



Comparative Analysis of Intraarticular Prolozone Therapy with Corticosteroids in Patients of Osteoarthritis Knee a Pilot Study

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Abstract

Aim: To evaluate and compare the effect of ozone therapy with intra-articular corticosteroids on functional quality of life of knee OA patients.

Patients and Methods: A total of 100 Grade I/II knee OA patients were randomized into two groups - Group I (n = 50): receiving intra-articular Prolozone (5% concentration O₂-O₃) and Group II (n = 50): receiving intra-articular steroid (Dexamethasone) 2 ml respectively. Both the groups were compared demographically, radiologically and functionally at baseline. Patients were followed up at 1, 4, 8 and 12 weeks intervals. Functional outcome was assessed in terms of WOMAC scores. Data was analyzed using SPSS 20.0, χ^2 and 't'-tests were used to compare the data.

Results: At baseline mean WOMAC scores in Groups I and II were 62.48 ± 6.80 and 64.68 ± 4.77. In both the groups a decline in WOMAC scores was observed since week 1 itself. At week 12 Mean WOMAC scores were 23.42 ± 7.64 and 34.30 ± 5.24 respectively in Groups I & II. Statistically, the difference between two groups was significant statistically at all the follow up intervals except at baseline and week 4.

Conclusion: Ozone therapy was found to have a better and sustainable positive effect on functional quality of life of knee OA patients.

Keywords: Ozone Therapy; Prolozone; Corticosteroids; Knee OA; Dexamethasone

Introduction

Knee osteoarthritis (OA) is one of the leading causes of global disability. Globally, of the 291 conditions, hip and knee OA was ranked as the 11th highest contributor to global disability and 38th highest in DALYs¹. OA is a degenerative joint disease involving the articular cartilage and many of its surrounding tissues. In addition to damage and loss of articular cartilage, there is remodelling of subchondral bone, osteophyte formation, ligamentous laxity, weakening of periarticular muscles, and, in some cases, synovial inflam-

mation². These changes may occur as a result of an imbalance in the equilibrium between the breakdown and repair of joint tissue.

Knee OA has great physical and economic impacts. The disease usually evolves with increasing levels of pain, mobility restriction, and physical disability^{3,4}. The disability associated with knee OA leads to reduction in hours of working, truncation of work-life and high costs of care have an economic impact on an individual as well as society^{5,6}. Moreover, the quality of life of a patient is also affected owing to chronic pain and decreased joint function which

¹Cross M, Smith E, Hoy D, et al. The global burden of hip and knee osteoarthritis: estimates from the Global Burden of Disease 2010 study. *Ann Rheum Dis.* 2014 Jul;73(7):1323-30.

²Hutton CW. Osteoarthritis: the cause not result of joint failure? *Annals of the Rheumatic Diseases.* 1989;48(11):958-961.

³Davis MA. Epidemiology of osteoarthritis. *Clin Geriatr Med* 1988;24:766-7.

⁴Altman RD. The syndrome of osteoarthritis. *J Rheumatol* 1997;24:766-7.

⁵McLean CH, Knight K, Paulus H, Brook RH, Shekelle PG. Cost attributable to osteoarthritis. *J Rheumatol* 1998; 25: 2213- 8.

⁶Lanes SF, Lanza LL, Radensky PW, Yood RA, Meenan RF, Walker AM, et al. Resource utilization and cost of care for rheumatoid arthritis and osteoarthritis in a managed care setting. *Arthritis Rheum* 1997;40:1475- 81.

eventually makes the patients susceptible to various physical and psychological comorbidities and finally a possible impact on overall life expectancy^{7,8}.

Unfortunately, there is no specific cure for OA and the severity of condition varies from individual to individual. Although joint replacement surgery is a often mooted as an option, however, this option has its own risks and limitations. Among different pharmacological treatment options available use of steroids is most common, however, their use is often criticized owing to associated side effects⁹, moreover intra-articular glucocorticoid injection offer only moderate and short-lived reduction in pain and hence their use is related with inconvenience too¹⁰. Hence, there is need for search of a more viable and useful treatment modality, that can attenuate the burden of pain and has a sustained effect on quality of life of knee OA patients.

In recent years ozone therapy has emerged as a useful management option for knee osteoarthritis patients. Although medical use of ozone is reported to be quite diversified¹¹ yet intra-articular administration for osteoarthritis of the knee is a recent development that has shown a positive impact on attenuation of pain, stiffness and physical disability without any significant adverse effect¹². Ozone has very good analgesic and anti-inflammatory property because it blocks phosphokinase-A2¹³. Unfortunately, despite its reported usefulness, there is almost no clinical trials available reporting the usefulness of ozone therapy in knee osteoarthritis patients. Prolozone is a technique that combines the principles of neural therapy, Prolotherapy, and ozone therapy. It involves injecting com-

binations of procaine, anti-inflammatory medications, homeopathics, vitamins, minerals, proliferatives, and ozone/oxygen gas into degenerated or injured joints, and into areas of pain¹⁴.

Hence, the present study was planned to evaluate the evaluate the role of prolotherapy in management of osteoarthritis as compared to intraarticular corticosteroids.

Material and Method

The present study was carried out as a prospective randomized controlled study at Department of Orthopaedics, Era's Lucknow Medical College & Hospital, Lucknow over a period of two years starting from January, 2015 to December, 2017. A total of 100 patients with radiological grade I/II primary knee osteoarthritis having WOMAC score >1 for pain, stiffness and disability with symptoms of osteoarthritis for at least 3 months after getting usual conservative treatment e.g. Paracetamol, NSAIDS, Opioid, Physiotherapy were enrolled in the study. Patients with neurological complications, secondary osteoarthritis, patients with recent knee traumas or suspected associated knee lesion and those who were on drug treatment for osteoarthritis or any other disease for the last 3 months were excluded from the assessment.

All the patients underwent a thorough physical examination by the attending clinician and relevant clinical history was also taken. All the participants were subjected to WOMAC questionnaire to assess the presence and severity of the disease, thereafter, bilateral knee radiograph was obtained.

⁷Yelin E, Lubeck D, Holman H, Epstein WV. The impact of rheumatoid arthritis and osteoarthritis: the activities of patients with rheumatoid arthritis and osteoarthritis compared to controls. *J Rheumatol* 1987;14:701-7.

⁸Bellamy N, Bradley L. Workshop on chronic pain, pain control and patient outcomes in rheumatoid arthritis and osteoarthritis. *Arthritis Rheum* 1996;39:357- 62.

⁹Hochberg MC, Altman RD, Brandt KD, Clark BM, Dieppe PA, Griffin MR, Moskowitz RW, Schnitzer TJ. Guidelines for the medical management of osteoarthritis. Part II. Osteoarthritis of the knee. *American College of Rheumatology. Arthritis and Rheumatism*. 1995;38:1541-1546.

¹⁰Raynauld JP, Buckland-Wright C. Safety and efficacy of longterm intra-articular steroid injections in osteoarthritis of the knee: a randomized, double-blind, placebo-controlled trial. *Arthritis Rheum* 2003;48:370-7.

¹¹Elvis AM, Ekta JS. Ozone therapy: A clinical review. *Journal of Natural Science, Biology, and Medicine*. 2011;2(1):66-70.

¹²Mishra SK, Pramanik R, Das P, Das PP, Palit AK, Roy J, Halder RN. Role of intra-articular ozone in osteo-arthritis of knee for functional and symptomatic improvement. *IJPMR* (22) September 2011, 65-69.

¹³Bocci V, Luzzi E, Corradeschi F, Paulesu L, Di Stefano A. Studies on the biological effects of ozone, 3. An attempt to define conditions for optimal induction of cytokines. *Lymphokine Cytokine Res*. 1993 Apr;12(2):121-6.

¹⁴Shallenberger F. Prolozone – Regenerating Joints and Eliminating Pain. *Journal of Prolotherapy*. 2011;3(2):630-638.

All the participants were randomly divided in two groups as under:

- **Group I (n = 50):** Patients were subjected to Intra-articular injection of Prolozone (5% concentration O₂-O₃) in the knee joint along with Dextrose and a local anaesthetic at admission, (and thereafter at week 4, Week 8 and Week 12.
- **Group II (n = 50):** Patients were subjected to intra-articular steroid (Dexamethasone) 2 ml in the knee joint along with a local anaesthetic at admission and thereafter at Week 8.

Patients were followed up at Weeks 1, 4, 8 and 12 respectively. Change in functional quality of life was evaluated using WOMAC scoring. Radiological change was evaluated at 12 weeks. Records of side effects during the follow up period were noted.

Statistical analysis

Data was analyzed using Statistical Package for Social Sciences (SPSS) version 20.0. Chi-square and Independent samples ‘t’ tests

were used to compare the data. ‘p’ value less than 0.05 was considered statistically significant.

Results

Age of patients ranged from 40 to 80 years. Mean age of patients in Groups I and II was 55.24 ± 10.04 and 57.98 ± 10.16 years respectively. In both the groups majority of patients were males. Proportion of males was slightly higher in Group I (66%) as compared to that in Group II (54%). Pre-treatment WOMAC score was 62.48 ± 6.80 and 64.68 ± 4.77 respectively in Groups I and II. In Group I, 42 (84%) had radiological grade I and remaining 8 (16%) had Grade II whereas in Group II, 47 (94%) had grade I and 3 (6%) had grade II. Statistically, there was no significant difference between two groups with respect to demographic profile and baseline WOMAC and radiological grade (p > 0.05) (Table 1).

Mean WOMAC score at week 1, week 4, week 8 and week 12 intervals was 39.14 ± 6.52, 32.82 ± 6.67, 27.60 ± 6.74 and 23.42 ±

SN	Characteristics	Group I (n = 50)	Group II (n = 50)	Statistical significance ('p' value)
1.	Mean Age ± SD (Range) in years	55.24 ± 10.04 (42-80)	57.98 ± 10.16 (40-79)	0.178
2.	M:F	33:17	27:23	0.221
3.	Pre-treatment WOMAC (Mean ± SD)	62.48 ± 6.80	64.68 ± 4.77	0.064
4.	Radiographic grade (KL Grade)			0.110
	I	42 (84%)	47 (94%)	
	II	8 (16%)	3 (6%)	

Table 1: Demographic Profile and Baseline Characteristics of Patients in two study groups.

7.64 respectively in Group I and 44.06 ± 3.20, 35.14 ± 5.15, 34.56 ± 5.10 and 34.30 ± 5.24 respectively in Group II. Statistically, the difference between two groups was significant statistically at all the follow up intervals except at week 4 (Table 2 and Figure 1).

SN	Time interval	Group I (n=50)	Group II (n=50)	Statistical significance ('p' value)
1.	Week 1	39.14 ± 6.52	44.06 ± 3.20	<0.001
2.	Week 4	32.82 ± 6.67	35.14 ± 5.15	0.055
3.	Week 8	27.60 ± 6.74	34.56 ± 5.10	<0.001
4.	Week 12	23.42 ± 7.64	34.30 ± 5.24	<0.001

Table 2: Comparison of WOMAC scores between two groups at different follow-up intervals.

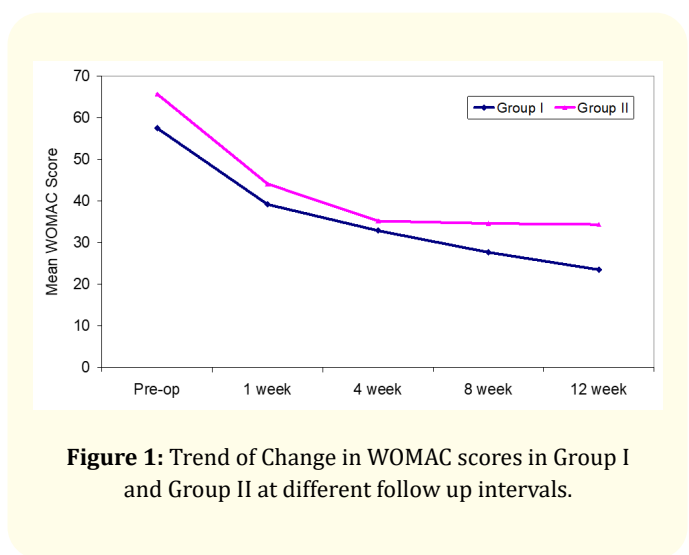


Figure 1: Trend of Change in WOMAC scores in Group I and Group II at different follow up intervals.

No change in radiographic grade of any patient in either of two groups was observed at 12 months.

None of the cases had any side effect.

Discussion

The present study showed a declining trend in WOMAC scores indicative of increase in functional quality of life of patients in both the groups. Use of corticosteroids like dexamethasone for knee OA is quite popular and has been reported to be quite effective. In present study, in both the groups significant reduction in WOMAC scores was observed starting from the first week itself. At all the follow-up intervals, WOMAC scores in prolozone group were lower as compared to that in steroid therapy group and the difference between two groups was also significant statistically at all the follow up intervals except at week 4. The percentage decline in WOMAC scores in prolozone group was nearly 37% at week 1 which reached to its nadir at 12 weeks with a % decline of 62.5%. In dexamethasone group too, the percentage decline was nearly 32% at week 1 which showed an almost stabilization at week 8 when the % decline from baseline was 46.6% and between 8 and 12 weeks there was no practical change in WOMAC scores in this group. In contrast, in prolozone group, at 8 weeks and 12 weeks, WOMAC scores showed a decline of 56% and 62.5% respectively, thus showing that the decline in WOMAC scores continued the declining trend beyond 8 weeks time too. The outcome of prolozone therapy, thus showed a continued and better efficacy as compared to dexamethasone for prolonged duration. In present study, both the groups were found to be efficacious in reducing the WOMAC scores up to 12 weeks interval. The usefulness of corticosteroids in symptomatic reduction in knee OA patients. In a study by Grecomoro, *et al.* (1992) dexamethasone showed a continuous decline in symptoms up to 60 days. In another study, they have been showed to be effective upto 24 weeks¹⁵. However, as far as efficacy of ozone therapy is concerned, it has been shown to be effective upto 10 months¹⁶. Although, in present study, owing to limitations of time, we could not assess the entire duration of efficacy of either of two therapies, yet a higher efficacy of ozone therapy as compared to corticosteroid therapy at different follow up intervals indicated that it can be used for long-term. One of the reasons for higher efficacy of ozone therapy in present study could be attributed to be the intermittent reinforcement of ozone therapy at week 4, 8 and 12

follow-up intervals. The findings of present study endorsed the observation made by Mishra, *et al.* [12] who also found ozone therapy to provide a better outcome as compared to corticosteroids upto three months of evaluation.

In present study, no change in radiological grade of patients was noted in either group. Both corticosteroid and ozone therapy are indicated to have impact on functional quality of life only and as such none of the previous studies have reported their ability to change radiological grade. However, the positive finding of the study was that despite being administered more frequently, ozone therapy did not produce any side effect. Although, effectively, ozone therapy required more frequent reinforcement as compared to corticosteroid therapy yet the benefit of ozone therapy as compared to corticosteroid therapy lies in the fact that it can be used for long-term without the associated side effects of corticosteroids.

Thus the present study showed that ozone therapy is a feasible option for improvement in functional quality of life of knee OA patients. Its long-term efficacy and better safety profile needs to be explored in further clinical trials.

Conclusion

Within the limitations of present study, ozone therapy proved to be provide better and sustainable functional outcomes as compared to corticosteroid therapy.

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¹⁶Al-Jaziri AA; Mahmoodi SM. Painkilling effect of ozone-oxygen injection on spine and joint osteoarthritis. *Saudi Med J.* 2008 Apr; 29(4): 553-7.

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