10.5005/jp-journals-10046-0047

ORIGINAL ARTICLE

A Comparison of Intradiscal Ozone with Transforaminal Triamcinolone and Bupivacaine to Ozone Therapy alone in the Treatment of Discogenic Sciatica

[1]Kawsar Sardar, [2]M Omar Faruque, [3]Gautam Das, [4]Richard Hubbard, [5]Nicholas CH Liang
[6]Harvey Finkelstein, [7]Pankaj N Surange, [8]Geeta Joshi

ABSTRACT

Introduction: Ozone disk nucleolysis is a nonsurgical percutaneous procedure for the treatment of discogenic sciatica, and published success rates of ozone disk nucleolysis vary significantly. This study assesses the outcome difference between two treatment modalities among patients with discogenic sciatica secondary to a herniated disk in Bangladesh: Intradiscal ozone injection and combination therapy with intradiscal ozone and transforaminal triamcinolone and bupivacaine injection.

Materials and methods: Prospectively recruited 50 patients (group I) received intradiscal injections of an oxygen–ozone mixture and 150 patients (group II) received identical oxygen–ozone injections, followed by transforaminal triamcinolone 20 mg in 2 mL of 0.25% bupivacaine, in relevant foramen. Discography was noted for each case. All patients underwent follow-up examinations at 1-week, 1-month, and 6-month time points. Clinical outcome was evaluated by using the verbal rating scale (VRS) and modified Macnab method.

Results: According to the modified Macnab method, group II showed "excellent and good" result of about 97, 90, and 88% in 1-week, 1-month and 6-month time points respectively, whereas group I showed 70, 70, and 68% at the same time point. The difference is significant in each time point. Groups I and II demonstrated similar VRS scores prior to intervention, but patients in group II had significantly better VRS pain scores at all three time points.

Conclusion: A combination of transforaminal triamcinolone and local anesthetic with intradiscal ozone provides clearly superior outcomes when compared with ozone therapy alone in discogenic sciatica.

Keywords: Discogenic sciatica, Ozone, Transforaminal.

How to cite the article: Sardar K, Faruque MO, Das G, Hubbard R, Liang NCH, Finkelstein H, Surange PN, Joshi G. A Comparison of Intradiscal Ozone with Transforaminal Triamcinolone and Bupivacaine to Ozone Therapy alone in the Treatment of Discogenic Sciatica. J Recent Adv Pain 2016;2(3):77-81.

Source of support: Nil

Conflict of interest: None

[1]Associate Professor and Pain Consultant, [2]Associate Professor [3]Director, [4]Resident Anesthesiologist, [5]Senior Consultant and Director, [6]Director Emeritus, [7]Director and Chairman, [8]Professor

[1]Department of Anesthesiology, BIRDEM General Hospital and Ibrahim Medical College, Shahbag, Dhaka, Bangladesh

[2]Department of Nutrition and Food Engineering, Daffodil International University, Dhaka, Bangladesh

[3]Department of Pain Medicine, Daradia: The Pain Clinic, Kolkata India

[4]Department of Anesthesiology, University of Pittsburgh Pittsburgh, Pennsylvania, USA

[5]Department of Anaesthesiology and Pain Medicine, Specialist Pain International Clinic, Mt Elizabeth Hospital, Singapore, Singapore

[6]Department of Anaesthesiology and Pain Medicine, Pain Care Medicine of Long Island, New York, USA

[7]Department of Anaesthesiology and Pain Medicine, Interventional Pain and Spine Centre, New Delhi, India

[8]Department of Anaesthesiology, Pain and Palliative Medicine Gujarat Cancer and Research Institute, Ahmedabad, Gujarat, India

Corresponding Author: Kawsar Sardar, Associate Professor and Pain Consultant, Department of Anesthesiology, BIRDEM General Hospital and Ibrahim Medical College, Shahbag, Dhaka Bangladesh, e-mail: kawsardr@yahoo.com

INTRODUCTION

Mixter and Barr reported the important causes of low back pain and radicular pain in 1934 for the first time. They identified the herniated nucleus pulposus as an important cause for this pain condition.[1] Decompression of nerve roots is the main goal of treatment in this condition. It can be done by removing the disk surgically or percutaneous minimally invasive procedure. The reported success rate of lumbar disk surgeries is between 49 and 95%.[2] Short-term success rate after surgery is around 95 to 98%, with a 2 to 6% incidence of recurrence, but in the long-term, it decreases to 80%; 20% of the patients developed failed back surgery syndrome because of recurrence and/or hypertrophic scarring.[3,4] These results have encouraged researchers to develop newer less invasive techniques to improve clinical outcome. Among the percutaneous techniques by interventional procedures, chemonucleolysis and percutaneous disk decompression procedures are mostly reported. Decompressor and nucleoplasty have the best grading at 2B+ with chymopapain, automated percutaneous lumbar discectomy, and percutaneous laser disk decompression ranging between 2C+ and 2B+/–. Targeted disk decompression has the lowest grade at 0.[5] These are less invasive than surgery, and by avoiding the spinal canal they help to avoid complications, such as postsurgical infection and epidural fibrosis which are often responsible for recurrence of pain.[4,6,7]

Though ozone therapy is used to treat a variety of pain conditions, it is yet unknown to most of the physicians. Ozone (O_3) is an allotropic form of oxygen found in nature (most famously in the protective "ozone layer"), which is also used for industrial and clinical purposes in humans. Questions do persist about its potential toxicity as an oxidant agent, and this possible side effect must be weighed against its potential for therapeutic benefit. Such risks must also be considered in light of other options with known, relatively high complication rates, for example, surgical intervention. Multiple studies have suggested a low complication rate for this ozone disk nucleolysis, with reported success rates varying from 65 to 80% in different studies.[8]

Ozone nucleolysis is being used in multiple countries for over three decades. Leonardi popularized fluoroscopic-guided ozone disk nucleolysis globally.[8,9] Though ozone is toxic in high concentrations, it is applied by mixing with oxygen at nontoxic concentrations. The concentration range of ozone for clinical application in humans is 1 to 40 µg per mL of oxygen.[10]

Multiple mechanisms of action have been identified to explain the efficacy of ozone therapy. Among the mechanisms of action, anti-inflammatory, analgesic, and oxidant actions on proteoglycans in nucleus pulposus are predominant. Free radical oxygen atoms are produced during the breakdown of ozone molecules inside intervertebral disk. These free radicals react with proteoglycan bridges in the nucleus pulposus and destruct the proteoglycan bridges. Ultimately, proteoglycan loses its water holding capacity, which mummifies and shrinks the nucleus pulposus.[11,12] As a result, the intradiscal volume and pressure are reduced. This ultimately reduces the nerve root pressure followed by elimination of radicular pain.

In clinical practice, intradiscal ozone alone or intradiscal ozone with transforaminal steroid is practiced in Bangladesh. This study is designed to assess the outcome difference between these two approaches in the Bangladeshi population.

MATERIALS AND METHODS

Subjects

Two hundred patients (22–70 years of age) were recruited prospectively into this study from the outpatient department of BIRDEM General Hospital, Dhaka, Bangladesh, between March 28, 2011, and December 2014. All patients were recruited after failure of conservative therapy for 1 month and refusal to surgical treatment.

Inclusion criteria of the subjects were as follows: (i) One level herniated disk in lumbar region by history and physical examination matched with magnetic resonance imaging (MRI) and (ii) corresponding radicular pain of 7/11 or more on a verbal rating scale (VRS). Exclusion criteria for oxygen–ozone therapy were progressive motor loss, infection, bleeding disorders, red flag's sign, glucose-6-phosphate deficiencies, and patient's refusal.

After obtaining permission from the ethical review committee of the hospital, 200 patients were recruited prospectively into this study. Subjects were randomized and allocated as follows: Every fourth patient was considered as group I (50) and the other 150 considered as group B. Group I received an intradiscal (4–6 mL) injection of an oxygen–ozone mixture with an ozone concentration of 30 µg/mL, and group II received intradiscal identical oxygen–ozone injections, followed by transforaminal 20 mg triamcinolone in 2 mL of 0.25% bupivacaine for each side. The proceduralist was blinded to the allocation of patients to either group. Procedures were done with all aseptic precautions under fluoroscopy as standard protocol. Discography was performed before giving intradiscal ozone, and the presence of contained *vs* noncontained disks was noted. Quincke-type needle (10–15 cm, 22 G) was used for each case. One to two grams (depending on patient weight) of intravenous ceftriaxone was given for prophylactic antibiosis, followed by 500 mg of oral flucloxacilline every 6 hours for 7 days. Standard safety measures for monitored anesthesia were ensured before each procedure. Ozone was injected within 10 seconds of image generation.

At the end of the procedure, patients were advised to rest in supine decubitus position for 2 hours. All patients were discharged after 4 hours while they were hemodynamically stable and could walk without support. On discharge, patients were advised for back extension exercise and to increase motor activity gradually. All patients underwent person-blinded follow-up, either in person or over telephone, at 1 week, 1 month, and 6 months posttreatment.

Clinical outcome was assessed by applying the modified Macnab method and VRS. According to the modified Macnab method, patients were asked to rate his or her level of well-being, before intervention and at the different time points during follow-up. The patients chose one of the four: Excellent (which comprises no pain, no restriction of mobility, return to normal work), Good (which comprises occasional nonradicular pain, relief of presenting symptoms, able to return to modified work), Fair (which comprises some improved functional capacity, still handicapped and/or unemployed), and Poor (which comprises continued objective symptoms, additional operative intervention needed). Similarly, VRS was recorded (0–10), where 0 is no pain and 10 is maximum pain.

Table 1: Status of pain after different time periods of injection according to modified Macnab scale

Postintervention period	*Groups*	*Excellent, n (%)*	*Good, n (%)*	*Fair, n (%)*	*Poor, n (%)*
1 week	I (n = 50)	10 (20)	25 (50)	10 (20)	5 (10)
	II (n = 150)	75 (50)	70 (47)	5 (3)	0 (0)
		$\chi^2 = 36.9$, p = 0.0001			
1 month	I (n = 50)	14 (28)	21 (42)	14 (28)	1 (2)
	II (n = 150)	70 (47)	65 (43)	14 (9)	1 (1)
		$\chi^2 = 13.13$, p = 0.004			
6 months	I (n = 50)	15 (30)	19 (38)	15 (30)	1 (2)
	II (n = 150)	72 (48)	60 (40)	17 (11)	1 (1)
		$\chi^2 = 9.19$, p = 0.027			

Excellent: No pain, No restriction of mobility; Good: Occasional nonradicular pain, relief of presenting symptoms, and able to return to modified work; Fair: Some improved functional capacity, still handicapped and/or unemployed; Poor: Continued objective symptoms of root involvement

Statistical Analysis

Results of the modified Macnab scores were expressed as frequencies, and the significance of the difference between the two procedures was calculated with χ^2-test using Statistical Package for the Social Sciences (SPSS) 17.0 for Windows version. The VRS scores were expressed as median (range), and the difference between the groups was measured using Mann–Whitney test.

RESULTS

All the patients were followed up in three different time points, namely 1 week, 1 month, and 6 months after intervention. All were assessed by both modified Macnab method and VRS. At the 1-week time point, 20% of patients of group I showed excellent, 50% good, 20% fair, and 10% poor improvement in modified Macnab method. Comparatively, 50% patients of group II showed excellent improvement, 47% good improvement, and 3% fair improvement. In modified Macnab method, the improvement in group II was significantly ($\chi^2 = 36.9$, p = 0.0001) higher than in group I when χ^2-test was performed (Table 1).

At the 1-month time point, group II continued to demonstrate superior improvement (47% excellent, 43% good, 9% fair, 1% poor improvement) when compared with group A (28% excellent, 42% good, 28% fair, 2% poor improvement). In modified Macnab method, the difference of improvement between the groups was significant ($\chi^2 = 13.13$, p = 0.004) in χ^2 (Table 1).

At the 6-month time point, patients in group II (48% excellent, 40% good, 11% fair, 1% poor improvement) continued to show improved outcomes ($\chi^2 = 9.19$, p = 0.027) when compared with group I (30% excellent, 38% good, 30% fair, and 2% poor improvement) in modified Macnab method (Table 1).

The VRS in both groups was similar before intervention. After 1 week of intervention, the median (range) of group I was 3 (3–7), whereas in group II, the value was 2 (2–3). The improvement was significantly (p < 0.001) higher in group II when Mann–Whitney test was performed. At the 1-month time point, the median value of VRS in groups I and II was 4 (3–7) and 3 (3–4) respectively, and the difference between the groups was shown to be significant (p < 0.01). After 6 months of intervention, the values of VAS in groups I and II were 4 (3–7) and 3 (3–7) respectively, and the improvement was still significantly (p < 0.05) better in group II compared with group I (Table 2).

Table 2: Verbal rating scale score among the groups

Groups (200)	*Before intervention, median (range)*	*1 week, median (range)*	*1 month, median (range)*	*6 months, median (range)*
I (50)	8 (7–9)	3 (3–7)	4 (3–7)	4 (3–7)
II (150)	8 (7–9)	2 (2–3)***	3 (3–4)**	3 (3–7)*

***p < 0.001, **p < 0.01, *p < 0.05 in Mann–Whitney test

Table 3: Discography among the groups

Groups (200)	*Contained disk n (%)*	*Noncontained disk n (%)*
I (50)	30 (60)	20 (40)
II (150)	80 (53)	70 (47)

Discography demonstrated 60% contained and 40% noncontained disk in group I, whereas in group II, it was 53 and 47% respectively (Table 3).

DISCUSSION

There are a good number of percutaneous procedures practiced for discogenic sciatica in different parts of the world. The beauty of these procedures is that they are less invasive and they decompress the nerve roots without alteration in the structure of the spine. Transforaminal epidural steroid injection has been practiced since long for herniated lumbar disk. Success rates up to 84% have been reported for these procedures in different literatures, but several authors have also reported its high

recurrence rate.[13,14] Chemonucleolysis using chymopapain is another frequently practiced percutaneous procedure for discogenic sciatic pain in the last few years. Authors reported approximately 66% success rate at 1 year follow-up, but chances of anaphylaxis during the procedure made it unpopular.[15,16] Injection of ozone for discogenic radiculopathy has developed as an alternative to chemonucleolysis and disk surgery. Bonetti et al[17] reported excellent outcome in 74.4% patients at the 6-month follow-up study. Ozone therapy for slip disk became popular worldwide because of its high success rate, limited side effects, less invasiveness, and cost-effectiveness properties.[12,18,19]

After an extensive meta-analysis on ozone therapy in herniated disk, Magalhaes et al[20] reported that ozone therapy resulted in positive outcome with lower incidence of morbidity. Buric et al studied a series of 45 patients with noncontained lumbar disk herniation. They showed the differences in outcome between application of oxygen–ozone mixture in lumbar herniated disk and microdiscectomy surgery in patients with noncontained lumbar disk herniations; they documented that 90% of the patients in the ozone group showed significant improvement in pain score, whereas 93.3% patients in the microdiscectomy group showed the same clinical improvement.[21] Das et al conducted a cohort study in Indian population with 53 selected patients with lumbar disk herniation. Diagnosis was made by specific history and physical examination and confirmed by positive findings in computed tomography (CT) and MRI technique. All patients received intradiscal oxygen–ozone mixture in herniated disk once. They showed significant VAS change to 2.64 from 7.58 at 2 years' follow-up. At the same time, they reported no major complication in this cohort study.[11] In a report of 187 patients with sciatica and low back pain with positive straight leg raising test with supportive CT and MRI exhibiting evidence of disk protrusion and nerve root compression, Xu et al compared the effectiveness of intradiscal oxygen–ozone mixture with three treatment variabilities of duration. The groups received 1 week (103 cases), 2 weeks (61 cases), and 4 weeks (23 cases) treatment sessions of intradiscal ozone therapy. They were evaluated by Macnab criteria at 48 months, with a success rate of 82.52, 85.24, and 95.65% respectively.[22]

A meta-analysis of 12 studies from multicenter data was conducted by Steppen et al to determine the effectiveness of oxygen/ozone treatment in lumbar disk herniation having the specific focus on reduction of pain, functional improvement, and complication rate. This meta-analysis showed the average improvement in VAS as 3.9 and 25.7 in Oswestry Disability Index. They showed the very minimum complication rate, which was 0.064%.[23]

Our study demonstrated both short-term and long-term improvement in functional abilities and pain scores in both treatment arms; however, clear statistical superiority was demonstrated at all time points for combined therapy with ozone disk nucleolysis and transforaminal epidural steroid injection. Overall, 88% success rate ("excellent" and "good" improvement) in the combined treatment group at 6 months was demonstrated, while only ozone therapy showed a 68% success rate in the same interval. The most impressive difference in success rates is at the 1-week interval, with 97% improvement in group II, compared with 70% in group I. This may be due to additional anti-inflammatory actions of triamcinolone, as well as the breakage of the "pain circuit" by bupivacaine.

The results reported in this study are supported with a little difference in percentage by previous work of Andreula et al,[24] where a 78.3% success rate in patients treated with ozone therapy and periganglionic steroid injection was compared with a 70.3% rate in those treated with ozone therapy alone. Oder et al[25] also demonstrated significantly better values on the VAS score 6 months after treatment with the combined method in patients younger than 50. Conversely, work by Zhang et al[26] showed no significant statistical difference between treatment of injection of oxygen–ozone combined with steroid and ozone only in the 6 and 12 months follow-up.

Of note, discography completed during our study showed that 40% of patients in group I had noncontained disk, whereas 47% of patients in group II had noncontained disk. Interestingly, group B showed better result than group I in both modified Macnab and VRS scores. In the published literature, almost all studies showed intradiscal ozone works better in the contained disk group than in the noncontained disk. Our result indicated that transforaminal steroid and local anesthetic may alter the outcome. Local anesthetic and anti-inflammatory action of triamcinolone may take part in this alteration. Further advanced study may be needed to explore definite cause.

In conclusion, a combination of transforaminal triamcinolone and local anesthetic with intradiscal ozone provides clearly superior outcomes when compared with ozone therapy alone in discogenic sciatica pain. Though clearly inferior to combination therapy, patients treated with ozone therapy alone did have "excellent" or "good" outcomes in greater than two-thirds of cases. In order to fully elucidate the contribution of ozone disk nucleolysis in the treatment of discogenic sciatica pain, further studies would be required comparing combination ozone therapy and transforaminal epidural steroid injection with transforaminal epidural steroid injection alone.

ACKNOWLEDGMENT

Authors are grateful to the authority of BIRDEM General Hospital for allocation of space and manpower facility for this research.

REFERENCES

1. Mixter WJ, Barr JS. Rupture of the intervertebral disc with involvement of the spinal canal. N Engl J Med 1934 Aug; 211(5):210-215.
2. Kumar VS. Total clinical and radiological resolution of acute, massive lumbar disc prolapse by ozonucleolysis. Rivista Italiana di Ossigeno-ozonoterapia 2005;4:104-106.
3. Gallucci M, Splendiani A, Masciocchi C. Spine and spinal cord: neuroradiological functional anatomy. Rivista di Neuroradiologia 1997 Jun;11(3):293-304.
4. Gangi A, Dietemann JL, Mortazavi R, Pfleger D, Kauff C, Roy C. CT-guided interventional procedures for pain management in the lumbosacral spine. Radio Graphics 1998 May;18(1):621-633.
5. Ong D, Chua NHL, Vissers K. Percutaneous disc decompression for lumbar radicular pain: a review article. Pain Pract 2016 Jan;16(1):111-126.
6. Berger O, Dousset V, Delmer O, Pointillart V, Vital JM, Caille JM. Evaluation of the efficacy of foraminal infusions of corticosteroids guided by computed tomography in the treatment of radicular pain by foraminal injection. J Radiol 1999 Sep;80(9):917-925.
7. Buchner M, Zeifang F, Brocai DR, Schiltenwolf M. Epidural corticosteroid injection in the conservative management of sciatica. Clin Orthop Relat Res 2000 Jun; 375:149-156.
8. Buric J, Rigobello L, Hooper D. Five and ten year follow-up on intradiscal ozone injection for disc herniation. Int J Spine Surg 2014;8.
9. Muto M, Andreula C, Leonardi M. Treatment of herniated lumbar disc by intradiscal and intraforaminal oxygen-ozone (O_2-O_3) injection. J Neuroradiol 2004 Jun;31(3):183-189
10. Bocci VA. Scientific and medical aspects of ozone therapy. State of the art. Arch Med Res 2006 May;37(4):425-435.
11. Fabris G, Tommasini G. Oxygen-ozone therapy in percutaneous treatment of lumbar HNP. Rivista di Neuroradiologia 1999;12:23.
12. Das G, Ray S, Iswarari S, Roy M, Ghosh P. Ozone nucleolysis for management of pain and disability in prolapsed lumbar intervertebral disc: a prospective cohort study. Interv Neuroradiol 2009 Sep;15(3):330-334.
13. Vad VB, Bhat AL, Lutz GE, Cammisa F. Transforaminal epidural steroid injections in lumbosacral radiculopathy: a prospective randomized study. Spine 2002 Jan;27(1):11-16.
14. Ng LC, Sell P. Outcomes of a prospective cohort study on peri-radicular infiltration for radicular pain in patients with lumbar disc herniation and spinal stenosis. Eur Spine J 2004 Jul;13(4):325-329
15. Krugluger J, Knahr K. Chemonucleolysis and automated percutaneous discectomy – a prospective randomized comparison. Int Orthop 2000;24(3):167-169.
16. Revel M, Payan C, Vallee C, Laredo JD, Lassale B, Roux C, Carter H, Salomon C, Delmas E, Roucoules J, et al. Automated percutaneous lumbar discectomy versus chemonucleolysis in the treatment of sciatica. A randomized multicenter trial. Spine 1993 Jan;18(1):1-7.
17. Bonetti M, Fontana A, Cotticelli B, Volta GD, Guindani M, Leonardi M. Intraforaminal O_2-O_3 versus periradicular steroidal infiltrations in low back pain. Randomized controlled study. Am J Neuroradiol 2005 May;26(5):996-1000.
18. León Fernández OS, Pantoja M, Díaz Soto MT, Dranguet J, García Insua M, Viebhan-Hánsler R, Menéndez Cepero S, Calunga Fernández JL. Ozone oxidative post-conditioning reduces oxidative protein damage in patients with disc hernia. Neurol Res 2012 Jan;34(1):59-67.
19. Lehnert T, Mundackatharappel S, Schwarz W, Bisdas S, Wetter A, Herzog C, Balzer JO, Mack MG, Vogl TJ. Nucleolysis in the herniated disk. Radiologe 2006 Jun; 46(6):513-519.
20. Magalhaes FN, Dotta L, Sasse A, Teixera MJ, Fonoff ET. Ozone therapy as a treatment for low back pain secondary to herniated disc: a systematic review and meta-analysis of randomized controlled trials. Pain Physician 2012 Mar-Apr; 15(2):E115-E129.
21. Buric J, Molino Lova R. Ozone chemonucleolysis in non-contained lumbar disc herniations: a pilot study with 12 months follow-up. Acta Neurochir (Suppl) 2005;92:93-97.
22. Xu L, Li ZL, He XF, Xiang DC, Ma J, Hong CJ, He JX, Yang L, Gong ZH, Qiu J. Evaluation of the clinical curative effect of an O_2-O_3 mixture to treat lumbar disc herniation with different treatment sessions. Interv Neuroradiol 2009 Jul;15(2):159-163.
23. Steppan J, Meaders T, Muto M, Murphy KJ. A metaanalysis of the effectiveness and safety of ozone treatments for herniated lumbar discs. J Vasc Interv Radiol 2010 Apr; 21(4):534-548.
24. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen ozone therapy for lumber disc herniation. Am J Neuroradiol 2003 May;24(5):996-1000.
25. Oder B, Loewe M, Reisegger M, Lang W, Ilias W, Thurnher SA. CT-guided ozone/steroid therapy for the treatment of degenerative spinal disease: effect of age, gender, disc pathology and multi-segmental changes. Neuroradiology 2008 Sep;50(9):777-785.
26. Zhang Y, Ma Y, Jiang J, Ding T, Wang J. Treatment of the lumbar disc herniation with intradiscal and intraforaminal injection of oxygen-ozone. J Back Musculoskelet Rehabil 2013;26(3):317-322.