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Original Research

Intradiscal ozone therapy for lumbar disc herniation

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Abstract: The rationale behind intradiscal O_2-O_3 therapy is the pain elicited by the mechanical compression of the nerve root, which is associated with periganglionic and periradicular inflammation. This study aimed to determine the effect of intradiscal ozone injection on pain score and satisfaction of patients with low back pain (LBP) secondary to disc herniation. Patients with LBP diagnosed with disc herniation were enrolled in this clinical trial. After prepping and draping the area, intradiscal injection of ozone/oxygen mixture (10 ml, 25µg/ml) was performed under fluoroscopy guide (c-arm). Pain score and patient satisfaction were assessed prior to the injection (baseline) and 1, 3, 6, 12 and 24 months after the injection. Sixty three patients (24 males, 39 females) with mean age of 53.3 ±2.0 y enrolled in the study. The mean±standard deviation (SD) of pain score before intervention was 6.968 ±0.11. Pain score was reduced to 4.25±0.19 at 1 month, 4.33±0.20 at 3 months, 4.87 ±0.21 at 6 months and 5.22 ±0.20 at 24 months. According to the modified MacNab scale success of pain relief was as follows: excellent: 4 (6.3%), good: 17 (26.98 %), sufficient: 13 (20.63 %), poor: 13 (20.63 %), no result: 11 (17.46%), negative: 4 (6.3 %). Intradiscal ozone therapy was determined to provide improved outcomes in patients with single level of bulging and protrusion.

Key words: Intradiscal ozone; Lumbar disc herniation; Pain score; Patient satisfaction.

Introduction

Low-back pain is the most common spinal disease that leads to loss of work-power in developed countries. About 80% of adults complain of low-back pain at least once in their lifetime, 55% of which is related with radicular syndrome (1). While there is no identifiable specific reason for pain among 60-80% of patients, it can be linked to muscle or ligament strains in many patients and to degenerative joints and disc lesions in 5-15% of patients (2). Herniation of the disc or nucleus pulposus is one of the most important disc lesion. Short-term success rate of the surgical treatment of the herniated disc is about 85-90%, with a 2-6% of recurrence rate. In long-term (>6 months), this diminishes up to 70-80% along with symptoms of failed back surgery syndrome (3). Therefore, researchers tend towards less invasive and safer methods. These minimal invasive techniques may include intradiscal steroid, chemonucleosis, intradiscal decompression, laser, discectomy, and annuloplasty. Most important characteristic of these methods is to directly intervene into the target disc structure without affecting the spinal canal (4). Beside biochemical, immunological, and inflammatory alterations in the area surrounding the disc, herniation leads to mechanical compression. Intradiscal injections are minimal invasive applications which lead to regression of the disc and subsidence of nerve root inflammation (4). Intradiscal ozone injection was first used in 1980 for the management of disc herniation (5). Half-life of the ozone, recently applied across Europe including Italy, Germany, and Spain is 45 minutes, which is also unstable and colorless, and has disturbing odor. It is a potent oxidant with additional antiseptic, disinfecting, and antiviral properties. It is obtained by transformation of little amount of medical oxygen into the ozone by applicable generators (6). The rationale behind O_2-O_3 therapy is the pain elicited by the mechanical compression of the nerve root, which is associated with periganglionic and periradicular inflammation. Despite being not clearly elucidated, mode of action of O_2-O_3 gas mixture involves several mechanisms. These result in anti-inflammatory effect induced by the oxidation of chemical mediators of the pain, resolution of the venous stasis which decreases nerve root edema and ischemia and increases local oxygen support, and shrinkage and dehydration of the disc after improved microcirculation and direct effect imposed on the water-containing mucopolysaccharide structure in nucleus pulposus (7). The latter was also histologically demonstrated by the dehydration of the fibrillary matrix of nucleus pulposus of discs in which underwent initial ozone treatment followed by microdiscectomy (8). By directly acting on disc structure and inhibiting inflammatory reaction, ozone provides rapid and long-lasting relief of pain through a minimal invasive technique without any adverse effects.

In this study we aimed to determine the effect of intradiscal ozone injection on pain score and satisfaction of patients with low back pain (LBP) caused by herniated disc.

Materials and Methods

Participants

The study was reviewed and approved by Firat University Ethics Board Committee. All patients gave their written informed consents prior to enrollment. After ethical approval, 63 patients who were referred to the pain clinic due to LBP with or without radicular pain were enrolled in the study.

Inclusion criteria

Lumbar disc pathologies documented on MR images, pain for at least 8 weeks that does not respond to conservative treatment, and initial mean VAS ≥4.

Exclusion criteria

Allergies to medications administered during procedures, pregnancy, presence of bleeding disorder, local infection, uncontrolled or degenerative spine disease and major neurologic deficits.

Primary outcome of this study was to assess the visual analogic scale (VAS) before and after intradiscal injection of ozone. Secondary outcome was to assess the Modified MacNab after injection.

Clinical Measures

Demographic data, including gender, age, weight and size, initial pain score (using VAS) and MR images concurring with dermatome pattern of pain were obtained. Patients were assigned to five groups according to MR images, bulging (n = 23), protrusion (n = 23), bulging + protrusion (n = 3), extruded disc herniation + protrusion (n = 4) and spinal stenosis + protrusion (n = 10). Pain score was measured prior to injection (baseline) and then at 1st, 3th, 6th, 12th and 24th months after injection. Patient satisfaction was evaluated with the modified MacNab classification (Table 1).

Modified Mac Nab Classification

Procedure

All procedures were performed in operation room under fluoroscopy guidance with the patients in prone position. Patients were monitored for heart rate and oxygen saturation by pulse oximetry. An i.v. line access was inserted, and sedation was performed with administration of 0.02 mg/kg midazolam and 1 µg/kg fentanyl. After prep and drape, C-arm fluoroscopy was placed in the anteroposterior position to display to disc space to be treated. Then an oblique projection was taken of the facet joint in the direction of the posterior third of the intervertebral space. Once 22 G, 15-20 cm chiba needle was inserted in the muscle the lateral view was resumed and the needle inserted into the nucleus pulposus (Fig.1). An intradiscal injection was made inserting10 ml of O_2-O_3 mixture at a concentration of 25µg/ml. Discography was not performed because a contrast material injected during discography fills the potential intradiscal space that may prevent injection of the optimal amount of the drug. At the end of the treatment patients were antagonized with flumazenil 0.2 mg and taken to the recovery room and followed for about 4 hours then discharged without any sensory or motor deficits. All patients were reassessed after the procedure at the end of convalescence, 1 and 3 months later. Other reassessments were made by phone, and patients were asked to report any possible late complications.

Table 1. Modified Mac Nab Classification.

Successful of Treatment		
Excellent Disappearance of symptoms Complete recovery of working and sports activities	**Good** Occasional episodes of low back pain or sciatica	**Sufficient** Improvement in symptoms. Limitation of normal physical activity
Failure of Treatment		
Poor Insufficient improvement of symptoms Periodic use of analgesic medications	**No Result** No improvement of symptoms Need for surgical operation	**Negative** Worsening of symptoms Need for surgical operation

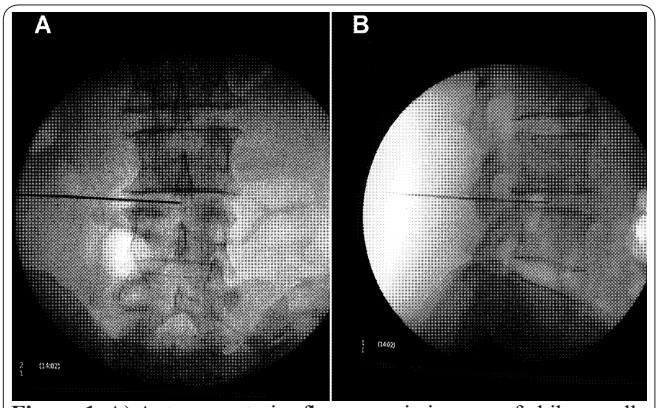

Figure 1. A) Antero-posterior fluoroscopic images of chiba needle inserted in L3-L4 interdiscal space. B) Lateral fluoroscopic images of chiba needle inserted in L3-L4 interdiscal space.

Statistical Analysis

Data are expressed as mean±SD except where otherwise stated. Statistical analysis was performed using SPSS 22.0 for Windows (SPSS Institute, Chicago, IL, USA). Number of patients were determined by power analysis on a pilot study with an alpha error of 0.05 and a beta error of 0.20 revealed that a minimum of 17 patients was required in each group for the study. Variables were compared among groups using ANOVA followed by Bonferroni correction for pair-wise comparisons. Macnab classification was compared using Yates' corrected chi-square test. $P<0.05$ was considered statistically significant.

Results

Sixty three patients (24 males, 39 females) with the mean age of 53.3 ± 2.0 y enrolled to the study. Intradiscal ozone injections were performed at a single level in 60 patients which were L4-5 (n=41), L3-4 (n=10), and L5-S1 (n=9). Two patients were treated at two levels which were L4-5 and L5-S1 (n=1), L3-4 and L4-5 (n=1) and one patient was treated at 3 levels which were L3-4, L4-5 and L5-S1. The mean ± standard deviation (SD) of pain score before intervention was 6.968 ± 0.11. After

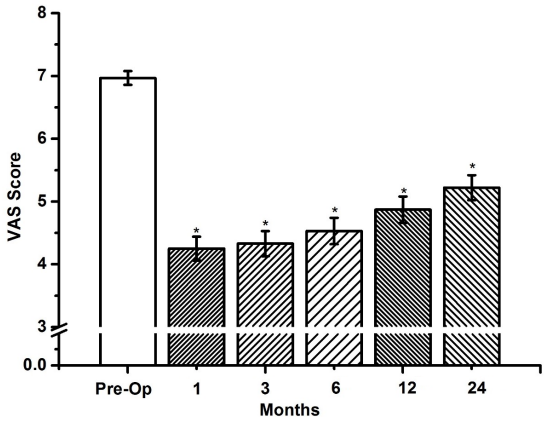

Figure 2. Time course for analgesic effect of intradiscal ozone administration on VAS score in patients with lumbar disc herniation. VAS scores are recorded just before (pre-op) and at 1, 3, 6, 12 and 24 months after the intradiscal ozone administration. Each point represents the mean and SD of sixty three patients. *; P<0.05 as compared with the respective values of the pre-op patients. Post-op (1, 3, 6, 12 and 24 months).

one month, pain score was reduced to 4.25 ± 0.19, 4.33 ± 0.20 at 3 month, 4.87 ± 0.21 at 6 month and 5.22 ± 0.20 at 24 month (Fig.2, p<0.05). There was no statistically significant difference in terms of pain scores when the groups were evaluated among themselves

Results according to the modified MacNab scale were as follows (Fig.3):

- Excellent: 4 (6.3 %),
- Good: 17 (26.98 %),
- Sufficient: 13 (20.63 %),
- Poor: 13 (20.63 %),
- No result: 11 (17.46 %),
- Negative: 4 (6.3 %)

Four patients were referred to neurosurgery who evaluated result of treatment as a negative (1 patient with bulging, 1 patient with extruded disc hernia + protrusion, 2 patients with spinal stenosis + protrusion).

Discussion

Pathology of disc herniation originates from mechanical (nerve root compression) and associated-biochemical (immunological and inflammatory) factors around the disc area (9). To date variety of minimally invasive percutaneous techniques have been introduced for the treatment of lumbar disc herniations. The main common targets of implementing these techniques are to reduce intradiscal pressure and create the space necessary for retropulsion or digestion of the disc. They all require a short hospital stay and eliminate the risk of postoperative infections and hypertrophic scarring, which is responsible for the recurrence of symptoms. Ozone injection is a minimally invasive and inexpensive procedure minimizing inflammation in intradiscal area and decreasing intraforaminal adhesion bands (10, 11). As also seen in our study, intradiscal ozone injection leads to a reduction in pain score and provides consequent patient satisfaction lasting up to 24 months.

Intradiscal ozone injection was first introduced by Muto *et al*. with favorable outcomes (12). After 18 months of follow-up in 2200 patients to whom intradiscal and foraminal ozone injection were applied, they

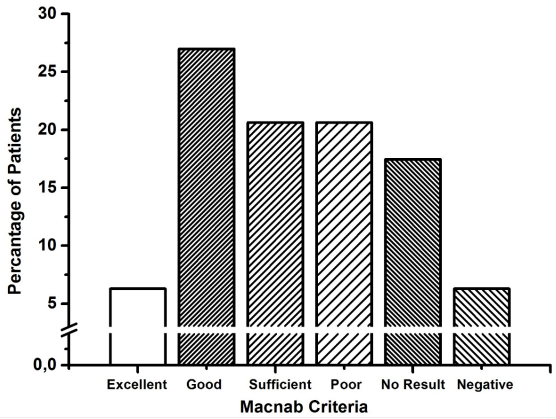

Figure 3. Effects of Intradiscal Ozone Administration on Macnab scores in Patients with Lumbar Disc Herniation.

reported that this method was most effective in patients with single level of disc herniation with 64% excellent and 14% good results. They also concluded that the effect tended to reduce in the presence of disc degeneration, calcified disc, and stenosis (13). In another study, 77 patients who were administered intraforaminal and intradiscal steroid and local anesthetics were compared with 82 patients who were applied 5-7 mL intraforaminal and 5-7 mL intradiscal ozone in a 28 µg/mL concentration in an add-on setting to steroid and local anesthetic injections. While short-term outcomes did not significantly differ, 6-month follow-up data showed success rates of the steroid treatment and intradiscal ozone injection by 47% and 74%, respectively, where authors reported this difference to be driven by the longer duration of action of ozone compared to the steroid treatment (14). In our study, 63 patients which we applied intradiscal ozone were followed for 24 months with a success rate of 53.96 (6.3% excellent, 26.98% good, and 13% satisfactory outcomes). This treatment was determined to provide better outcomes in bulging and protrusion groups, with a trend to decline in stenotic cases.

In a 12-month study, where respectively 3-4 ml and 10 ml of O_2-O_3 gas mixture of 30-40 µg/ml concentration was applied into the disc and the foramen of 2900 patients, success rates was detected to be 75-80% in soft disc herniation, followed by 70% in multiple disc herniation, and 55% in failed back surgery (15). In our study, 10 ml of mixture of O_2-O_3 at 25 µg/ml concentration was injected into the disc. A higher volume was preferred to avoid potential triggering of pain by high concentrations. Hashemi *et al.* performed intradiscal ozone injection to 30 patients with a follow-up of 6 months and detected reduced pain score to 3.2±0.6 from 8.1±0.8 and about 50% regression in Oswestry disability index (ODI) (16). We followed our patients for 24 months and found reduced VAS scores (1st month, 4.25±0.19; 3th month, 4.33±0.20; 6th month, 4.53±0.21; 12th month, 4.87±0.21; and 24th month, 5.22±0.20) compared to baseline score (6.968±0.11). Groups did not significantly differ in terms of MRI pathology.

Lehnert assessed disc volume of 283 radiculopathy patients treated with intradiscal injection. Disc volume was measured by MRI before and 6 months after the O_2-O_3 injection as 3 ml into the disc and 7 ml into the periganglionic area, where a mean of 8% reduction was

detected in disc volume (17). One hundred and eight patients who were administered intradiscal ozone injection were evaluated after 5 and 10 years by MRI and 79 patients were reported to have a mean of 56% reduction in their disc volume (18). In our study, disc volume was not measured. Patients were assessed by VAS scoring and modified Mac Nab classification.

There were several limitations in this study. First, this study had no control group. Thus there could be criticism that it was difficult to differentiate natural pain remission from pain reduction by treatment effects. But we did not establish control group because main purpose of this study was to assess the clinical efficacy of intradiscal ozone injection. Second, this study was retrospective design so that only who completed the 24 months follow up were included in this study.

Cost-effectiveness and lack of complications make O_2-O_3 discolysis a reliable and competitive treatment option compared with other percutaneous techniques. In our study intradiscal ozone therapy was determined to provide improved outcomes in patients with single level of bulging and protrusion, which tended to diminish in the presence of stenosis.

Conflict of interest

The authors of this article have no conflicts of interest to disclose.

Author's contribution

Sibel Ozcan: Study design, manuscript preparation.
Arzu Muz: Collected of Data
Aysun YILDIZ ALTUN: Statistically analysis and help to Collected of Data
Selami Ates ONAL: Study design, help to manuscript preparation.

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