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Study to compare the effectiveness of 25% dextrose prolotherapy and ozone therapy in primary osteoarthritis of knee in terms of pain and improvement of knee function

Medical Science

KEYWORDS: WOMAC, VAS, KL grade, Prolotherapy

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ABSTRACT

Limited studies are available in management of primary osteoarthritis of knee with prolotherapy with 25% dextrose and ozone therapy. A randomized controlled trial was conducted to study the effectiveness of 25% dextrose prolotherapy and ozone therapy in primary osteoarthritis of knee in terms of pain and improvement of knee function in sixty-six patients in age group of 50 to 70 yrs attending PMR department, RIMS, Imphal. The study group received of 25% dextrose 6 ml, 3 times at baseline, at 1 month and 6 month and the control group received 15 ml of ozone intra- articularly. In both the groups 50 mg of tramadol tablet and isometric strengthening exercise of quadriceps was given. Assessment was done at baseline, at 1 month and 6 months in terms of VAS and WOMAC. Statistically significant improvement was noted in VAS (7.48±0.91 to 1.94±0.70) and WOMAC score (83.21±3.66 to 15.24±2.25) at 6 month follow up in control group. Significant difference was also noted in VAS (7.27±1.10to 3.24±1.09) and WOMAC score (79.33±16.67 to 28.42±11.55) among study group. It was concluded that Ozone therapy was more effective than dextrose prolotherapy in management of primary osteoarthritis of knee.

Introduction

Osteoarthritis (OA) is the commonest joint disease affecting the human body and is an important cause of disability. It is characterized by focal loss of cartilage with evidence of accompanying peri-articular response in the form of subchondral bone sclerosis and attempted new bone formation in the form of osteophytes. According to WHO, Osteoarthritis is the 2nd most common musculoskeletal problem in world population after back pain (Das, 2009).

Prolotherapy is also known as "proliferation therapy or regenerative injection therapy or proliferative injection therapy" It involves injecting an otherwise non-pharmacological and non-active irritant solution into the body, generally in the region of tendons or ligaments for the purpose of strengthening weakened connective tissue and alleviating musculoskeletal pain. The precise mechanism of action for prolotherapy is currently unclear. Prolotherapy, in clinical practice most commonly, hyperosmolar dextrose (a sugar) is the solution used. Lidocaine (a commonly used local anesthetic), phenol and sodium morrhuate (a derivative of cod liver oil extract) are other commonly used agents (Rabago, Slattengren & Zgierska, 2010; Baurer, 2015; Alderman, 2007).

Numerous studies have been conducted on corticosteroids, and its optimal dosing regimen for the intra-articular treatment of osteoarthritis. However, consensus has still not been established. Recently intra-articular injection of ozone-oxygen mixture (O_3-O_2) in therapeutic concentration (30 micro g/ ml of ozone in oxygen) gained popularity for relief of pain, stiffness and physical disability without any significant adverse effect(Di Paolo, Bocci & Gaggiotti, 2004).

Ozone referred to as O_3, is the tri-atomic state of oxygen, a molecule that consists of three oxygen atoms in a dynamically unstable structure. The gas is colourless, acrid/pungent in odour and explosive in liquid or solid form. (Di Paolo, Bocci & Gaggiotti, 2004).

Ozone is gradually gaining popularity in various medical fields especially in pain management. Newer modification in techniques and administration of ozone, more and more publication of scientific materials in the medical journals and animal studies are making it more acceptable to the medical community and gradually it is becoming more popular. (Di Paolo, Bocci & Gaggiotti, 2004).

Hence, this study was undertaken to compare the effectiveness of intra-articular 25% Dextrose prolotherapy and Ozone therapy in primary osteoarthritis knee for pain control and functional improvement.

Methods:

A randomized controlled trial was conducted in the Department of Physical Medicine and Rehabilitation, RIMS, Imphal during October, 2014 to April, 2016. Sixty-six patients with primary knee osteoarthritis, in the age group of 50-70 years, with KL grade 2 and 3 and who gave informed consent were included in the study. The diagnosis of knee osteoarthritis was made on the basis of the results of clinical examination and antero-posterior standing radiography. All patients with inflammatory joint diseases, metabolic diseases of the bone, known blood diseases, systemic metabolic diseases including uncontrolled diabetes, immunodeficiency, Hepatitis B or C, systemic and local infections, severely moribund patients and KL grade 4 were excluded from the study.

Before the start of the study, the pain intensity was determined by using Visual Analogue Scale (VAS). In this scale, 0 indicated no pain and 10 indicated the worst pain. All patients also completed the Western Ontario and Mc Master University Arthritis index (WOMAC) assessment, which ranges from 0 to 100 and lower scores indicate better knee status.

The patients were randomized into two groups (ozone group and dextrose group) by using block randomization.

Patients were made to lie down in supine position and the knee was kept in slightly flexed position.

The intervention group was injected with 6 ml of 25% of dextrose

intra articularly through the supero-lateral approach. 50 mg of tramadol tablet along with isometric strengthening of Quadriceps was given.

The control group was injected with 15 ml of ozone intra-articularly through the supero-lateral approach. 50 mg of tramadol tablet along with isometric strengthening of Quadriceps was also given.

The injections were repeated three times, first one at baseline, second at one month after the onset of study and the third at six month. Follow up was done at one month and six month and the outcomes, i.e. pain intensity and function were determined by visual analogue scale (VAS) and Western Ontario McMaster University Osteoarthritis Index (WOMAC) scores.

Ethical Approval: All the participants were informed about the nature of the project and informed consent was taken. Ethical approval was taken from Institutional Ethics Committee, RIMS, Imphal.

Statistical analysis:
Statistical analyses were performed by SPSS statistical software version 21. The pre-treatment and post-treatment outcomes within the group were compared using paired t- test. Comparison between the two groups was done by independent samples t-test for quantitative data and chi-square test and Fisher exact test for qualitative data. P-value of <0.05 was taken as statistically significant.

Results:
The background characteristics of the study groups are presented in table 1 which shows no statistically significant difference between the two groups. Before treatment, the VAS score and WOMAC score were the same in both the groups (P>0.05). The VAS score reduced significantly from 7.27±1.10 at baseline to 6.45±0.56 at first follow up and (P<0.05) among the dextrose group. It further reduced significantly to 3.24±1.09 at second follow up. Among the ozone group(control), there was significant reduction in VAS score from 7.48±0.91 at baseline to 4.36±0.55 at first follow up (P<0.05). It further reduced significantly to 1.94±0.70 at second follow up. The WOMAC score among dextrose group reduced significantly from 79.33±16.67 at baseline to 54.76±22.21 at first follow up and 28.42±11.55 at second follow up. There was also significant reduction among the ozone group (control), 83.21±3.66 at baseline to 40.76±7.05 at first follow up and 15.24±2.25 at second follow up.

Table 1. Baseline characteristics of study group

Variables		25% Dextrose group n(%) N=33	Ozone group n(%) N=33	P value
Age (year)	50-60	23(69.7%)	23(69.7%)	0.752
	61-70	10(30.3%)	10(30.3%)	
SEX	Female	26(78.8%)	21(63.6%)	0.174
	Male	7(21.2%)	12(36.4%)	
Duration(month)	1-6	17(51.5%)	18(54.5%)	0.496
	7-12	7(21.2%)	8(24.2%)	
	13-24	2(6.1%)	3(9.1%)	
	25-36	4(12.1%)	2(6.1%)	
	>36	3(9.1%)	2(6.1%)	
BMI(Kg/m^2)				0.073
	18.5-25	3(9.1%)	9(27.3%)	
	25-30	30(90.9%)	24(72.7%)	
	Mean ± SD	27.73±1.67	26.90±2.02	
Occupation	Housewife	23(69.7%)	22(66.7%)	0.895
	Govt. Employee	2(6.1%)	4(12.1%)	
	Business	2(6.1%)	3(9.1%)	
	Shopkeeper	2(6.1%)	2(6.1%)	
	Laborers	1(3%)	1(3%)	
	Veg seller	1(3%)	1(3%)	
	Actress	1(3%)	0(0%)	
	Soldier	1(3%)	0(0%)	
Side Affected	Left	17(51.5%)	17(51.5%)	0.687
	Right	13(39.4%)	15(45.5%)	
	Both	3(9.1%)	1(3%)	
VAS (mean±SD)		7.27±1.10	7.48±0.91	0.395
WOMAC (mean±SD)		79.33±16.67	83.21±3.66	0.196

Table 2. Comparison of VAS Score between the two groups

Duration	VAS score	P- value	
	25% Dextrose (Mean ±SD)	Ozone (Mean±SD)	
Baseline	7.27±1.10	7.48±0.91	0.395
1st follow up	6.45±0.56	4.36±0.55	0.001
2nd follow up	3.24±1.09	1.94±0.70	0.001

Table 2 shows that VAS score differed significantly between the two groups at both follow ups. At first follow up, VAS score in dextrose group was 6.45±0.56 and 4.36±0.55 in ozone group. At second follow up, VAS score in dextrose group was 3.24±1.09 and 1.94±0.70 in ozone group and these differences were found to be statistically significant.

Table 3. Comparison of WOMAC score between the two groups.

Duration	WOMAC score		P- value
	25% Dextrose (Mean ±SD)	Ozone (Mean±SD)	
Baseline	79.33±16.67	83.21±3.66	0.196
1st follow up	54.76±22.21	40.76±7.05	0.001
2nd follow up	28.42±11.55	15.24±2.25	0.001

Table 3 shows that at baseline WOMAC score in dextrose group was 79.33±16.67 and in ozone group was 83.21±3.66 and the difference was not statistically significant. However, at first and second follow up, the WOMAC score was significantly different between the two groups.

DISCUSSION
In this study, it was observed that there was significant improvement in functional disability at six month of follow up. At baseline, the mean WOMAC score was 79.33±16.67 in the dextrose group and 83.21±3.66 in ozone group. WOMAC score was 28.42±11.55 in the dextrose group and 15.24±2.25 in the ozone group at second follow up, i.e. at the end of six month. The improvement in WOMAC score was more in the ozone group with improvement in score of 67.97 as compared to dextrose group with improvement of 50.81 from baseline.

A study on a total of 24 female patients (average age: 58.37 ± 11.8 years old). The patients received 3-monthly injection of 20% Detrose prolotherapy. Before the treatment mean VAS scale at was 8.83 ± 1.37. At the end of 24 week pain severity decreased to 4.87 ± 1.39, 45.86% (p < 0.001). (Eslamian & Amouzandeh, 2015)

In a study, 128 patients compared the effect of prolotherapy with 25% Dextrose intraarticular and 15% Dextrose extra-articular in osteoarthritis of knee. It was reported that there was significant improvement in WOMAC and VAS (p < 0.001). (Soliman, Sherif &

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Omar, 2016).

This study also shows that all subjects had some degree of improvement in pain and functional score in both the groups. Improvement in VAS score at 6th month in the dextrose group is 4.03. The improvement in pain with ozone therapy corresponds to a study where the pain killing effect of ozone injection on osteoarthritis of the joints and spine was shown. Another study also validated ozone having anti-inflammatory and analgesic effect(Al-Jaziri & Mahmoodi, 2008; Bocci, 2006).

In this study, it has been observed that there was significant improvement in VAS score in the ozone group. The mean VAS score was 7.48±0.91 at baseline, which improved 1.94±0.70 follow up at 6^{th} month ($p<0.05$).

This study also showed functional improvement as measured by WOMAC score in both the groups. The WOMAC score in the ozone group was83.21±3.66 at baseline, which reduced to 15.24±2.25 at second follow up at eight month ($p<0.001$).

No adverse reaction occurred in any patient in both the groups, which suggests that the ozone therapy in osteoarthritis knee is safe, if not otherwise contraindicated.

In a study done on ozone therapy, they established that ozone therapy is a simple technique with no complication for pain relief in knee pain particularly in early OA and soft tissue inflammation. Another study done also concluded that ozone therapy is a much safer agent in osteoarthritis knee for relief of pain (Qing & Feng, 2005; Gheza & Bissolotti, 2003).

Limitations of the study: Small sample size in each group, short period follow up period of only 6 months, which is relatively short for a chronic disease like osteoarthritis of knee.

Since this study is the first of its kind to compare the effectiveness of 25% dextrose prolotherapy and ozone in primary osteoarthritis of knee in terms of pain and improvement of knee function, there are no directly comparable results in literature.

However, our study results are generally consistent with other studies on prolotherapy with 25% D and Ozone in subjects with osteoarthritis of knee. The results of this study introduce intervention therapies that resulted in significant reduction in pain and improvement in function, which is main focus in the treatment of osteoarthritis of knee. As such these interventions may be a possible treatment for patients with osteoarthritis of knee (OA).

Conclusion:

From the study it was found that ozone was better than 25% dextrose prolotherapy in long term (6^{th} month) for pain relief and functional improvement in patients of primary KL Grade 2 and 3 osteoarthritis of knee.

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