

# Comparative Efficacy of Intraarticular Injection of Combination of Ozone and Steroid and Ozone alone in Patients with Primary Knee Osteoarthritis: A Prospective and Randomized Clinical Analysis

<sup>1</sup>Mayank Chansoria, <sup>2</sup>Sachin Upadhyay, <sup>3</sup>Sheetal Panwar, <sup>4</sup>Piyush Shivhare, <sup>5</sup>Neha Vyas

## ABSTRACT

**Background:** Osteoarthritis (OA) is the most prevalent chronic degenerative joint disorder worldwide and is associated with significant pain, disability and economic impact on society. The primary objective of the present research is to validate the hypothesis that combination of intraarticular injection of ozone and steroid has better outcome than using ozone alone in patients with primary knee OA.

**Materials and methods:** Cohort comprises of 80 patients of American Society of Anesthesiologists (ASA) I and II between age 45 and 70 years of either sex with primary knee OA with radiographic evidence (grade 0, I, and II; Lawrence and Kellgren radiological criteria) of severity of knee joint. The patients were randomized to receive single intraarticular injection of either ozone alone or combination of ozone with steroid. All patients were assessed using Western Ontario and McMaster University Osteoarthritis (WOMAC) index, and the visual analog pain scale (VAS) at 1, 3, and 6 months of follow-up. Statistical Package for the Social Science (SPSS) for Windows software was used for data management and statistical analysis. The level of significance was set at 0.05 for all statistical tests.

**Result:** Both the group treated with the combination of ozone and steroid and the group treated with ozone alone demonstrated improvements from baseline parameters. At 1 month patients in both group showed significant improvement in VAS and WOMAC ( $p < 0.05$ ). Group treated with combination of ozone and steroid showed significant difference ( $p < 0.05$ ) with respect to WOMAC, or VAS results at the end of 6 months of follow-up.

**Conclusion:** Ozone treatment was highly effective in relieving pain and improving functional outcome in patients with primary knee OA. Significant differences were detected between patients

treated with intraarticular injections combination of ozone and steroid and those treated with the ozone alone with respect to pain relief or function at 6 months of follow-up.

**Keywords:** Intraarticular injections, Osteoarthritis, Ozone, Steroid.

**How to cite this article:** Chansoria M, Upadhyay S, Panwar S, Shivhare P, Vyas N. Comparative Efficacy of Intraarticular Injection of Combination of Ozone and Steroid and Ozone alone in Patients with Primary Knee Osteoarthritis: A Prospective, Randomized Clinical Analysis. *J Recent Adv Pain* 2016;2(1):11-14.

**Source of support:** Nil

**Conflict of interest:** None

## INTRODUCTION

Knee osteoarthritis (OA) is a degenerative disease with multifactorial etiopathogenesis characterized by cartilage degradation, painful joints, articular stiffness, and decreased joint movements and joint deformity in advanced stages.<sup>1</sup> With rising life expectancy and increasing obesity within the population, OA arises as a major public health concern. Pain relief is still a primary goal in treating patients along with optimal joint function and mobility. The various conservative treatment modalities available for these patients is a multimodal approach that includes physical therapy, anti-inflammatory drug use, cryotherapy and heat therapy like transcutaneous electrical nerve stimulation (TENS). Minimally invasive therapy includes intraarticular injection of steroid and lignocaine and hyaluronic acid for relief of pain and improvement of joint functions.<sup>2</sup> In recent years, the ozone therapy emerged as a recognized novel modality especially for musculoskeletal disorders, including low back pain, lumbar disk herniation, failed back surgery syndrome, degenerative spinal diseases, shoulder disorders, and OA.<sup>3-5</sup> The hyperoxygenation following neoangiogenesis, anti-inflammatory properties and analgesia through the stimulation of the antinociceptive system may explain the therapeutic effects of ozone in musculoskeletal disorders.<sup>3,6</sup> Literature revealed that intraarticular ozone therapy may provide short-term pain relief in patients with knee OA with low risk of adverse effects. We postulated that ozone injection

<sup>1</sup>Associate Professor and Consultant, <sup>2</sup>Assistant Professor and Consultant <sup>3,4</sup>Resident, <sup>5</sup>Consultant

<sup>1,3,4</sup>Department of Anesthesia, NSCB Medical College, Jabalpur Madhya Pradesh, India

<sup>2</sup>Department of Orthopedics, NSCB Medical College; Trauma and Minimal Invasive Surgery Specialist, Shalby Hospital Jabalpur, Madhya Pradesh, India

<sup>5</sup>Department of Endodontics, Sparsh Dental Centre, Jabalpur Madhya Pradesh, India

**Corresponding Author:** Mayank Chansoria, Associate Professor and Consultant, Department of Anesthesia, NSCB Medical College Jabalpur, Madhya Pradesh, India, e-mail: mayankchansoria@gmail.com

may have beneficial effects but its combination with corticosteroids may yield a slightly better outcome both short-term as well as long-term. Furthermore, there is a paucity of data on the efficacy of combination of ozone and steroid in improving clinical outcomes. The primary objective of the present pilot study is to test the hypothesis that there are statistically significant differences between the intraarticular injections of combination of ozone and steroid over ozone alone in terms of pain relief and functional recovery of their daily activities as determined by validated scoring scales.

**MATERIALS AND METHODS**

The present single-center, randomized, prospective clinical research was carried out in the Department of Anesthesiology and Orthopedics, NSCB Medical College, Jabalpur. The research was approved by the Institutional Review Board. A total 80 patients of American Society of Anesthesiologists (ASA) I and II between ages 45 and 70 years were enrolled. All patients gave their written informed consent before the study. Primary OA of knee joint with radiographic evidence (grades 0, I, and II; Lawrence and Kellgren radiological criteria<sup>7</sup>) of severity were stringent inclusion criteria. The exclusion criteria included severe OA (grades III and IV); any systemic diseases, such as cardiovascular, diabetes, asthma, anticoagulant use, previous ozone therapy or any intraarticular injection during previous year, infections or inflammatory arthritis, patients on nonsteroidal anti-inflammatory drugs (NSAIDs), pregnant or lactating mothers. The cohort was randomized based on odd/even number. Each group had equal number (n = 40) of patients. They were divided into two groups with odd numbers (group A) assigned to combination of 5 ml (25 µg/ml) injection ozone + 5 ml injection lignocaine 1% + injection depomedrol (40 mg) treatment and even numbers (group B) to 5 ml (25 µg/ml) injection ozone + 5 ml injection lignocaine 1% treatment. All procedures were performed in the operating room. Patients were monitored for heart rate, blood pressure, and oxygen saturation by pulse oximetry. Under aseptic precautions, all injections were performed in a similar manner by one of the physician. A 22-gauge needle was positioned superolaterally into the suprapatellar pouch, injection 5 ml (40 mg) depomedrol, and 5 ml injection lignocaine 1% was injected slowly

(over 1–2 minutes) to avoid the reflux of steroid along the needle trajectory. The needle was left in space for the 5 ml (25 µg/ml) ozone injection. Afterward, patients were monitored for extra 4 hours in the recovery room for vital signs. Patients were advised to avoid strenuous activity for 2–3 days with other precautions following the intraarticular injections. Demographic variables, such as age, sex, and the occupation during the study period were recorded. Baseline parameters using Western Ontario and McMaster Universities Arthritis (WOMAC) index and VAS were collected. All patients were evaluated critically at 1, 3, and 6 months of follow-up.

The data were analyzed with the software (SPSS, version 20.0). The pretreatment (baseline data) and post treatment outcomes were compared by using a paired t-test for quantitative data and McNemar test was used for qualitative data. p < 0.05 was considered significant.

**RESULTS**

No significant differences between the treatment groups were found with respect to demographic variables (Table 1; p > 0.05) and baseline parameters (pretreatment scores) (p > 0.05) (Table 2). A significant difference was detected for both groups with respect to pain relief and function improvement at 1 month when compared with the baseline data (Table 2; p < 0.05). At 6 months, the WOMAC scores and the scores on the VAS improved significantly for the patients treated with combination of ozone and steroid then the other group (Table 3; p < 0.05). There were no acute local reactions or infections in present research.

**Table 1:** Demographic data for knee OA patients

Parameters	Group A	Group B	p-value
Age (Yrs)	57 ± 16.7	59 ± 12.88	0.346
Sex ratio (M:F)	16:24	18:22	0.491
Weight (kg)	56.5 ± 3.8	55.8 ± 7	0.114

**Table 2:** Comparison of the VAS and WOMAC scores between the two groups

Groups	Group A	Group B	p-value
<b>VAS score</b>			
Before	8.9 ± 1.3	8.1 ± 1.1	0.146
After (1 month)	2.8 ± 1.1	3 ± 1.2	0.001
<b>WOMAC score</b>			
Before	56.3 ± 11.5	58.5 ± 13.3	0.173
After (1 month)	86.6 ± 13.7	83.7 ± 15.3	0.004

**Table 3:** Results from follow-up

Groups	VAS score				WOMAC score			
	Pre-treatment	1 month	3 months	6 months	Pre-treatment	1 month	3 months	6 months
Group A	8.9 ± 1.3	2.8 ± 1.1	3.4 ± 1.3	5.1 ± 1.4	56.3 ± 11.5	86.6 ± 13.7	76.6 ± 10.7	70.23 ± 14.3
Group B	8.1 ± 1.1	3 ± 1.2	5.93 ± 1.2	6.24 ± 1.6	58.5 ± 13.3	83.7 ± 15.3	72.37 ± 13.4	61.43 ± 12.7
p-value		0.001	0.001	0.532		0.004	0.002	0.598



## DISCUSSION

Osteoarthritis is a gradually progressive articular disease characterized by joint pain, stiffness, and loss of full range of motion. Degeneration of cartilage is among the most prominent pathological changes. Clinical OA is a complex interaction of degradation and repair of the cartilage, bone, and synovium with secondary components of inflammation.<sup>8,9</sup> Although ozone is being increasingly used worldwide, its mechanism of action in pain relief is not yet clearly understood. Several mechanisms have been proposed, such as accelerating the healing process of damaged tissue.<sup>10,11</sup> It promotes cartilage growth. It stimulates the synovial tissue to produce more lubrication and to produce more cartilage. It also helps to reduce venous stasis caused by compression of vessels, and hence improve 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 proinflammatory prostaglandins, release of bradykinins and algogenic compounds.<sup>10,12</sup> Ozone also increases the release of antagonists to proinflammatory cytokines.<sup>12,13</sup> The use of intraarticular injections of corticosteroids for arthritis is more than 2 decades old. Intraarticular steroid injections caused a significantly greater reduction in pain and tenderness, but the benefit was transient.<sup>14,15</sup> Intraarticular steroids also exert protective effect and reduce the severity of cartilage lesions and the size of osteophytes.<sup>16,17</sup> These effects would seem to be the result of the suppressive action of glucocorticoids on the synthesis by connective tissue cells of a number of cytokines and metalloproteases associated with cartilage degradation.<sup>16</sup> To the best of our knowledge, the present research is the first prospective, randomized analysis involving a comparison of combination of ozone and steroid and ozone alone using specific instruments, such as WOMAC index in patients with primary knee OA. The preliminary results of the present research suggest that both intraarticular ozone and its combination with steroids are beneficial in patients with primary knee OA when compared with the baseline parameters. Furthermore, the authors speculated that ozone in combination with steroid have a remarkable synergistic effect on pain relief and improvement in functional outcome. These synergistic effects were strong that improves the efficacy of the combination. In current pilot research, authors have found intraarticular injection of combination of ozone and steroid to be safe and effective for primary knee OA of the knee. There is need for further studies with bigger cohort and longer follow-up to compare and generalize our outcomes. Small sample size, short follow-up, inclusion of only grade 0, I, and grade II

Kellgren and Lawrence radiological assessment of OA, and no attempts made to measure cartilage thickness neither through imaging nor at molecular level were the limitations of the present research.

## CONCLUSION

Both ozone and the combination of ozone and steroid provided patients with modest improvements in function and pain relief, but at 6 months the patient treated with combination has better outcome in term of pain relief and functional outcome than those treated with ozone alone. However, larger scale studies are required to prove the efficacy of ozone and steroid combination, as steroid has its own limitations too.

## REFERENCES

1. Hawamdeh ZM, Al-Ajlouni JM. The clinical pattern of knee osteoarthritis in Jordan: a hospital based study. *Int J Med Sci* 2013;10(6):790-795.
2. Jordan KM, Arden NK, Doherty M. Evidence exists for 33 different treatment options for osteoarthritis of the knee. *Evid Based Med* 2004;9:81.
3. Andreula CF, Simonetti L, De Santis F, Agati R, Ricci R, Leonardi M. Minimally invasive oxygen-ozone therapy for lumbar disk herniation. *Am J Neuroradiol* 2003;24(5):996-1000.
4. Mishra SK, Pramanik R, Das P, Das PP, Palit AK, Roy J, et al. Role of intra-articular ozone in osteoarthritis of knee for functional and symptomatic improvement. *Ind J Phys Med Rehabil* 2011;22(2):65-69.
5. Bonetti M, Fontana A, Martinelli F, Andreula C. Oxygen-ozone therapy for degenerative spine disease in the elderly: a prospective study. *Acta Neurochir Suppl* 2011;108:137-142.
6. Elvis AM, Ekta JS. Ozone therapy: a clinical review. *J Natural Sci Biol Med* 2011;2:66-70.
7. Kellgren JH, Lawrence JS. Radiological assessment of osteoarthrosis. *Ann Rheum Dis* 1957;16:494-502.
8. Pelletier JP, Howell DS. Etiopathogenesis of osteoarthritis. In: McCarty DJ, Koopman WJ, editors. *Arthritis and allied conditions: a textbook of rheumatology*. 12th ed. Philadelphia: Lea & Febiger; 1993. p. 1723-1734.
9. Kelly's text book of rheumatology. 2nd ed. 2:1514-1515.
10. Hazucha MJ, Bates DV, Bromberg PA. Mechanism of action of ozone on the human lung. *J Appl Physiol* 1989;67:1535-1541.
11. Sharma M, Hudson JB. Ozone gas is an effective and practical antibacterial agent. *Am J Infect Control* 2008;36:559-563.
12. Johansson E, Claesson R, van Dijken JW. Antibacterial effect of ozone on cariogenic bacterial species. *J Dent* 2009;37:449-453.
13. Bocci V, Luzzi F, et al. Studies on the biological effects of ozone—III: an attempt to define conditions for optimal induction of cytokines. *Lymphokine Cytokine Res* 1993;12:121-126.

14. Dieppe PA, Sathapatayavongs B, Jones HE, Bacon PA, Ring EF. Intra-articular steroids in osteoarthritis. *Rheumatol Rehabil* 1980;19:212-217.
15. Gaffney K, Ledingham J, Perry JD. Intra-articular triamcinolone hexacetonide in knee osteoarthritis: factors influencing the clinical response. *Ann Rheum Dis* 1995;54:379-381.
16. Pelletier JP, Martel-Pelletier J, Cloutier JM, Woessner JF Jr. Proteoglycan-degrading acid metalloprotease activity in human osteoarthritic cartilage, and the effect of intraarticular steroid injections. *Arthritis Rheum* 1987;30:541-548.
17. Williams JM, Brandt KD. Triamcinolone hexacetonide protects against fibrillation and osteophyte formation following chemically induced articular cartilage damage. *Arthritis Rheum* 1985;28:1267-1274.