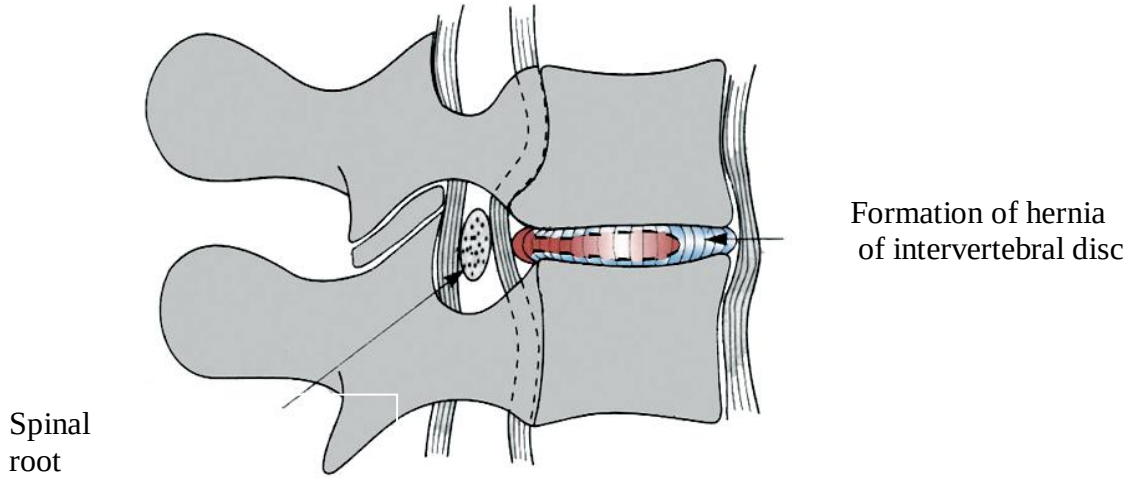

Fig. 1. Scheme of Intervertebral Disc Hernia Development (according to R. V. Deev, 2005)

But often patients delay surgery and prefer conservative methods. One alternative is the chemonucleolysis method, i.e. the splitting or degradation of the nucleus pulposus as a result of a chemical reaction after percutaneous injection directly into the tissues of the disc of a substance for the nucleolysis of the degenerated disk. In most cases, papain and chemopapain are used for this purpose. Papain is a monothiolic cysteine endoprotease, by nature of enzymatic action called ‘plant pepsin’. But unlike pepsin, papain is active not only in acidic, but also in neutral and alkaline environments, as well as in a wide temperature range (up to 50–60 °C). Advantages of the method are low traumatism and preservation of the regenerative potential of the nucleus pulposus.

But this method of treatment is often associated with pyrogenic and allergic reactions. For the first time this procedure was carried out in the 50s and is still in use. According to the American Pain Society Clinical Practice Guideline of 2009, chemonucleolysis ranks well in the list of conservative spinal pain therapy methods [8]. The limitation in the use of the technique is due, firstly, to serious complications of the procedure, namely allergic reactions to as much as anaphylactic shock expressed by neurotoxic action of proteolytic enzymes in contact with subarachnoid space if the injection was made with undue care, and, secondly, is due to the fact that high qualification of medical personnel is required. However, since 1975 chemonucleolysis was performed for about 16,000 patients, 70–90 % of them with a good and excellent rating [6]. Papain causes dehydration of nucleus pulposus proteoglycans, thereby reducing intra-disc pressure and mechanically reducing protrusion of disc elements [7].

In the territory of the former USSR since the 70s, polyenzymatic drugs (Papain, Lekozim, Caripazim) have also been used to treat degenerative spinal diseases. Different methods of administration of drugs were studied and applied – intradisc, intramuscular or subcutaneous with subsequent galvanization or ultrasound treatment, percutaneous electrophoresis.

Now in our country only one proteolytic enzyme complex – Karipain, (**manufacturer is NPC AS-COM, Moscow**) formulated of three enzymes (papain, chymopapain, proteinase) and lysozyme. Karipain is a medicinal product of plant origin derived from papaya latex. **Papaya** is also known as **mamão, pawpaw, melon tree** (*Carica papaya*).

Karipain is allowed only for external use, therefore in our study the effect of Karipain on vertebral pain syndrome administered by electrophoresis method was studied.

Therefore, **the aim of our study** was to study the efficacy and safety of electrophoresis with Karipain as part of the complex treatment of vertebral pain syndrome caused by degenerative and dystrophic changes in the intervertebral discs of the lumbosacral spine.

Material and Methods The study was conducted in the Department of Clinical Physiology and Pathology of the Musculoskeletal System of the Institute of Gerontology of the AMS of Ukraine.

Criteria for the inclusion of patients in the study:

– Age 30–65 years
– Men and women
– Osteochondrosis of the lumbar spine and associated pain syndrome
– Pain at the time of the initial examination is over 4 cm by VAS
– Presence of compression and root syndrome in the form of sensitive or reflex disorders
– Presence of intervertebral disc protrusions in the lumbar spine, size from 3 to 6 mm according to MRI data.

Exclusion criteria:

– Compression-root syndrome with motor disorders, pelvic dysfunction, reduced sensitivity, in the perineum zone
– The presence of signs of intervertebral disc sequestration according to MRI data
– Hypersensitivity to any component of the drug that is investigated
– Skin pathology in the area of electrophoresis
– Pathology of the cardiovascular system or oncological diseases that are contraindications to electrophoresis.

The study included 15 patients between 30 and 65 years of age (mean age 47.1 ± 4.2 years). Among them 8 are women (53 %) and 7 are men (47 %). In all patients prior to the examination, magnetic resonance imaging (MRI) of the lumbar spine was performed, with which protrusions of intervertebral discs were diagnosed at the level of lumbar spine, size from 3 to 6 mm. In 9 patients IVD

protrusions were at level L_5-S_1, in 6 patients at level L_4-L_5. The duration of the pain syndrome was at least 2 months. In all patients since MRI, there was no significant deterioration in the clinical condition which could indicate the progress of IVD protrusion or rupture of the fibrosis ring.

All patients received complex treatment, which included non-steroidal anti-inflammatory drugs, muscle relaxants, therapeutic exercise and electrophoresis with Karipain on the lumbar spine.

Electrophoresis Procedure

1 g of dry substance was diluted in 5–10 mL of saline, 2–3 drops of dimexide were added and applied on a fabric pad, the size of 100 cm^2. The solution was injected from the anode. Electrophoresis was performed by a two-channel device for electrotherapy in pulse mode (MIT EF 2). Electrodes were placed paravertebrally across the longitudinal method at a distance of 10–15 cm one from the other. The modulating frequency was 37 Hz. The duration of the first procedure is 10 minutes, followed by a 3-minutes increase each next procedure up to 20 minutes. For the course 10 procedures daily, with a possible 1-2 days' break.

The condition of patients was assessed twice: before treatment and 14 days after treatment. All patients were examined according to a plan acceptable to the orthopedic patient. Next to general clinical and radiological studies, the intensity of pain syndrome was determined according to the four-part visual analogue scale (VAS) for pain and the McGill Pain Questionnaire, the Roland Morris Low Back Pain Disability Questionnaire, the Oswestry Questionnaire and the Zung Questionnaire. In addition, all patients completed the European Quality of Life Questionnaire – 5 directions (EvroQol-5D).

Study Results and Discussion Indicators of pain syndrome intensity according to the McGill Pain Questionnaire before treatment were: descriptors – 11.3 ± 1.6 points, ranks – 25.0 ± 4.6 points, pain index – 5.3 ± 0.3 which indicates moderate severity of pain, duration of pain syndrome at least 2 months. The level of anxiety on the Zung questionnaire was 14.0 ± 2.6 points. The vital activity disorder associated with vertebral pain syndrome was 27.6 ± 2.3 and 10.3 ± 1.0 points respectively according to Roland the Oswestry Disability Index and Roland-Morris Disability Questionnaire.

After the treatment course, a significant decrease in the intensity of pain syndrome was determined in patients according to the indicators of VAS (Fig. 2) and McGill Pain Questionnaire (Fig. 3) and a significant improvement of activities of daily living by questionnaires of Zung, Roland Morris, Oswetsry (Fig. 4) and EvroQol-5D (Table 1).

Table 1. Dynamics of Intensity of Vertebral Pain Syndrome on the Background of Complex Treatment using Electrophoresis with Karipain in Patients with Lumbar Osteochondrosis

Method of study	Indicator	Before treatment, scores	After treatment, scores	Value dynamics, %	t	P
McGill Pain	Pain index	5.3 ± 0.3	2.4 ± 0.4	53.6 ± 7.5	7.5	0.0001

Questionnaire	Total amount of descriptors, points	11.3 ± 1.6	6.5 ± 1.0	34.6 ± 8.9	4.0	0.002
	Total rankings, points	34.6 ± 8.9	25.0 ± 4.6	47.9 ± 7.9	4.5	0.001
4-component VAS	Scale 1, cm	5.3 ± 0.5	2.60 ± 0.5	56.6 ± 7.4	8.7	0.001
	Scale 2, cm	5.4 ± 0.4	3.1 ± 0.2	44.6 ± 6.0	5.6	0.001
	Scale 3, cm	2.9 ± 0.5	1.5 ± 0.2	40.8 ± 9.2	4.0	0.001
	Scale 4, cm	7.8 ± 0.4	5.7 ± 0.3	29.4 ± 5.1	5.3	0.001
Roland-Morris Disability Questionnaire	Total points	10.3 ± 1.0	3.7 ± 0.8	57.8 ± 10.0	5.6	0.001
Oswetsry Questionnaire	Total points	27.6 ± 2.3	18.2 ± 1.9	33.4 ± 5.1	7.8	0.001
Zung Questionnaire	Total points	14 ± 2.6	7.3 ± 2.1	50.2 ± 8.2	5.3	0.003
EvroQol-5D	Points	6.11 ± 0.38	5.3 ± 0.45	10.0 ± 9.13	4.0	0.001

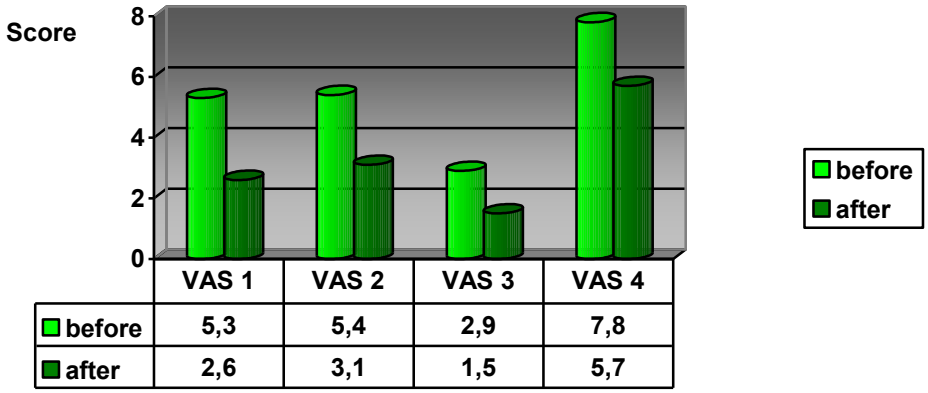

Fig. 2. Dynamics of Severity of Pain Syndrome in the Lower Back in Patients with Osteochondrosis of the Lumbosacral Spine according to the 4-component of VAS on the Background of the Treatment with Karipain

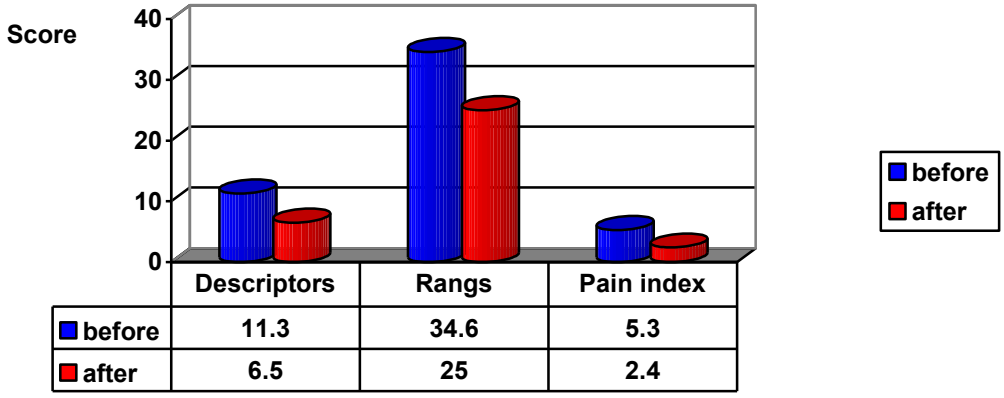

Fig. 3. Dynamics of Severity of Pain Syndrome in the Lower Back in Patients with Lumbar Sacral Osteochondrosis according to the Mac-Gill Questionnaire on the Background of the Treatment with Karipain

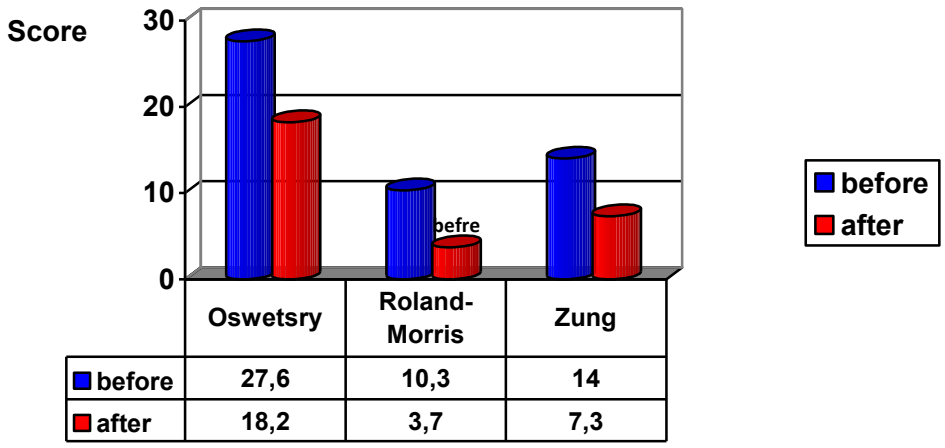

Fig. 4. Dynamics of the General State associated with Lower Back Pain on the Background of the Treatment with Karipain

Degenerative processes in the nucleus pulposus caused by a variety of factors are accompanied by inflammation and swelling of tissues, lead to increased pressure inside the disc and thus disrupt the processes of diffusion, necessary to maintain normal tissue metabolism of the disc, and therefore degenerative changes are progressing. Therefore, reduction of intra-disc pressure is a pathogenetic method of treatment, and contributes not only to reduction of manifestations of radiculopathy, but also to reduction of vertebral pain syndrome.

In the study conducted in the State Institution Institute of Neurology, Psychiatry and Narcology of AMS of Ukraine, positive results were obtained in 77.27 % of patients, according to the intensity of pain syndrome, pain decrease was about 34 % on VAS [12]. Similar data are obtained in our study: reduction of pain syndrome intensity from 29.4 ± 5.1 % to 56.6 ± 7.4 % on different sub-scales of the four-component VAS. According to the report of Kharkov researchers, side effects were uncommon: one case (5 %) of generalized allergic reaction which led to discontinuation of treatment, 3 (13 %) cases of local reactions in the form of redness and rash, with no need of change the treatment regimen. There were no adverse reactions in our study, which, in our opinion, is due to fewer studies and shorter treatment courses. The results presented in the paper are preliminary. In our opinion, the use of Karipain is a promising method in the conservative treatment of complicated osteochondrosis, which is the basis for the continuation and planning of new studies.

Conclusions Complex treatment of patients with osteochondrosis of the lumbosacral spine with intervertebral disc protrusions using electrophoresis with Karipain causes a decrease in intensity vertebral pain syndrome by 53.6 ± 7.5 % and increases daily activity and level of life of patients from 33.4 ± 5.1 to 57.8 ± 10.0 % according to different questionnaires. The noted method of treatment is safe for use in both inpatient and outpatient settings.

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Efficacy of complex treatment of vertebral pain syndrome with electrophoresis with Karipain in patients with lumbosacral osteochondrosis

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Summary

Study of the effectiveness and safety of electrophoresis with Karipain was conducted in the complex treatment of vertebral pain syndrome caused by degenerative-dystrophic changes in the intervertebral discs of the lumbosacral spine in the Department of Clinical Physiology and Pathology of the Musculoskeletal System of the State Institution Institute of Gerontology of the Academy of Medical Sciences of Ukraine. After the course of treatment in patients there is definitely a significant decrease in the intensity of pain syndrome according to the indicators of VAS and McGill Questionnaire and significant improvement of activities of daily living by questionnaires of Zung, Roland Morris, Oswetsry and EvroQol-5D.