

Retrospective observational study of intramuscular oxygen-ozone therapy for the treatment of neck pain: cervical paravertebral injection

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Abstract

Neck pain is one of the major pathologies responsible for loss of labor. Many conservative treatment methods for neck pain have been described. The purpose of this study was to obtain pain scores for patients undergoing paravertebral ozone-oxygen (O_3/O_2) injections for neck pain caused by cervical disc disease. Over the last 6 months of 2018, 72 patients who undergoing intramuscular O_3/O_2 injections to treat neck pain were examined retrospectively in this multicenter study. Patients were injected with 30 mL of 20 $\mu\text{g}/\text{mL}$ O_3/O_2 gas (into the paravertebral space). Subjects were treated once a week for 6 weeks. The visual analog scale pain scores and Japanese Orthopedic Association scores were obtained before (pre-injection) and after treatment (i.e., at 2 and 6 months). Significant improvements were observed in visual analog scale and Japanese Orthopedic Association scores at both 2 and 6 months versus the pre-injection scores. There was no significant difference in the visual analog scale or Japanese Orthopedic Association scores between 2 and 6 months. Paravertebral O_3/O_2 injection is a reliable and effective treatment of neck pain caused by cervical disc disease. The study was approved by Umraniye Education and Research Hospital, University of Health Sciences, Turkey (Reference Number: 00102187854) on September 25, 2019.

Key words: cervical disc; cervical discogenic pain; ozone treatment; paravertebral ozone

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INTRODUCTION

Neck pain secondary to disc degeneration or hernia is a significant health problem resulting in disability. After back pain, neck pain is the musculoskeletal condition most responsible for primary care consultations worldwide.¹ The majority of adults experience at least one significant episode of axial neck pain during their lives.^{2,3} Based on studies using the same definition of neck pain, the prevalence ranges from 16.7% to 75.1% (mean, 37.2%) within the entire adult population (aged 17–70 years).^{1,4} Muscle strains and ligament sprains are common causes of acute axial neck pain. Spondylotic or degenerative causes include disc degeneration, facet arthrosis and, less commonly, segmental instability. Degenerative discs may lead to generalized axial neck pain. Consensus exists regarding surgical indications for several common cervical spine disorders, such as myelopathy, radiculopathy, and traumatic conditions characterized by instability or neurologic deficit.^{5,6} Recently many treatment methods have been tried to decrease the pain, particularly because of cervical disc disease.^{7,8} Especially, insufficiency of some drugs (paracetamol, non-steroidal anti-inflammatory, and myorelaxant) to effectively treat neck pain has prompted a search for alternative treatments.^{9,10}

Paravertebral injection with O_3/O_2 (ozone-oxygen mixture) is a technique that can be applied easily. Ozone gas is derived from a variety of sources and shows numerous beneficial

effects, including inhibition of inflammation, correction of ischemia and venous stasis, and antinociceptive activity in reflex therapy.^{11,12} Paravertebral injection with O_3/O_2 has mostly been used in the treatment of lower back pain¹³⁻¹⁶; few studies have applied this technique to cervical pain.¹⁷⁻¹⁹

Ozone therapy for disc diseases is generally applied using the intradiscal method. In this study, we show that paravertebral ozone injection administered via an “intradiscal external method” can provide the same effects. However, the optimal dose of ozone remains unclear. The aim of our multicenter study was to demonstrate the efficacy and reliability of ozone gas administered by injection for treating neck pain.

SUBJECTS AND METHODS

Design

This study was allowed by Umraniye Education and Research Hospital, University of Health Sciences, Turkey (Reference No. 00102187854) on September 25, 2019. Patients undergoing intramuscular oxygen-ozone injections for neck pain were examined retrospectively over the last 6 months of 2018 in Umraniye Education and Research Hospital, Basari Hospital, Sancaktepe Ilhan Varank Education and Research Hospital. Only patients aged between 18 and 70 years were included. Patients with cervical discogenic pain²⁰ were enrolled regardless of whether disc degenerative disc was found on magnetic resonance imaging (MRI) in the past year. Other patients for



enrollment included patients with spinal stenosis, who are not considered as surgical candidates, patients with radial root compression, and patients with pain for over 6 weeks and a visual analog scale (VAS)²¹ score above 5. The patients did not receive physical therapy during ozone therapy, and patients who underwent physical therapy up to 3 months before starting ozone therapy were excluded from the study. Patients were free to use non-steroidal anti-inflammatory drugs during treatment.

A total of 72 patients analyzed retrospectively in this study. Study was conducted in accordance with principles for human experimentation as defined in the *Declaration of Helsinki*. An informed consent was obtained from all the patients prior to the injection.

Treatment procedure

Patients received paravertebral oxygen-ozone injections (30 mL of 20 µg/mL O₃/O₂ gas) in the paravertebral space once a week for 6 weeks. Injection performed all patients with gas produced by ozone generator system (TURKOZONE Blue S; Ozon Sağlık, İstanbul, Turkey). Subjects with cervical discogenic pain received injection in the left and right side up to C3–T1.

The patient is placed in the prone position with the neck flexed at 30°, and the C7 cervical spinous process is palpated. Spinous protrusions of the vertebrae above and below the disc with cervical discopathy can be located using the C7 spinous protrusion as a guide. The area is cleaned with alcohol and a 13-mm needle tip is injected vertically 2 cm above and below the disc, starting 1 cm lateral to the spinous protrusion in the region of the disc. An average of 15 mL of O₃/O₂ is injected into the right and left side of the disc.

Outcomes

The VAS scores and Japanese Orthopedic Association (JOA) scores²² were measured before paravertebral ozone injection, and at 2 and 6 months after the last injection. The scores of the patients were performed by an orthopedist who did not know the radiological images of the patients and did not apply the ozone injection.

Statistical analysis

The statistical analysis was performed using IBM SPSS Sta-

tistics 22 software (IBM Corp., Armonk, NY, USA). Pre- and post-injection values were compared using the Mann Whitney *U* test. A *P* value of < 0.05 was considered significant.

RESULTS

O₃/O₂ injections were applied in 72 patients with neck pain (32 males and 40 females). The mean age was 55 years (range: 30–70 years). At 6 months after the O₃/O₂ injections, the final assessments were performed. On MRI, 30 subjects had bulging disc herniations, and 22 had degenerative discs and facet arthrosis. Furthermore, 10 had radicular pain and 10 had mechanical neck pain. The mean duration of pain before injection was 6.2 months (3–18 months).

We found a significant improvement in the VAS and JOA scores at 2 and 6 months after O₃/O₂ injection relative to the pre-injection scores (*P* < 0.001). No significant difference in the VAS or JOA scores between 2 and 6 months after O₃/O₂ injection (*P* > 0.05) (Table 1). No complications of neck pain patients with O₃/O₂ injection were observed.

DISCUSSION

In addition to drugs, physical therapy, and steroid injections, physicians have used conservative and non-invasive methods to manage cervical symptoms. According to recent studies, the pain-reducing effects of ozone may be similar, if not identical, to those of steroid injection.^{15,23} Similar to steroids, the anti-inflammatory effect of ozone had been exploited in joint and paravertebral muscle injections.²⁴ Ozone is typically mixed with oxygen when administered for common spine conditions. Ozone is a three-molecule atom with less stability than oxygen. Thus, it evokes a larger biological response. Ozone blocks an inflammatory enzyme known as phospholipase A2, which is also blocked by pain-relieving steroid injections.²³ The limited (if any) side effects of ozone represent an important advantage over steroid injections.

Complications of ozone injection have not been widely described in the literature.²³ However, gas embolism related to paravertebral ozone injection has been reported in the last few years as a major complication. Freund et al.²⁵ reported a 34-year-old man with chronic neck pain who was treated with regular cervical paravertebral ozone injections. After the last injection, multifocal stroke occurred. Angiography

Table 1: Visual analog scale pain scores and Japanese Orthopedic Association scores of neck pain patients with cervical paravertebral O₃/O₂ injection

	Visual analog scale score	Japanese Orthopedic Association score
Pre-injection	8.5 ± 1.3 (5–10)	12.2 ± 3.2 (10–15)
2 mon after injection	3.5 ± 1.6 (0–6)	15.8 ± 2.2 (12–17)
6 mon after injection	4.0 ± 1.1 (0–7)	16 ± 2.8 (13–17)
<i>P</i> ₁	0	0
<i>P</i> ₂	0	0
<i>P</i> ₃	0.459	0.344

Note: Data are expressed as the mean ± standard deviation (range), and were analyzed by Mann Whitney *U* test. *P*₁: *P* value of comparing pre-injection and month 2 scores; *P*₂: *P* value of comparing pre-injection and month 6 scores; *P*₃: *P* value of comparing month 2 and 6 scores.



revealed intra-arterial gas in the right vertebral artery, although the size of the injector tip was not reported. We use a 13-mm injector tip and recommend that the cervical artery be avoided. Chirchigilla et al.²⁶ observed a case of embolism after intradiscal ozone injection, which was preferred over paravertebral administration. Intradiscal high dose O₃/O₂ gas injection is performed using fluoroscopy. Although complications are rare, intradiscal ozone injection can cause embolism and serious infection. In our study, similar improvements in pain scores were observed when paravertebral ozone injection was performed instead of intradiscal ozone injection. Paravertebral ozone injection carries no risk of embolism. It is important that a bacterial filter be fitted to the device used for sterilizing the injection area. Ozone doses over 40 µg/mL have toxic effects even if applied locally, so local injections should not be performed above this dose. Ozone is used for sterilization and we do not believe that ozone applied using a device with a bacterial filter is a potential source of infection.

Ozone therapy has been used for treating musculoskeletal diseases in recent years.²⁷ Intramuscular ozone injections are normally used for long-term relief of lumbar back pain.^{14,16} However, few studies have evaluated the efficacy of paravertebral ozone injection therapy for treating cervical disc diseases.^{17,19}

Ozone gas injection into the paravertebral muscle has been characterized as “chemical acupuncture,” where both the needle itself and the gas elicit a complex series of chemical and neurological reactions leading to a reduction in pain in the majority of patients with mild spinal pain.²⁸ The gas rapidly dissolves in interstitial water and quickly reacts with antioxidants.

We found few studies in the literature of patients with neck pain treated using paravertebral ozone injections.¹⁷ Intradiscal ozone injections have been used most commonly for treating patients with cervical pain. Consoletti et al.¹⁷ explored the effectiveness of intramuscular paravertebral injection of O₃/O₂ in patients with chronic pain due to cervical bulging or herniated discs (cervicobrachialgia). They reported effective pain reduction in 29 patients. Beyaz et al.¹⁹ treated 44 patients who had chronic neck pain due to disc herniation with intradiscal ozone injections. In a follow-up analysis of their VAS pain scores, significant pain reduction was observed compared to the preoperative levels and no complications were reported.

It has been established that the ozone concentration should be between 18–25 µg/mL.²⁵ We administered 20 µg/mL paravertebral ozone injections. There is no consensus optimal dose in the literature; Consoletti et al.¹⁷ did not specify the dose they used in their cervical paravertebral study, while Biazzo et al.¹⁶ used a 27 µg/mL dose and Özcan et al.¹² administered 15 µg/mL lumbar paravertebral ozone injections.

The retrospective design and lack of any control group represent the limitations of this study, which aimed to demonstrate that cervical paravertebral ozone injection is an easy, effective and minimally invasive treatment for relieving the pain caused by disc disease and degeneration.

Author contributions

DU, BYU, and ÇÖ designed this study. DU and SU conceived and supervised the study. ÖP and MAÇ assisted with the treatment. ÇÖ and BYU assisted with the statistical analysis. DU and ÇÖ wrote the paper. All authors were involved in and contributed to the manuscript.

Conflicts of interest

The authors have no conflict of interest to declare.

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Institutional review board statement

The study was approved by Umraniye Education and Research Hospital, University of Health Sciences, Turkey (Reference Number: 00102187854) on September 25, 2019.

Declaration of patient consent

The authors certify that they have obtained patients consent forms. In the form, patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published.

Reporting statement

The writing and editing of the article were performed in accordance with the Transparent Reporting of Evaluations with Nonrandomized Designs (TREND) Statement.

Biostatistics statement

The statistical methods of this study were reviewed by the biostatistician of Umraniye Education and Research Hospital, University of Health Sciences.

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The data could be shared if requested.

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REFERENCES

1. Babatunde OO, Jordan JL, Van der Windt DA, Hill JC, Foster NE, Protheroe J. Effective treatment options for musculoskeletal pain in primary care: A systematic overview of current evidence. *PLoS One*. 2017;12:e0178621.
2. Scott KM, Saha S, Lim CCW, et al. Psychotic experiences and general medical conditions: a cross-national analysis based on 28 002 respondents from 16 countries in the WHO World Mental Health Surveys. *Psychol Med*. 2018;48:2730-2739.
3. Chiu TT, Lam TH, Hedley AJ. A randomized controlled trial on the efficacy of exercise for patients with chronic neck pain. *Spine (Phila Pa 1976)*. 2005;30:E1-7.
4. Malfliet A, Lluch G, Pecos-Martin D, Gallego-Izquierdo T, Valera-Calero A. The influence of treatment expectations on clinical outcomes and cortisol levels in patients with chronic neck pain: an experimental study. *Pain Pract*. 2019;19:370-381.
5. Kaya BB, Atış G, Başoğlu F. Incidence of brachioradial pruritus in patients with C5/C6 pathology. *Acta Med Mediterr*. 2019;35:1009-1012.
6. Bakhsheshian J, Mehta VA, Liu JC. Current diagnosis and management of cervical spondylotic myelopathy. *Global Spine J*. 2017;7:572-586.
7. River Y, Levital T, Belgrade M. Computerized mobilization of the cervical spine for the treatment of chronic neck pain. *Clin J Pain*. 2012;28:790-796.



8. Peng B, DePalma MJ. Cervical disc degeneration and neck pain. *J Pain Res.* 2018;11:2853-2857.
9. Peloso PM, Khan M, Gross AR, et al. Pharmacological interventions including medical injections for neck pain: an overview as part of the ICON Project. *Open Orthop J.* 2013;7:473-493.
10. Yang XN, Geng ZS, Zhang XL, et al. Single intracutaneous injection of local anesthetics and steroids alleviates acute nonspecific neck pain: A CONSORT-perspective, randomized, controlled clinical trial. *Medicine (Baltimore).* 2018;97:e11285.
11. Smith NL, Wilson AL, Gandhi J, Vatsia S, Khan SA. Ozone therapy: an overview of pharmacodynamics, current research, and clinical utility. *Med Gas Res.* 2017;7:212-219.
12. Özcan Ç, Polat Ö, Çelik H, Uçar BY. The effect of paravertebral ozone injection in the treatment of low back pain. *Pain Pract.* 2019;19:821-825.
13. Paoloni M, Di Sante L, Cacchio A, et al. 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;34:1337-1344.
14. 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;26:317-322.
15. Lu W, Li YH, He XF. Treatment of large lumbar disc herniation with percutaneous ozone injection via the posterior-lateral route and inner margin of the facet joint. *World J Radiol.* 2010;2:109-112.
16. Biazzo A, Corriero AS, Confalonieri N. Intramuscular oxygen-ozone therapy in the treatment of low back pain. *Acta Biomed.* 2018;89:41-46.
17. Consoletti L, Di Francesco N, D'Antini D, Mirabella L, Di Foggia T, Dambrosio M. Oxygen/ozone therapy for cervicobrachialgia: clinical outcome in the short term: 14AP2-6. *Eur J Anaesthesiol.* 2013;30:209.
18. Alexandre A, Corò L, Azuelos A, et al. Intradiscal injection of oxygen-ozone gas mixture for the treatment of cervical disc herniations. *Acta Neurochir Suppl.* 2005;92:79-82.
19. Beyaz SG, Sayhan H. Six-month results of cervical intradiscal oxygen-ozone mixture therapy on patients with neck pain: preliminary findings. *Pain physician.* 2018;21:E449-E456.
20. Gebremariam L, Koes BW, Peul WC, Huisstede BM. Evaluation of treatment effectiveness for the herniated cervical disc: a systematic review. *Spine (Phila Pa 1976).* 2012;37:E109-118.
21. Heller GZ, Manuguerra M, Chow R. How to analyze the Visual Analogue Scale: Myths, truths and clinical relevance. *Scand J Pain.* 2016;13:67-75.
22. Azimi P, Mohammadi HR, Montazeri A. An outcome measure of functionality and pain in patients with lumbar disc herniation: a validation study of the Japanese Orthopedic Association (JOA) score. *J Orthop Sci.* 2012;17:341-345.
23. 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;66:377-384.
24. Duymus TM, Mutlu S, Dernek B, Komur B, Aydogmus S, Kesiktas FN. Choice of intra-articular injection in treatment of knee osteoarthritis: platelet-rich plasma, hyaluronic acid or ozone options. *Knee Surg Sports Traumatol Arthrosc.* 2017;25:485-492.
25. Freund PR, Alshafai L, Margolin EA. Multifocal stroke from ozone gas emboli. *J Neuroophthalmol.* 2019;39:518-519.
26. Chirchiglia D, Chirchiglia P, Strocio C, Volpentesta G, Lavano A. Suspected pulmonary embolism after oxygen-ozone therapy for low back pain. *J Neurol Surg A Cent Eur Neurosurg.* 2019;80:503-506.
27. Seyam O, Smith NL, Reid I, Gandhi J, Jiang W, Khan SA. Clinical utility of ozone therapy for musculoskeletal disorders. *Med Gas Res.* 2018;8:103-110.
28. Bocci V, Borrelli E, Zanardi I, Travagli V. The usefulness of ozone treatment in spinal pain. *Drug Des Devel Ther.* 2015;9:2677-2685.

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