Local ozone therapy options for lumbosacral dorsopathy

Lev G. Agasarov (1,2,3), Tatiana V. Konchugova (1,2), Detelina B. Kulchitskaya (1), Olga S. Davyan (3), Tatiana V. Apkhanova (1), Anatoliy D. Fesyun (1), Andrey P. Rachin (1), Maxim Yu. Yakovlev (1), Kirill V. Terentev (4), Natalia P. Sanina (4)

(1) Federal State Budgetary Institution "National medical research center for rehabilitation and balneology", Ministry of Health of Russia, Moscow, Russia; (2) Federal State Autonomous Educational Institution of Higher Education I.M. Sechenov First Moscow State Medical University, Ministry of Health of Russia, Moscow, Russia; (3) Non-profit Partnership "Professional association of reflexologists"; (4) *State Budgetary Healthcare Institution of Moscow region, M. F. Vladimirsky Moscow Regional Research and Clinical Institute, Moscow, Russia.*

This article is distributed under the terms of the Creative Commons Attribution Noncommercial License (CC BY-NC 4.0) which permits any noncommercial use, distribution, and reproduction in any medium, provided the original author(s) and source are credited.

Abstract

The characteristic resistance of dorsopathies to conventional therapy explains the attention to new technologies that combine several therapeutic links and, in particular, ozone therapy. The study involved 90 patients under the age of 55 in the exacerbation phase of lumbar and sacrum dorsopathy with the leading vascular component. The patients were divided into three groups, in which basic medical and physical treatment was given. At the same time, ozone therapy was used the first two groups: the 1st group received standard ozone therapy, with a predominant selection of algic zones, the 2nd - according to the rules of biopuncture, affecting the complex of segmental, distant and "vascular" points. In the 3rd control group, the correction was limited to a standard therapeutic complex. The verification of the observed changes was carried out through clinical, psychological and electrophysiological analysis. As a result, both ozone therapy schemes (effective in 69% and 73% of observations respectively) were found to have a reliable advantage over the base complex, where 49% of patients demonstrated improvement. Differences within the ozone therapy groups themselves related to the achievement of a stable effect (in the 2nd group 2.6 days earlier) and the degree of reduction of vaso-reflex reactions (observed in 50% and 75% of observations respectively). Thus, by bringing in additional control methods, it has been proven that the implementation of ozone therapy in compliance with the rules of biopuncture ensures faster and more sustainable effects.

Key Words: Dorsopathy; biopuncture; local ozone therapy; tetrapolar reovasography; thermography; laser doppler flowmetry.

Eur J Transl Myol 32 (3): 10684, 2022 doi: 10.4081/ejtm.2022.10684

The range of diffusion at the pandemic level and the protracted course of lumbosacral dorsopathies up to the disability of the patients underline their socio-medical significance.[1,2] Furthermore, the characteristic resistance of the process to common therapies explains attention of specialists to new types of treatments uniting several therapeutic approaches.[3]

One of them is the method of local ozone therapy, characterized by anti-inflammatory and analgesic effects as a result of the addition of reflex and specific responses (the action of the gas itself).[4,5] According to the standard technique the gas mixture is administered intra- or sub-cutaneously to the areas of maximum pain, including the paravertebral lines. In the course of refining the method, we suggested to perform it in accordance with the biopuncture rules, that is, by to impact not only on algic, but also in combination of segmental, distant and "vascular" acupuncture points.[6]

The hypothesis was based on data of the high efficacy of biopuncture performed in cases of dorsopathies with the help of other agents. in particular, drugs.[7]

The efficacy of the new developed option of biopuncture performed with local ozone therapy was previously confirmed by us in practice.[4] Based on new data here reported, our aim is to strengthen the evidence of the applicability of the method.

Materials and Methods

The study involved 90 patients (41 women and 49 men) under the age of 55 years, who were seeking medical assistance in connection with the onset or exacerbation of lumbosacral dorsopathy.

The inclusion criteria were the presence of vertebrogenic reflex and radicular syndromes with the dominance of the vascular component of the process. Excluded were patients suffering with protrusion of intervertebral discs over 7 mm, radiculomyeloischemia, as well as neoplasms or organ decompensation, as basic contraindications to reflex therapy.

Proper neurological and vertebrological examinations were performed according to a well-known scheme,[2] including fixation of algia using a visual analogue scale (VAS). Pathological changes in the vertebral tissues were identified by means of radiography and / or computer and magnetic-resonance imaging. The psychological study included unassisted execution of Minnesota Multiphasic Personality Inventory tests (MMPI) and health-activity-mood (HAM). The electrophysiological unit was presented by thermography methods (AGA-782 apparatus, "AGEMA") tetrapolar rheovasography (Bioset-6001) and ultrasonic Doppler examination of the lower limb arteries (Acuson X300, Siemens).

The conditions of microcirculatory bloodstream were assessed according to the data of laser Doppler flowmetry (LDF) using the LAKK-01 apparatus. In the treatment phase the patients were divided into 3 randomized groups (30 persons in each), in which they were prescribed medicines (analgetics, non-steroidal anti-inflammatory and selectively, psychotropic drugs), methods of manual therapy, massage and exercise therapy.

This management in the first two groups was supplemented with ozone therapy: in the 1st group, that of comparison, the gas was administered according to the existing scheme paravertebrally and into the algic zones, while in the 2nd, main group, a combination of segmental and distant points was targeted. Besides, distal "vascular" (F2.3, RP6) points were selected. Ozone-oxygen mixture was administered in both groups subcutaneously in a volume of 1 ml, based on 2.0 μg / ml (ozonizer "Medozons BM", oxygen concentrator – "JAY-5A").

Course exposure included 10 procedures performed every other day. The exposure in the 3rd control group was limited by standard, above-mentioned combined therapy. The treatment efficacy was defined "significant improvement", "improvement" and "no effect" and correlated to reslts in the three groups of patients The statistical analysis was based on the results of parametric and nonparametric calculations using Statistica for Windows v.7 program.

Results and Discussion

According to distribution of syntoms that reflect the disorders, in 74 observations dominated positive shifts. The intensity of algia moderation, corresponding to 5 points of the VAS, waspresented in 58% of patients. By clinical and psychological analysis, 75% of patients demonstrated persistent astheno-neurotic changes. Meanwhile, an evident increase was evident in the average of the 1st scale (up to 73 T-points) of the Comprehensive Personality Study Profile and a less pronounced increase in the 6th-8th positions were combined with a decrease in the scores of HAM (health, activity and mood) test to 41-44 points. Visually, and according to the results of the Goldflamm-Samuels and Opel-Verbov vascular tests, 75% of patients demonstrated domination of the vascular spastic component of the process. This was confirmed by the temperature increase in the lumbosacral region (Δt 1.36 ± 0.11°C) against the background of distal hypothermia-(Δt 1.3 ± 0.04°C in the legs on the "affected" side. The temperature shifts were consistent with the results of rheovasography in the form of limitation of pulse blood filling of the lower limbs, with a reliable, more often unilateral, drop in the rheographic index (RI) of the legs to 0.04 ± 0.005 Ohm. Ultrasonic Doppler examination showed a decrease in blood flow in the posterior tibial and dorsal arteries on the side of the algia (to 3.9 ± 0,9 and 3.0 ± 0,9 mL/min respectively) with less informativeness of the linear velocity indicators due to their multidirections. By LDF, indicating disorders in the system of the microcirculatory bloodstream, 76% of cases demonstrated spastic, 22% hyperemic and only

Table 1. *Therapeutic efficacy of the compared methods.*

Groups	Results							
	Significant improvement		Improvement		No effect		Deterioration	
	Abs.	%	Abs.	%	Abs.	%	Abs.	%
1 (30)	10	33.3	11	36.6	8	26.6	1	
2 (30)	12	40.0	10	33.3	8	26,.	-	-
3 (30)	7	23.3	8	26.6	15	50,0	-	-
Pearson criterion χ^2	$\chi^2_{1,2}$=1.69 (p > 0.05) $\chi^2_{1,3}$=10.2 (p< 0.05) $\chi^2_{2,3}$=11.7 (p< 0.05)							

Note: in brackets the number of observations.

Table 2. *Changes in thermoasymmetry at the level of the legs in patients (M ± m).*

Groups of patients	Severity of the assymentry (Δt°C)	
	Before	After
1	1.28 ± 0.10	**0.78 ± 0.09***
2	1.28 ± 0.10	**0.71 ± 0.11***
3	1.27 ± 0.13	1.18 ± 0.12

*Note: * reliability (**p<0.05**) of the changes.*

2% of observations normal circulatory reaction type. The ischemic type manifested itself in the decrease in blood flow in the nutrition vessels as a result of super tension of arterioles and congestion in the venular link of the microcirculatory bloodstream. In case of hyperemic type of reaction an increase of blood volume in the arterioles was accompanied by congestive phenomena in the resistive and nutrition vessels of the microcirculatory bloodstream. The positive follow-up confirmation of the conditions of the patients under study made it possible to move on to the actual evaluation of the mechanisms and effectiveness of the approaches compared. In the meantime, the positive results in response to ozone therapy (a single case of worsening in the 1st group) have definitely exceeded the indicators of the 3rd group (Table 1).

The advantage of both options of ozone therapy manifested itself in the distinct regression of neurological symptoms, including a definite lessening of pain, on average by 64%, against 45% in the 3rd group. However, there are also differences in the groups of ozone therapy: the long-lasting effect in the 1st group was achieved after 7.5 gas injections, while in the 2nd group after 6.2. Considering the periodicity of injections due result in the groups was observed after 15 and 12.4 days respectively. Besides, reduction (by visual characteristics) of vasospastic manifestations was also different in 50% and 75% of observations, i.e. 1.5 times oftener in case of ozone therapy observing the rules of biopuncture. In the course of psychological testing the analysis of Minnesota Multiphasic Personality Inventory tests (MMPI) in the patients of the ozone therapy group demonstrated a drop ($p < 0.05$) of the peak on the 1st scale with more favorable places of the positions in the right part of the chart. The observed shifts spoke of a decrease in anxiety and the need to control the character of the symptoms of illness. Simultaneously, a steady increase in the average indicators of HAM (Health, activity, mood) was observed. Dynamic changes of electrophysiological indicators, on the whole, corresponded to the shifts of clinical characteristics. Particularly, the severity of temperature asymmetry at the segmental level significantly reduced only in the groups of ozone therapy, by 45% on average. The asymmetry levels in the area of the legs in these groups also decreased (in the 2nd group it was a little more pronounced), unlike the control group (table 2). The rheographic characteristics were undergoing similar changes: against the background of the ozone therapy, unlike the basic exposure, there was an improvement in indicators (moreover, of the rheographic index, RI – significantly) in the area of the lower limbs. The shifts of the analyzed characteristics at the level of the legs are given in table 3. The results of ultrasonic Doppler examination also confirmed positive effect of the compared options of

Table 3. *Changes in the indicators of rheovasograms of the legs in the groups (M ± m).*

Groups	Indicators					
	RI (Ohm)		DI		RT (s)	
	before	after	before	after	before	after
1 (25)	0.044± 0.005	0.062± 0.006*	0.35± 0.05	0.37± 0.07	0.12± 0.006	0.11± 0.008
2 (23)	0.045± 0.006	**0.062**± **0.007***	0.35± 0.06	0.36± 0.06	0.12± 0.008	0.11± 0.01
3 (25)	0.044± 0.007	0.049± 0..007	0.34± 0.06	0.35± 0.08	0.12± 0.009	0.12± 0.01
Control	0.07±0.01		0.39±0.06		0.09±0.007	

*Note: In brackets the number of observations; DI, dicrotic index; RT , rise time of the pulse wave; *, reliability (**p < 0.05**) of the changes.*

Table 4. *Changes in blood flow in the vessels on the side of pain (M±m).*

Groups	Arteries, blood flow level (mL / min)			
	Posterior tibial		Dorsum of foot	
	Before	After	Before	After
1 (19)	3.9±1.4	4.1±1.3	3.1±0.8	3.2±0.7
2 (20)	4.0±1.5	4.4±1.5	3.1±0.7	3.4±0.6
3 (17)	3.9±1.6	3.9±1.4	3.0±0.6	3.1±0.9
Control	4.9±1.9		3.6±0.6	

Note: in brackets the number of observations.

ozone therapy, manifesting itself in the decrease (unreliable, in the form of a trend) in the tone of the examined arteries. The effect of the basic therapy in this case was less pronounced (table 4).

It is important that reliable changes in the indicators of ultrasonic Doppler examination were observed only in the process of ozone therapy. Particularly, a specific improvement of blood flow at the spastic type of microcirculation was explained by the decrease in the tone of arterioles, a verified drop in index ALF/CKOx100% in the first two groups from 141.2 ± 1.3 down to 135.1 ± 1.5 ($p < 0.05$) and from 141.4 ± 1.3.down to 131.0 ± 2.1 ($p < 0.001$), respectively.

Simultaneously, it reduced the contribution of respiratory fluctuations to the general spectrum of oscillations confirmed by the drop in AHF/CKOx100% (from 64.3 ± 1.2 down to 59.1±1.2, $p < 0.05$ and from 64.2 ±1.3 down to 54.7 ± 1.2, $p < 001$, respectively), thus, demonstrating decongestion in the venular link of the microcirculatory bloodstream. In case of the hyperemic type normalization of the blood volume in the resistive and nutrition vessels of the microcirculatory bloodstream was observed as a consequence of the prevalence of active mechanisms of blood flow modulation, at the increase in ALF/CKOx100% from 91.1 ± 2.1 down to 106.4 ± 3.1 ($p < 0.05$) and from 91.2 ± 2.3 down to 116.9±2.1 ($p < 001$), respectively. It is also necessary to point out restriction of passive me. hanisms – a drop in index ACF/CKOx100% from 49,9± 1.4 down to 41.9 ± 1,.4 ($p < 0.05$) and from 49.6 ± 1.7 down to 38.9 ± 1.3 ($p < 0.001$), respectively, confirming the improvement of the microcirculatory bloodstream. The 3rd group, both in case of the spastic and in case of hyperemic type of reaction, demonstrated a trend to improvement of some indicators of ultrasonic Doppler examination, however, beyond the reliability of their changes. On the whole, an unambiguous priority of the local ozone therapy in the recovery of the microcirculation level was confirmed, with an advantage for the 2nd group, i.e. in reaction to the application of the biopuncture scheme. As a result of the follow-up analysis, carried out 6 months later, dorsopathy relapses were observed in 32% of observations, unlike the ozone therapy groups, where they occurred significantly less often, in 21% and 18% of observations, respectively. At the same time, it should be noted that the exacerbations in the 2nd group were less pronounced and were in a “milder” form. Correspondingly, if the 1st and the 3rd group demonstrated clinically an increase in the spastic vascular response, then, a positive effect, on the whole, persisted in the 2nd group. These data were complemented with electrophysiological data, the shifts of which were not reliable, reflected the direction of the reaction. For example, unlike the 2nd group, in which the achieved thermography indicators were relatively stable, the other two groups demonstrated an increase (on average by 15%) in thermoassymentry in the area of the limbs. Other electrophysiological characteristics (Rheographic Index of the legs and the blood flow in the arteries of the dorsum of the foot, the indicators of the microcirculatory flow level) underwent similar shifts, differing in a certain preservation in the 2nd group and deterioration in the other groups, by 12-16% on average.

The ozone therapy method is becoming more and more popular all over the world. This is due to the ozone properties to influence oxygen transport and its release in tissues, its bactericidal effect. The ozone molecule has a special structure, formed by three oxygen atoms, which makes ozone very active when attaching to living cells and ensures its oxidation capacity. At present, it has been established that ozone activates metabolism, induces optimizations of pro- and antioxidant systems, anti-inflammatory, analgesic and detoxification effects. When treating degenerative and dystrophic spine disorders various approaches to ozone therapy are used.

RCS were conducted to assess the efficacy of oxygen-ozone nucleolysis, a minimally invasive procedure of intradiscal administration of the mixture[8-10]

A pronounced analgesic action was observed in most patients with herniation of intervertebral disk, who did not respond to conservative therapy. At the same time, any significant statistical differences between the effect from oxygen-ozone nucleolysis and its combination

with steroid drugs after 6 and 12 months study were not found.

A multicenter placebo-controlled study to examine the efficacy of intramuscular paravertebral administration of the ozone-oxygen mixture to patients with a sharp backache, caused by lumbar spine herniation, was conducted. Credible differences between the results in the main group and in the placebo group about the severity of the pain syndrome were established, while the need to take steroidal anti-inflammatory drugs has reduced seriously. These have been no observations of adverse reactions to administration of the of the ozone-oxygen mixture.[11]

The authors of a systematic review that included 438 scientific publications and dedicated to the analysis of the efficacy of ozone therapy for backache came to the conclusion that almost all studies demonstrated credible differences in the influence on the pain syndrome between the patients receiving the ozone therapy and the patients of the control groups. Also, no complications have been registered after administering ozone.[12] The efficacy of ozone therapy was also demonstrated in 576 patients with non-discogenic lower back pain.[13] Other authors had the objective to study mechanism(s) of action of the ozone-oxygen mixture.[14-19] It was established that administration of ozone can reactivate innate antioxidant system that induces a correction of the oxidative stress, which is typical of chronic inflammatory diseases.

Therapeutic effects of ozone therapy are achieved due to the improvement of oxygenation of tissues, the acceleration of the use of glucose in the cellular metabolism, the improvement of the protein metabolism, increased activity of the erythrocytes, the inhibition of inflammation mediators, reducing prostaglandins synthesis and oxidative stress in biological tissues.

It is very important that some studies found not only the analgesic effect of ozone therapy, but a significant improvement of motor functions that were disordered against the background of compression of nerve roots in patients with herniation of intervertebral disks as well.[20] It was also demonstrated that ozone therapy is effective for elderly people with signs of spondyloarthrosis and degeneration of the disk of the lumbar spine, who have contraindications to analgetics and non-steroidal anti-inflammatory drugs.[21] On the whole, it can be said that the efficacy of oxygen-ozone nucleolysis or paravertebral injections is the best studied area. Currently, primary biochemical mechanisms of the main clinical effects of ozone therapy have been identified.[22]

Meanwhile, many authors noted the need of further studies in order to define more clearly optimal parameters and methodological approaches in case of the ozone therapy for patients with dorsopathies. The rate of development and stability of positive effects in dorsopathies that were pointed out in this study are explained by the peculiarities of the compared exposure variants.[23] Meanwhile, once again, it was confirmed that using ozone therapy by biopuncture scheme ensures, compared with other methods, the achievement of a faster and more sustainable effect. The explanation for this phenomenon is the plane of combination of reflex and specific mechanisms of the developed technology.

List of acronyms

ALF/CKOx - Standard Deviation of the amplitude of low-frequency oscillations
HAM - Health-activity-mood
LDF - Laser Doppler flowmetry
MMPI - Minnesota Multiphasic Personality Inventory Tests
RCS - Randomized Controlled Studies
RI - Rheographic Index
VAS - Visual Analogue Scale

Contributions of Authors

LGA: concept development, editing; TVK: editing; DBK: writing of the text; OSD: collection and processing of the material; TVA: statistical processing of the material, ADF: administrative support; APR: scientific consultant; MyuY: bibliographical search and data collection; KVT: statistical analysis; NPS: informational support. All authors have read and approved the final edited version.

Acknowledgments

None

Funding

None.

Conflict of Interest

The authors declare no conflict of interests.

Ethical Publication Statement

We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

Corresponding Author

Kirill V. Terentev, State Budgetary Healthcare Institution of Moscow region, M. F. Vladimirsky Moscow Regional Research and Clinical Institute, Moscow, Russia
ORCID iD: 0000-0003-0858-1906
E-mail: kirillterentev184@gmail.com

E-mails and ORCID iD of co-authors

Lev G. Agasarov: lev.agasarov@mail.ru
ORCID iD: 0000-000-5218-1163
Tatiana V. Konchugova: umc-rnc@mail.ru
ORCID iD: 0000-0003-0991-8988
Detelina B. Kulchitskaya: deti_ku@mail.ru
ORCID iD: 0000-0005-1231-8082
Olga S. Davyan: davianolga@gmail.com
ORCID iD: 0000-0002-9630-1355

Tatiana V. Apkhanova: apkhanova@yandex.ru
ORCID iD: 0000-0003-3852-2050
Anatoliy D. Fesyun: fad68@yandex.ru
ORCID iD: 0000-0003-3097-8889
Andrey P. Rachin: RachinAP@nmicrk.ru
ORCID iD: 0000-0003-4266-0050
Maxim Yu. Yakovlev: masdat@mail.ru
ORCID iD: 0000-0002-5260-8304
Natalia P. Sanina: nataliasanina2@yandex.ru
ORCID iD: 0000-0001-8597-1962

References

1. Agasarov LG. [Reflexology for common diseases of the nervous system]. 2017; 240. Russian.
2. Popelyansky YYu. [Diseases of the peripheral nervous system]. 2005; 463. Russian.
3. Podchufarova EV. [Topical issues of acute and chronic pain in the lumbosacral region]. Neurology, neuropsychiatry, psychosomatics. 2012;1:27-35. Russian.
4. Agasarov LG, Davyan OS, Tarasova LYu. [Electrophysiological correlates of the efficacy of local ozone therapy in vertebral pathology]. Attending physician. 2017;10:58-60. Russian.
5. Gustov AV, Kontorshchikova KN, Potekhina YuP. [Ozone therapy in neurology]. 3rd ed., Revised edition. 2012;192. Russian.
6. Agasarov LG. [Pharmacopuncture]. 2015:192. Russian.
7. Kuzmina IV. [Optimization of reflex methods of exposure to dorsopathies]. Author's abstract dis. Ph.D. (Medicine). 2015;23. Russian.
8. Oder B, Loewe M, Reisegger M, Lang W, Ilias W, Thurnher S. CT-guided ozone/steroid therapy for the treatment of degenerative spinal disease--effect of age, gender, disc pathology and multi-segmental changes. Neuroradiology. 2008 Sep;50(9):777-85. doi: 10.1007/s00234-008-0398-2.
9. Zhang Y, Ma Y, Jiang J, Ding T, Wang J. Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone. J Back Musculoskelet Rehabil. 2013;26(3):317-22. doi: 10.3233/BMR-130386
10. Elawamy A, Kamel EZ, Hassanien M, Wahba OM, Amin SE. Implication of Two Different Doses of Intradiscal Ozone-Oxygen Injection upon the Pain Alleviation in Patients with Low Back Pain: A Randomized, Single-Blind Study. Pain Physician. 2018 Jan;21(1):E25-E31.
11 Paoloni M, Di Sante L, Cacchio A, Apuzzo D, Marotta S, Razzano M, Franzini M, Santilli V. Intramuscular oxygen-ozone therapy in the treatment of acute back pain with lumbar disc herniation: a multicenter, randomized, double-blind, clinical trial of active and simulated lumbar paravertebral injection. Spine (Phila Pa 1976). 2009 Jun 1;34(13):1337-44. doi: 10.1097/BRS.0b013e3181a3c18d.
12. Costa T, Linhares D, Ribeiro da Silva M, Neves N. Ozone therapy for low back pain. A systematic review. Acta Reumatol Port. 2018 Jul-Sep;43(3):172-181. English.
13. Bonetti M, Zambello A, Princiotta C, Pellicanò G, Della Gatta L, Muto M. Non-discogenic low back pain treated with oxygen-ozone: outcome in selected applications. J Biol Regul Homeost Agents. 2020 Jul-Aug;34(4 Suppl. 1):21-30. SPECIAL ISSUE: OZONE THERAPY
14. Bocci V, Borrelli E, Zanardi I, Travagli V. The usefulness of ozone treatment in spinal pain. Drug Des Devel Ther. 2015 May 15;9:2677-85. doi: 10.2147/DDDT.S74518
15. Akkawi I. Ozone therapy for musculoskeletal disorders Current concepts. Acta Biomed. 2020 Nov 12;91(4):e2020191. doi: 10.23750/abm. v91i4.8979.
16. de Sire A, Agostini F, Lippi L, Mangone M, Marchese S, Cisari C, Bernetti A, Invernizzi M. Oxygen-Ozone Therapy in the Rehabilitation Field: State of the Art on Mechanisms of Action, Safety and Effectiveness in Patients with Musculoskeletal Disorders. Biomolecules. 2021 Feb 26;11(3):356. doi: 10.3390/biom11030356.
17. Bhatia A, Munk P, Lee D, Elias G, Murphy K. Percutaneous Ozone Treatment for Herniated Lumbar Discs: 1-Year Follow-up of a Multicenter Pilot Study of a Handheld Disposable Ozone-Generating Device. J Vasc Interv Radiol. 2019 May;30(5):752-760. doi: 10.1016/j.jvir.2018.09.037. Epub 2019 Mar 25.
18. Melchionda D, Milillo P, Manente G, Stoppino L, Macarini L. Treatment of radiculopathies: a study of efficacy and tollerability of paravertebral oxygen-ozone injections compared with pharmacological anti-inflammatory treatment. J Biol Regul Homeost Agents. 2012 Jul-Sep;26(3):467-74.
19. Özcan Ç, Polat Ö, Çelik H, Uçar BY. The Effect of Paravertebral Ozone Injection in the Treatment of Low Back Pain. Pain Pract. 2019 Nov;19(8):821-825. doi: 10.1111/papr.12812. Epub 2019 Jul 11.
20. Dall'Olio M, Princiotta C, Cirillo L, Budai C, de Santis F, Bartolini S, Serchi E, Leonardi M. Oxygen-ozone therapy for herniated lumbar disc in patients with subacute partial motor weakness due to nerve root compression. Interv Neuroradiol. 2014 Oct 31;20(5):547-54. doi: 10.15274/INR-2014-10078. Epub 2014 Oct 17
21. Bonetti M, Fontana A, Martinelli F, Andreula C. Oxygen-ozone therapy for degenerative spine disease in the elderly: a prospective study. Acta Neurochir Suppl. 2011;108:137-42. doi: 10.1007/978-3-211-99370-5_21.
22. Hammad EV, Nikitin IG, Fedorova KV. [Ozone therapy in Patients with the New Coronavirus Infection COVID-19]. Bulletin of Rehabilitation

Medicine. 2020;5 (99):94-100. Russian. doi: 10.38025/2078-1962-2020-99-5-94-100.
23. Nuvakhova MB. [Innovative Technologies in the Health-Resort Treatment of Patients with Dorsopathy]. Bulletin of Rehabilitation Medicine. 2020;6(100):66–74. Russian. doi: 10.38025/2078-1962-2020-100-6-66-74.

Disclaimer

All claims expressed in this article are solely those of the authors and do not necessarily represent those of their affiliated organizations, or those of the publisher, the editors and the reviewers. Any product that may be evaluated in this article or claim that may be made by its manufacturer is not guaranteed or endorsed by the publisher.

Submission: June 15, 2022
Accepted for publication: June 21, 2022