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ORIGINAL ARTICLE

OZONE NUCLEOLYSIS IN LUMBAR INTERVERTEBRAL DISC HERNIATION: NON-RANDOMIZED PROSPECTIVE ANALYSIS

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ABSTRACT: STUDY DESIGN: Non-randomized, prospective analysis of 68 patients of lumbar disc herniation treated with ozone nucleolysis. **OBJECTIVE:** To assess the patients with lumbar disc herniation treated with intradiscal ozone, pre and post ozone nucleolysis, for pain using Visual Analog Scale (VAS) functional & disability score using Japanese Orthopedic Association (JOA) Clinical Symptom Score. **SUMMARY OF BACKGROUND DATA:** Ozone therapy for disc herniation is becoming popular because of its minimal invasive, lesser recurrences and remarkably fewer side effects. Successful outcomes of ozone therapy have been reported from various European & Indian centers. **METHODS:** A series of 68 patients were treated with ozone therapy for lumbar disc herniation from January 2009 to January 2012. The procedure is done under C-arm guidance under local anesthesia by "Single sitting double injection technique". All patients were assessed using VAS for radiation pain & back pain, Clinical Symptom Score of the Japanese Orthopaedic Association (JOA) for a Patient with Lumbar Disc Herniation, pre op and post op, on day one, after a week, two weeks, first month, third months, sixth month one year second year. Were classified them as Good, Moderate & Poor outcome. **RESULTS:** Out of 68 patients 89.7% (61/68) patients had good outcome, 7.35% (5/68) patients had moderate outcome, 2.95% (2/68) had poor outcome. Intra-op in 1 patient where ozone spread in Para spinal muscles but had no postoperative problem.4 patients had mild nausea, 2 had mild headache & No infection. **CONCLUSIONS:** Ozone nucleolysis is a new, minimally invasive procedure done under local anesthesia & has shown effective results in the treatment of contained intervertebral disc herniation with no side effects.

KEYWORDS: Ozone nucleolysis, Disc Herniation, Injection technique.

INTRODUCTION: Low back pain is an extremely common ailment encountered in our day to day practice. 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] Low backache is one of the leading causes of lost working days all over the world. The symptoms of 80-90% of patients with disc prolapse usually resolve with conservative treatment. Most episodes resolve spontaneously or after conservative therapy.[2,3] For disc induced low back pain the modalities of treatment are conservative, root block, epidural steroid, radio nucleoplasty, endoscopic discectomy, micro discectomy & classical laminectomy and discectomy.

Surgery is reserved for those who fail to respond to conservative management. Traditionally, Open Discectomy has stood the test of time for the treatment of prolapsed intervertebral disc. Endoscopic & micro discectomy have good results but due to associated surgical complications & epidural scar formation in a substantial proportion of patients, the preoperative symptoms recur after primary successful surgical treatment.

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Newer trend of minimal invasive technique, which is cost effective with minimal hospital stay and least complications, for discogenic low back pain has been in research for some time now, giving rise to modern techniques came into being that are minimally invasive and share the principle of acting directly on disc content without accessing spinal channel. Image guided percutanous intradiscal injection techniques are chemodiscolysis by chimopapain or by Ozone nucleolysis. Chemodiscolysis by chimopapain is based on an enzymatic dissolution of the nucleus. Although purified prepared enzymes are used, anaphylactic shock can occur.[4]

Ozone is a tri-atomic Oxygen molecule, O3, with a different molecular structure from Oxygen. Its name is derived from the Greek word “ozein” meaning "to smell". Ozone, an emerging medical drug, is used in disc hernaition because of its property to break down the proteo-glycan bridges in the nucleus pulposus of disc along with an anti-inflammatory action.[5]

In this study we aim to assess the effectiveness of ozone nucleolysis in lumbar intervertebral disc herniation. This study is done over a period of three years, wherein 68 individuals with complaints of low backache and radiation pain due to disc herniation were taken as subjects and were treated with ozone injection in the herniated disc followed up for 2 years.

Ozone & How Ozone Acts: 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 proteo-glycan bridges in the jelly-like 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 or ozonucleolysis. 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.

Ozone has a dose-related biological action. At high concentrations (30-70µg/ml 02), it may cause alterations of tissue structure; at medium concentrations (20-30µg/ml 02) it seems to affect the regulation of the immune system and at low concentrations (<20µg/ml 02) it improves the microcirculation.[5, 6,7] 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.[8,9] The specific feature of oxygen ozone therapy noted in disc specimens was dehydration of the fibrillary matrix of the nucleus pulposus, revealing collagen fibers and signs of regression (Vacuole formation and fragmentation)—a sort of disk “mummification.”[10]

MATERIAL & METHODS: A series of 68 patients were treated with ozone therapy for lumbar disc herniation from January 2009 to January 2012. All patients age group 18 yrs to 60 yrs who presented with clinical signs of disc compressing the nerve root & whose MRI showed evidence of contained disc herniation [Figure 1], with duration of symptoms more than six weeks and had failed to respond conservative treatment with Non-steroidal anti-inflammatory medical therapy and physical therapy were included.

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Exclusion Criteria: Previous lumbar spine surgery, possible pregnancy. Current fracture, infection, and/or deformity (greater than 15 degrees of lumbar scoliosis, using Cobb's measure technique) of the spine. Calcified or migrated herniated disc, signifiant glucose-6-phosphate-dehydrogenase deficit, active hyperthyroidism. cauda equina syndrome or progressive neurological deficit (Usually requiring urgent surgery), loss of control of urination & defecation.

All patients were orally informed about the procedure and potential risks of treatment. Written informed consent was obtained from all patients. The procedure followed was approved by the committee on Human Experimentation of our institution.

The procedure is done under C-arm guidance under local anesthesia. All patients were assessed using VAS for radiation pain, Clinical Symptom Score of the Japanese Orthopaedic Association (JOA) for a Patient with Lumbar Disc Herniation [11], pre op and post op, day one, after a week, two weeks, first month, third months, sixth month one year &second year. Were classified as good, moderate & poor outcome according to [Table 1] which included VAS for radiation pain & JOA score.

PROCEDURE: The patient is taken to the operation theatre lying on oblique position with a pillow under lower abdomen. The side of pain turned upwards. The area is prepared and draped in sterile manner. It is done usually under local anaesthesia Intravenous antibiotic ceftriaxone 1G should be given 30minutes before the procedure. An intravenous line & Pulse oxymeter are secured before the procedure. The procedure is done under C-arm guidance. C-arm first should be focused to a pure anterior-posterior view to view the diseased disc. Then C-arm is cranially tilted to abolish any double end-plates and thereby getting widest possible view of disc space. Then C-arm is focused in a away such that facet joint come at the center of the end plates. On the side of maximum pain, the needle entry point is marked just lateral to the superior pars/articular pillar exactly at the center of the disc [Figure 2].

Local 2% xylocaine is infiltrated, then 22 G Chiba, 178mm long spinal needle is introduced into the diseased disc under fluoroscopic guidance [Figure 3]. The position of needle tip is confirmed in AP & lateral view. The ozone oxygen mixture gas is collected from the ozone generator at 6 Lt's of oxygen, concentration of 40µgm ozone in a 20 cc syringe. Initial 10 to 15 cc is injected with needle placed just ahead of midline. As Ozone gas is injected in the disc, the disc appears radiolucent and illuminated [Figure 4 a, b].Usually after injecting 10 to 15 cc there is resistance the syringe is held in place under pressure for 5 min. Then the trochar is placed back and waited for 10 minutes. Again fresh ozone is collected from ozone generator and 5 to 10 cc of ozone is injected in the disc with needle 2-3mm posterior of the midline. So this act as 2 injection in one sitting, as the half-life of ozone is around 20 minutes" single sitting double injection". Then needle is removed and aseptic spray is applied. Patient is advised bed rest for 2 hrs. later patient can mobilize according to his comfort.

RESULTS: Of 68 patients 41 were male & 27 female. Mean age was 34 years.L4-5 disc protrusion in 38 pts, L5-S1disc protrusion in 23 Pts &doth L4-L5and L5-S1dics protrusion in 7 patients. Data analysed by using SPSS (Statistical Package for social sciences) version 17.0 We have used paired t-test to find out the significance between the pre-operative and post-operative pain score and JOA score at 5% level of significance (95% C.I.) if the p-value < 0.05 then there is significant difference between pre & post-operative score.

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Patients with VAS score for radiation pain [Table 2] in leg reduced from pre-op (Average7.09) to 6 months post op for good outcome (Average 0.95), 2nd year (Average 0.4), for moderate (Average 3.2), 2nd year (Average 0.6). Patients VAS score for low back pain [Table 3] reduced significantly from pre op(Average 6.03) to good outcome 6months post op (average1.08), 2nd year (average 0.8), moderate 6th month (Average 3.4) 2nd year (Average 2.6). JOA scores [Table 4] pre-op score (Average 15.4). Post–op JOA score in good outcome at 6th month Average (27.23), 2nd year (Average 28.2), in moderate outcome (Average 20.40) at 6th month, (Average 21.3) at 2nd year. & Average (13.25) in poor outcome. JOA Postoperative improvement in percent average 97%.The patients with poor outcome underwent surgical micro discectomy after one month.

Complication: Intra-op in 1 patient where ozone spread in Para spinal muscles [Figure 5] but had no post-operative problem.4 patients had mild nausea, 2 had mild headache & No infection.

Final Outcome: Out of 68 patients 89.7% (61/68) patents had good outcome, 7.35% (5/68) patients had moderate outcome, 2.95% (2/68) had poor outcome. Four patients had repeat MRI after six months which showed disc herniation size decrease more than 50%.

DISCUSSION: Disc Herniation is defined as a localized displacement of disc material beyond the limits of the intervertebral disc space. Partial tear of annular ligament with herniation of the nucleolus pulposus is termed as contained disc herniation. Diagnosing contained disc herniation on MRI becomes crucial as ozonucleolysis as its treatment has better prognosis as compared to disc protrusion.

Clinical signs and symptoms of disc herniation are not only caused by mechanical compression but also by biochemical factors that play an important role in inflammatory sensitization and immune response in the epidural environment of the nerve root.[12,13,14] Pain and inflammation developed from the pressure of the herniated material on the posterior longitudinal ligament and the dura mater, may ultimately affect the nerve roots. The patients who fail to respond to medical treatment including analgesics and physiotherapy are one who require decompression of nerve roots either by surgery or some percutaneous intradiscal or foraminal procedure.

Use of medical ozone for treatment of low back pain was advocated by orthopaedic surgeon 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.[15] Leonardi popularized fluoroscopy guided ozone injection into the intervertebral disc.

Nowadays, ozone therapy is understood to be a genuine treatment method in complementary medicine, encouraging the scientific dialog between traditional medicine and complementary methods. Critical discussions have activated basic research in the field of ozone therapy including the revision of highly complicated treatment methods. It has been published in Anesthesia and pain journals that up to 85% of disc surgeries can be avoided with these non-surgical interventions. Success rate is about 88% which is comparable to surgical discectomy (50% to 90%). Complications are remarkably low and much less than surgery.

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In Our Study: We had good result in 87.9% of the patients selected for the study, who had complaints of low back ache lasting longer than 6 weeks, refractory to all conservative treatment with NSAIDs and physiotherapy. VAS for radiation pain & JOA pre operatively as well as on various specified intervals post operatively had shown significant difference.

Ozonucleolysis caused a more significant improvement of radiation pain in those patients who had complaints of low backache along with radicular pain. Patients with moderate (7.35%) outcome used occasional analgesic and physical therapy. Two patients (2.95%) had poor outcome who underwent surgical discectomy.

Bonetti et Al also reported excellent results in 74.4% patients after six months.[16] A success rate of 70.3% was noted by Cosma F. Andreula et Al.[10] Successful outcomes of ozone therapy have been reported from various European centers. Other studies as Treatment of Intraforaminal and intradiscal injections of a steroid, an anesthetic, and O2-O3 are more effective at 6 months than injections of only a steroid and an anesthetic in the same sites.[17]

Technique: 'Single sitting double injection technique' in which 15 -25 cc of freshly prepared oxygen-ozone mixture was given twice intra discally with a time gap of 10 minutes. This technique was used to increase the tissue destruction property of ozone and considering its half-life that is about 20 minutes.

We used a 178 mm long 22 guage Cheba needle. The advantage of using a thin bore needle is that it reduces tissue injury and patient discomfort. All patients were discharged & made to walk the same day or the next day as per patients comfort.

Most of the studies used radio opaque dyes for confirmation of needle in the disc & its containment. The use of intradiscal contrast reduces the discal absorption of ozone and the space available for the action of ozone. Hence, no intradiscal dye was used in our study.

Under C-arm guidance. At the time of injection of ozone, the patient complaints of increase in pain symptom initially and reduction eventually. This is because the intradiscal pressure rises with the injection of ozone and reduces with tissue destruction that it causes.

We used ozone in concentration of 40 microgram per millilitre of oxygen to increase its tissue destruction property. Paoloni et Al in their study used a concentration of 20 mc/ml**[18]**.Bonetti et Al used a concentration of 25mc/ml.[12] Viebahn reported that the nontoxic concentration of ozone varies from one to 40 microgram per millilitre of oxygen and concentration should not exceed 40 mc/.[19]

Complications of ozone therapy are very rare. They include post-procedural transient muscle spasm & burning pain. No patients had infection or discitis (Very rare due to the bactericidal effect of ozone).

Intra-op, in one of our patients where ozone had spread in Para spinal muscles. Patient had mild burning pain for 7to 8 minutes but had no postoperative problem. Review with literature showed intramuscular ozone therapy in treatment of acute back pain has shown to reduce disability & the intake of analgesic drugs in a study with no complications.[19]

A case being reported of the complication: Acute fatal septicemia should be considered among the major complications of the oxygen-ozone therapy in the treatment of a herniated lumbar disc. The patient developed a fulminant septicemia. An abdominal-pelvic and chest computed tomography and blood culture led to the diagnosis of pyogenic lumbar muscle involvement, accompanied with septic pulmonary embolism secondary to Escherichia coli infection.[20]

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In our experience the failure has been mostly related to patients with some amount of spinal canal stenosis, recurrent herniated disc and small descending herniated disk of the lateral recess with significant compression of the nerve sheath.

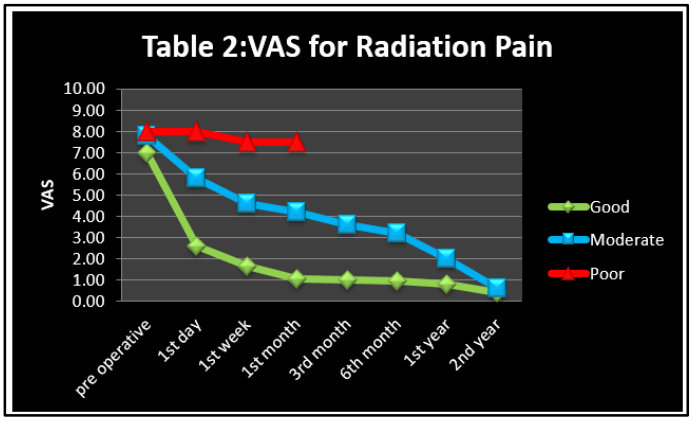
On the basis of our results and the assessment of our failures, we recommend careful selection of patients to avoid broadening the indications for treatment, thereby ensuring a high success rate.

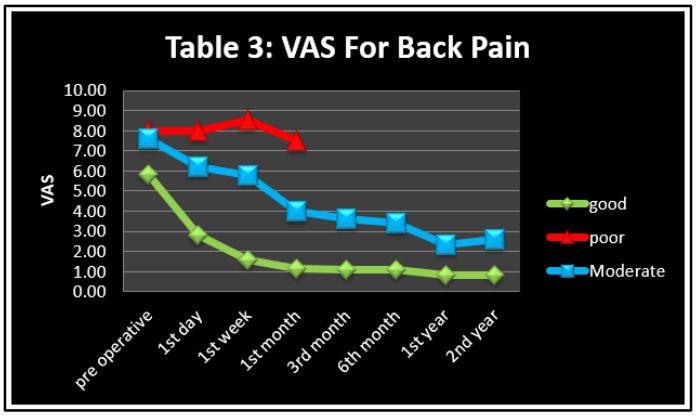
Ozone nucleolysis being a minimally invasive technique allows for early mobilization of the patient as well as early recovery, reduced hospital stay and working days lost of the population. Ozone nucleolysis has a success rate of about 87.9% and remarkably few side effects.

CONCLUSION: Ozone nucleolysis is a new, minimally invasive procedure done under local anesthesia & has shown effective results in the treatment of contained lumbar intervertebral disc herniation with remarkably few side effects. Ozone therapy is a good option to treat lumbar disc herniation that has failed to respond to conservative management, before recourse to medications or surgery.

Post-operative at 6 months	Good	Moderate	Poor
Vas back pain	≤ 2	≤5	>5
VAS radiation Pain	≤ 2	≤5	>5
JOA score	≥ 25	≥19	<19

Table 1





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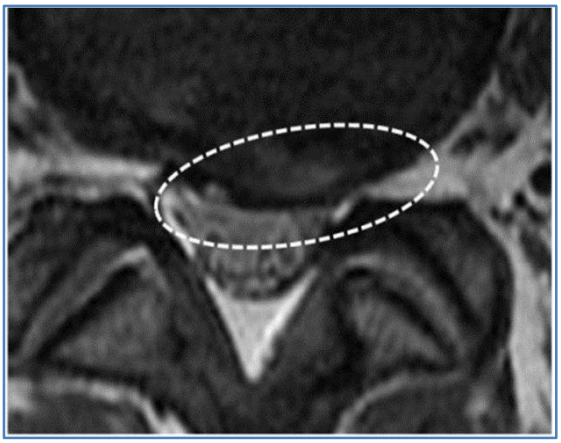

Figure 1

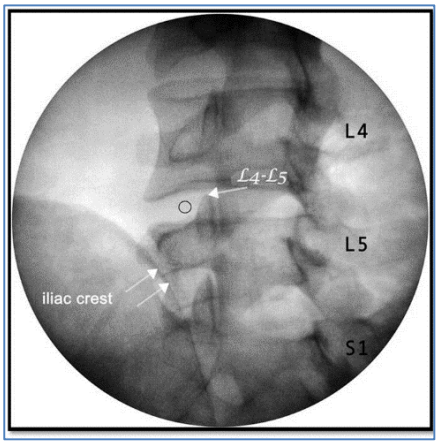

Figure 2

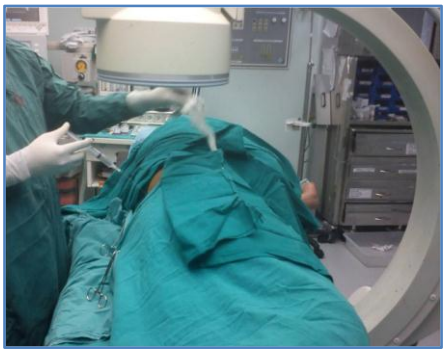

Figure 3

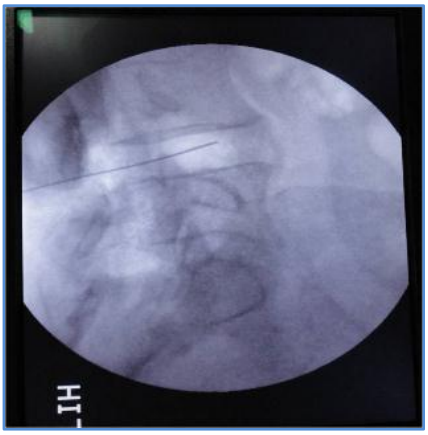

Figure 4a

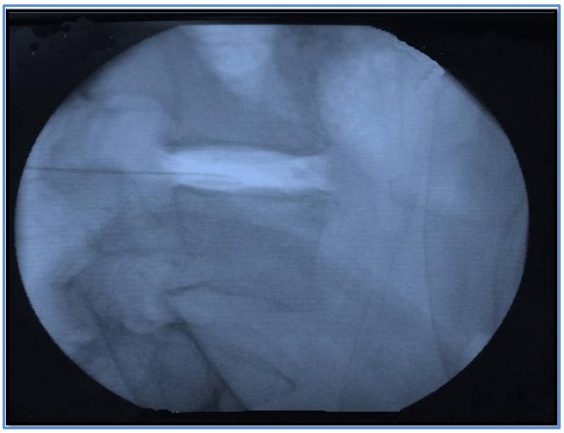

Figure 4b

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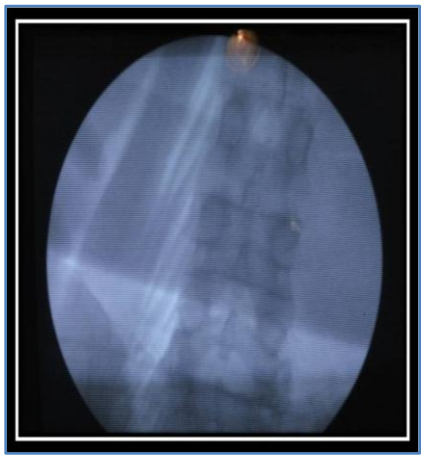

Figure 5

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