



## Application of Viprazan in physiopharmacotherapeutic techniques at treatment of patients with osteoarthritis of knee joints

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### ABSTRACT

We have examined 45 men and women at the age of 45 to 59 with osteoarthritis of the knee joints complained of a pain syndrome and limitation of motion in the lower extremities. All patients were divided into 3 groups: in the first group the basic medical treatment was supplemented with ultraphonophoresis of chitosan gel Viprazan with adder venom on the affected joints; in the second group it was carried out placebo procedure of ultraphonophoresis; in the third group the basic treatment was supplemented with application of Viprazan gel on painful zones during three weeks. Based on the research findings we have established that introduction by ultrasound of the gel Viprazan in circumarticular tissues promotes the decrease of indicators of the pain, constraint and functional insufficiency. According to WOMAC questionnaire the indicators of the pain, constraint and functional insufficiency were decreased 1.3 times, and total index – 1.2 times. Upon completion of a therapeutic course in patients of the first group it was noted the increase of degree of restoration of function of a joint up to 84.2% and an index of efficiency of microcirculation 2.1 times that was not observed in the placebo and comparison groups.

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### Introduction

Osteoarthritis is one of the most important medico-social problems of modern society that is caused by its high prevalence and a co-morbidity [1]. Side effects from the administered drugs are the main deficiency of drug therapy. It makes important the development of effective methods of correction of the clinical functional disturbances in patients with osteoarthritis [2]. In this regard traditional methods of rehabilitation can be optimized by use of natural drugs both independently and in combination with physiotherapeutic technologies.

The data of the expressed anesthetizing action of venoms of adder are presented in literature. It allows to use these data in treatment of diseases of musculoskeletal system and peripheral nervous system: osteoarthritis, dorsopathies, neuralgia, etc. [3]. It is supposed that the antinociceptive effect can be caused by influence of specific peptides on the receptor apparatus and a condition of the membranous apparatus of nervous cells [4]. Introduction of snake venom into tissues implies the existence of system carrier, which is often chitosan serves. Biomedical properties of chitosan are well-known [5].

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## Aim of the Research

The purpose is to estimate the influence of ultraphonophoresis of chitosan gel Viprazan with viper a venom on expression of pain syndrome and clinical functional parameters in patients with gonarthrosis.

## Materials and Methods

We examined 45 men and women of 45 to 59 years with osteoarthritis of knee joints in phase of the fading exacerbation with I–II X-ray stage according to Kellgren – Lawrence and first degree of joint dysfunction. The main implications of illness in the examined patients were the pain (100.0% of cases) and dysfunction of a joint (82.5% of cases). We verified the diagnosis basing on clinical functional probes, X-ray and ultrasound studies.

Criteria of exception were: 1) malignant neoplasms; 2) general diseases of blood; 3) decompensated conditions of endocrine and cardiovascular systems, liver, and kidneys; 4) bleeding, pneumorrhagia; 5) hypersensitivity to meloxicam and other nonsteroidal anti-inflammatory drugs; 6) aspirin-sensitive asthma. Permission from the Local Ethical Committee was got for carrying out the study. All patients signed informed consent sheet to participate in the study.

The basic treatment course included magnetotherapy of the affected joints area, manual massage of lower extremities, and physiotherapy exercises.

By random sampling, all patients were divided into three groups: in the first group (25 people) the basic treatment was combined with ultraphonophoresis of the affected joints with chitosan gel (Viprazan) containing venom of adder; in the second group (10 people) the basic treatment was combined with placebo procedure of ultraphonophoresis; in the third group (10 people) basic treatment was combined with rubbing gel Viprazan into painful zones in the morning and in the evening for three weeks.

We assessed the pain in joints (at rest, at night, when relying on the leg, at passive movements, after a day of usual loading, when walking the stairs, starting pain), joint stiffness, and functional failure of an extremity in daily activity – according to the WOMAC index [6]. We estimated the volume of movements in the affected joints by means of the goniometer with mathematical calculation of extent of restoration of function of a joint: the value  $96.8 \pm 3.2\%$  was considered as “excellent”;  $83.7 \pm 7.3\%$  – as “good”; “satisfactory” was the indicator  $67.7 \pm 6.6\%$  – “satisfactory”;  $55.8 \pm 4.2\%$  – “unsatisfactory” [7].

We carried out the Laser Doppler Flowmetry with the device LAKK-0 selectively in patients of the first and second groups. Sensors were fixed by a sticky ring to the skin surface in the area of maximum painfulness. Examination was carried out during primary survey and upon completion of treatment course.

Ultraphonophoresis was carried out with the device UZT-101F when 2–3 g of Viprazan gel were applied on skin in projection of the affected joint. After full absorption of the gel we additionally applied a mix of lanolin and vaseline as the contact substance. Then we performed the procedure of ultraphonophoresis. In placebo group we applied on skin only mix of vaseline and lanolin before ultrasonography. The influence technique was slow roundabouts (speed of 1–1.5 cm/s) of ultrasonic radiator on the chosen zones contactly with ultrasound intensity of  $0.8 \text{ W/cm}^2$  in continuous mode. Daily exposure time on a single zone was 3–5 min, on a session 6–10 min. During a single procedure the influence was applied on 1–2 joints depending on the area of lesion. The treatment course included 12 procedures which are carried out 5 times a week.

Statistical processing of the obtained data was carried out with software package SPSS 17.0. For estimating the differences between the groups we used nonparametric methods: Kolmogorov – Smirnov’s criterion, and angular criterion of Fischer. Comparative intra group assessments of results before and after treatment we performed according to Wilcoxon’s criterion. We also used the method of variation statistics: calculation of arithmetic mean (M) and mean arithmetic error (m). The level of the statistical significance was assumed as 0.05.

## Results and Discussion

Initial values of total index WOMAC of osteoarthritis in the studied groups varied from  $122.5 \pm 20.3$  to  $127.3 \pm 21.8$  points. This proved the presence of clinical functional disturbances (Table 1). In particular, high levels of pain and malfunction were noted in all patients according to results of testing with separate subscales of questionnaire. After 2.5 weeks of treatment in patients of the first group the indicators of pain, constraint and functional insufficiency have been decreased by 1.29 times ( $p = 0.024$ ), 1.26 ( $p = 0.036$ ) and 1.24 times ( $p = 0.042$ ) respectively, and the total WOMAC index has been decreased 1.2 times ( $p = 0.043$ ). At patients in the second and third groups the changes were less significant and ranged within 7–12%. At the same time in the group of treatment with Viprazan gel applications the patients noted higher effectiveness concerning algias and functioning of the affected joints, than in placebo group.

**Table 1**

Indicators of pain, constraint in joints and functional insufficiency of extremity in patients with gonarthrosis in dynamics of treatment according to WOMAC, points

Indicator	1 group (n = 25)		2 group (n = 10)		3 group (n = 10)	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Pain	25.7 ± 4.2	19.8 ± 3.7*	26.7 ± 4.4	24.8 ± 4.2	25.9 ± 4.5	23.5 ± 4.1
Constraint in joints	9.7 ± 1.8	7.7 ± 1.6*	9.4 ± 1.7	8.4 ± 2.0	9.5 ± 1.6	8.1 ± 1.6
Functional insufficiency	88.4 ± 7.9	71.3 ± 9.2*	87.9 ± 9.6	84.6 ± 10.3	87.3 ± 11.2	84.2 ± 10.5
Total point	124.5 ± 20.5	103.6 ± 21.6*	125.7 ± 21.1	118.4 ± 21.7	124.2 ± 20.3	115.5 ± 22.8

\* Criterion of reliability of intra group differences.

**Table 2**

Indicators of peripheral microcirculation in patients with gonarthrosis in dynamics of treatment

Indicator	1 group (n = 25)		2 group (n = 10)	
	Before treatment	After treatment	Before treatment	After treatment
Peripheral microcirculation, perf. units	8.91 ± 0.06	17.6 ± 0.18* <sup>^</sup>	9.9 ± 1.3	11.9 ± 0.63*
Mean square deviation, perf. units	4.30 ± 0.41	5.16 ± 0.40* <sup>^</sup>	4.20 ± 0.31	4.20 ± 0.26*
Coefficient of variation, %	49.90 ± 1.8	35.5 ± 2.01* <sup>^</sup>	48.80 ± 2.42	47.01 ± 2.3*
Index of efficiency of microcirculation, c.u.	0.70 ± 0.07	1.47 ± 0.10*	0.61 ± 0.08	0.81 ± 0.12*

\* Criterion of reliability of intergroup differences.

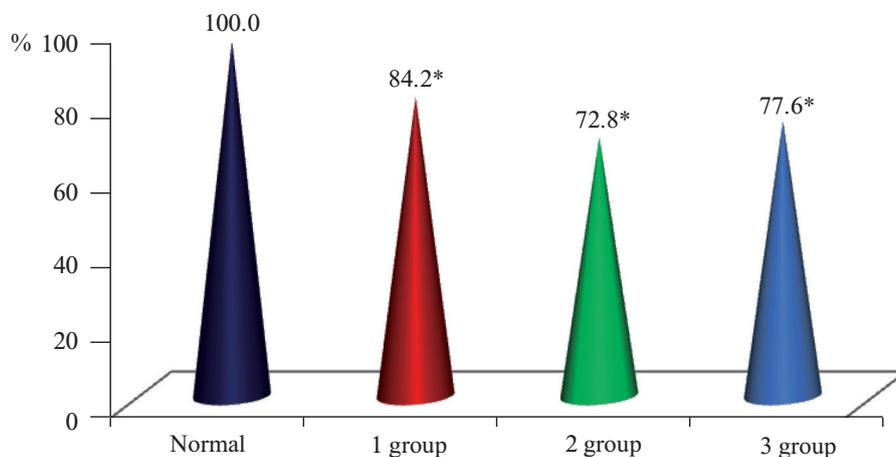
<sup>^</sup> Criterion of reliability of intra group differences.

Upon completing of therapeutic course we observed the increase in extent of restoration of function of joint in all patients. At the same time the results were the best in the first group where the indicator of restoration was 84.2% whereas in the second group it was only 72.8%, and in the third – 77.6% (Figure 1).

At initial examination in patients of both groups we taped the depression of a basal blood flow which was  $8.91 \pm 1.62$  perfusion (perf.) units, that is 1.9 times lower than standard parameters (Table 2). After

the end of the observation period the indicator of basal microcirculation in the first group was enlarged 1.9 times (from  $8.91 \pm 0.06$  to  $17.6 \pm 0.18$  perf. units,  $p < 0.05$ ) whereas in the second group the changes were less expressed.

The decrease of an index of efficiency of microcirculation making in the first and second groups  $0.70 \pm 0.07$  and  $0.61 \pm 0.08$  standard units proved initial reduction of perfusion of blood through fibers, the phenomena of ischemia and stagnation at the level of microcirculatory bloodstream. Upon



**Figure 1.** Extent of restoration of function of a joint in patients with gonarthrosis to completing of the treatment (\*Criterion of reliability of differences in comparison with standard indicators ( $p < 0.05$ ))

completing the treatment in the main group the index of efficiency of microcirculation has grown 2.1 times and made  $1.47 \pm 0.10$  standard units ( $p = 0.024$ ), whereas in comparison group it has been increased only 0.4 times ( $p < 0.05$ ). Increase of fiducially lowered value of the average square deviation by 1.2 times ( $p = 0.041$ ) and also decrease in originally raised variation coefficient by 1.4 times ( $p = 0.028$ ) demonstrated the correction of active vasomotor mechanisms in the first group, whereas in the second group these indicators authentically have been not changed.

## Conclusion

Introduction in treatment course of ultraphonophoresis with Viprazan gel for patients with gonarthrosis in a phase of the fading exacerbation reduces expression of pain and constraint, increases extent of restoration of function of joints, promotes activation of microcirculatory and trophic processes, improving a condition of articulate surfaces, that differs from the results received in groups of placebo and standard treatment.

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