



EFFECTIVENESS OF INTRA ARTICULAR OZONE THERAPY ON QUALITY OF LIFE AND KNEE FUNCTION COMPARED WITH INTRA ARTICULAR STEROID IN PATIENTS WITH PRIMARY OSTEOARTHRITIS OF KNEE: A RANDOMIZED CONTROLLED TRIAL

Physical Medicine & Rehabilitation

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ABSTRACT

Background And Objectives: Knee osteoarthritis is the commonest rheumatological condition causing functional impairment, disability, and diminished quality of life. Treatment should aim improve function and quality of life. This study compares the effectiveness of two nonoperative treatment option for osteoarthritis of knee, intraarticular ozone and intraarticular steroid injection, on quality of life and knee function.

Methods: It is a randomized control study done in the Department of Physical Medicine and Rehabilitation, Regional Institute of Medical Sciences, Imphal. Study population is the patient with knee pain attending OPD. Study group received intraarticular injection of ozone and control group received intraarticular injection of steroid. The outcome variables, WOMAC index and SF36 score, were measured before the intervention and at 1st, 4th and 12th week post intervention. Data analysed by using SPSS Version 21.

Results: There was a significant improvement in knee function and quality of life in both groups in all the follow up periods ($p < 0.05$). When comparing between the groups, the steroid group shows significant improvement in both WOMAC and SF36 score at 1st week and ozone group shows significant improvement in SF36 score (p value= 0.018) at 12th week follow up. At 4-week follow up there were no significant difference between the two groups ($p > 0.05$).

Interpretation And Conclusion: Although intraarticular injection of ozone and steroid have good and similar effectiveness in improvement of knee function and quality of life in osteoarthritis knee, ozone injection in long term follow up has more significant improvement

KEYWORDS

Knee osteoarthritis, Ozone, Steroid, Quality of life, knee function

INTRODUCTION:

Knee osteoarthritis is a progressive chronic degenerative musculoskeletal disease of knee joint which is the commonest rheumatological condition causing functional impairment, disability, and diminished quality of life.^{1,2} In 2025, due to the aging of the world population, the prevalence of knee osteoarthritis is expected to be increase by 40%.³ There will be involvement of the entire joint and related structures, such as articular cartilage, capsule, subchondral bone, ligaments, synovial membrane and muscles acting on the joint. The disease has a multifactorial aetiology and it is characterized by synovitis with cartilage destruction and subchondral bone remodelling. There will be degeneration of ligaments and hypertrophy of joint capsule.³ Most common symptoms of osteoarthritis include pain, stiffness, swelling, crepitus, and functional limitation of movement. It can occasionally lead to joint and limb deformity in advanced stage.⁴

There is no cure for osteoarthritis and treatment should aim to relieve pain, improve function, limit disabilities and improve quality of life. Various conservative treatments include lifestyle modification, muscle strengthening exercises, orthotics, physical therapy and NSAIDs. Intra-articular injection of corticosteroid, hyaluronic acid, dextrose, normal saline, glucosamine, and platelet-rich plasma (PRP) are also found to be effective.⁵ Intra articular injection of steroid is the most common intervention done in osteoarthritis because of its anti-inflammatory action and it also reduces the structural change in arthritis.^{6,7} Latest evidences are there which supports the role of ozone injection in management of knee osteoarthritis. Ozone therapy induces anti-inflammatory and analgesic effects within its therapeutic concentrations and improves knee function without serious adverse effects.^{8,9}

The aim of this trial was to determine the effectiveness of intra-articular ozone injection on knee osteoarthritis on quality of life and knee function compared to intra-articular steroid therapy.

MATERIALS AND METHOD:

A randomized controlled trial was conducted in the Department of Physical Medicine and Rehabilitation (PMR), Regional Institute of Medical Sciences (RIMS), Imphal, Manipur. The study comprised patients with osteoarthritis of the knee who attended the PMR OPD during September, 2019 to August, 2021. The study was approved by the Research Ethics Board (REB), RIMS, Imphal on September 24, 2019 and registered in Clinical Trials Registry of India and the registration number was CTRI/2019/11/022182.

Eligible patients were both males and females aged between 50 and 70 years, with osteoarthritis of knee as defined by the American College of Rheumatology (ACR, 2016) criteria¹⁰ and a confirmatory knee X-ray diagnosis (Kellgren Lawrence grades II – III)¹¹, who were willing to participate in the study, signed the informed consent prior to enrolment of the trial and comply with treatment and follow up were included in the study. Patients with history of recent knee trauma or knee surgery, any other knee disease or infection, intra articular steroid injection to the knee during past 3 months, metabolic disease of bone, cognitive impairment, uncontrolled systemic disease, bleeding disorders, recent myocardial infarction or stroke were excluded from the study.

Taking the mean WOMAC score in the ozone therapy group as 44.06 (SD=3.20) and the mean WOMAC in the steroid group as 39.14 (SD=6.52) with pooled SD of 5.13¹² at 5% significance level and 90% power and group ratio of 1:1, sample size was calculated to be 22 per group. The sample size was inflated to 27 per group after taking into consideration dropout rate of 20%.

Patients were randomized into the intervention and control groups by block randomisation. It was decided prior to intervention that the group A would be the intervention (ozone) group and group B would be the control (steroid) group. A block size of four was used and the possible combinations were numbered 1 to 6. A computer-generated list was then generated to select 14 blocks and the sequence of the

interventions was then generated according to the sequence in each of the selected block. Opaque envelopes containing the group to which each patient would belong were sequentially numbered and closed by an individual not involved in the study. The patients in the intervention group received one intra-articular injection of 10 ml Ozone (20µg/ml) and the control group received an intra-articular steroid injection of Methyl prednisolone (80mg). Blinding was not done for this study.

Study participants were assessed at baseline, 1 week, 4 weeks and 12 weeks after the injections for background characteristics, Quality of life, knee function and knee pain by using a questionnaire that includes: Short-Form Health Survey (SF-36)¹³ and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)¹⁴. Statistical analysis was done using IBM-SPSS version 21. Data were analysed by using descriptive statistics like mean, standard deviation and percentages. Independent t-test for continuous variables and Chi-square test for categorical variables were used to test for significance. For comparison between the groups, independent t- test was used and repeated measures ANOVA was used to compare the means obtained on repeated measurements within each group. When statistical significance was observed in repeated measures ANOVA, the analysis was followed by post hoc analysis (Bonferroni) to establish between which groups the differences in the scales occurred.

RESULTS

The base line characteristics of the patients in both groups were comparable (Table 1). The mean age of patients was 53.49 (SD=5.3) years and there was female predominance (65%). Among them 68% were having a KL grade II with predominant right sided affection. Base line values of WOMAC score and SF-36 score were also comparable between intervention and control groups (Table1).

Table 1: Base line characteristics of the patients in both groups (N=54)

Characteristics	Groups		P value*
	Intraarticular ozone (n= 27) n (%)	Intraarticular steroid (n= 27) n (%)	
Age in completed years (Mean ± SD)	54 ± 5.4	53 ± 5.3	0.838
Gender			1.00
Male	9 (33.3%)	10 (37%)	
Female	18 (66.7%)	17 (63%)	
Duration of symptom			0.640
< 8 months	8 (29.7%)	11 (40.7%)	
9-16 months	9 (33.3%)	10 (37%)	
>17-24 months	10 (37%)	6 (22.3%)	
Occupation			0.574
Homemaker	11 (40.7%)	7 (25.9%)	
Farmer	6 (22.2%)	5 (18.5%)	
Manual labourer	4 (14.8%)	6 (22.2%)	
Shop keeper	6 (22.2%)	9 (33.3%)	
Side of affection			0.78
Right	17 (63%)	16 (59.3%)	
Left	10 (37%)	11 (40.7%)	
KL grade			0.78
2	10 (37%)	11 (40.7%)	
3	17 (63%)	16 (59.3%)	
WOMAC score	57±10	57±9	0.931
SF36 score	36±7.5	36±8.1	0.967

Post intervention mean WOMAC score and SF-36 score of both study and control group at base line and post intervention at 1 week, 4 weeks, 12 weeks are shown in Table 2. The results show significant differences in both outcome measures at all time-points of follow-up within the group (p value<0.05).

Table 2: Within the group comparison of outcome measures in both groups

Parameter	Group	Base line	1 weeks	4 weeks	12 weeks	P value*
WOMAC	Ozone	57.4±9	44.8±7.5	29.2±2.8	21.9±2.3	0.00
	Steroid	57.2±9.6	34.7±5.4	26.9±4.3	24.9±3.0	0.00
SF36	Ozone	36.5±7.7	49.3±5.6	63.4±3.3	72.6±2.5	0.00
	Steroid	36.6±8	58.8±4.3	66.3±3.2	68.2±2.6	0.00

Post hoc analysis shows differences in both WOMAC score and SF36 at each follow up from base line and from previous follow up time point and the difference is more in steroid group initially and ozone group later (Table 3).

Table 3. Post hoc analysis of WOMAC score and SF36 score in study and control group

	Intraarticular ozone group				Intraarticular steroid group			
	SF 36		WOMAC		SF 36		WOMAC	
	Mean difference	P value*	Mean difference	P value*	Mean difference	P value	Mean difference	P value
Base line to 1 st week	-12.74	0.00	12.667	0.00	-21.939	.000	22.250	.000
Base line to 3 rd week	-26.89	0.00	28.222	0.00	-30.007	.000	30.643	.000
Base line to 12 th week	-36.048	0.00	35.519	0.00	-32.150	.000	32.893	.000
1 st to 4 th week	-14.148	0.00	15.556	0.00	-8.068	.000	8.393	.000
1 st to 12 th week	-23.304	0.00	22.852	0.00	-10.211	.000	10.643	.000
4 th to 12 th week	-9.156	0.00	7.296	0.00	-2.143	.002	2.250	.002

Between the two groups mean change of SF36 from baseline shows significant improvement in steroid group (p=0.00) at 1st week follow up and ozone group at 12th week follow up (p=0.018). There was no significant difference the two groups at 4week follow up. Mean change from baseline of WOMAC score also shows significant improvement in steroid group at 1st week follow but doesn't show any significant difference at the remaining follow up (table 4).

Table 4: Comparison of mean change of WOMAC score and SF36 score from the base line between the two group

Follow up	Mean changes from base line of WOMAC score		p-value	Mean changes from baseline of SF36 score		p-value
	Intra-articular ozone (Mean ± SD)	Intra-articular steroid (Mean ± SD)		Intra-articular ozone (Mean ± SD)	Intra-articular steroid (Mean ± SD)	
1 week	12.8±3.5	22.52±5.9	0.00	12.8± 3.3	22.3± 5.3	0.00
4 weeks	28.2±7.1	30.22±7.4	0.316	26.9± 5.7	29.7± 6.5	0.102
12 weeks	35.4±7.8	32.26±7.8	0.144	35.7± 5.6	31.3± 7.6	0.018

DISCUSSION

Osteoarthritis is one of the leading causes of disability in the world which cause reduced quality-of-life especially in geriatric population. Large number of researches were conducted to formulate treatment for osteoarthritis knee. These were mainly focusing on relieving pain, improving function, and limiting disabilities and improving quality of life. Now a days more researches are conducting on regenerative methods in knee osteoarthritis which include platelet-rich plasma (PRP), hyaluronic acid, dextrose, normal saline.⁵

There is no consensus in the use of intra articular injection of ozone in management of osteoarthritis knee. Several studies are conducted which shows that ozone is effective and the effect last longer so can be used in the management. The study intended to compare two different intervention, intraarticular ozone and steroid injection for the treatment of knee osteoarthritis in intervals up to 12 weeks follow-up.

The data shows that WOMAC and SF36 score was improved from base line to first, second and third follow up significantly in both groups and there is improvement in quality of life of participants in both group after injection. In study group mean WOMAC score at base line was 57.4±9 and score improved to 21.9±2.3 at 12th week. SF36 score at base line was 36.5±7.7, which was improved to 72.6±2.5 at 12th week. Control group also shows similar improvement were WOMAC score improved from 57.2±9.6 at base line to 24.9±3 at 12th week and

SF36 score improved from 36.6 ± 8 at base line to 68.2 ± 2.6 at 12th week. In a study conducted by Ghazani AB et al¹⁵ on ultrasound guided intraarticular oxygen-ozone and steroid in osteoarthritis knee, they found that both steroid and oxygen ozone injections are effective in patients with knee osteoarthritis. The findings were consistent with our results. In this study they use ultrasound guided injection of ozone oxygen and triamcinolone which is not similar to our study, where we are using methyl prednisolone. In a placebo-controlled study conducted by Jesus LCC et al¹⁶ on effectiveness of ozone injection in pain relief, functional improvement and quality of life of osteoarthritis knee patients shows similar results as our study.

While comparing the improvement in quality of life and functional status of patient between the two group, improvement was more in steroid group after 1 week (p value, 0.05). The difference was not significant 4-week post intervention (p value > 0.05). But there presents a significant difference (p value = 0.018) in improvement in quality of life as evidenced by improvement in SF36 score in study group (intraarticular ozone group) compared with control group (intraarticular steroid group). This shows that after intervention, improvement in both knee function and quality of life is seen at all levels of follow up in both groups, but intraarticular steroid injection produces more improvement in quality of life and functional improvement 1 week after injection, which become almost similar in both groups by 4 weeks as the effect of steroid reduces, and intraarticular ozone showed more improvement in quality of life after 12 weeks post intervention. Ghazani AB et al¹⁵ demonstrated that both ozone and steroid are effective in osteoarthritis knee. Steroid injection shows earlier improvement in symptoms but effect of oxygen ozone injection last longer than those of steroid injection into the knee joint. These findings were in consensus with our findings. In another study Saurabh A et al¹² found that Ozone therapy was found to have a better and sustainable positive effect on functional quality of life of knee OA patient than steroid both the groups. The results are not in complete agreement with our study where both groups found to have a sustainable effect on functional quality of life with steroid showing more improvement at initial follow up.

Most of the study comparing ozone and steroid injection shows that both the intervention improves pain, functional outcome and quality of life, but ozone is having a better and prolonged effectiveness. This study also shows the same result that both interventions were having good efficacy. But the difference was that the initial improvement is better for steroid group and ozone has got better long-term effect. Some other study shows that repeated injection of ozone has got more prolonged effect. Further studies are required to find ideal schedule of intra articular ozone injection to produce a long-term effect in osteoarthritis knee.

To summarize the findings in this study, intra articular injection of both ozone and steroid shows improvement in functional outcome and quality of life. Intra articular steroid has got better improvement in early period but intra articular ozone showed a long-term improvement in quality of life compared to steroid. So Intra articular injection of ozone is a simple, safe and easy procedure with good and long-term improvement functional outcome and quality life in osteoarthritis of knee.

In this study there were no serious complication in both groups after procedure. There was mild erythema at the injection site that subsided by itself. Limitations of this study include small sample size, no blinding, short follow up periods.

Although intraarticular injection of ozone and steroid have good and similar effectiveness in improvement of knee function and quality of life in osteoarthritis knee, ozone injection in long term follow up has more significant improvement. For better understanding of improvement in quality of life in long run, further study is required with large sample size and longer follow up

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