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## ORIGINAL ARTICLE

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# The Effect of Paravertebral Ozone Injection in the Treatment of Low Back Pain

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### ■ Abstract

**Aim:** Paravertebral ozone injection is a new treatment method described in the literature for low back pain. The aim of this study was to compare the pre- and post-treatment pain scores of patients undergoing paravertebral ozone/oxygen (O<sub>3</sub>/O<sub>2</sub>) injections for low back pain.

**Methods:** From September 2018 to December 2018, 122 patients who underwent paravertebral ozone injections due to low back pain were examined retrospectively; 62 patients who met the study criteria were included. The patients were injected with 15 µg/mL (50 mL) O<sub>3</sub>/O<sub>2</sub> gas in the paravertebral space. The subjects were treated every 7 days for 6 total session. The VAS and Oswestry Disability Index (ODI) scores were assessed before treatment and after treatment (first and third months). The patients' body mass indexes (BMIs) were measured before the injections.

**Results:** There were 12 male patients and 50 female patients. The mean age was 51.9 (range 25 to 71) years. The mean duration of pain was 9.1 (3 to 24) months. Significant improvements were observed in the statistical comparison of VAS and ODI scores between the pre-injection and first month controls ( $P < 0.000$ ). There was no significant difference in the statistical comparison of VAS and ODI scores between the first and third months ( $P < 0.05$ ). There was no

statistically significant difference between BMI and pain scores ( $P > 0.213$ ).

**Conclusion:** Paravertebral O<sub>3</sub>/O<sub>2</sub> gas is a reliable and effective treatment for the treatment of lumbar disc herniation, radicular pain, and mechanical back pain due to low back pain. ■

**Key Words:** low back pain, ozone injection, ozone therapy, lumbar disc hernia, back pain, lower back pain

### INTRODUCTION

Low back pain is a common and important health problem worldwide.<sup>1</sup> The prevalence of the annual incidence varies between 25% and 65%. Mild to moderate low back pain is seen in 80% of the world's adults at some point in their lives.<sup>2</sup> Disc degeneration and accompanying vertebral diseases constitute many causes of low back pain in the elderly population. Frequent imaging can show the cause of low back pain. Patients who do not respond to conservative therapies, present neurological findings, or have complaints related to compression are candidates for surgery. The rate of recurrence after surgery in these patients is as high as 40%.<sup>3</sup> Therefore, nonsurgical treatments are needed before surgery.

In recent years, many treatment strategies have been developed in the literature to reduce pain, especially due to nerve root compression. In particular, the ineffectiveness of medical treatments (with paracetamol, nonsteroidal anti-inflammatory drugs, and myorelaxant drugs) in the management of low back pain has led to

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the search for different treatments.<sup>4</sup> It is often preferable to treat low back pain with minimally invasive therapies because they are both reliable and easy to apply.

The application of paravertebral injection with ozone/oxygen (O<sub>3</sub>/O<sub>2</sub>) gas is a minimally invasive technique. It is safe and practical.<sup>5</sup> The literature states that injecting ozone gas into paravertebral muscles and discs can neutralize proteoglycan and the negative burden of sulphate side chains. This treatment reduces water retention and can decrease hernia volume.<sup>2,6,7</sup> The aim of this study was to demonstrate the efficacy and reliability of the ozone gas applied with paravertebral injection in the treatment of low back pain.

## METHODS

The study protocol was approved by Health Science University Umraniye Training and Research hospital (Registry Number:00091932884). We obtained informed consent from all patients. All procedures involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

### Study Design

Patients who underwent paravertebral ozone injections due to low back pain were examined retrospectively in our clinic between September 2018 and December 2018. The criteria included patients between 18 and 70 years of age. Patients with lumbar disc herniation were enrolled regardless of whether there was a degenerative disc as seen on the MRI in the prior year. Other candidates included patients with spondylolisthesis, spinal stenosis (not due to surgery), mechanical low back pain with unknown etiology (nonradicular pain), or radial root compression, all of whom had these pains for over 4 weeks and had a VAS score > 5.

The followed subjects were excluded: 3 patients who had acute or chronic infections, 16 patients who had signs of diabetic neuropathy, 21 patients who had spinal deformity or disc hernia, 3 patients who had lumbosacral anomalies, 2 patients who had scoliosis Cobb angle > 20 degrees, 4 patients who had a body mass index (BMI) > 32, and 11 patients who did not complete the 6 sessions or subsequently did not come to follow-up checks. These patients were all removed from the study. Thus, 122 patients with low back pain who had

paravertebral ozone injections were analyzed, and 62 patients who met our criteria were included in the study.

### Treatment Application Methods

All patients were treated with injections using the same medical ozone generator (TURKOZONE Blue S 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<sub>3</sub>/O<sub>2</sub> gas administered through ozone-resistant injectors. In patients with a disc hernia, the ozone gas was applied to the region, with disc herniation starting 2 cm lateral to the spine. The injections were made 3 cm above the lesion and 3 cm below the lesions in patients with root pressure. The subjects with mechanical back pain received a paravertebral injection of 50 mL O<sub>3</sub>/O<sub>2</sub> gas to the left and right sides up to T10–L5.

The disc levels were determined before the ozone injection by assessing lumbar anteroposterior and lateral marked radiographs. Paravertebral ozone injections were applied to patients for a total of 6 sessions every 7 days. The consent form was completed during the first visit.

### Outcome Measures

The outcomes were measured before the paravertebral ozone injection, 1 month after the last session, and again 3 months after the last session. The metrics included the patients' VAS and Oswestry Disability Index (ODI) scores as determined by an orthopedic specialist. The following question was rated on the VAS: "Referring to the worst pain you have experienced in your life, how would you rate (out of 10) the relative level of your back pain or spreading pain compared to this pain?"

The patients' scores were made by an orthopedist specialist without knowledge of the patients' MRI and x-ray data. Another orthopedic specialist who did not know the patients' scores applied the ozone injections in a blinded manner. A detailed physical examination was performed when patients were called in for their final evaluations. Data were collected related to the patient's BMI, physiological profile, and quality of life.

### Statistical Methods

The findings of the study were evaluated using the IBM SPSS Statistics 22 (IBM SPSS, Armonk, NY, U.S.A.)

program for statistical analysis of the pre-and post-injection values of the patients using the Mann–Whitney *U* test;  $P < 0.05$  was considered meaningful. The Pearson test was used for correlation comparisons of parameters showing a normal distribution when evaluating the study data.

## RESULTS

The O<sub>3</sub>/O<sub>2</sub> paravertebral injections were performed in 62 patients recruited for low back pain. Twelve of the 62 patients were male, and 50 were female. The mean age was 51.9 (range 25 to 71) years. Three months after the O<sub>3</sub>/O<sub>2</sub> injections over 6 sessions, the patients completed their final controls, and their scores were recorded. The MRI showed that 34 subjects had bulging disc herniations, 12 with hernia disc pain, 10 with radicular pain, and 6 with mechanical low back pain (nonradicular pain). When the patients were questioned on quality of life, 28 of them were not working, 32 patients smoked, and 21 complained of severe work/life problems. The mean duration of pain in patients was 9.1 (range 3 to 24) months.

Before the ozone injection, the mean ( $\pm$  standard deviation [SD]) VAS score was  $8.02 \pm 1.18$  (range 5 to 10), and the mean ( $\pm$ SD) ODI score was  $65.52 \pm 6.13$  (range 48 to 78). One month following the injections, the VAS score was  $3.10 \pm 1.49$  (0 to 7), and the ODI score was  $32.39 \pm 12.09$  (4 to 58). Three months following the injections, the VAS score was  $3.22 \pm 1.50$  (0 to 7), and the ODI score was  $34.35 \pm 12.67$  (8 to 62). There was a significant improvement in the statistical comparison of VAS and ODI scores between the pre-injection and first month controls according to the Mann–Whitney *U* test ( $P < 0.000$ ). There was no significant difference in the statistical comparison of VAS and ODI scores between the first and third months ( $P < 0.05$ ) (Table 1). Pearson correlation values were evaluated among patients in terms of BMI and 1-month post-treatment VAS and ODI scores. There was no

statistically significant difference between BMI and pain scores ( $P > 0.213$ ).

Mild ecchymosis was observed at the injection site in 14 of the 62 patients who underwent paravertebral injection. These patients were evaluated for this minor complication. No other complications were encountered.

## DISCUSSION

Ozone medical gas is a treatment method that provides treatment with wide application areas and low incidence of side-effects for many diseases. It can increase the efficiency of treatment.<sup>8,9</sup> Ozone is a 3-molecule atom and is less stable than oxygen. Thus, its biological response is higher than that of oxygen.

Paravertebral ozone injection for low back pain is an issue that is currently discussed in the literature. The O<sub>3</sub>/O<sub>2</sub> gas is applied directly to the disc or to the paravertebral muscles. The ozone gas enters the nucleus pulposus in the disc through the proteoglycan structure and is then oxidized. There is a decrease in intradiscal pressure and shrinking of the disc after reabsorbing the water inside the disc. Thus, the pressure of the disc herniation on the root is eliminated.<sup>10,11</sup>

The ozone injected into the paravertebral muscle is rapidly dissolved in the interstitial water and quickly reacts with antioxidants. It can affect an area up to 3 cm from the injection site depending on the dose. In our study, the levels were determined by assessing the marked x-ray, and paravertebral ozone injection was applied from the closest location to the disc pathology. Paravertebral ozone injection has a better effect on the combination of biochemical effects in the muscle (improved oxygenation, correction of local acidosis, and loss of venous and lymphatic stasis).<sup>10,12</sup> It also shows a paradoxical mechanism of useful action<sup>12</sup> that increases the immunosuppressive cytokines (interleukin-10 and transforming growth factor- $\beta$ ) in these injected regions.

**Table 1. Pain Scores**

	Pre-injection Mean $\pm$ SD (range)	1 <sup>st</sup> Month Mean $\pm$ SD (range)	3 <sup>rd</sup> Month Mean $\pm$ SD (range)	<i>P</i> <sup>†</sup>	<i>P</i> <sup>§</sup>
VAS	8.02 $\pm$ 1.18 (5 to 10)	3.10 $\pm$ 1.4 (0 to 7)	3.22 $\pm$ 1.50 (0 to 7)	0.000	0.647
ODI	65.52 $\pm$ 6.13 (48 to 78)	32.39 $\pm$ 12.09 (4 to 58)	34.35 $\pm$ 12.67 (8 to 62)	0.000	0.730

<sup>†</sup>Mann–Whitney *U* test statistical analysis between pre-injection and first month.

<sup>§</sup>Mann–Whitney *U* test statistical analysis between the first and third months.

ODI, Oswestry Disability Index; SD, standard deviation.

Ozone gas can be used alone or it can be used with a corticosteroid.<sup>13</sup> Andreulla et al.<sup>5</sup> reported intradiscal and periganglionic ozone applied to a group of patients with lumbar disc herniation. One group had a corticosteroid applied with ozone injection. A significant improvement was seen in both groups. However, the group receiving corticosteroids showed significantly improved clinical scores vs. the other groups. Our study only used ozone gas isolation, and there was significant improvement in clinical scores in accordance with the literature.

Biazzo et al.<sup>14</sup> studied 109 patients who had low back pain and underwent 5 sessions of paravertebral ozone injections. On a follow-up analysis of their VAS scores, 79% of the patients showed a decrease to 2.3 in terms of VAS this was a significant change. It has been argued that ozone injection can be easily applied, is safe and reliable, and must be applied to patients before surgery. Our results were similar to those of Biazzo et al. In our study, the VAS scores fell below 3 in 67% of patients.

Costa et al.<sup>15</sup> published a meta-analysis of non-ozone injection systems in which control groups were given ozone injections. They found 7 studies that included non-ozone injections; results of paravertebral ozone injection therapy were meaningful, with aggregated scores showing a reduction. No complications were found in 2 studies, and minor side effects were mentioned in 5 studies. We found a significant decrease in pain scores consistent with the literature; 14 patients had ecchymosis as a minor complication.

Complications after paravertebral ozone injection are often described in the literature as minor. We had 14 patients with ecchymosis at the injection zone. In the literature, there were complications such as gas embolism in the cervical artery in patients who received injections due to cervical pain other than in the lumbar region.<sup>16</sup> A 13-mm injector tip is recommended to avoid the cervical artery in these patients.<sup>17</sup> Our study used a 13-mm injector tip. A case of cardiopulmonary arrest has been reported after O<sub>3</sub>/O<sub>2</sub> injection in the epidural cavity.<sup>18</sup> No major complication has been reported with lumbar paravertebral ozone injection.

For intradiscal ozone injection, the complication rate is low, and the method is less painful. The pain score reduction is similar in both paravertebral injection groups and intradiscal injection groups. There have been serious adhesions and bone hardening in the disc region, especially after intradiscal ozone injection.<sup>19</sup> This is why we used paravertebral ozone injection. The ozone is rapidly dissolved in the injected region, and the

bolus spreads rapidly into the tissues; it has the same effect on the area near the disc.

We used 15 µg/mL of paravertebral ozone. The literature has not reached consensus on a standard dose for paravertebral ozone injection. Paoloni et al.<sup>20</sup> treated 60 patients with 20 µg/mL of O<sub>3</sub>/O<sub>2</sub> in 20 mL in the paravertebral space over 5 sessions. This included injections of 10 mL to the right side of the disc and 10 mL to the left of the disc. Biazza et al. applied 27 µg/mL ozone in 20 mL via paravertebral injection over 12 sessions.<sup>5</sup> We used 50 mL of 15 µg/mL via paravertebral injection. The application amount was slightly higher than in the literature, but this ozone dose is low compared to that of the patients who underwent paravertebral ozone treatment in the literature. However, we obtained similar results, as described in the literature. The standard treatment dosage and amount of paravertebral ozone injection have not yet been specified in the literature.

The 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 disc herniation, radicular root pain, and mechanical low back pain. There are insufficient studies on this treatment method. More prospective randomized and controlled trials are needed to increase the reliability of paravertebral injection therapy.

## CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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