Original article
https://doi.org/10.18019/1028-4427-2024-30-3-345-352

Interstitial electrical stimulation for middle-aged, and elderly adults with early stages of knee osteoarthritis

N.A. Burmatov[1]✉, K.S. Sergeev[1], S.N. Luneva[2], A.A. Gerasimov[3], S.A. Kopylov[4], N.A. Spiridonova[5]

[1] Tyumen State Medical University, Tyumen, Russian Federation
[2] Ilizarov National Medical Research Centre for Traumatology and Orthopedics, Kurgan, Russian Federation
[3] Ural State Medical University, Ekaterinburg, Russian Federation
[4] Omsk State Medical University, Omsk, Russian Federation
[5] Industrial University of Tyumen, Tyumen, Russian Federation

Corresponding author: Nikita A. Burmatov, burmatov.n@yandex.ru

Abstract

Introduction The adequate, pathogenetically substantiated pain management is essential for treatment of early stages of deforming osteoarthritis of the knee joint. There is a need to explore the effectiveness and mechanisms of modern methods of electrical therapy and their impact on the quality of life due to close cause-and-effect relationship between the pain, inflammatory and destructive components of osteoarthritis (OA) as one of the most common conditions.

The objective was to evaluate the effect of interstitial electrical stimulation (IES) as a monotherapy in the course of conservative treatment of early stages of gonarthrosis based on clinical and biochemical findings.

Materials and methods Radiographic findings, skin electrometry (objective parameters of pain intensity), limb weight-bearing capacity, biochemical parameters of connective tissue matrix degradation in blood serum and 24-hour urine samples, and treatment satisfaction were explored in 43 patients. Patients who received a course of IES were assigned to the treatment group (n = 22) and patients who received standard treatment without IES constituted the control group (n = 21).

Results Electrometric analysis showed a higher effectiveness of pain relief in the treatment group compared to the controls with asymmetry coefficient measuring 3.2 ± 0.31 versus 1.9 ± 0.4 at $p > 0.05$. The weight-bearing scored 3.59 ± 0.34 versus 3.26 ± 0.2 at $p > 0.05$. The treatment group showed shorter treatment length with 13.21 ± 1.2 days versus 18.3 ± 1.2 days in the control group at $p > 0.05$ and a higher degree of satisfaction with outcomes scored 96.2 ± 2.59 in the treatment group versus 86.2 ± 3.17 in the control group. A statistically significant difference ($p > 0.05$) was established in the levels of free and total hydroxyproline characterizing the different intensity of collagen breakdown in the groups at the end of treatment.

Discussion The IES used as an analgesic and anti-inflammatory therapy was shown to be highly effective with changes in the hydroxyproline level in the media suggesting a chondroprotective effect. The analysis and comparison of objective parameters demonstrated high effectiveness of IES in the treatment of early stages of gonarthrosis in middle-aged and elderly adults.

Conclusion The IES used for treatment of early stages of gonarthrosis helps pain reducing the intensity of collagen destruction and improving weight-bearing.

Keywords: osteoarthritis, joint diseases, interstitial electrical stimulation, rehabilitation, gonarthrosis

For citation: Burmatov NA, Sergeev KS, Luneva SN, Gerasimov AA, Kopylov SA, Spiridonova NA. Interstitial electrical stimulation for middle-aged, and elderly adults with early stages of knee osteoarthritis. *Genij Ortopedii*. 2024;30(3):345-352. doi: 10.18019/1028-4427-2024-30-3-345-352

INTRODUCTION

Knee osteoarthritis is a degenerative musculoskeletal disease [1] and is diagnosed in nearly 240 million people globally [2]. The prevalence of knee OA is 40–70 % in individuals aged 60 to 70 years with 40 to 65 % of cases being associated with a genetic factor [3]. With the known prevention and treatment measures, the incidence of knee OA is rising and there is an increase in the incidence of arthritis affecting young people that impairs the quality of life in all aspects [4]. Although more effective treatments are available osteoarthritis (OA) is associated with an extremely high economic burden and has an economic impact of 2.5 % of GDP in industrialized countries [5]. There is a search for pathogenetically substantiated methods of treating primary knee OA based on a complex set of biochemical and structural changes that involve all articular components including hyaline cartilage and subchondral bone [6–8]. Different methods for treating the painful and inflammatory components of OA and their combinations including intra-articular injections of blood components, bone marrow and various pharmacological and physiotherapeutic modalities have been shown to be effective. The problem of pain relief in OA is not completely solved and, therefore, is relevant. Bone tissue is rich in osteoreceptors that respond to a decrease in the partial pressure of oxygen in bone vessels, caused by hypoxia and venous stagnation in the subchondral bone [9, 10]. Poor circulation causes chronic bone pain, characteristic of knee OA. It has been proven that the worse the blood supply to the bone, the more intense the pain. Impaired subchondral microcirculation leads to a sharp decrease in the diffusion of essential nutrients into the cartilage matrix. Reduced intraosseous pressure eliminates one of the obstacles to adequate trophism of hyaline cartilage, which is confirmed clinical and biochemical findings. The purpose of the work was to evaluate interstitial electrical stimulation as a monotherapy option in the course of conservative treatment of early knee OA based on clinical and biochemical findings.

MATERIAL AND METHODS

The study included a cohort of patients of both sexes aged 45–65 years ($n = 43$). The clinical examination included a specific assessment of anthropometric parameters and calculation of body mass index (BMI) using the well-known formula:

$$I = \frac{m}{h^2}, \text{ kg/m}^2,$$

where I is body mass index, m is body weight in kilograms, h is height in meters. To rule out obesity, we were guided by body mass index, the presence and severity of concomitant diseases, according to the Clinical Guidelines for the treatment of gonarthrosis (Approved by the Ministry of Health of the Russian Federation on September 3, 2021). The numerical parameter of the comorbidity index (CI) was calculated using the "Environmental Comorbidity Calculator" [11].

Inclusion criteria included:

— a history of an established diagnosis of "knee OA", "arthrosis of the knee joint" (code M17 according to ICD-10);

— disease grade I-II (according to Kellgen-Lawrence) [12];

— one-sided involvement.

Exclusion criteria:

— systemic, allergic, rheumatoid and tumor lesions of joints, aseptic necrosis, obesity grade 1 and over;

— a musculoskeletal pain phenotype being different from mechanical;

— knee surgical interventions;

— kidney pathology;

— diseases of a tumor and endocrine nature;

— Hauser Ambulatory Index of less than 5 [13].

Based on treatment methods, the patients were divided into 2 groups. The control group ($n = 21$) consisted of patients who received treatment including medications, physiotherapy and kinesiotherapy, as featured in the current Order of the Ministry of Health of Russia dated October 27, 2022 No. 706 "On approval of the standard of medical care for adults with gonarthrosis (diagnosis, treatment and dispensary observation)". Individuals who received interstitial electrical stimulation (IES) as monotherapy according to Gerasimov were assigned to the treatment group ($n = 22$). The distribution of the parameters show that the groups are comparable ($p < 0.05$) (Table 1).

Table 1

Characteristics of the patients in the groups

Description		Treatment group	Controls
Male	abs.	10	10
	%	45.5	47.6
Female	abs.	12	11
	%	54.5	52.4
Age (years)		70.00 ± 2.65	69.60 ± 2.93
CI (score)		9.42 ± 0.86	9.73 ± 0.42
BMI (score)		23.85 ± 3.24	23.33 ± 2.3

Note: CI, comorbidity index; BMI, Body Mass Index

The duration of treatment and the number of procedures were individual (from 7 to 21 days) and varied based on the need and condition of the patient. Subjective assessment of the pain intensity was measured with visual analog scale VAS (from 0 to 10 points). Characteristics of pain intensity were determined by skin electrometry according to Gerasimov [14]. The SupportTest original software was used to calculate the lower extremity support ability [15]. The examination was performed with floor scales. The subject stood with one foot on the scales and the other foot on the stand. The scale readings were recorded every 15 seconds within 5 min. The patient's body weight (P) was previously determined on the same scales and was taken as 100 %. The mean P1 was calculated based on the readings of the scales for the leg standing and then the value of the limb's support ability (X) was determined using the formula:

$$X = \frac{P1 \times 100}{P}, \%.$$

The percentage of body weight distribution to the other leg was calculated by subtracting the resulting value from 100 %. The weight-bearing ability of a limb was considered restored if the parameters of the affected limb reached a value of at least (80 ± 10) % of the healthy one. In the absence of impairments and with complete (100 %) restoration of OS, 5 points were awarded; 4, 3 and 2 scored for values of 90, 80 and 70 %, respectively. Markers of cartilage tissue degradation (free and total hydroxyproline) were explored with blood serum and 24-hour urine according to the method offered by Sharaev [16]. Biological material was collected before the treatment and at 45 days of the last procedure or stay in the rehabilitation department. Similar parameters of healthy individuals aged between 45 and 65 years were used as reference values. Satisfaction with treatment was determined according to a personalized assessment of treatment results [17] using the WOMAC (Western Ontario and McMaster University Osteoarthritis Index) scale as the base scale. The research results were processed by nonparametric methods of variation statistics for small samples. Statistical significance of differences was confirmed at $p < 0.05$. The parameters were tested for normality using the Shapiro – Wilk and Tietjen – Moore tests.

RESULTS

Standard radiographs of patients in both groups revealed radiological signs characteristic of the knee OA as described by J. Kallgren and J. Lawrence [12] with a zero value indicating the absence of changes, with a value of I (doubtful degree) showing minor osteophytes. Grade II (minimal) is characterized by clearly defined osteophytes. Minimal narrowing of the joint space (less than 2/3 compared to normal values) was seen in 11 patients with subchondral cysts and minor marginal bone growths noted. No visible changes in bone structure or joint anatomy were detected in 32 cases (Fig. 1).

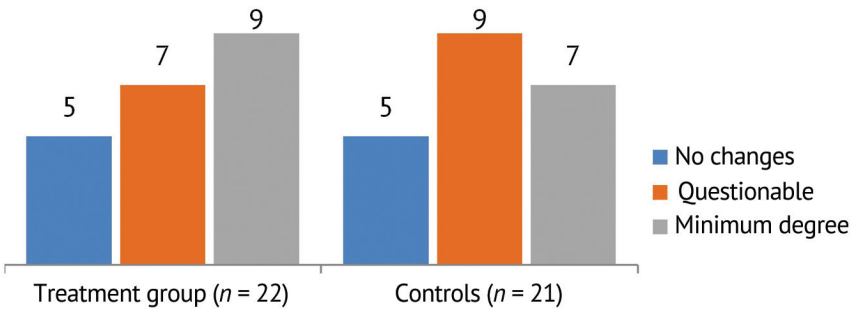

Fig. 1 Distribution of patients according to the Kellgren & Lawrence classification

Objective parameters characterizing the ability to support the limb and the pain were comparable in both groups (Table 1). Preoperative locomotion testing demonstrated impaired ability to support the limb in 70 % of patients in the treatment group and 70 % controls. A comparative analysis of the parameters at a long term revealed a statistically confirmed difference in the values ($p < 0.05$) which indicated a more effective restoration of limb support in the treatment group: (3.59 ± 0.31) versus (3.26 ± 1.2). Preoperative measurements of the skin electrical potential showed presence of pain of varying intensity (from moderate to severe) in the majority of the patients. An objective quantitative measurement of electrical potential in the form of the coefficient of asymmetry (CA) consistently correlated ($r = 0.97$) with similar subjective VAS parameters (Table 2). A clinical and electrometric study confirmed the presence of pain of varying intensity in an equal number of patients, with static and night pain experienced by 55 % ($n = 11$) of patients in the treatment group and 57 % ($n = 11$) of controls. Pain relief was achieved in all patients of the treatment group and in 65 % of controls. Comparison the numerical values of CA at a long term, the presence of mild to moderate pain was established in 15 controls and in 2 patients of the treatment group. The result was confirmed by VAS score. A statistically confirmed difference ($p < 0.05$) was revealed in parameters characterizing the presence and degree of pain intensity at a long term indicating a higher effectiveness of pain therapy in the treatment group.

Table 2

Distribution of anthropometric, locomotor, electrometric and clinical parameters during different periods of treatment

Description	Treatment group ($n = 22$)		Controls ($n = 21$)	
	Pre-op	Post-op	Pre-op	Post-op
VAS (score)	6.7 ± 2.6	0.6 ± 0.02	6.5 ± 2.3	4.6 ± 0,02*
CA (score)	3.2 ± 0.3	1.1 ± 0.1	3.1 ± 0.3	1.9 ± 0,4*
LSA (score)	3.4 ± 0.31	3.59 ± 0.14	3.21 ± 0.2	3,26 ± 0,15*

Note: CA, coefficient of asymmetry; VAS, visual analogue scale; LSA, limb support ability; *, differences between groups are significant at $p \leqslant 0.05$

Similar findings were obtained in biochemical parameters in young healthy individuals aged 30–45 years, who made up the reference group ($n = 20$) and were used as reference values. Preoperative biochemical analysis revealed equally elevated levels of the serum total and free hydroxyproline in both groups ($p > 0.05$). The free hydroxyproline in 24-hour urine tests was

increased, and the values obtained differed from those in the controls indicating increased collagen destruction in both groups (Tables 3, 4).

Table 3

Comparative analysis of biochemical findings in patients' blood serum

Description	Reference group (n = 20)	Treatment group (n = 22)		Controls (n = 21)	
		pre-op	post-op	pre-op	post-op
Total hydroxyproline (mmol/l)	3.28 ± 0.11	3.43 ± 0.08	3.31 ± 0.07*	3.46 ± 0.07	3.06 ± 0.05
Free hydroxyproline (mmol/l)	0.29 ± 0.10	0.25 ± 0.13	0.27 ± 0.06	0.24 ± 0.09	0.28 ± 0.06

Note: *, differences between groups are significant at $p \leqslant 0.05$

Table 4

Biochemistry of 24-hour urine collection from patients of both groups

Description	Reference group (n = 20)	Treatment group (n = 22)		Controls (n = 21)	
		pre-op	post-op	pre-op	post-op
Free hydroxyproline (mmol/l)	0.12 ± 0.01	0.17 ± 0.04	0.12 ± 0.05	0.17 ± 0.02	0.15 ± 0.02*

Note: *, differences between groups are significant at $p \leqslant 0.05$.

A comparative analysis of preoperative and postoperative biochemical parameters measured at a long term of 45.3 ± 1.22 days in the treatment group and at 44.1 ± 1.03 days in the controls revealed statistically significant differences (p > 0.5) indicating improved biochemical parameters of connective tissue metabolism in the treatment group. Personalized assessment of treatment results [17] showed different degrees of treatment satisfaction in the treatment and control groups ($p < 0.05$). The WOMAC score was used as a baseline for assessing knee function [18]. The patients' expectations included pain relief, improved weight-bearing ability, functionality and quality of life. Higher rates of treatment satisfaction were recorded in 95 % of patients in the treatment group and in 55 % of controls. Based on the results of the introductory testing, each group was divided into 2 subgroups (Table 5). The "A" subgroup consisted of patients whose expectations were in the "excellent" range or at the upper limit of the "good" (n = 21). The IE scored ⩾ 85. Subgroup "B" included patients whose expectations were at the lower limit of the "good". The "B" subgroup included patients whose expectations were at the lower limit of the "good". The subgroup consisted mostly of elderly patients with impaired limb support. The IE scored ⩽ 84 in the patients. Analysis of the treatment effectiveness revealed different degrees of treatment satisfaction in patients of the treatment and control groups. The majority of patients in the treatment group were satisfied with outcomes with the intended effect being superior in 25 %. There were less patients in the control group being satisfied with outcomes as compared to those in the treatment group. Two poor outcomes were identified due to low effectiveness of analgesic and anti-inflammatory therapy. Interstitial electrical stimulation and the course of treatment were terminated in the treatment group due to pain relief and the restored limb support. The treatment length differed in the groups measuring 13.21 ± 1.2 days in the treatment group versus 18.3 ± 1.2 days in the control group.

Table 5

Personalized assessment of the results and duration of treatment

Description	Treatment group			Controls		
	A, n = 11	B, n = 6	C, n = 21	A, n = 12	B, n = 7	C, n = 22
IE (score)	91.8 ± 3.8	77.5 ± 6.09*	87.05 ± 8.28	96.2 ± 3.25	85.5 ± 5.68*	92.6 ± 6.59
RO (score)	96.2 ± 3.25	85.5 ± 5.68*	92.6 ± 2.59	89.1 ± 3.68	81.1 ± 2.79	86.21 ± 3.17**
CR (score)	104.9 ± 4.43	110.89 ± 11.3	106.9 ± 7.66	97.9 ± 5.97	106.9 ± 5.15	101.24 ± 7.1
Treatment length (day)	8.2 ± 1.2	11.3 ± 2.2	13.21 ± 1.2	10.2 ± 2.3	13.5 ± 3.4	18.3 ± 1.2**

Note: A, a group of patients with expectations in the "excellent" range or at the upper limit of the "good"; B, patients whose expectations are at the lower limit of the "good"; C, a group of patients with expectations of "excellent" and "good"; IE, intended effect; RO, result obtained; CR, cumulative result; *differences between A and B subgroups are significant at $p \leqslant 0.05$; **, differences between C subgroups of the treatment and control groups are significant at $p \leqslant 0.05$.

DISCUSSION

Early stages of OA are characterized by chronic bone pain of varying intensity and accompanied by characteristic changes in the biomechanical and strength bone properties caused by restructuring and changed quality. Our own clinical observations, confirmed by literature data, indicated the most intense pain being localized in the bradytrophic zones of the bones forming the knee joint (tibial metaphysis) [1, 4]. In addition to pain relief IES can help to restore local microcirculation of the bone and cartilage tissue in the early stages of OA [19]. The previous polarographic and rheographic findings showed a significantly accelerated latent period of oxygen delivery and utilization in bone tissue after a course of electrical stimulation. Restoration of microcirculation and vascularization enhances the activity of energy metabolism processes leading to the elimination of local foci of aseptic inflammation of the bone and restoration of the piezoelectric and biochemical properties [19]. The specificity of markers of degradation and synthesis of cartilage tissue and subchondral bone as the main pathogenetic links of OA is reported [20] with the relationship between structural disorders of the hyaline cartilage and systemic manifestations of the inflammatory response to various (including preclinical) stages of the disease explored [22, 23]. The destruction of collagen fibers is accompanied by an increased excretion of hydroxyproline and an increased content in the blood serum. Hydroxyproline tested in blood serum and urine is a product of collagen breakdown with the free fraction of GP being considered as a marker of destruction, and the bound fraction being a marker of connective tissue metabolic activity [23–26]. A decrease in the total and free hydroxyproline in the blood serum and daily urine was observed in patients of the treatment group after a course of interstitial electrical stimulation suggesting a more active inhibition of the processes of collagen breakdown and restoration of the metabolic activity of connective tissue in this cohort of patients [27, 29]. The biochemical markers we explored had low specificity and high diagnostic significance being an indirect sign of inhibition of collagen breakdown. However, changes in biochemical markers in combination with clinical and electrometric findings suggested a chondroprotective effect of interstitial electrical stimulation with a high degree of probability.

CONCLUSION

IES used for early stages of knee OA can help pain relief reducing the intensity of collagen destruction and improving weight-bearing capacity. Interstitial electrical stimulation is an effective, pathogenetically substantiated method of treating patients with knee OA accompanied by chronic pain.

Conflicting Interests *The authors declared no potential conflicts of interest with respect to the authorship and/or publication of this article.*

Funding *The authors received no financial support for the research and/or authorship of this article.*

Ethical Approval *The local ethics committee decided that the IES method has been introduced into routine clinical practice, has a 15-year period of use, and does not require approval by the local ethics committee for use. Permission to use medical technology "Treatment of pain syndromes of the spine and joints with interstitial electrical stimulation" was issued by the Federal Service for Surveillance in Healthcare and Social Development, FS 210/379 dated 10.26.10. The Vector-MS device used has been in serial production since 2003, registration certificate No. RZN 2013/1050 dated 14.08.13.*

Written ***informed consent*** *for the participation in the research project was obtained from the subject's parent/ legally acceptable representative.*

REFERENCES

1. Helo MJ, Akhtiamov IF, Abdullah AM, Said FM Treatment of arthrosis of the knee, current trends and issues. *Practical Medicine*. 2018;16(7 (part 1)):48-53. (In Russ.) doi: 10.32000/2072-1757-2018-16-7-48-53
2. Katz JN, Arant KR, Loeser RF. Diagnosis and Treatment of Hip and Knee Osteoarthritis: A Review. *JAMA*. 2021;325(6):568-578. doi: 10.1001/jama.2020.22171
3. Novakov VB, Novakova ON, Churnosov MI. Polymorphism of LYPLAL1 and TGFA Genes Associated With Progression of Knee Osteoarthritis in Residents Central Chernozem Region of Russia. *Traumatology and Orthopaedics of Russia*. 2022;28(4):42-53. (In Russ.) doi: 10.17816/2311-2905-1979
4. Alekseeva LI, Taskina EA, Kashevarova NG. Osteoarthritis: epidemiology, classification, risk factors, and progression, clinical presentation, diagnosis, and treatment. *Modern Rheumatology Journal*. 2019;13(2):9-21. (In Russ.) doi: 10.14412/1996-7012-2019-2-9-21
5. Povzun AS, Mazurov VI, Povzun KA, Kostenko VA. Assessment of the current economic efficiency of treatment of patients with osteoarthritis in Saint-Petersburg and its perspectives. *Herald of the Northwestern State Medical University named after I.I. Mechniko*. 2017;9(3)89-96. (In Russ.)
6. Rizk E, Tajchman S, Fink E, et al. Quality indicators for osteoarthritis pain management in the primary care setting. *BMC Musculoskelet Disord*. 2023;24(1):538. doi: 10.1186/s12891-023-06637-x
7. Eymard F, Ornetti P, Maillet J, et al. Intra-articular injections of platelet-rich plasma in symptomatic knee osteoarthritis: a consensus statement from French-speaking experts. *Knee Surg Sports Traumatol Arthrosc*. 2021;29(10):3195-3210. doi: 10.1007/s00167-020-06102-5
8. Fiz N, Delgado D, Garate A, et al. Intraosseous infiltrations of Platelet-Rich Plasma for severe hip osteoarthritis: A pilot study. *J Clin Orthop Trauma*. 2020;11(Suppl 4):S585-S590. doi: 10.1016/j.jcot.2019.12.012
9. Abuseva GR, Kovlen DV, Ponomarenko GN, et al. Physical Methods of Rehabilitation for Patients with Osteoarthritis: A Scientometric Analysis of Evidence-Based Studies. *Traumatology and Orthopedics of Russia*. 2020;26(1):190-200. (In Russ.) doi: 10.21823/2311-2905-2020-26-1-190-200.
10. Garvey WT, Garber AJ, Mechanick JI, et al. American association of clinical endocrinologists and american college of endocrinology position statement on the 2014 advanced framework for a new diagnosis of obesity as a chronic disease. *Endocr Pract*. 2014;20(9):977-989. doi: 10.4158/EP14280.PS
11. Ragozin ON, Malakhov YuV, Dyachkova EE, Ragozin RO. *Calculator of environmental comorbidity*. Certificate of state reg. computer programs No. 2017663878. 2017. Available at: https://www.fips.ru/registers-doc-view/fips_servlet. Accessed Apr 09, 2024.
12. Kellgren JH, Jeffrey M, Ball J. *Atlas of standard radiographs*. Vol 2. Oxford: Blackwell Scientific; 1963.
13. Kovalenko AP, Kamaeva OV, Misikov VK, Poleshchuk YuR, Koshkarev MA. Scales and tests in the rehabilitation and treatment of patients with spasticity of the lower limbs. *S.S. Korsakov Journal of Neurology and Psychiatry*. 2018;118(5):120-128. (In Russ.) doi: 10.17116/jnevro201811851120
14. Gerasimov AA Method of objective diagnostics of pain syndromes. *Russian journal of pain*. 2013;1(36):76-77. (In Russ.)
15. Burmatov NA, Sergeev KS, Kopylov SA, et al. *Method for calculating objective indicators of lower limb support ability (SUPPORTTEST)*. Certificate RF of state registration of a computer program No. 2023616226, 2023. Available at: https://www.fips.ru/registers-doc-view/fips_servlet. Accessed Apr 10, 2024. (In Russ.)
16. Sharaev PN, Sakhabutdinova EP, Lekomtseva OI, Koshikova SV. Determination of free and peptide-bound hydroxyproline in blood serum. *Clinical laboratory diagnostics*. 2009;(1):7-9. (In Russ.)
17. Garkavi D, Garkavi A, Lychagin A. A universal method for personalized assessment of treatment in outcomes orthopedic trauma patients. *Physician*. 2014;(7):31-34. (In Russ.)
18. Irzhanski A.A., Kulyaba T.A., Kornilov N.N. Validation and cross-cultural adaptation of rating systems WOMAC, KSS and FJS-12 in patients with knee disorders and injuries. *Traumatology and Orthopedics of Russia*. 2018;24(2):70-79. (In Russ.) doi: 10.21823/2311-2905-2018-24-2-70-79
19. Gerasimov A.A. T*reatment of patients with dystrophic diseases of the joints and spine using interstitial electrical stimulation: abstract of thesis. Autoref. Dokt. Dis*. Saint Petersburg; 1995;27. Available at: https://medical-diss.com/medicina/lechenie-bolnyh-s-distroficheskimi-zabolevaniyami-sustavov-i-pozvonochnika-sposobom-vnutritkanevoy-elektrostimulyatsii. Accessed Apr 10, 2024.
20. Belova SV, Gladkova EM, Ulyanov VYu, Blinnikova VV. Metabolic shifts in subjects with potential risk of primary osteoarthritis. *Saratov Journal of Medical Scientific Research*. 2018;14(3):511-514. (In Russ.)
21. Gladkova EV, Ivanov AN. The correlation between structural changes in articular hyaline cartilage and the parameters of systemic manifestations of inflammatory reaction in the pathogenesis of early stages of primary osteoarthritis. *Saratov Journal of Medical Scientific Research*. 2018;14(3):518-523. (In Russ.)
22. Galashina EA, Bondarenko AS, Ulyanov VYu, Klimov SS. The role of skeletal tissue remodeling markers in the pathogenesis of implant-associated inflammation after primary knee arthroplasty. *Saratov Journal of Medical Scientific Research*. 2018;14(3):515-518. (In Russ.)
23. Nosivets D.S. Biochemical markers for pathology of cartilage and bone tissue. *Materials of the scientific and practical conference with international participation dedicated to the 90th anniversary of Professor N.P. Demicheva "Modern aspects of traumatology, orthopedics and reconstructive surgery", Astrakhan, March 22-23, 2019*. Astrakhan: Astrakhan State Medical University Publ.; 2019:90-92. (In Russ.)
24. Ruslanova NM, Pospelova KI, Bakhtin VM, et al. Clinical significance of hydroxyproline in the diagnosis of connective tissue dysplasia. *Materials of the VI International Scientific and Practical Conference of Young Scientists and Students, dedicated to the year of science and technology "Current issues of modern medical science and healthcare", Ekaterinburg, April 8-9, 2021*. Ekaterinburg: USMU Publ.; 2021:369-374. (In Russ.)
25. Kurd MF, Kreitz T, Schroeder G, Vaccaro AR. The Role of Multimodal Analgesia in Spine Surgery. *J Am Acad Orthop Surg*. 2017;25(4):260-268. doi: 10.5435/JAAOS-D-16-00049
26. Rasskazov NI, Kolokoltsev VV, Rasskazov DN. Prospects for the study of autoantibodies to collagens. *Bulletin of Dermatology and Venereology*. 1994;(3):12-15. (In Russ.)

27. Luneva SN, Sazonova NV, Malceva LV, Matveeva EL. Effectiveness of Theraflex® evaluation in early stages of osteoarthritis treatment and its influence on articular cartilage structure and metabolism. *Consilium Medicum*. 2018;20(9):63-70. (In Russ.) doi: 10.26442/2075-1753_2018.9.63-70
28. Parry DDA, Squire JM. Fibrous proteins: new structural and functional aspects revealed. In: *Advances in protein chemistry*. Elsevier Publ.; 2005:1-10.

The article was submitted 17.05.2023; approved after reviewing 24.01.2024; accepted for publication 08.04.2024.

Information about the authors:

Nikita A. Burmatov — Candidate of Medical Sciences, traumatologist-orthopedist, Assistant at the Department, burmatov.n@yandex.ru;

Konstantin S. Sergeev — Doctor of Medical Sciences, Professor, Head of Department, https://orcid.org/0000-0002-6621-9449;

Svetlana N. Luneva — Doctor of Biological Sciences, Professor, Leading Researcher, luneva_s@mail.ru, SPIN-code: 9572-2655, https://orcid.org/0000-0002-0578-1964;

Andrey A. Gerasimov — Doctor of Medical Sciences, Professor, Professor, https://orcid.org/0000-0002-3581-1917;

Semyon A. Kopylov — student, 5th year, https://orcid.org/0009-0001-7031-2646;

Natalia A. Spiridonova — Candidate of Physical and Mathematical Sciences, https://orcid.org/0000-0002-2918-6609.