Original Paper

Role of intra-articular ozone in osteo-arthritis of knee for functional and symptomatic improvement

Swapan Kr Mishra, Rajesh Pramanik**, Pallab Das***, Partha Pratim Das****, Asim Kumar Palit*****, Jayanta Roy******, Rathindra Nath Halder********

Abstract

This prospective randomised controlled study aiming to evaluate the role of intra-articular ozone in OA knee patients was conducted in pain clinic, Sambhu Nath Pandit Hospital, Kolkata from February 2008 to November 2008. One group of patients received three injections of O3 (one month apart) and other group received injection methylprednisolone and a cross over was done (ie, one injection of O3 given to those failed patients on methylprednisolone). The data was assessed and it was concluded that intra-articular injection of O_3-O_2 relieved pain, stiffness and physical disability better than intra-articular injection of methylprednisolone.

At the end of the study it was noted that when both (ozone + local anaesthetics and injection steroid + injection local anaesthetics) are given together at the intra-articular space in OA knee then that can relieve all those symptoms much more efficiently in all those cases who are refractory to conservative treatment.

key words **: Intra-articular oxygen-ozone, osteo-arthritis knee, minimal invasive procedure.**

Osteo-arthritis (OA) knee is a chronic progressive painful condition mainly affecting middle aged people. In OA main pathological changes are progressive loss of cartilage, meniscus and capsule of the joint. In the ealier age group both sexes are equally affected but later on (>50 years) females are mainly affected. Obesity, family history, high body mass index (BMI) and repeated trauma are the susceptible precipitating factors to develop OA[1].

Pain, stiffness and functional limitation of movement are other major symptoms.Restriction of joint movement, bony swelling and crepitus are common earlier signs and joint deformity occurs in advanced stage[2].

Radiological disease progression is measured by Kellgren-Lawrance (KL) Score (adapted by WHO)[3].

Osteophyte, joint space narrowing (JSN), subchondral sclerosis and cyst etc are main radiologic findings[4].

Main goal of treatment of OA are to relieve pain, to achieve optimal joint function and mobility, to educate the patients regarding avoidance of precipitating and aggravating factors, management options etc[5]. Even in the era of modern medicine there is no drug available which can cure OA. Non- pharmacological therapy like cryotherapy, heat therapy like SWD, UST, TENS, shoe modification and shock absorbing foot wear, exercise, assistive devices are helpful for symptomatic and functional improvement[6]. There is paucity of evidence regarding definite roles of symptomatic slow acting drugs of OA (SYSADOA) eg, injection hyaluronic acid and oral glucosamine and chondroitin sulfates and structure modifying mrugs (DMOAD) eg, glucosaminoglycan, doxy- and minocycline etc to reduce disease activity[6].

Author's affiliations

Department of PMR, Institute of Post Graduate Medical Education & Research, Kolkata, West Bengal

*MBBS, DNB (PMR), RMO-cum-Clinical Tutor

**MBBS, MD (PMR), MRCP (UK), Assistant Professor

***MBBS, MD (PMR), Assistant Professor

****MBBS, MD (PMR) DNB, Assistant Professor

*****MBBS, MD (PMR), DNB (PMR), Associate Professor

******MBBS, MD (PMR), DNB (PMR), Associate Professor, Department of PMR, RG Kar Medical College& Hospital, Kolkata, West Bengal

*******MBBS, MD, Head of the Department

Address of Correspondence *:*

Dr Swapan Mishra,

Flat-B/10," ABAKASH", 121/24/F, Kalitala Road, North Purbachal, Kolkata-700 078, West Bengal, Telephone: 09433165142, 09432650923, 033-24844488, Email : drswapanmishra@gmi.com

Received on 07/07/2011, Revised on 04/08/2011,

Accepted on 20/08/2011

Invasive management are possibly better for those patients not showing improvement after conservative management for 3-6 months, mild / no radiological deformity (KL Score ≤ 3), pain, stiffness and physical disability score (WOMAC ≥ 2 in Likert Scale / ≥ 40% in VAS) and last but not the least for those patients tried with popular minimal invasive procedures (MIP) e.g. intra-articular injection steroid + injection lignocaine + injection hyaluronic Acid[6].

Recently intra-articular injection of ozone-oxygen mixture (O_3-O_2) in therapeutic concentration (30 µg/ml of ozone in oxygen) gained popularity for relief of pain, stiffness and physical disability without any significant adverse effect. Ozone possesses bacteriostatic, fungicidal and viricidal property, that's why no antibiotic required after the procedure[7,8]. Lastly ozone has very good analgesic and anti-inflammatory property because it blocks phosphodiasterase-A2 [9, 10].

Materials and Methods

This prospective randomised, controlled, double-blind, cross-over study was conducted at Pain Clinic, PMR Department Sambhu Nath Pandit Hospital, Kolkata, West Bengal from February 2008 to November 2008. Permission of Institutional Ethical Committee and informed consent was taken from all patients before the study. Meticulous history taking and thorough clinical examination was done for every patient. Patient selection was done with following criteria

Inclusion criteria :

Patients of primary OA presents in:

Radiologically early stage i.e. KL Score ≤ 2.

WOMAC Score ≥ 2 for pain, stiffness and physical disability.

Having no other medical and/or neurological complication.

Having the symptoms of OA for at least 3 months after getting usual conservative treatment e.g. paracetamol, NSAIDs, opioids, physical therapy and Therapeutic exercises

Exclusion criteria :

Patients who are suffering from:

Secondary OA

Primary OA but:

(I) WOMAC Score < 2 in for pain, stiffness and physical disability

(II) Radiologically in advanced stage (K L Score>2).

(III) Having associated medical and / or neurological complications to any intervention eg, T_2DM-HTN,

(IV) Having contra-indication for steroid use.

Then the patients were divided randomly into two groups (group A & B). VCTC counselling and all necessary preoperative investigations were done in all patients. Both the groups received baseline conservative management like lifestyle modifications, therapeutic exercise regimen, orthosis (in case mediolateral instability), three weeks course of paracetamol (1 g thrice daily), superficial heat etc.

Apart from these, patients of group A received three injections [at first visit after randomisation, after 1month, after 2 months] of O_3-O_2 (30 µg /ml of O_3 in O_2—10 ml) + injection lignocaine (2%-2 ml). Group - B patients received one injection methylprednisolone (40 mg) + injection lignocaine (2%—2ml) at first visit after randomisation. One injection [after 3 months 2] of O_3-O_2 (30 µg /ml of O_3 in O_2—10 ml.) + injection lignocaine (2%-2 ml) was given to those patients of group B who failed to respond at first follow up.

After the procedure every patient was advised to take rest for 1-2 hours at recovery room with knee functional position, to avoid strenuous activity for 2-3 days, then to resume activity of knee joint gradually. All patients were assessed after 3 months of first injection at 1st follow-up (F.U-1) and after 6 months of first injection at the 2nd follow-up (F.U-2).

Assessment tools :

Outcome was measured by marker of success and failure comprising

(1) Overall post - treatment satisfaction assessment in patient asking...***Yes/No.***

(2) Modified Mac Nab Method of symptoms assessment.

(3) WOMAC Score of OA knee symptoms assessment for pain, stiffness and physical disability.

Based on the above mentioned markers of outcome assessment we used the following criteria of success and failure of treatment outcome in our study.

CRITERIA FOR ASSESSMENT FOR SUCCESS & FAILURE		
	SUCCESS	**FAILURE**
Overall satisfaction of patient after treatment (Yes/No)	Satisfied	Not satisfied
per format)	Excellent/Good/ fair	Mediocre/ No result /bad
WOMAC Index -Likert	< 2	> 2

modified Macnab (As

Results :

In this prospective study total numbers of patients were 46. Total 48 patients were selected but two patients (one from each group) were unable to continue the whole procedure due to their personal problems. At the end of the study it was noticed that age distribution of patient population was 38-58 years (mean age 42 ± 4). Females slightly outumbers the male group (male: female = 22:24).

It is interesting to note that group A patients responded well by ozone with a success rate of 80 % at first follow-up (3 months) and improvement sustained up to 6 months. But in group B (on methylprednisolone) patient's response rate was not so good (with success rate 60 %). Although after cross over (one injection of ozone to the failed patients at 3 months), success rate peaked up to 91% (Table 1).

Similar type of improvement pattern was noted in Modified Mac Nab Method. In this analysis it was noted that success rate for group A was initially 80% then became 90% at the end of 6 months. In group B it was topped up to 91% (at 3 months) from 60% (at 6 months) (Table 2).

Discussion

Analysis of result findings on overall post -treatment satisfaction assessment in patient, Modified Mac Nab Method, WOMAC Score (Table 3) and All Data together in Table 4 strengthen the hypothesis that invasive technique like intra-articular ozone therapy is an effective

Table 1 — *Overall Post-Treatment Satisfaction (Responding Yes/No)*

	Group-A (No of Cases)		**Group-B (No of Cases)**	
	1st follow-up (3 months)	**2nd Follow-up (6 months)**	**1st Follow-up (3 months)**	**2ndFollow-up (6 months)**
Success	**18 (80%)**	**20 (90%)**	**14 (60%)**	**21 (91%)**
Failure	**5 (20%)**	**3 (10%)**	**9 (40%)**	**2 (9%)**
TOTAL	**23 (100 %)**	**23(100 %)**	**23(100 %)**	**23(100 %)**

Table 2 — *DATA in Modified Mac Nab Method*

	Group-A (No of Cases)				**Group-B(No of Cases)**			
	1st follow-up (3-months)		**2nd follow-up (6-months)**		**1st follow-up (3-months)**		**2nd follow-up (6-months)**	
Success	**10 (E) 6 (G) 2 (F)**	**80 %**	**14 (E) 4 (G) 2 (F)**	**90 %**	**9 (E) 3 (G) 2 (F)**	**60 %**	**13 (E) 4 (G) 4 (F)**	**91%**
Failure	**3 (M) 2 (NR)**	**20 %**	**2 (M) 1(NR)**	**10 %**	**5 (M) 3(NR) 1(B)**	**40 %**	**1 (M) 1(NR)**	**9%**
—		—					—	

Table 3 — *WOMAC Score*

	GROUP-A(n)			GROUP-B(n)		
	0-Day	1st FU	2nd FU	0-Day	1st FU	2nd FU
Pain :						
Extreme	1	—	—	1	1	—
Severe	17	2	1	16	6	1
Moderate	5	3	2	6	2	1
Slight	—	15	5	—	10	10
Nil	—	3	15	—	4	11
Stiffnness :						
Extreme	1	1	—	1	1	—
Severe	15	2	1	15	6	1
Moderate	7	2	2	7	2	1
Slight	—	14	6	—	11	9
Nil	—	4	14	—	3	12
Physical disability :						
Extreme	1	—	—	1	1	—
Severe	14	1	—	13	4	1
Moderate	8	4	3	9	4	1
Slight	—	14	4	—	12	8
Nil	—	4	16	—	2	13

of OA knee. There are evidences which showed intra-articular ozone has bacterostatic, viricidal, anti-inflammatory property.

According to Quing and Feng[7] it is much safer agent in OA knee for relief of all those symptoms. Similarly it was established by Gheza *et al*[11], it is a simple technique with no complication for pain relief in knee pain particularly in early OA and other soft tissue inflammation also. Our study also supported this data. According to our study is significant success rate (80% after 3 months, 90% after 6 months) with intraarticular O3 injections to the patient of group A. On the other hand methyl prednisolone is not so effective to reduce symptoms of OA (success rate 60% after 3 months). But interestingly success rate improved dramatically after one injection of O_3 to those failed patients on methylprednisolone. Two patients were unable to continue the study. Among the failure patients of gr.-B in 1st follow-up, 80 % shows success after cross over with injection O_3-O_2 mixture.

Intraarticular injection of O_3-O_2 + injection lignocaine relieves pain, stiffness and physical disability better than intra-articular injection of methylprednisolone + injection lignocaine. When both are given together (crossover) reliefs of all those symptoms much more efficiently than either of the procedure.

At the end of study it can be concluded that intraarticular ozone is definitely helpful to reduce pain, stitiffness, disability. Intra-articular ozone therapy has better efficacy than intra-articular methylprednisolone. But when both (Ozone + local anaesthetics and injection steroid + injection local anaesthetics) are given together at the Intra-articular space in OA knee then that can relief all those symptoms much more efficiently in all those cases who are refractory to conservative treatment.

FOOT NOTES: KL Score= Kellgren –Lawrence score, WOMAC= Western Ontario and McMaster University, OA= Osteoarthritis, MM & DR=Clinicians involved in assessment of patients during follow up after the procedures.

Table 4 — *All Data Together*

	GROUP-A				GROUP-B			
	1st Follow Up		2nd Follow Up		1st Follow Up		2nd Follow Up	
	S	F	S	F	S	F	S	F
Post-treatment satisfaction (Y/N)	**18 (80%)**	**5 (20%)**	**20 (90%)**	**3 (10%)**	**14 (60%)**	**9 (40%)**	**21 (91%)**	**2 (9%)**
WOMAC	**18 (80%)**	**5 (20%)**	**20 (90%)**	**3 (10%)**	**14 (60%)**	**9 (40%)**	**21 (91%)**	**2 (9%)**
Modified Mac Nab	**18 (80%)**	**5 (20%)**	**20 (90%)**	**3 (10%)**	**14 (60%)**	**9 (40%)**	**21 (91%)**	**2 (9%)**

References

1 Oxford textbook of Rheumatology; 2nd edition: 259-267

2 Kelly's Text Book of Rheumatology 2nd Ed: 2:1514 -1515.

3 T.M. Link, MD, L.S. Steinbch, MD, S.Ghoah, MS, M. Ries, MD, Y. Lu, PhD, N. Lane MD & S. Majumder, PhD: Osteoarthritis: MR Imaging findings in different stages of disease and correlation with clinical findings; *Am J Rontgend* 2002; **22:** 476-88.

4 Pavelka K, Gatterova J, Altman RD — Radiographic progression of knee osteoarthritis in czech cohort. *Clin Experiment Rheumatology* 2000; **18:** 473-7.

5 Narayanan K — Recent advances in management of osteoarthritis.www.natboard.edu.in.:recent advances.

6 Grainger , Cicuttini FM — Medical Management of osteoarthritis of knee and hip joints. MJA 2004; **180:** 232-6.

7 Quing H, Feng D — Clinical observation of O_2-O_3 treating common kinetic system soft tissue injury pain (141) cases. *Rivista Italiana di Ossigeno-Ozonoterapia* 2005; **4:** 155-8.

8 Genovese E, Bonnetti M, Fontana A — CT Guided O_2-O_3 Infiltration in to the main joints: *Rivista Italiana di Ossigeno-Ozonoterapia* 2004; **3:** 121-30.

9 Spinal Ozone Therapy in Lumber Spinal Therapy: *International Journal of Ozone Therapy* 2007; **6:** 17-4.

10 Bocci V, Luzzi E, *et al* — Studies on the biological effects of ozone, III an attempt to define condition for optimal induction of Cytokines. *lymphokines-Cytokines Res* 1993; **12:** 121-6.

11 Gheza G, Bissolotti L — Servizio di Radiologia, Casa di Cura S. Anna, Brescia* Servizio di Recupero e Rieducazione Funzionale Casa di Cura Domus Salutis, Brescia. Intra-articular Oxygen-Ozone Injection for Knee Disease—Proposed Guidelines: *Italy Published in Rivista Italiana di Ossigeno-Ozonoterapia* 2003; **2:** 63-6.