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Original Research Article

Role of ozone nuleolysis in management of discogenic pain in lumbar and lumbosacral disc prolapse

Kuldeep Yadav[1], Priyesh Bhaskar[2]*, Anita Jagetia[3], Mohd. Kaif[1]

[1]Department of Neurosurgery, Dr Ram Manohar Lohia Institute of Medical Sciences, Lucknow, Uttar Pradesh, India
[2]Department of Anaesthesia, Career Institute of Medical Sciences, Lucknow, Uttar Pradesh, India
[3]Department of Neurosurgery, Maulana Azad Medical College and Associated G. B. Pant Hospital, New Delhi, India

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***Correspondence:**
Dr. Priyesh Bhaskar,
E-mail: priyesh.bhaskar@yahoo.com

ABSTRACT

Background: Discogenic low back pain is a common symptom. Over the years many percutaneous minimally invasive therapeutic modalities have evolved. Intradiscal oxygen-ozone therapy is one of them and has showed promising results. We undertook a prospective study to evaluate the therapeutic outcome of intradiscal oxygen-ozone therapy on patients with lumbar and lumbosacral disc prolapse in the Indian population.
Methods: Fifty consecutive patients complying with selection criteria were included in this study with clinico-radiologic diagnosis of lumbar and/or lumbosacral disc prolapse. All patients received ozone-oxygen mixture in the disc, in neural foramen and root canal and in facet join region and para-vertebral muscles at concentration of 29-40 mcg/mL. Therapeutic outcome was assessed after four weeks, three months, and six months post-procedure, on visual analog scale (VAS), Oswestry low back pain disability questionnaire (ODI) and Modified MacNab methode.
Results: Pain intensity was significantly reduced following treatment (from baseline mean VAS 8.46±0.67 to 3.8±1.29 at one month, at three months 3.1±0.7 and at six months follow up 3.78±1.13, $p < 0.0001$). Similarly the ODI and modified MacNab criteria showed a remarkable improvement in the functional status of the patients ($p<0.05$). No minor or major complications were observed in this case series.
Conclusions: It can be concluded that oxygen-ozone treatment is highly effective in relieving low back pain due to lumbar and lumbosacral disc prolapse.

Keywords: Discogenic low back pain, Fluoroscopic, Minimally invasive, Ozone nucleolysis, Percutaneous

INTRODUCTION

In every day's life lower back pain is a major cause of morbidity. In 50% cases it is associated with radicular symptoms.[1] The causes of variable success are considered to be epidural fibrosis, arachnoidal adhesions, muscle and fascial fibrosis, and or mechanical instability. Mixter and Barr proposed prolapsed lumbar and lumbosacral inter-vertebral disc as a cause of low back pain.[2] For the reasons of safety and efficacy ozone nucleolysis is becoming widely used intermediate procedure between conservative therapy and surgery, to alleviate pain, decompress the nerve roots and to maintain the structural stability, in cases of disc prolapse.[3] A prevalence of 30 percent has been found to be associated with chronic low back pain in Unites States.[4]

The mechanisms of action include analgesic, anti-inflammatory and oxidant actions which work together to cause symptomatic and radiological improvements in disc prolapse. Active oxygen atom is liberated from breaking down of ozone molecule. When ozone is injected into the

disc the active oxygen atom, attaches with the proteoglycan bridges in the nucleus pulposus. The proteoglycan bridges in the nucleus palposus are broken down so their water holding capacity is lost, resulting in reduction of volume of nucleus palposus. Additionally ozone also causes cellular degeneration and shrinkage of matrix of nucleus palposus. This results in reduction in the size of the prolapsed disc portion and decompression of the nerve root. Anti-inflammatory action is produced by decreased concentration of inflammatory mediators and inflammatory cells.[4-6]

METHODS

This prospective study is designed to evaluate ozone nucleolysis in lumbar and lumbosacral disc prolapse. This study includes 50 patients of either sex of all ages since 2012- 2015 with clinico-radiologic diagnosis of low back pain with or without radicular pain due to lumbar or lumbo-sacral disc prolapse.

None of the patient had sensory or motor deficit, bladder bowel involvement, and trauma. All the patients were non-responder to conservative treatment for minimum 3 months. Dynamic X-ray of lumbosacral spine was one in all the patients to exclude instability in the lumbosacral spinal segment. Computed tomography was done to exclude patients having bony lumbar canal stenosis, fracture or calcified disc. Magnetic resonance imaging was one to exclude any disc fragment as it was contraindicated in sequestrated disc prolape.

Untreated hyperthyroidism, known case of glucose-6 phosphatase (G-6PD) deficiency (Favism), Pregnancy, active untreated systemic infection, local skin infection or untreated discitis, bleeding disorder and anticoagulant medication were other contraindications for ozone nucleolysis. Patients were screened and evaluated by taking thorough history and detailed clinical examination to ensure proper selection and follow up. Hematological investigations included routine, thyroid profile and ESR. Informed consent was taken after explaining procedure and side effects of O_3 nucleolysis. Pre-procedural severity of symptoms was subjectively quantified by self-reported questionnaires using following scales Visual analogue pain Intensity Scale (VAS), Oswestry low back pain disability questionnaire (ODI), modified MacNab's criterion.

The patient was made to lie on prone position on Mizuho operating table with spinal attachment (Allen Medical System). Patient was positioned in such a way that there is break at lower lumbar region. Intravenous access, non-invasive blood pressure monitoring, electrocardiographic monitoring and pulse oxymetery was established. The procedure was done under local anesthesia with intravenous sedation.

All emergency medicines, facilities for intubation and oxygenation were kept on standby. Patient was given sedation of 1 mcg/kg dose of fentanyl and 1-2 mg of midazolam. Lidocaine 2% infiltrated at puncture site. Right or left side injection was planned based on the radiation of pain in unilateral radicular pain. In bilateral pain, the side of radiation which was first in chronology on history or the side with more severity of pain was chosen as the side of injection.

The procedure was done under fluoroscopic-arm guidance. Fluoroscopic-arm is positioned at the same side from where the procedure was planned. C-arm was focused to take antero-posterior view to localize the diseased disc. Then fluoroscopic-arm was rotated cranially/caudally to abolish any double end-plates and thereby getting widest possible view of disc space. Fluoroscopic-arm was rotated obliquely away from vertebral column (towards the side of concern, approximately 600) in such a way that facet joint come at the center of the end plates and Scotty dog appearance is obtained. Needle entry point at skin was 8-10 cm lateral to midline at the disc level concerned and the needle entry point at disc level was just lateral (anterior) to the superior articular process exactly at the center of the disc .Before proceeding from skin entry point end on view of the needle is obtained. Quincke type spinal needle (BD,18G ,9 cm) was introduced percutaneously into the concerned disc using tunnel vision (end on view, so that needle was seen almost as a single point and the tip of needle is in the centre of disc, anterior to the lateral surface of superior articular process of inferior vertebrae) under fluoroscopic guidance.

Now the inner Quincke type spinal needle (VYGON, 22G, 15 cm) was introduced into outer needle under same setting and advanced into the posterolateral part of disc through the Kambin's triangle bounded by lateral surface of superior articular process of inferior vertebrae and dura with traversing nerve root posteriorly, exiting nerve root anterolaterally and superior end plate of inferior vertebrae inferiorly, using Kambin's triangle transforaminal approach. The position of needle tip was double confirmed by pure antero - posterior and lateral views. The needle was advanced in lateral position after confirmation on anteroposterior view.

The needle tip was aimed at the centre of the disc. For injection oxygen-ozone mixture was always freshly prepared on site from an ozone generator (Ozomed, Kastner Praxisbedarf GmbH Medizintechnik, Germany) for immediate administration. The gas was collected in BD polypropylene 10 cc leur lock with leur mount syringe through (minisart, sartorius stedim) millipore bacterial filter. Injection time was 15 seconds as after 20 seconds ozone starts decaying at the rate of 2 mcg/second.[7] Six to eight cc of oxygen-ozone mixture (at a concentration of 29-40 microgram/ml.) was injected into the disc. Then needle was withdrawn a few millimeters and 15-20 cc of gas mixture was injected into neural foramen and root canal. By further withdrawing

the needle 8-10 cc of gas mixture was injected into facet joint region and para-vertebral muscles.

Immediately after the procedure the patient was kept in supine position without changing posture for 4 hours and the patient was advised to have bed rest for next 12 hours and he/she was discharged next day in the morning. He/she was advised to avoid strenuous activity for 3 days post procedure. Clinical follow up data was collected at 4 week, 3 months and 6 months post procedure and all the patients were evaluated using - visual analogue pain intensity scale (VAS) Oswestry low back pain disability questionnaire (ODI) and, modified MacNab method at each visit and these values were compared with preoperative values. If Patient showed 50% reduction in symptom, repeat ozone injection 4-6 weeks after initial procedure was considered. If patient showed 70-80% reduction in symptoms, no further therapy except physiotherapy was advised. If patient showed only 10-20% reduction in symptoms, no further ozone injection was advised and the patient was considered for standard surgical microscopic discoidectomy. All patients were advised to have magnetic resonance imaging of lumbar and lumbosacral spine at 6 months post procedure to document reduction in size of prolapsed disc in the question.

RESULTS

Total number of patients was 50. Age range of patients was 22-62 (mean age 41.62 years). Pain was significantly reduced following ozone therapy.

The reduction of VAS score from baseline to one month following treatment was 8.46±0.67 to 3.8±1.29, at three months 3.1±0.7 and at six months follow up 3.78±1.13 p value was < 0.0001 (Wilcoxon signed rank test, graph Pad software) which is significant (Table 5). Oswestry low back pain disability score showed a significant improvement in functional status of the patients.

Reduction of Oswestry disability index from baseline to one month, three months and six months following treatment was 35.52±1.58 to 22.61±5.53, 23.28±3.8,and 20.52±3.41 p value was <0.0001(Wilcoxon signed rank test, Graph Pad software) (Table 6). Results according to modified MacNab criterion were as following (Table 1).

At one month post procedure

Excellent 4%, good 16%, fair 68%, poor 12%

At 3 months post procedure

Excellent 4%, good 28%, fair 60%, poor 8%

At 6 months post procedure

Excellent 2%, good 76%, fair 18%, poor 4%

There were no complications such as allergy, stroke, systemic hypotension, bradycardia, vagal.

Table 1: MacNab grading.

	Excellent	Good	Fair	Poor
One month follow up	2 (4%)	8 (16%)	34 (68%)	6 (12%)
Three months follow up	2 (4%)	14 (28%)	30 (60%)	4 (8%)
Six months follow up	1 (2%)	38 (76%)	9 (18%)	2 (4%)

Table 2: At 6 months follow up MacNab grade (disc prolapse level wise).

	Excellent	Good	Fair	Poor
L4-L5 and L5-S1 [15 patients-(30%)]	0	8 (16%)	5 (10%)	2 (4%)
L4-L5 [33 patients (66%)]	1 (2%)	30 (60%)	2 (4%)	0
L3-L4 and L4-L5 [2 patients (4%)]	0	0	2 (4%)	0

Table 3: Disc prolapse grade 54 (percentage of length between posterior margin of ring epiphysis of vertebrae and level of facet joint) and MacNab outcome grades at 6 months follow up.

	Excellent	Good	Fair	Poor
grade one (less than 25%) total 37 patients	1 (2%)	30 (60%)	6 (12%)	0
grade two (25%-75%) total 11 patients	0	8 (16%)	2 (4%)	1 (2%)
grade three (76%-90%)total 2 patients	0	0	1(2%)	1 (2%)

Table 4: Age related outcome.

	Excellent	Good	Fair	Poor
20-30 years (10)	1 (2%)	9 (18%)	0	0
31-40 years (17)	0	16 (32%)	1 (2%)	0
41-50 years (14)	0	12 (24%)	1 (2%)	1 (2%)
51-60 years (8)	0	1 (2%)	7 (14%)	0
61-70 years (1)	0	0	0	1(2%)

Table 5: VAS Score.

	Minimum	Maximum	Mean	Median	Standard deviation
Pre-operative vas score	7	9	8.46	9	0.67
Vas score at 1 month follow up	0	6	3.8	4	1.29
Vas score at 3 months follow up	1	4	3.1	3	0.7
Vas score at 6 months follow up	2	6	3.78	4	1.13

Table 6: ODI scores.

	Minimum	Maximum	Mean	Median	Standard deviation
Pre-operative ODI score	32	38	35.52	36	1.52
ODI score at 1 month	16	30	22.61	20	5.53
ODI score at 3 months	16	28	23.28	24	3.8
ODI score at 6 months	12	26	20.52	20	3.41

Table 7: Outcome using MacNab criterion at 6 months.

	Excellent	Good	Fair	Poor
History < 6 months (total 26 patients	2%	56%	4%	0
History >6 months (total 24 patients)	0	20%	14%	4%

DISCUSSION

The intervertebral discs occupy one third of the height of the spinal column .The lumbar intervertebral discs are 7-10 mm thick and 4 cm in diameter. Lumbar intervertebral disc is wedge shaped and anterior thickness is more than posterior thickness. This wedge shape is mainly responsible for lumbar lordosis. The disc herniation is classified on various basis. It may be central, subarticular, foraminal, extraforaminal and anterior in axial plane. It may be pedicular, suprapedicular or infrapedicular in coronal plane. It is also classified as mild, moderate and severe herniation but interobserver and intraobserver differences are much.

Later modification came (nomenclature committee of North American Spine Society) which stated that herniated disc occupying less than 25% of the distance between posterior ring epiphysis and facet joint is called mild, 25-75% is called moderate, 76%-90% is called moderately severe and 90%-100% is called severe herniation.[8]

This nomenclature is more precise and simple and correlates well with symptoms and response to therapy and is based on axial magnetic resonance imaging view. We have adopted this nomenclature in our study for these reasons. Disc prolapse is called when the base of the herniation is more in dimension than herniated portion but is less than 1800 of disc circumference. Extrusion of the disc is called when base is shorter than the dimension of herniated portion. The disc material may migrate either sub ligamentous or trans-ligamentous, either upward, downward or centrally.

Disc bulge is the term used when more than 180 o of the disc circumference is outside the boundary of ring epiphysis. Disc prolapse means nucleus palposus material coming out of annular confines, whatever the direction, volume, extent, base or migration is. We have used the term “prolapse” in our study. The herniated nucleus palposus material act as antigen and inflammatory response is initiated around it with formation of granulation tissue, neovascularization and innervations by nerve fibres.[9,10]

Based on this theory of ozone nucleolysis, this prospective as well as retrospective study was undertaken in 50 adult patients suffering from low back pain and lumbar and lumbosacral prolapsed intervertebral disc on

magnetic resonance imaging with clinicoradiological correlation. Six to eight cc of oxygen-ozone mixture (at a concentration of 29-40 microgram/ml.) was injected into the disc. Then needle was withdrawn a few millimetres and 15-20 cc of gas mixture was injected into neural foramen and root canal. By further withdrawing the needle 8-10 cc of gas mixture was injected into facet joint region and para-vertebral muscles.

The mean concentration of ozone was 29.4 mcg/ml, which is absolutely safe for the patient. Viebahn reported that the nontoxic concentration of ozone varies from one to 40 microgram per millilitre of oxygen and concentration should not exceed 40 mcg/ml.[11,12] 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.[13,14]

Following intradiscal administration of ozone- oxygen mixture, patients were followed-up at one month, three months and six months interval using the visual analogue scale, Oswestry low back pain disability index and modified MacNab criterion.[15-17] The reduction of VAS score from baseline (mean 8.46±SD 0.67) to one month following treatment was 3.8±1.29, at three months 3.1±0.7 and at six months follow up 3.78±1.13 (p value using Wilcoxon's paired signed rank test, was < 0.0001 which is significant) (Table 5).

Likewise reduction of Oswestry disability index (ODI) from baseline to one month, three months and six months following treatment was 35.52±1.58 to 22.61±5.53, 23.28±3.8,and 20.52±3.41, p value was <0.0001 (Table 6). Thus significant improvement was observed in the functional status of all patients and severity of pain was also significantly reduced. According to modified MacNab criterion there was 2% of patient population (N = 50) had excellent outcome, 76% had good, 18% had fair outcome and 4% patients failed to respond (poor outcome) at six months post-procedure (Table 1).

The two (4%) patients who did not respond to the treatment were subjected to surgical microdiscoidectomy. Patients having L4-L5 level disc prolapse were having superior results[good outcome in 30 patients out of 50(60%), excellent outcome in 1 patient(2%), fair outcome in 2 patients out of 50(4%)] (Table 2). Also the younger age group patients with short duration of low back pain history were benefited the most [in age group 20-30 years 20% patients had excellent to good outcome in 31-40, 34% patients were having good to fair outcome, in age group 41-50 years 28% patients had good to fair outcome at six months follow up] (Table 4 and Table 3). Bonetti et Al also reported successful results in 74.4% patients after six months.[13,14]

Most of the authors reported 65%-85% successful outcome in their studies.[4-7,18] In our study, Ozone not only reduces 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.

Ozone breaks down inflammatory cascade and reduces pain associated with neuronal hypoxia. Ozone has analgesic as well as anti-inflammatory effects as it inhibits synthesis of pro-inflammatory cytokines (IL-1, IL-2, IL-8, IL12, IL-15, INF-alpha, TNF-alpha) prostaglandins(PG-E2), phospholipase -A2, bradykinins and algogenic compounds(matrix metalloproteinases, MMPs) Ozone also increases the release of antagonists to proinflammatory cytokines (TGF-beta, IL-10, IL-4).[18,19] Patients who had improvement of only 10%-20% of VAS score after six month follow up were taken for standard surgical microscopic discoidectomy. The patients who had improvement of 50%, were considered for repeat ozone nucleolysis and patients who had improvement of 70%-80%, were advised only physiotherapy.

CONCLUSION

Ozone nucleolysis provides excellent pain relief in patients with prolapsed lumbar or lumbosacral intervertebral disc and concordant low back pain with or without radiation, who failed to respond to conservative therapy for at least 3 months. Complications if any are least and the procedure can be repeated and the cost is low. The limitations of this study are lack of control and lack of blinding due to ethical constraints.

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