Ozone Nucleolysis for Management of Pain and Disability in Prolapsed Lumber Intervertebral Disc

A Prospective Cohort Study

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Summary

The prevalence rate of low back pain in a number of studies ranged from 22% to 65% in one year, and lifetime prevalence ranged from 11% to 84%. Over the years many percutaneous minimally invasive therapeutic modalities have evolved. Intradiscal oxygen-ozone therapy has also showed promising results. We undertook a prospective cohort study to evaluate the therapeutic outcome of oxygen-ozone therapy on patients with lumber disc herniation in the Indian population.

After obtaining ethical committee and investigational review board permission, 53 consecutive patients complying with selection criteria were treated with a single session of oxygen-ozone therapy. All presented with clinical signs of lumber nerve root compression supported by CT and MRI findings. All patients received 3-7 ml of ozone-oxygen mixture at an ozone concentration of 29-32 mc/ml of oxygen. Therapeutic outcome was assessed after three weeks, three months, six months, one year and two years on a visual analog scale and Oswestry low back pain disability questionnaire.

Pain intensity was significantly reduced following treatment (VAS baseline 7.58±0.86, after three weeks 2.75±1.42 and after two years 2.64±2.14). Similarly the Oswestry disability index showed a remarkable improvement in the functional status of the patients ($p<0.05$). No major complication was observed in this case series. Oxygen-ozone treatment is highly effective in relieving low back pain due to lumber disc herniation.

Introduction

The prevalence rate of low back pain in a number of studies ranged from 22% to 65% in one year and the lifetime prevalence ranged from 11% to 84%[1]. In 1934 Mixter and Barr drew worldwide attention by stating that herniated disc or nucleus pulposus is one of the important causes of low back pain[2]. Various treatment modalities for herniated disc include conservative management, minimally invasive procedures such as intradiscal steroids, chemonucleolysis, intradiscal decompression, laser discectomy, annuloplasty and surgical management. Non-invasive conservative treatment is the first choice in most cases, but when patients fail to respond, minimally invasive percutaneous measures or surgery is warranted. The success rate of lumber disc surgeries ranges from 49% to 95%. Therefore, there has been continuous search for safer alternative methods. Use of medical ozone for treatment of low back pain was advocated by orthopaedic surgeon Verga in the 1980s. In 1998 Muto and Avella suggested intradiscal injection of ozone for disc herniation under CT guidance[3]. After that successful outcome have been reported by many European centers[4-6]. Therefore the present study was carried out in an Indian popula-

tion to establish the efficacy of oxygen-ozone therapy:

- For relieving pain due to disc prolapse.
- For reducing disability of patients due to disc prolapse.

Material and Methods

This open label prospective study was carried out after obtaining permission from the ethical committee and investigational review board between March 2006 and December 2008 at the Pain Clinic, Charnock Hospital, Kolkata, India. Fifty-six consecutive adult patients with low back pain due to lumber disc prolapse were included in this study over a period from March 2006 to December 2008. There was a drop-out of three patients during follow-up.

Table 1 **Changes in VAS score over time.**

	Obs	Total	Mean	Variance	Std Dev
Baseline	53	402.0000	7.5849	.7475	.8646
3 weeks	53	146.0000	2.7547	2.0348	1.4265
3 months	53	128.0000	2.4151	3.0552	1.7479
6 months	53	103.0000	1.9434	3.3621	1.8336
1 year	53	123.0000	2.3208	3.6067	1.8991
2 years	53	140.0000	2.6415	4.5806	2.1402

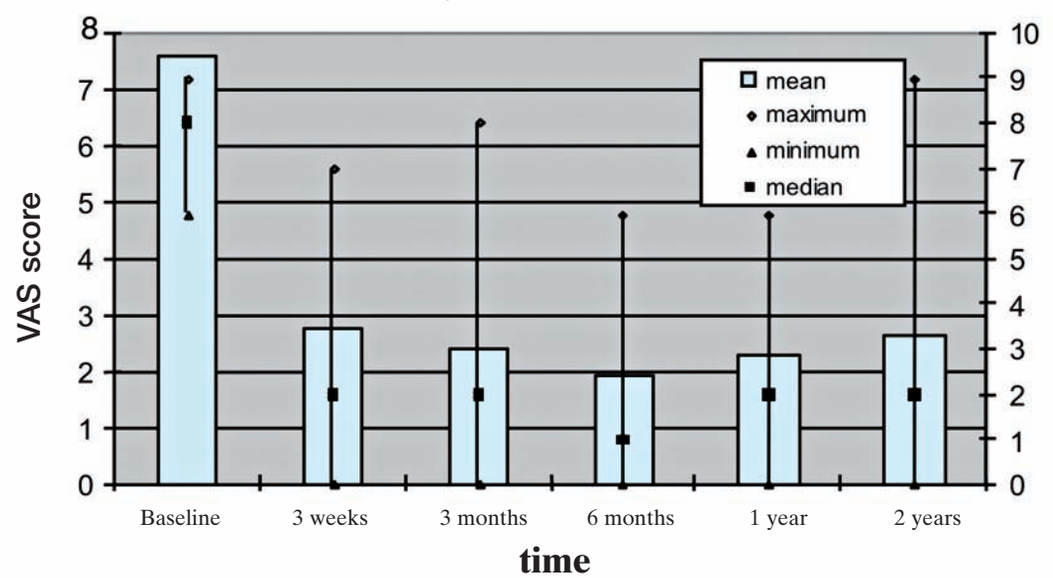
Selection criteria

All patients were referred after failure to respond to conservative therapy for four weeks and refusal or non-feasibility of surgical intervention. To our knowledge/review no such study has been undertaken among the Indian population. So we included all the patients available during the recruitment period of six months. The period of study was from March 2006 to December 2008 with a follow-up period fixed at intervals of three weeks, three months, six months, one year and two years. Patients with the following inclusion criteria were selected in this study:

- VAS score >= 6.
- Radicular pain concurring with imaging for more than four weeks and less than one year.
- MRI/CT images concurring with dermatomal pattern of pain.
- SLR $\leq 45°$.
- Femoral stretch test positive.
- Dural stretch test positive.
- Functional impairment.

P-value <0.0001

Graph depicting the pattern of pain sensation score



Exclusion criteria
- Positive red flag.
- Presence of bleeding disorder.
- Local infection.
- G6PD deficiency.
- Uncontrolled diabetes.
- Caries spine.
- Hyperparathyroidism.
- Pregnancy.
- Patient refusal.

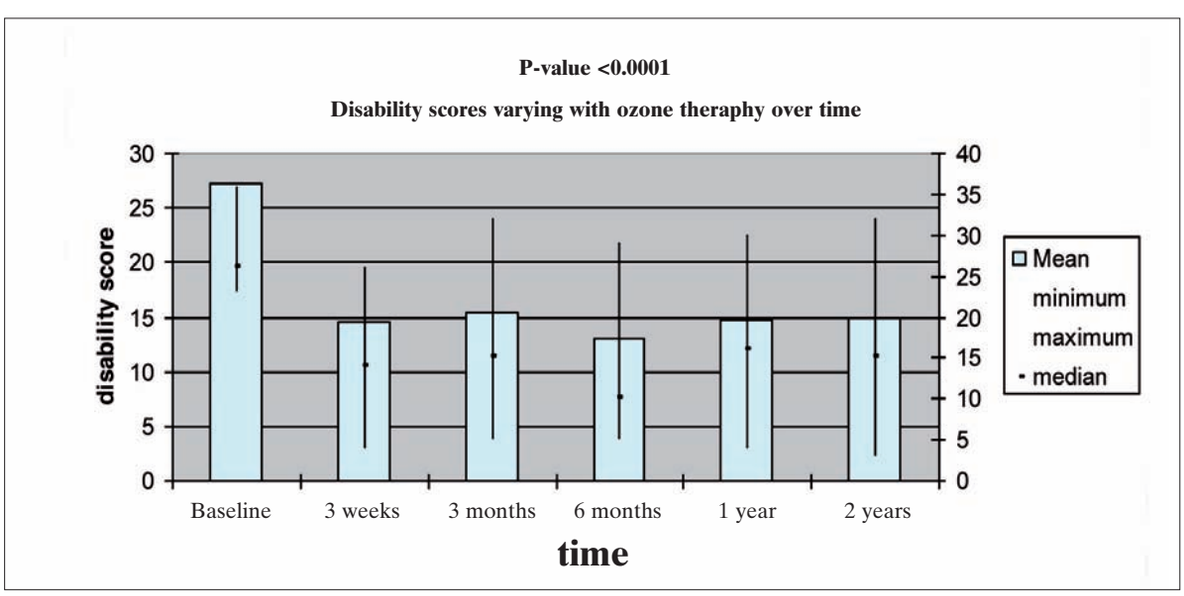
Informed consent was obtained from all the patients. Intravenous cannulation was done and midazolam 0.05 mg/kg was injected for conscious sedation. Patients were turned to a prone position and a pillow was placed under the lower abdomen. The procedure was performed under C-arm guidance. The C-arm was first focused to an antero-posterior view for identification of the diseased disc. Then the C-arm was angled cranially or caudally to abolish any double end-plates and to achieve the widest possible view of the disc space. Then the C-arm was rotated obliquely so that the image of the facet joint appeared at the centre of the end plates. At this stage needle entry point was just lateral to the superior articular process, which corresponds to the centre of the disc. The needle puncture site was identified and marked on the skin.

After antiseptic dressing and draping, the proposed site was infiltrated with local anaesthetic agent. A 22 gauge 12 cm long needle was introduced needle through needle into the affected disc using the tunnel view under fluoroscopic guidance. The position of the needle was confirmed by AP and lateral view of the spine and 3-7 ml of oxygen-ozone mixture at a concentration of 29-32 mc/ml was injected in the disc by ozone resistant syringe over a period of 15-20 seconds.

At the end of the procedure, patients were advised to rest in supine decubitus position for at least two hours. All patients were discharged on the same day evening, and were advised to gradually resume motor activity. All patients underwent follow-up examination at three weeks, three months, six months, one year and two years after the procedure. Pain intensity was assessed by 0-10 points visual analog scale (VAS) and Oswestry low back pain disability questionnaire[7] was used to assess functional

Table 2 **Changes in Oswestry disability index over time.**

	Obs	Total	Mean	Variance	Std Dev
Baseline	53	1445.0000	27.2642	8.3904	2.8966
3 weeks	53	768.0000	14.4906	32.4470	5.6962
3 months	53	816.0000	15.3962	45.3592	6.7349
6 months	53	690.0000	13.0189	46.6343	6.8289
1 year	53	785.0000	14.8113	53.4253	7.3093
2 years	53	792.0000	14.9434	50.2083	7.0858



impairment. Oswestry disability index was used on a 0-5 point score to assess limitations of daily activities due to pain.

The index includes;
1 pain intensity
2 personal care (washing, dressing)
3 lifting of weight
4 walking
5 sitting
6 standing
7 sleeping
8 social life
9 traveling
10 changing degree of pain.

Statistical analysis was done using ANOVA test. Microsoft Epi info. Version 3.4.1 software was used for data analysis, and results were considered statistically significant if p value < 0.05.

Results

Patients' range of age was 21-65 (average 46.04) years. There were more men than women (male: female ratio 32: 21). Intensity of pain was significantly reduced following ozone therapy (Table 1). The reduction of VAS score from baseline to three weeks following treatment was 7.58 ± 86 to 2.75 ± 1.42, and at the end of the study, that is two years after treatment 2.64 ± 2.14, p value was < 0.0001 which is significant. Oswestry low back pain disability score showed a significant improvement in functional status of the patients. Reduction of Oswestry disability index from baseline to three weeks and two years following treatment was 27.26 ± 2.89 to 14.49 ± 5.69 and 14.94 ± 7.08, p value was < 0.0001 (Table 2).

There were no complications such as systemic hypotension, bradycardia, vagal shock, meningeal irritation or neurological deficit observed in this series.

Discussion

The intervertebral discs occupy one third of the height of the spinal column and consist of an outer annulus fibrosus and inner nucleus pulposus. The nucleus pulposus is sandwiched inferiorly and superiorly by cartilage endplates. In childhood the annulus fibrosus is separated from the nucleus pulposus by a transitional zone. In the growing phase during skeletal maturation the boundary between annulus and nucleus becomes less obvious. The nucleus pulposus is a ball of transparent jelly which consists of collagenous fibres, cells and mucopolysaccharides.

Disc prolapse results from herniation of soft disc material from the nucleus pulposus through a tear in the annular ligament. Pain and inflammation develop from the pressure of the herniated material on the posterior longitudinal ligament and the dura mater, which may ultimately affect the nerve roots.

About 90% of patients respond to medical treatment including analgesics and physiotherapy. The remaining 10% require decompression of nerve roots either by surgery or some percutaneous intradiscal procedure.

Chemonucleolysis using chymopapain was the first intradiscal therapy done in human in 19638. Subsequently some other percutaneous therapeutic options evolved. The use of medical ozone in the treatment of low back pain was developed by orthopaedic surgeon Verga in 1980s. He has treated about 8000 patients over 15 years, and relapse of pain has occurred in less than 2% of cases. The injection is generally made into the paravertebral musculature and in the hernia zone. Ozone nucleolysis by intradiscal injection under CT guidance was first suggested by Muto et Al in 1998 [3]. The action of ozone is due to the active oxygen atom released by the breakdown of the ozone molecule. This active oxygen atom or singlet oxygen is attached to the proteoglycan bridges of the nucleus pulposus. Due to this reaction proteoglycans in the nucleus pulposus is no longer able to hold water and there is shrinkage or mummification of the disc leading to decompression of nerve roots.

Based on this theory of ozone nucleolysis, this prospective study was undertaken in 53 adult patients suffering from lumber disc prolapse for more than four weeks duration. Three to seven ml of oxygen-ozone mixture at a concentration of 29-32 mc/ml were injected into the disc. The mean concentration of ozone was 30.2 mc/ml in this series, which is absolutely safe for the patient. Viebahn reported that the nontoxic concentration of ozone varies from one to 40 microgram per milliliter of oxygen and concentration should not exceed 40 mc/m [9]. The dose of ozone is crucial and must not exceed the capacity of antioxidant enzyme and glutathione to prevent accumulation of

the superoxide anion and hydrogen peroxide, which can cause cell membrane degradation [10,11].

Following intradiscal administration of ozone-oxygen mixture , patients were followed-up for two years using the visual analog scale and Oswestry low back pain disability index. A significant improvement was observed in the functional status of the patients and severity of pain was also significantly reduced (Tables 1 and 2). Bonetti et Al also reported excellent results in 74.4% patients after six months [5].

Ozone not only attenuates nerve root compression by reducing the size of the disc, 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 [12] as it inhibits synthesis of proinflammatory prostaglandins, release of bradykinins and algogenic compounds. Ozone also increases the release of antagonists to proinflammatory cytokines [13].

Patients who did not show much improvement following ozone therapy and whose Oswestry disability index remained high even after three months were referred to a neurosurgeon for surgical intervention if indicated.

To conclude, ozone nucleolysis provides excellent pain relief in most herniated disc patients who failed to respond to conservative therapy. The limitations of this study are lack of control and lack of blinding. Further study is necessary to evaluate the long-term outcome of ozone nucleolysis therapy.

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