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RETROSPECTIVE OBSERVATIONAL STUDY OF PARAVERTEBRAL INTRAMUSCULAR OZONE/OXYGEN INJECTION IN THE TREATMENT OF CHRONIC NONSPECIFIC LOW BACK PAIN

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ABSTRACT

Objective: Chronic non-specific low back pain is a very common musculoskeletal condition that affects the quality of life. It is critical to be treated with effective, safe and minimally invasive treatments. In this study, we analyzed the impact of paravertebral ozone/oxygen (O_3/O_2) treatment injection treatment on distress and disability in patients with chronic non-specific low back pain.

Materials and Methods: From January 2019 to December 2021, 426 patients who underwent paravertebral ozone injections due to low back pain were examined retrospectively; 305 patients who met the study criteria were included. The patients were injected with 15 Î¼g (50 mL) O_3/O_2 gas in the paravertebral muscle. Paravertebral O_3/O_2 injections were administered once a week for 5 weeks. Visual analog scale (VAS)-resting, VAS-activity and Istanbul Low Back Pain Disability Index (ILBPDI) were recorded at pre-treatment, post-treatment, and 6-month follow-ups.

Results: Of the patients included in the study, 158 (51.8%) were female, 147 (48.2%) were male and the mean age of all patients was 45.6±8.8.VAS-resting, VAS-activity decreased statistically significantly after treatment and 6 months after treatment compared to pretreatment ($p<0.001$). The mean ILBPDI score of the patients decreased statistically significantly after the treatment and at the 3rd month and 6th month after the treatment compared with the pre-treatment ($p<0.001$). There was no significant difference between the post-treatment and post-treatment 6-month measurements.

Conclusion: In our study, it was found that paravertebral O_3/O_2 therapy for treating chronic nonspecific low back pain was effective in improving pain, functional status and activities of daily living, and its effect continued in the long term.

Keywords: Non-specific low back pain, paravertebral ozone, intramuscular ozone, disability

INTRODUCTION

Chronic non-specific low back pain (CNLBP) is defined as low back pain lasting longer than 12 weeks, not due to a clearly defined anatomical or physiological cause[1]. Often, a specific pathology such as infection, tumor, fracture, or inflammatory disease that cause low back pain cannot be detected, and nonspecific low back pain is diagnosed in 80-90% of the cases[2,3]. It is known in many clinical studies that chronic nonspecific low back pain, which has been shown to cause not only nociceptive but also neuropathic pain, adversely affects functionality, social participation, and mental and financial well-being. Although most of the resources are allocated for the treatment of chronic low back pain, the success rate of treatment is low. For this reason, it is extremely important to investigate more effective methods for coping with chronic low back pain to improve the health and quality of life of patients[2-6].

Especially the ineffectiveness of medical applications (with paracetamol, nonsteroidal anti-inflammatory drugs, and myorelaxant) in the treatment of chronic nonspecific low back pain has led to different treatment searches[5,6]. Therefore, it is of great importance to treat chronic nonspecific low back pain with safe and practical minimally invasive techniques. Ozone/oxygen (O_3/O_2) gas therapy applied to the paravertebral muscles is a practical, safe and easy mini-invasive technique[7]. Multiple mechanisms of action have been demonstrated to explain the efficacy of ozone therapy, including analgesic, anti-inflammatory, and oxidant action on proteoglycans (eg in the nucleus pulposus)[8]. Ozone rapidly transforms into molecular oxygen and oxygen radicals in biological environments, creating a moderate oxidative stress in the body. In this way, ozone is perceived as an oxidative threat in the body. This results in the stimulation of enzymes working in antioxidant defense systems.

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The ozone dose should be sufficient to produce an acute, clear and temporary oxidative stress. Lower doses cause a placebo effect, while higher doses cause toxicity[9]. Therefore, it is very important to set ozone doses correctly. Moderate oxidative stress activates nuclear factor-erythroid 2-related factor-2 (Nrf2). Nrf2 triggers the transcription of antioxidant response elements. However, severe oxidative stress causes an inflammatory response by activating nuclear transcription factor kappa, resulting in tissue destruction by increasing cyclooxygenase-2, prostaglandin E2 and cytokine production[10]. The key point in ozone therapy is the regulation of oxidative stress level.

Many studies examining the efficacy responses of specific low back problems with paravertebral ozone therapy have been found, but no study has been found on paravertebral ozone therapy in patients with chronic non-specific low back pain. Accordingly, our study aimed to determine the effects of paravertebral O_3/O_2 therapy (OOT) on pain, functionality, and activities of daily living in patients with chronic nonspecific low back pain.

MATERIALS AND METHODS

A total of patients were analyzed retrospectively in this study. The study protocol was approved by the Yeditepe University Faculty of Medicine Ethics Committee (decision no: 2022/001, date: 09.06.2022). The registration number for the study is 2022/001. The study was conducted following the principles of the Declaration of Helsinki.

Study Design

Patients with CNLBP who had low back pain for at least 3 months and were administered paravertebral O_3/O_2 injection in the anamnesis of the patients who applied with the complaint of low back pain between January 2019 and December 2021 were included in the retrospective study. Patients diagnosed with nonspecific low back pain by a physiatrist according to magnetic resonance imaging findings and without radicular leg pain were included in the study.

Inclusion criteria for the study were: Being between the ages of 25 and 65, having nonspecific low back pain lasting longer than 3 months that did not respond to conventional conservative treatment methods, having a visual analog scale (VAS) score of 4 or higher in VAS evaluation and not be included in any other treatment for chronic low back pain during the study.

Exclusion criteria: Presence of a specific cause of low back pain such as lumbar spinal stenosis, radiculopathy, cancer, inflammatory arthritis, history of previous spinal surgery, presence of pathological findings in neurological examination (loss of sensation in lower extremities, loss of position sense, loss of motor muscle strength), severe cardiovascular or respiratory system pathologies, uncontrolled diabetes mellitus, unhealed fracture or open surgical wound, and the application of algological interventional treatment to the lumbar region in the last 6 months.

Treatment Procedure

All patients were treated with injections using the same medical ozone generator (Salutem model, İstanbul, Turkey). Injections were made into the paravertebral muscles using a 13 mm injector tip, with a total of 15 µg/mL in 50 mL of O_3/O_2 gas administered through ozone-resistant injectors. Paravertebral O_3/O_2 injections were administered once a week for 5 weeks.

While the patient is standing, the spinous process point which is the midpoint of the imaginary line passing over the crista iliacas in the lumbar region is determined as the L4 vertebra spinous process. The upper and lower spinous processes are then marked by palpation. The area is cleaned with alcohol and O_3/O_2 is injected vertically 2 cm above and below the spinous processes, starting 1 cm lateral to the spinous process, while the patient is in the prone position. The 21 gauge injector tip was applied at a depth of 3 cm. A total of 4 injections were applied to the paravertebral muscles at the level of L4 and L5 vertebrae bilaterally and no premedication or anesthesia was given. All paravertebral ozone applications were performed by an experienced specialist physician and all sessions were performed by the same person.

Before starting the treatment program, lumbar isometric exercises (pelvic tilt exercises, hamstring stretching, and modified straightening) were shown to all patients by the same physiotherapist and they were told that these exercises should be performed for 20 minutes a day, at least 5 days a week.

Evaluation Measures

VAS-resting, VAS-activity, and Istanbul Low Back Pain Disability Index (ILBPDI) were recorded at pre-treatment, post-treatment, and 6-month follow-ups.

Pain intensity was measured using the VAS. The patients were asked to rate their pain intensity on the scale by explaining what the numbers meant on a 10 cm-long horizontal line. Zero means no pain, and 10 means severe pain. The pain intensity of the participants was defined in 3 situations: At rest, during forward bending, and backward stretching movements. The point marked by the participants on the line was measured with a ruler, and the VAS value was recorded in cm[11].

ILBPDI, which evaluates functional status, is a specific scale developed for the evaluation of patients with chronic low back pain. ILBPDI contains 18 questions, each question is scored with a 6-point (0-5 points) Likert scale. The questions relate to the patients' activities of daily living during the past month. Total scores range from 0 to 90, with higher scores indicating greater disability. A validity and reliability study of ILBPDI was conducted[12]. The scores of the patients were made by a physiatrist who did not administer ozone injection.

Statistical Analysis

The data of the study were analyzed using the IBM SPSS Statistics 22 (IBM SPSS, Armonk, NY, U.S.A.) program, and $p<0.05$ was accepted as the significance level. In summarizing the data obtained from the study, descriptive statistics were tabulated as mean ± standard deviation or median, minimum and maximum depending on the distribution of continuous numerical variables. Pre- and post-injection data were compared using the one-way ANOVA test for repeated measures.

RESULTS

Four hundred twenty six patients who underwent paravertebral ozone injections due to low back pain were examined retrospectively; 305 patients who met the study criteria were included. Of the patients included in the study, 158 (51.8%) were female, 147 (48.2%) were male and the mean age of all patients was 45.6±8.8 years, the mean body mass index was 26.4±5.5 kg/m^2 and 132 patients smoked. Of the patients, 190 (62.2%) were working in a paid job and 106 (34.7%) had primary education. The mean duration of low back pain in the patients was calculated as 32±9.9 months. While the duration of symptoms was 12 months or less in 31.8% (n=97) of the patients, the duration of low back pain was over 12 months in 68.2% (n=208) of the patients. Table 1 shows the sociodemographic and clinical characteristics of the patients. According to the information determined from the recorded file data, no complications were observed during the injection. Post-injection pain and stiffness were observed in 154 patients within the first three days, after which it was reported that the symptoms regressed.

VAS-resting, VAS-activity decreased statistically significantly after treatment and 6 months after treatment compared to pretreatment ($p<0.001$). The mean ILBPDI score of the patients decreased statistically significantly after the treatment and 6th month after the treatment compared to the pre-treatment ($p<0.001$). The changes in the evaluation criteria before and after the treatment are shown in Table 2.

According to the pairwise comparisons of the evaluation criteria, statistical significance was found in all parameters when pre-treatment and post-treatment, and pre-treatment and post-treatment 6 months were compared ($p<0.05$). There was no significant difference between the post-treatment and post-treatment 6-month measurements. Pairwise comparisons of the evaluation criteria with the measurements made before and after the treatment are shown in Table 3.

DISCUSSION

In a global systematic study conducted in 2012, the point prevalence of chronic nonspecific low back pain in the adult population was 12%, and the lifetime prevalence was as high as 40%. The aim of the treatment of chronic non-specific low back pain is to relieve pain, restore function and prevent recurrence[13]. It is known that chronic low back pain is often not treated appropriately. Therefore, it is very important to determine the effectiveness of new, effective, and reliable treatment methods. Minimally invasive treatment methods have been developed (such as corticosteroid and anesthetic injections, acupuncture, mesotherapy, and platelet-rich plasma injection) in addition to physiotherapy and vertebral manipulation to treat chronic low back pain.

Ozone; it is a molecule formed by the coexistence of 3 oxygen atoms, and it is a treatment method that provides treatment for many diseases with wide application areas and low incidence of side effects. Paravertebral OOT is a treatment method that has become widespread and has direct and indirect mechanical and anti-inflammatory dual effects[14,15]. Dissolved ozone in body fluids reacts immediately with antioxidants and polyunsaturated fatty acids, resulting in rapid-acting reactive oxygen compounds [most importantly hydrogen peroxide (H_2O_2)] and lipid peroxidation products with longer half-lives[9]. In the first phase, H_2O_2 diffuses into the cell cytoplasm and acts as a trigger. It causes different chemical pathways according to the cell types it affects. Reactive oxygen products act as short-acting messengers and are removed by antioxidants in a very short time, but the complex pharmacodynamics of lipid peroxidase products allow them to be long-term messengers by minimizing their potential toxicity[10]. It is a less stable molecule than oxygen, it has a more biological response and blocks the phospholipase A2 enzyme, and suppresses inflammation[15].

Table 1. Sociodemographic and clinical characteristics of the patients

Variables	Mean ± SD (%)	Median (minimum-maximum)
Age	45.6±8.8	46.0 (29-63)
Gender (%)		
Female	158 (51.8%)	
Male	147(48.2%)	
BMI (kg/m)	26.4±5.5	26 (18.4-37.5)
Working condition (%)		
Working in paid job	190 (62.2%)	
Not working	115 (37.8%)	
Education (%)		
Primary education	106 (34.7%)	
High school	89 (29.1%)	
University	76 (24.9%)	
Graduate	34 (11.1%)	
Low back pain duration (months)	32±9.9	25.5 (6.0-45.5)

SD: Standard deviation, BMI: Body mass index

Table 2. Comparison of the evaluation criteria before treatment, after treatment, and 6 months after treatment

	Before treatment	After treatment	6 months after treatment	p values
VAS-resting	4.53±5.32 4 (0-9)	1.85±1.86 1 (0-5)	1.47±1.63 1 (0-5)	<0.001
VAS-activity	6.74±1.86 7 (3-9)	3.44±2.19 5 (0-8)	3.29±2.08 3 (0-8)	<0.001
ILBPDI	26.74±12.25 24 (8-42)	17.53±10.18 15 (0-33)	12.12±11.78 4 (0-45)	<0.001

VAS: Visual analog scale, ILBPDI: Istanbul Low Back Pain Disability Index

Table 3. Paired comparisons of assessment criteria before and after treatment and 6 months after treatment

	VAS-resting p	VAS-activity p	ILBPDI p
Before treatment-after treatment	<0.001	<0.001	<0.001
Before treatment-6 months after treatment	<0.001	<0.001	<0.001
After treatment-6 months after treatment	0.723	0.489	0.367

VAS: Visual analog scale, ILBPDI: Istanbul Low Back Pain Disability Index

Cantele et al.[16] reported that intramuscular paravertebral O_3/O_2 injections in 21 patients with chronic low back pain improved their pain and disability outcomes, along with a better outcome in psychological well-being due to lumbar low back pain.

In a systematic review that included 15 studies examining 2,597 patients in total, it was stated that OOT was effective in pain control and functional improvement. However, looking at the quality of the literature, none of the included studies reached the standard of "good quality", 3 were rated as "moderate" and the rest were rated as "poor"[17].

Lumbar paravertebral O_3/O_2 injections in the treatment of low back pain are minimally invasive, safe, cheaper, and effective in relieving pain as well as disability. It has been reported in the literature that only a very small proportion of patients have non-serious side effects. This technique is easy to apply and does not require premedication, CT, or surgery environment, it is an injection that can be done safely in outpatient clinic conditions[15]. In our study, it has been shown that paravertebral OOT is effective on pain, activities of daily living, and disability in patients with chronic nonspecific low back pain.

Patients with low back pain for at least 6 months who had previously received medical and physical therapy but did not benefit were included in our study. Therefore, when evaluating the results of our study, it should be taken into account that the pain of the patients is chronic and resistant. However, it is seen that the patient population is similar in the studies conducted[16-18].

Study Limitations

Limitations of this study include its retrospective design, absence of a control group, and lack of power analysis. Our results show that paravertebral ozone injections are a safe and easy treatment that is minimally invasive for patients with chronic nonspecific low back pain. There are not enough studies on this treatment method. More prospective randomized and controlled studies are needed to increase the safety of paravertebral injection therapy.

CONCLUSION

In our study, it was found that paravertebral OOT in the treatment of chronic nonspecific low back pain was effective in improving pain, functional status, and activities of daily living, and its effect continued in the long term. It is thought that paravertebral OOT can be recommended as an effective and safe treatment option in patients with CNLBP with appropriate indications. There is a need for randomized controlled studies with more patients.

Ethics

Ethics Committee Approval: The study protocol was approved by the Yeditepe University Faculty of Medicine Ethics Committee (decision no: 2022/0001, date: 09.06.2022).

Informed Consent: Informed consent was obtained from all patients before injection.

Peer-review: Externally and internally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.K., Concept: S.K., I.F.K., Design: S.K., I.F.K., Data Collection or Processing: S.K., Analysis or Interpretation: S.K., I.F.K., Literature Search: S.K., I.F.K., Writing: S.K., I.F.K.

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REFERENCES

1. Hayden JA, van Tulder MW, Malmivaara A, Koes BW. Exercise therapy for treatment of non-specific low back pain. Cochrane Database Syst Rev. 2005;CD000335.
2. Maher C, Underwood M, Buchbinder R. Non-specific low back pain. Lancet. 2017;389:736-47.

3. Ketenci A, Zure M. Pharmacological and non-pharmacological treatment approaches to chronic lumbar back pain. Turk J Phys Med Rehabil. 2021;67:1-10.
4. Chenot JF, Greitemann B, Kladny B, Petzke F, Pfingsten M, Schorr SG. Non-specific low back pain. Dtsch Arztebl Int. 2017;114:883-90.
5. Gianola S, Bargeri S, Del Castillo G, Corbetta A, Turolla A, Andreano A, et al. Effectiveness of treatments for acute and subacute mechanical non-specific low back pain: a systematic review with network meta-analysis. Br J Sports Med. 2022;56:41-50.
6. Chenot JF, Greitemann B, Kladny B, Petzke F, Pfingsten M, Schorr SG. Non-specific low back pain. Dtsch Arztebl Int. 2017;114:883-90.
7. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen-ozone therapy for lumbar disk herniation. Am J Neuroradiol. 2003;24:996-1000.
8. Magalhaes FN, Dotta L, Sasse A, Teixera MJ, Fonoff ET. Ozone therapy as a treatment for low back pain secondary to herniated disc: a systematic review and meta-analysis of randomized controlled trials. Pain Physician. 2012;15:E115-29.
9. Bocci V. Ozone as Janus: this controversial gas can be either toxic or medically useful. Mediators Inflamm. 2004;13:3-11.
10. Sagai M, Bocci V. Mechanisms of action involved in ozone therapy: Is healing induced via a mild oxidative stress? Med Gas Res. 2011;1:29.
11. McDowell I, Newell C. Measuring health: a guide to rating scales and questionnaires. Second Edition, Oxfort University Press, New York 1996;pp:354-55.
12. Duruöz MT, Özcan E, Ketenci A, Karan A. Development and validation of a functional disability index for chronic low back pain. J Back Musculoskelet Rehabil. 2013;26:45-54.
13. Ma K, Zhuang ZG, Wang L, Liu XG, Lu LJ, Yang XQ, et al. The Chinese Association for the Study of Pain (CASP): Consensus on the assessment and management of chronic nonspecific low back pain. Pain Res Manag. 2019;2019:8957847.
14. Alyan S, Zaghlol R, Mustafa AS. Efficacy of combined paravertebral ozone (O2O3) therapy with physiotherapy in patients with chronic mechanical low back pain. Egyptian Rheumatology and Rehabilitation. 2018;45:106-11.
15. Re L, Mawsouf MN, Menéndez S, León OS, Sánchez GM, Hernández F. Ozone therapy: clinical and basic evidence of its therapeutic potential. Arch Med Res. 2008;39:17-26.
16. Cantele F, Tognolo L, Caneva F, Formaggio E, Copetti V, Venturin A, et al. Influence of pain-related psychological factors on therapeutic outcomes in patients with chronic low back pain after oxygen-ozone treatment: a case-series. Eur J Transl Myol. 202;31:9906.
17. Sconza C, Leonardi G, Kon E, Respizzi S, Massazza G, Marcacci M, et al. Oxygen-ozone therapy for the treatment of low back pain: a systematic review of randomized controlled trials. Eur Rev Med Pharmacol Sci. 2021;25:6034-46.
18. Murphy K, Muto M, Steppan J, Meaders T, Boxley C. Treatment of contained herniated lumbar discs with ozone and corticosteroid: a pilot clinical study. Can Assoc Radiol J. 2015;66:377-84.