



Ozone Nucleolysis in the Management of Prolapsed Lumbar Intervertebral Disc in Reducing Pain and Disability: A Randomized Controlled Study

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| Nilachandra L | Assistant Professor, Department of PMR, RIMS, Imphal, Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Darendrajit L | Postgraduate Trainee, Department of PMR, RIMS, Imphal Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Joy Singh Ak | Professor, Department of PMR, RIMS, Imphal, Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Kanti RK | Postgraduate Trainee, Department of PMR, RIMS, Imphal Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Shibu B | Postgraduate Trainee, Department of PMR, RIMS, Imphal Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Tripti S | Postgraduate Trainee, Department of PMR, RIMS, Imphal Regional Institute of Medical Sciences, Imphal, Manipur, India |
| Aten J | Postgraduate Trainee, Department of PMR, RIMS, Imphal Regional Institute of Medical Sciences, Imphal, Manipur, India |

ABSTRACT

Low back pain affects people of all ages and is a very frequent reason for medical consultations. Forty percent of the people say that they have had low back pain within the past 6 months. Lifetime prevalence can be as high as 84%. Ozone therapy has emerged as an alternative non-surgical intervention for intervertebral disc prolapse. Despite its widespread use to treat a variety of conditions, ozone as a therapeutic modality remains unknown to most physicians. A reduction in herniated disc volume is one of the therapeutic goal for intradiscal administration of medical ozone, as a reduction in disc size reduces nerve root compression and venous stasis and hence improves the microcirculation and supply of oxygen. A randomized controlled study was conducted to assess the effectiveness of intradiscal ozone over and above transforaminal epidural steroid injection in reducing pain and disability in prolapsed lumbar intervertebral disc. Eighty patients enrolled in the study were allocated to 2 groups (Group A and B). Group A (n=40) received intradiscal ozone plus transforaminal epidural steroid injection while Group B (n=40) received transforaminal epidural steroid injection. Visual Analogue Scale (VAS) and Oswestry Disability Index (ODI) were used as outcome measures. Group A showed significant improvement in pain from baseline to 6 months as shown by reduction in VAS score from 7.13 ± 1.04 to 0.86 ± 0.69 and 7.25 ± 1.10 to 2.24 ± 0.93 in Group B ($p=0.000$). Reduction in ODI 70.90 ± 7.55 (baseline) to 18.28 ± 8.77 (6 months) in Group A was significantly ($p=0.000$) more than that of Group B, 73.05 ± 7.51 (baseline) to 29.00 ± 6.78 (6 months). The study concluded that the intradiscal ozone injection over and above transforaminal epidural steroid injection is effective in reducing pain and disability in prolapsed lumbar intervertebral disc.

KEYWORDS

Ozone, lumbar, prolapsed disc, VAS, ODI

Background

Low back pain affects people of all ages and is a very frequent reason for medical consultations. Forty percent of the people say that they have had low back pain within the past 6 months.¹ Studies have shown a lifetime prevalence as high as 84%.² The 2010 Global Burden of Disease Study highlighted that low back pain is among the top 10 diseases and injuries that account for the highest number of Disability-Adjusted Life Years (DALYs) worldwide.³

The disc consists of a central avascular nucleus pulposus— a hydrophilic gel made of protein-polysaccharide, collagen fibres, sparse chondroid cells and water (88%), surrounded by concentric layers of fibrous tissue known as the annulus fibrosus. Prolapsed intervertebral disc (PIVD) represents the tensile failure of the annulus fibrosus to contain the nucleus pulposus. It is a common manifestation of degenerative disease. The most common direction for a disc prolapse to occur is in the

posterolateral direction, where the annulus fibrosus is thin and not supported by the anterior or posterior longitudinal ligament.⁴ Prolapsed disc causes impairment of function by nerve root compression compelling the patient to seek medical advice for low backache.

Apart from conservative therapy, all other forms of treatment aim at decompressing the nerve root, which is considered as the cause of the patient's discomfort. These can be done by removing the disc either by surgery or by decompressing the disc by different interventions. Newer percutaneous techniques like chemonucleolysis with chymopapain, nucleolysis, LASER discectomy and recently nucleoplasty have minimized the invasive surgical techniques. Reducing intervertebral disc size by mechanical aspiration of disc fragments or partially dissolving the herniation by drying reduces the conic pressure on the torn annulus and creates the space necessary for retropulsion whenever the circular fibres of the annulus re-

gain a minimum capacity to contain the disc under tension.⁵

The action of ozone is due to the active oxygen atom or the free radical liberated from breaking down of ozone molecule. As ozone is injected into the disc the active oxygen atom attaches with the proteoglycan bridges in the jellylike material of nucleus pulposus. They are broken down and they no longer capable of holding water. As a result disc shrinks and mummified and there is decompression of nerve roots. It is almost equivalent to surgical discectomy and so the procedure is called ozone discectomy. It has an anti-inflammatory action due to inhibition of formation of inflammation producing substances, tissue oxygenation is increased due to increased 2, 3 diphosphoglycerate level in the red blood cells. All these leads to decompression of nerve roots, decreased inflammation of nerve roots, and increased oxygenation to the diseased tissue for repair work.⁶

Ozone therapy has emerged as an alternative to surgery or as an additional non-surgical intervention for PIVD. This procedure has been proven to be very safe and associated with high success rate for improving the physical function as well as pain sensation. The success rates reported in different studies vary from 65 to 80% of excellent or good results.⁷

Despite its widespread use to treat a variety of conditions, ozone therapy for PIVD remains unknown to most physicians. Ozone (O_3) is an allotropic form of oxygen, primarily known for its ecological properties, industrial applications and therapeutic effects. However, its potential toxicity as an oxidising agent versus its reported clinical efficacy remains to be answered.

Methods

A randomized controlled study on 80 patients presenting with low back pain radiating to the lower limb admitted in the Physical Medicine and Rehabilitation ward, Regional Institute of Medical Sciences (RIMS), Imphal, India, was conducted from February 2016 to October 2016

Approval from the Institutional Ethics Committee, RIMS, Imphal was taken before the start of the study and written informed consent was obtained from all the subjects.

Patients with back pain due to PIVD L3-L4, L4-L5 and L5-S1, confirmed by MRI (Grade II and III), age between 20 and 55 years, pain severity with minimum score of 5 based on 10 point scale VAS (Visual Analogue Score), ODI (Oswestry Disability Index) score more than 40, willingness to comply with treatment and follow-up assessments were included in the study. However, patients with cauda equina syndrome, mental or physical condition that would invalidate evaluation results, prior lumbar surgery at any level, multiple level disc prolapse, pregnancy, systemic or local infection at site of injection, known allergy to corticosteroids, contrast dye or anesthetics, history of any malignancy (including hematologic and non-hematologic malignancies), bleeding disorders, uncontrolled diabetes mellitus, uncontrolled hypertension, prior history of epidural steroid injection in the past 3 months and subjects who refuse to sign informed consent were excluded from the study.

The intervertebral disc to be treated was decided by the MRI finding in congruous with the neurological deficit.

Considering 80% power, 5% error rate and 10% drop out rate a total sample size of 80 was fixed (40 in each group).

Patients enrolled in the study were assigned to two groups (Group A and B) by block randomization method. Group A consisted of 16 males and 24 females while Group B consisted of 14 males and 26 females [Table 1].

Group A received fluoroscopic guided intradiscal ozone plus transforaminal epidural injection with methylprednisolone 80 mg while Group B received transforaminal epidural injection with methylprednisolone 80 mg only.



Figure 1. Preparation of the patient and level localisation

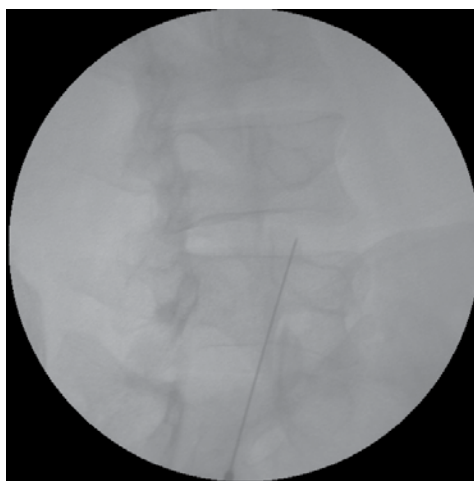


Figure 2. Needle entry point



Figure 3. Intradiscal needle placement

An intravenous line and pulse oxymeter were secured before the

procedure. Intravenous antibiotic coverage with piperacillin and tazobactam 4.5g was given just before the procedure after skin testing. The patient was placed prone with a pillow under lower abdomen. The area was prepared by antiseptics and draped in sterile manner. C-arm was first focused to obtain a pure antero-posterior view to localise the diseased disc. Then, it was cranially or caudally tilted to abolish any double end-plates and thereby getting widest possible view of disc space. C-arm was then focused in such a way that facet joint come at the center of the end plates. On the side of radiating pain, the needle entry point was marked just lateral to the superior articular process exactly at the center of the disc. Local 1% xylocaine without preservative was infiltrated to the skin and subcutaneous tissue, then a 12 cm long, 22 G Chiba spinal needle was introduced into the diseased disc in an end-on view until a firm feeling of the disc was felt. The position of needle tip was confirmed by lateral view. The needle was then advanced till it lies at the centre of the disc. The position of the needle tip was confirmed by the antero-posterior and lateral view. The ozone oxygen (O₂-O₃) mixture gas was collected from the ozone generator (Chemtronics, Made in India, Model No. MD/OG-60S) at 4 litre/ min of oxygen, concentration of 40µg/ml ozone in a 10 cc ozone resistant plastic syringe and injected into the disc over a period of 10 seconds. The needle was removed and sterile pad applied.

For transforaminal epidural injection, the needle was advanced from the same needle entry point using an ipsilateral oblique fluoroscopic view until the needle tip touched the lower edge of the Scottie dog eye, the junction of the transverse process and the superior articular process. The needle was then withdrawn for 2 to 3 mm and redirected inferiorly just under the lower edge of the transverse process for about 0.5 mm. Further advancement of the needle was done under AP and lateral views. The final needle tip position was kept at the posterior half of the neuroforamen just under the pedicle in the lateral view to minimize the potential injury to the vasculature, nerve root or dorsal root ganglion. In the AP view, the needle tip should not be medial to the medial edge of the pedicle to avoid penetrating the dura mater. If the patient complained of radicular pain or paresthesia, the needle was withdrawn and redirected superiorly. Once the needle was deemed at the proper position, approximately 1 mL of the non-ionic water soluble contrast was injected under live fluoroscopic view. With satisfactory needle position, the contrast often outlined the exiting spinal nerve and fills the neuroforamen with epidural spreading or an epidurogram. Injection methylprednisolone 80 mg was given slowly. Then, the needle was removed and covered with a sterile pad. Patient was advised bed rest in supine position for 2 hours. Follow up assessments were done at 1 week, 2 weeks, 3 months and 6 months.

Statistical analysis

Data analysis was done using Statistical Package for Social Sciences (SPSS) version 21. Descriptive analysis including mean, percentage, standard deviation were used. Mann-Whitney U-test was used for significant test between group comparison of mean scores and Friedman test was used for within group comparison over time. Value of p < 0.05 was considered to be statistically significant.

Results

Table 1. Baseline characteristics of the patients

| Characteristics | Group A n(SD/%) | Group B n(SD/%) | P value |
|-------------------|--------------------|--------------------|---------|
| Mean age (years) | 50.10 (6.61) | 52.50 (10.28) | 0.174 |
| Sex | | | |
| Male | 16 (40) | 14 (35) | 0.646 |
| Female | 24 (60) | 26 (65) | |
| Side of affection | | | |
| Right | 17 (42.5) | 18 (45) | 0.863 |
| Left | 23 (57.5) | 22 (55) | |
| Duration (months) | 9.50 (3.00) | 9.40 (3.04) | 0.862 |
| Level of prolapse | | | |
| L3-L4 | 4 (10) | 5 (12.5) | 0.522 |
| L4-L5 | 29 (72) | 24 (60) | |
| L5-S1 | 7 (17.5) | 11 (27.5) | |
| Grade | | | |
| 2 | 19 (47.5) | 17 (42.5) | 0.824 |
| 3 | 21 (52.5) | 23 (57.5) | |

Table 2. Mean improvement in VAS and ODI in the follow up

| TIME (N=No. of patients) | VAS | | | ODI | | |
|--------------------------------|----------------|----------------|---------|-----------------|-----------------|---------|
| | Group A | Group B | P value | Group A | Group B | P value |
| Baseline N(A)=40 N(B)=40 | 7.13 (1.04) | 7.25 (1.10) | 0.573 | 70.90 (7.55) | 73.05 (7.51) | 0.234 |
| 1 week N(A)=40 N(B)=40 | 3.50 (1.16) | 3.25 (1.03) | 0.317 | 38.98 (7.61) | 42.45 (9.97) | 0.213 |
| 2 week N(A)=39 N(B)=40 | 2.54 (0.89) | 2.75 (0.74) | 0.415 | 34.13 (7.94) | 36.20 (4.27) | 0.100 |
| 3 months N(A)=37 N(B)=38 | 1.54 (1.15) | 2.84 (0.64) | 0.000 | 25.14 (7.92) | 36.21 (4.67) | 0.000 |
| 6 months N(A)=36 N(B)=37 | 0.86 (0.69) | 2.24 (0.93) | 0.000 | 18.28 (8.77) | 29.00 (6.78) | 0.000 |

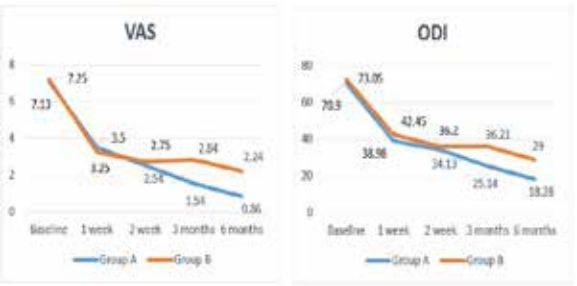


Figure 4. Line chart showing the improvement in VAS and ODI

There were no significant differences in the baseline characteristics of the two groups and hence were comparable.

Mean age of the patients in the Group A (Ozone) and Group B (Steroid) were 50.10±6.61 and 52.50±10.28 years respectively. Females constituted 62.5% (n=50) of the total patients. PIVD L4-L5 was found in 66.25% (n=53) of the patients. The reduction of pain intensity as measured by VAS score showed significant reduction at the follow up periods in both the groups. Group A showed better improvement in pain from baseline to 6 months as shown by reduction in VAS score from 7.13±1.04 to 0.86±0.69 and 7.25±1.10 to 2.24±0.93 in Group B (p=0.000) respectively.

Reduction in Oswestry Disability Index (ODI) from 70.90±7.55 to 18.28±8.77 in Group A was significantly more than that of Group B- 73.05±7.51 to 29.00±6.78 (p=0.000).

Reduction in pain and improvement in functional score are significantly more in patients receiving intradiscal ozone at 3 and 6 months follow ups (p=0.000, Mann-Whitney U test)

Four patients in Group A and two patients in Group B lost to follow up. One patient in the Group B underwent laminectomy and discectomy after 3 months follow up because of increasing pain with progressive neurological deficit.

There were no major complications following intradiscal ozone injection. One patient had mild paralumbar muscle spasm, another patient complaint of nausea and headache and were managed conservatively.

Discussion

A reduction in herniated disc volume is one of the therapeutic goal for intradiscal administration of medical ozone, as a reduction in disc size reduces nerve root compression. It also helps to reduce venous stasis caused by compression of vessels and hence improves the microcirculation and supply of oxygen. This reduces pain associated with neuronal hypoxia. Ozone has analgesic as well as anti-inflammatory effects as it

inhibits synthesis of pro-inflammatory prostaglandins, release of bradykinins and algogenic compounds. Ozone also increases the release of antagonists to proinflammatory cytokines.⁸

Use of medical ozone for treatment of low back pain was advocated by Verga in the 1980s, treated about 8000 of disc herniation patients over 15 years, in whom relapse of pain had occurred in less than 2% of cases. Muto suggested intradiscal injection of ozone for disc hernia in 1998 under CT guidance and Leonardi popularized fluoroscopy guided ozone injection into the intervertebral disc.⁹

Viebahn¹⁰ reported that the nontoxic concentration of ozone varies from one to 40 µg/ml of oxygen and concentration should not exceed 40 µg/ml. We used ozone in concentration of 40 µg/ml of oxygen to increase its tissue destruction property.

Ozone nucleolysis is mildly invasive entailing only a short hospital stay. By avoiding the spinal canal, this technique also eliminates the risk of post-operative scarring linked to surgery which is often responsible for recurrence of pain. In the present study there is significant reduction in pain and disability due to lumbar intervertebral disc in both the group of patients receiving intradiscal ozone plus transforaminal epidural and transforaminal epidural steroid in the follow up periods. The reduction in pain and improvement in functional activity of the patients were significantly more in patients receiving intradiscal ozone. Non-blinding nature of the study, small sample size and shorter follow up are the main limitations of the study.

Conclusion

Addition of ozone nucleolysis over and above the transforaminal epidural steroid injection is effective in reducing pain and functional disability in prolapsed lumbar intervertebral disc disease. However, the long term benefit of intradiscal ozone is to be determined by studies with a larger sample size and longer follow up period.

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