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Research Article

# The Possibilities of Using Chondroitin Sulfate in Patients with Chronic Back Pain

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## Abstract

**Objective:** To study the efficacy and safety of chondroitin sulfate (mucosat) in the treatment of chronic lower back pain.

**Material and Methods:** The medical documentation of 46 outpatients with chronic lumbosacral dorsalgia, who received 25 intramuscular injections of 2 ml mucosat, was studied. The assessment of patients' condition and efficacy and safety of the treatment was conducted based on the data of four visits (1st, 10th and 25th day and 3 months after the end of treatment). Results of the clinical-neurological examination, pain intensity at rest and at movement according to the Visual Analogue Scale (VAS) and the severity of Lasegue and Wasserman signs and limitation of movements in the lumbar spine were taken into account.

**Results:** The use of mucosat at a dose of 2 ml intramuscularly 1 time in 2 days led to a significant decrease in the severity of pain syndrome and increased mobility in the lumbar spine (before treatment, the level of pain at rest according to the VAS was 4.22 ± 1.28 scores, on the 25th day 2.13 ± 0.24, 3 month after treatment 2.37 ± 0.31; the level of pain at movement: 5.78 ± 1.15; 4.56 ± 0.47; 4.78 ± 0.22, respectively ($p < 0.01$). There was a reduction of the dose of previously used non-steroidal anti-inflammatory drugs in the end of treatment and maintenance of the results of therapy for 3 months after the end of treatment. Good tolerability of the drug and the absence of significant side-effects were shown as well.

**Conclusion:** This study showed the efficacy and safety of chondroitin sulfate (mucosat) in the treatment of outpatients with chronic lower back pain.

***Keywords:*** *Chronic Pain Syndrome; Chondroitin Sulfate; Chondroprotectors; Low Back Pain*

## Introduction

The problem of chronic pain is one of the most difficult in modern medicine. According to Russian and foreign researchers, diseases of the musculoskeletal system, namely pain in the joints and back, occupy the first place in terms of seeking medical help for chronic pain [1,2]. Both of them are the cause of long-term disability of patients [3]. From 50 to 85% of people have ever experienced pain in the lumbar spine [4], while a year after the onset of the disease, 33% of patients still experience moderate, and 15% - severe back pain. In 75% of patients, a relapse occurs after an episode of acute back pain [5].

Most researchers call degenerative-dystrophic lesions of the intervertebral discs and facet joints as the primary cause of dorsalgia. Further, the ligamentous apparatus, muscles, fascia, as well as spinal roots and nerves are involved in pathogenesis [6]. Ligament hypertrophy and persistent muscle spasm cause a change in the biomechanics of movements and impaired posture, which in turn support. Also,

the faster development of degenerative and dystrophic processes in this particular part of the spinal column is facilitated by a large range of movements in various planes, vertical static load, which causes increased pressure on the underlying vertebrae and discs. Repeated injuries, hereditary predisposition, excessive static or dynamic load, and also physical inactivity accelerate the processes of degeneration..

Depending on the duration of back pain, they are classified into three categories: acute (2 - 4 weeks), subacute (4 - 12 weeks) and chronic (> 12 weeks), which in turn are divided into permanent and episodic [7].

As you know, chronic pain differs from acute pain not only in temporal characteristics, but also in the complex neurophysiological mechanisms underlying it. If the leading role in the pathogenesis of acute pain is played by nociceptive afferentation from the structures of the affected spinal-motor segment, then the causes of the formation of chronic pain syndrome can be both peripheral nociceptive effects and dysfunction of the central structures of the somatosensory analyzer [8].

Recently, in the treatment of chronic back pain, non-invasive methods of therapy have been given preference. The goals of the therapeutic effect are not only the fight against pain, but also the early mobilization of the patient and, in the long term, his return to his usual way of life. In the treatment of patients with mild to moderate chronic back pain, non-drug methods, including kinesiotherapy, psychotherapy and cognitive-behavioral therapy, are preferable [9]. At the same time, with severe pain, topical pharmacotherapy remains, which includes the use of non-steroidal anti-inflammatory drugs (NSAIDs) as the first line and opioids or duloxetine as the second line of therapy [9,10]. When diagnosing the neuropathic component of pain, anticonvulsants can also be added to therapy [8].

NSAIDs are highly effective in stopping pain, however, their long-term use is limited by the risk of ulcerogenic damage to the gastrointestinal tract (GIT) [11]. The solution to this problem can be the use of selective cyclooxygenase-2 inhibitors, however, in this case there are restrictions in admission, in particular in elderly patients with coronary heart disease [12]. In general, there is no reliable information about the safety of long-term use of NSAIDs [13].

An analysis of clinical studies conducted in recent years also showed a lower effectiveness of NSAIDs in the treatment of chronic back pain than previously thought [14]. Limitations exist in the long-term administration of duloxetine, which may have a negative effect on hepatocytes [15].

In connection with the foregoing, of undoubted interest is the search for new drugs comparable in effectiveness with NSAIDs, but with a safer profile of use. In recent years, a number of clinical and experimental studies have been carried out to study drugs from the SYSADOA group (Symptomatic Slow Acting Drugs for Osteoarthritis) - slow-acting drugs for the symptomatic treatment of osteoarthritis [16]. The SYSADOA group includes various chondroprotectors, including glucosamine and chondroitin sulfate. The use of this group of drugs is pathogenetically justified, because, as already mentioned, one of the root causes of back pain is degeneration of facet joints.

Chondroitin sulfate (CS) - a natural glycosaminoglycan consisting of repeating disaccharide units of glucuronic acid and N-acetyl-D-galactosamine, plays an important role in biological processes. It is abundantly present in all connective tissues of mammals, especially in cartilage, skin, blood vessels, ligaments, tendons, axon terminals, in the extracellular matrix [17]. In clinical practice, the most widely used is the 4.6-sodium form of CS.

The main reasons for using CS as SYSADOA:

1. CS slows the development of osteoarthritis. This has been demonstrated in several clinical trials, while, unlike NSAIDs, it does not affect the gastrointestinal tract and kidneys in elderly patients.
2. The anti-inflammatory effects of CS were studied: stimulation of the synthesis of proteoglycans and hyaluronic acid, a decrease

3. Pain reduction and joint stiffness as a result of taking CS remain after the course of treatment for several months, which is never observed when using analgesics that require continuous use.
4. CS plays a role in the formation of new bones, cartilage and tendons, supports the structural integrity of tissues, and also heals damage well.
5. Provides specific biological functions in the cell: adhesion, morphogenesis, neural network formation and cell division [17].

The analysis of clinical and experimental studies demonstrates the efficacy and safety of the use of CS in the treatment of patients with osteoarthritis of the knee, which suggests that the drug is similarly effective in treating affected joints of a different location, including facet joints of the spine. Unfortunately, there is still insufficient clinical data on the use of chondroprotectors in the treatment of dorsalgia.

## Purpose of the Study

The purpose of the study was to determine the efficacy and safety of the use of the drug chondroitin sulfate (mucosate) in the treatment of chronic lower back pain.

## Materials and Methods

Retrospectively, outpatient records of 46 patients (27 women and 19 men) aged 42 - 65 years (mean age 53.8 ± 9.1 years) with chronic pain in the lumbar spine treated in the neurological department of the City Polyclinic nickname № 166 DZM. The inclusion criteria were the presence of pain in the lower back lasting from 6 months, the strength of 4 - 7 points, which required constant daily NSAID intake for the previous 3 months.

Chondroitin sulfate (mucosate) was prescribed in the course of 25 intramuscular injections of 2 ml every other day. The first 3 injections were performed at a dose of 1 ml (100 mg), the next at a dose of 2 ml (200 mg). If necessary, patients continued therapy with NSAIDs. A week or more before the start of injection therapy, muscle relaxants, glucocorticoids, and physiotherapy were canceled. Non-inclusion criteria were compression-radicular syndromes, injuries and a history of surgical interventions on the spine, the presence of blood diseases, prolonged use to anesthetize antidepressants and anticonvulsants.

The clinical examination included an assessment of the intensity of the pain syndrome according to the Visual Analogue Scale (VAS) at rest and during movement, the range of movements in the lumbar spine, the presence and severity of the symptoms of tension (Lasegue and Wasserman) during the initial intake, on the $10^{th}$, $25^{th}$ day of therapy and 3 months after the end of the course of treatment of CS. They also evaluated the need for NSAIDs during chondroitin therapy, the frequency and nature of side effects. Laboratory control included the assessment of coagulograms (INR, APTT, blood platelet count, coagulation time and bleeding time).

Statistical processing was performed using Microsoft Office Excel 2010 programs (Microsoft Corp., USA). Continuous parameters were taken into account in the form of means (M) and standard deviations (σ). For comparison in two groups of these parameters, under the assumptions of their normal distribution, the unpaired Student t-test was used for equal variances. To identify the dynamics of continuous indicators, paired Student t-test was used. To analyze the conjugation table 2´2, we used the Pearson $\chi^2$ criterion adjusted for Yates continuity. The significance level was assumed to be 0.05.

## Results

Prior to the start of therapy, limitation of mobility in the lumbar spine was noted in all patients, in 38 (82.6%) patients the presence of reflex muscular-tonic syndrome (pain and tension of the paravertebral muscles) was revealed. Radiographs of the lumbar spine in all patients showed structural changes in the vertebral-motor segments of a degenerative-dystrophic nature of varying severity. In 35 (76.08%) patients, a magnetic resonance imaging of the lumbar spine was performed to exclude compression-radicular pathology. Disc protrusions

of median and/or paramedian localization were detected without compression of the roots of the spinal cord and signs of spinal stenosis. Urinalysis, ultrasound examination of the pelvic organs, kidneys and abdominal cavity, gynecological examination in women revealed no pathology.

As a result of the treatment, a decrease in syndrome was noted already on the 10th day of therapy, but statistically significant differences were revealed at the end of the course. The severity of spontaneous pain according to VAS before treatment averaged 4.22 ± 1.28 points, with movement - 5.78 ± 1.15 points, by the 25$^{th}$ day of therapy, the severity of pain at rest decreased to 2.13 ± 0, 24 points, and during movement - up to 4.56 ± 0.47 points ($p < 0.01$). By the 3$^{rd}$ month there was no increase in pain (the severity of pain at rest was 2.37 ± 0.31 points on average, and 4.78 ± 0.22 points ($p < 0.01$) when moving).

Also, in patients after treatment with chondroitin sulfate, the need for NSAIDs was significantly reduced. Before treatment, drugs from the NSAID group were constantly (5 - 7 times a week) taken by 36 (78.26%) patients. By the 25$^{th}$ day from the start of therapy in 21 (58.33%) patients, the need for NSAIDs decreased to 2 times per week, 10 patients (27.77%) completely refused to take NSAIDs. 3 months after the end of taking CS, the need for NSAIDs remained in 24 (52.17%) patients, i.e. another 2 patients completely refused to take painkillers. The frequency of NSAIDs has remained unchanged. Along with the relief of pain in patients, an improvement in mobility in the lumbar spine was recorded.

Among the undesirable effects in 3 (6.5%) patients, dyspepsia was noted, which stopped on its own. Significant changes in blood tests were noted.

## Discussion

The data obtained by us on the effectiveness of chondroitin sulfate in reducing pain in patients with chronic back pain are similar to the results of the analgesic effect of CS in osteoarthritis of the knee joint. For instance, clinics in Belgium, France, and Switzerland conducted a multicenter, randomized, double-track, placebo-controlled study in which 353 patients of both sexes over 45 years old with osteoarthritis of the knee participated [18]. Minimum inclusion criteria: indicator of the algo-functional index M. Lequesne, equal to 7 or more, and pain strength, equal to 40 mm or more, according to the VAS. Patients received CS at a dose of 1200 mg/day (once or in three doses of 400 mg) for 3 months. As a result of the treatment, the value of the algo-functional index decreased significantly by almost 40% compared with the initial level and the level of pain according to the VAS decreased by 45%. There were no statistically significant differences between the forms of administration of the drug, which was also noted by researchers as a positive point, as non-compliance by patients with the regimen of drug administration is one of the frequent reasons for the ineffectiveness of the prescribed treatment.

Mitsuhiro Morita., *et al*. in his study [19] compared the effects of different doses of chondroitin in patients with radiologically confirmed knee osteoarthritis: one group of patients received 260 mg/day, the other 1560 mg/day. Patients were randomly divided into groups. Symptoms were assessed by Lequesne and VAS. The algo-functional index in both groups rapidly decreased during the first 3 months of treatment and then continued to gradually decrease until the end of the course of therapy. The analgesic effect of the dose of 1560 mg/ day was more pronounced than that of the dose of 260 mg/day, but this difference was observed only in the subgroup of patients with severe symptoms. In patients with less severe disorders in the joint, no differences were observed when taking small and large doses of CS, both doses showed comparable effectiveness. Researchers also noted that the drug was well tolerated.

Also, many researchers compared the effectiveness of chondroitin versus other chondroprotectors and NSAIDs. Comparative tests of glucosamine and chondroitin in therapy of patients with osteoarthritis of the hip and/or knee joints [20] showed that chondroitin was more effective in relieving pain and increasing the physical activity of patients, whereas glucosamine only contributed to a decrease in the stiffness of the affected joint.

A comparative analysis of glucosamine and diacerein [21] showed that both drugs alleviate the symptoms of gonarthrosis equally effectively, but the first has a significant advantage in the form of an almost complete absence of side effects.

In a six-month CONCEPT study in five European countries, 604 patients with osteoarthritis of the knee joint compared a 6-month administration of 800 mg of CS, placebo, and 200 mg of celecoxib. Both drugs effectively reduced leg pain and increased joint functional activity [22].

Experimental studies of the anti-inflammatory effect of chondroprotectors (CS, glucosamine, and a combination of avocados and soybeans) in combination with NSAIDs carprofen showed that when combined with chondroprotectors, the anti-inflammatory effect of carprofen was significantly enhanced [23]. In addition, Belgian researchers studied the anti-inflammatory effect of chondroitin sulfate in 72 patients with osteoarthritis of the knee. Patients received a dose of 800 mg/day for six months. As a result, after 3 and 6 months from the start of therapy in the blood of patients, the level of Coll2-1 cartilage tissue decay biomarker significantly decreased, and by the end of treatment a significant reduction in pain and an improvement in joint mobility were noted [24].

## Conclusion

A retrospective analysis of the efficacy and safety of the use of the injectable form of chondroitin sulfate (mucosate) in the treatment of patients with chronic pain in the lower back who underwent treatment on an outpatient basis confirmed the hypothesis that it is possible to use chondroprotectors in a complex therapy for chronic back pain.

## Conflict of Interest

The authors declare no conflict of interest.

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