Effect of Intra-Articular Ozone Injection on Osteoarthritic Knee Joint Pain and Range Of Motion

Nahla M. ElAmrawy, MSc 1, Fatmaa Sedeek, PHD 2, Ehab E.Kamel, PHD 3, Maha M. Mohammed, PHD 4

(1)Deputy Head of Physical Therapy department, El-Raml pediatric hospital, Ministry of health in Alexandria, Egypt.

(2) Professor, department of Basic Science, Faculty of Physical Therapy Cairo University, Egypt.

(3) Assistant Professor of Diving and Hyperbaric, Medicine Military Medical Academy, Ex-Dean of Naval and Hyperbaric Medical Institute, Egypt.

(4) Lecturer, department of Musculoskeletal disorders and its surgery, Faculty of physical therapy, Cairo University, Egypt.

ABSTRACT

Background: Osteoarthritis is a disabling disease that leads to severe morbidity and deterioration of physical activity. The intra-articular injections of ozone have been documented as a treatment of osteoarthritis. **Purpose**: To examine the effect of intra-articular ozone injection on osteoarthritic knee treated with traditional physical therapy program in terms of knee joint pain and range of motion. **Methods**: Thirty participants with grade II knee osteoarthritis (Kellgren and Lawrence classification) with age ranged from 40-55 years, were randomly assigned into 2 equal groups: the control group (group A), and the experimental group (group B). All patients received assessment for knee pain intensity using visual analogue scale and knee joint range of motion using the digital water level (inclinometer) pre and post treatment. Both groups received traditional physical therapy program three sessions a week, for 6 weeks and group B received intra-articular ozone injections two sessions a week, for 6 weeks. **Results**: There was a significant improvement in both groups as regard to knee joint pain and range of motion with a statistically significant difference between both groups in favor of group B ($P < 0.05$). **Conclusion**: Adding intra-articular ozone injection to physical therapy program can soothe pain and increase range of motion in patients with osteoarthritic knee more than using the traditional physical therapy alone.

Key Word: knee osteoarthritis, Intra-articular Ozone injection, Physiotherapy.

INTRODUCTION

Osteoarthritis (OA) is a disabling disease that leads to severe morbidity and deterioration of physical activity (1). It is the most common joint problem and is one of the main causes of disability in the elderly (2).

The increased prevalence of OA and the medical costs associated with total knee replacement surgery for terminal stage OA motivate a search for agents that can decelerate OA progression (3).

The primary osteoarthritic symptoms are pain, stiffness and limited range of motion (ROM) (4). Pain is one of the most commonly reported and prominent factors that are responsible for physical inactivity in patients with knee OA (5). This impairment in physical activity associated with knee OA has important implications for aerobic power and cardiovascular health. Hence, patients with OA are at a particular risk of poor health outcomes (6).

Pain pattern and severity of knee OA as either absent, mild, moderate, severe, or very severe could affect the ROM that involves daily activities and quality of life. Moreover, muscle weakness in knee OA usually results in joint stiffness and decreasing ROM that involves daily activities (7).

Management of pain in knee OA is a multidisciplinary approach. Physiotherapy, as a mainstay of conservative treatment for OA knee involves the use of various modalities such as manual therapy, exercises, thermal modalities and electrical stimulations as a direct or an indirect pain reduction method (8).

Ozone therapy has been widely used in the treatment of OA (9). The application of ozone seems to be empirical and there are limited studies showing the histological and biochemical evidence for the effects of its use (10).

Ozone therapy is an approach proving to have therapeutically efficiency with analgesic effect by activating cellular metabolism; regulating the membrane capacity and making fluids run normally in the inflamed tissues. The anti-inflammatory and anti-oxidant effects help immunomodulation by activating immune-competent cells and it protects against the endothelial dysfunction (11).

The intra articular injection of ozone has been suggested for the treatment of osteoarthritis and has yielded positive results since the 1995s (12).

Intra-articular ozone injections in acute and chronic, painful joint conditions represents a complementary treatment method providing rapid pain relief, decongestion, reduction in inflammation, and an improvement in motility (13).

So this study was conducted to investigate the combined effect of intra-articular ozone injections and physical therapy rehabilitation program on knee OA pain and range of motion.

MATERIALS AND METHODS

Design

The study was designed as a pre-test-post-test controlled study.

It was conducted in the outpatient clinic of Underwater and Hyperbaric Medical Institute, Military Medical Academy and Wengat care Hospital, Ministry of Health in Alexandria through the period from February 2018 to April 2019.The protocol was approved by the Research Ethics Committee of the Faculty of Physical Therapy, University of Cairo (**No:** P.T.REC/012/00745).

Patients:

Thirty patients from both sexes diagnosed as unilateral knee OA grade 2 on Kellgren and Lawrence classification(The Kellgren and Lawrence system is a method of classifying the severity of knee O.A using five grades; Grade 0: no radiographic features of O.A are present, Grade 1: doubtful joint space narrowing (JSN) and possible osteophytic lipping, Grade 2: definite osteophytes and possible JSN on anteroposterior weight-bearing radiograph Grade 3: multiple osteophytes, definite JSN, sclerosis, possible bony deformity and Grade 4: large osteophytes, marked JSN, severe sclerosis and definite bony deformity).

Patients were recruited according to the following criteria: aged between 40-٥٥ years, and they are able to walk with painful knee OA without assistive devices.

The participants were excluded if they had any history of congenital or acquired inflammatory or neurological (systemic or local) diseases involving the knee, joint replacement surgery in either Knee or/and hip joints , received supplementing anti-oxidant vitamins, intra-articular steroid injection, any anti-inflammatory drugs during the period of treatment and or had any psychiatric disorder.

Outcome Measures:

Intensity of knee pain was measured by using visual analogue scale (VAS) and knee ROM using of the digital water level (inclinometer) pre and post treatment.

Procedures:

Informed consent was obtained from all the patients after the detailed explanation of the study**.**

All Patients were evaluated before starting treatment program and after 6 weeks at the end of the study period.

1-The Intensity of Knee Pain:

The VAS was used to assess the knee pain intensity. Every patient was asked to report her/his pain on the VAS before the first session, and at the end of the study period (6 weeks). It consists of a continuous 10 cm line. The patient was instructed to place a vertical mark to indicate the intensity of pain, ranging from no pain or discomfort (0), to the worst pain could possibly feel (10) The VAS score is determined by measuring in 10 cm from the left hand end of the line to the point that the patient marks. The VAS is generally regarded as a valid and reliable tool for pain measurement **(14)**.

2-Knee Range of Motion:

A professional 9 inches multi-function HUSKY digital level was used in this study to measure knee range of motion. This inclinometer (digital level) has been used as a manual leveling tool. Mainly, it is used to measure the horizontal and vertical alignment of objects, with a measuring range of 360°. The accuracy of its fluid vials is ±0.029º for level, while the accuracy of digital display is ± 0.1º for level and ± 0.2º for all angles **(15).**

The digital inclinometer was accurate method of knee angle measurement

and it provides a valid and reliable method for assessing knee ROM **(16, 17, 18).**

A) Knee Flexion Rage of Motion Measurements:

The patient was instructed to lie in prone lying position with both feet out of plinth. Each patient was asked to maintain his trunk completely rested on the plinth, the contra lateral limb as well as the pelvis were well supported with two belts one around the hip joint and the other one around the thigh just above knee joint to avoid any substitutions of movements and 3inch towel roll under the anterior surface of the distal femur**(17).**

The towel roll allowed for full knee extension so that an accurate measurement of active knee flexion could be obtained. Stabilization of the subjects' hip was provided by different researchers to eliminate compensation and further increase the accuracy of measurement **(17).**

The digital level was stabilized to the long axis of the fibula in line with the head of fibula and lateral malleolus by two adhesive straps. Patient was asked to flex his knee till the end position then data was recorded. Flexion was measured 3 successive times and the mean was taken **(17).**

B) Knee Extension Rage of Motion Measurements:

Measurements were taken when the patient in sitting position at the edge of the table with hip and knee flexed 90 degrees; the patient`s thigh was supported with examiner hand or with a belt to avoid the substitutions.

The digital level was stabilized to the long axis of the fibula in line with the head of fibula and lateral malleolus by two adhesive straps and the patient was asked to extend his knee as much as possible. Extension was measured 3 successive times and the mean was taken. **(18)**.

Interventions:

Group (A): received traditional physical therapy program while group (B) received same program as group A in addition to intra-articular ozone injections. Treatment program of physiotherapy was applied for 6 weeks, 3 sessions per week and ozone therapy was applied for 6 weeks, 2 sessions per week.

Treatment Procedure:

All Patients in Both Groups (A and B) received:

Traditional physical therapy program three sessions a week, for 6 weeks (18 sessions) and group B received intra-articular Ozone injections two sessions a week, for 6 weeks(12 sessions).

I) Traditional Physical Therapy Program which consisted of:

1. Ultrasound.
2. Transcutaneous Electrical Neuromuscular stimulation.
3. Quadriceps setting.
4. Straight leg raising exercise.
5. Isotonic contraction exercise.
6. Stretch the hamstrings.

7-Self-stretch of the hamstrings:

1- Ultrasound:

The patient was in relaxed supine lying position with the affected knee semi flexed supported on a pillow, after applying an acoustic gel to the skin. The treatment head was placed on the skin before the output was

turned on and then moved continuously over the surface of the skin on medial aspect of knee in circular movements with the probe at right angles to ensure maximum absorption of the energy **(19)**.

In the ultrasound (US) therapy session US waves used for 5 minutes and with 5 centimeter diameter applicator, with intensity 0.3 - 0.8 Watt/centimeter square (W/cm^2) and pulsed waves (50% duty cycle). Ultrasound was applied using 1 megahertz (MHz) frequency because it is absorbed less rapidly with progression through the tissues and therefore will be more effective at greater depth **(19)**.

2-Transcutaneous Electrical Neuromuscular stimulation:

The patient was positioned in the supine lying position with a roll under his knees. The per-cutaneous electrodes for the electrical stimulation were placed on the anterior medial and lateral portions of the knee **(20)**.

Transcutaneous Electrical Neuromuscular stimulation was applied using a frequency of 100Hertz (Hz) and pulse width of 50 microseconds (μs), intensity milliampere (mA) set at the individual subject's sensorial threshold, modulation up to 50% of variation frequency with rectangular biphasic symmetrical pulse and a length of application of 20 minutes. The type of electrode was carbon silicone padded by gauze **(20)**.

3-Quadriceps Setting:

The patient was in supine or sitting with both arms beside or behind the body to give support. With leg straight then he/she was asked to tighten the muscle in front of his/her thigh as much as he/she can and dorsiflex the ankle, pushing the back of the knees flat against the plinth causing the patella glide proximally. Hold for about 10 seconds, then rest up to 10 seconds and repeated this exercise for 10 times then relaxes **(21)**.

-Straight Leg Raising Exercise:٤

The patient was positioned in the crook lying position with the unexercised limb is the flexed one then the patients was asked to contract the quadriceps muscle and elevate the limb to 45 degrees and hold for 6 seconds, slowly lower the limb and then relax for 6 seconds, and repeated this exercise for 10 times then relaxed **(21).**

As the exercise progresses the patient was asked to lift his/her limb to 30 degree of hip flexion and hold the position. Later, the patient was asked to flex the hip to only 15 degrees. The most significant resistance to the quadriceps is during the first few degrees of Straight leg raising (SLR) **(21).**

-Isotonic Contraction Exercise:٥

The patient was in sitting position at the edge of the table, with his back supported. The therapist was sitting on low chair beside the patient`s affected limb stabilizing the lower thigh by left limb **(22).**

The patient was asked to extend his leg as much as possible (active free against gravity),then asked the patient to do this again against slight resistance through full range of knee extension with a resistance to the anterior aspect of the lower leg just above ankle joint **(22).**

The patient was asked to extend his leg against manual resistance that was at the initiation, middle and end of the range in each of them patient hold of 10 seconds then continued the range and then repeated this exercise (combination of isometric and isotonic contraction)**(22).**

6-Stretch the Hamstrings:

With the patient's knee fully extended, the patient's lower leg was supported with

the therapist shoulder. The therapist stabilized the opposite extremity along the anterior aspect of the thigh with a belt or with the assistance of another person **(23).**

With the knee at 0 extension, and the hip in neutral position, therapist applied 3forces first by therapist shoulder moved the limb forward, second force with right hand down ward above knee joint and the third force with the left hand around calcaneus toward dorsiflexion then the therapist moved the patient hip into flexion up to pain limit with knee full extended, hold for 30 seconds then relax and repeated again from 3 to 5 times, with 30 seconds rest between each one **(23).**

7-Self-Stretch of the Hamstrings:

Patient was in supine lying position with unaffected limb extended and supported with the therapist hand or a belt to avoid substitution.

The patient put the belt around the foot with holding it with his hands to stretch the hamstring muscle from extended hip then from 50 degree of hip flexion hold for 30 seconds repeated 3 to 5 times each with rest for 1 minute in between different angles **(23).**

The patient instructed to do SLR and quadriceps setting exercises 10 times for each group 3 times per day as a home program and to do self-stretching of hamstring 3 to 5 times per day (**21).**

II) Intra-articular Ozone Injection:

Patients were in a relaxed comfortable sitting position with the treated knee in 90 degree knee flexion at the edge of the table.

Intra-articular ozone injections were done as follows: aseptic condition was done around a knee joint with betadine and alcohol. Ozone injection was done in medial aspect of the knee joint using needle of 1 milliliter (ml) 100 unit(U) insulin syringe **(24**).

Ozone was administered under supervision of the same physician, a course of 12 intra-articular injections of ozone in concentrations 7-10 gamma in 10 milliliter of oxygen (twice per week).

At the end of the injections the patient was asked to move several times in successive flexion/extension motions for a better distribution of the gas at the level of articulation **(24**).

Statistical Analysis:

Descriptive statistics and unpaired t-test were conducted for comparison of age and BMI between both groups. Chi- squared was carried out for comparison of sex, affected side and dominant side distribution between groups. Normal distribution of data was checked using the Shapiro-Wilk test for all variables. Levene's test for homogeneity of variances was conducted to test the homogeneity between groups. Paired t-test was conducted for comparison between pre and post treatment in each group. Unpaired t-test was conducted to compare the mean values of VAS, flexion and extension ROM between the group A and B. The level of significance for all statistical tests was set at $p < 0.05$. All statistical analysis was conducted through the statistical package for social studies (SPSS) version 25 for windows (IBM SPSS, Chicago, IL, USA).

RESULTS

Subject Characteristics:

Table (1) showed the subject characteristics of the group A and B. There was no significant difference between both groups in the mean age and BMI ($p > 0.05$). Also, there was no significant difference in sex, affected side and dominant side

distribution between groups (p > 0.05).

Table 1. Basic Characteristics of Participants:

Items	Group A	Group B	Comparison
	mean ± (SD),	mean ± (SD),	**p-value**
Age (years)	49 ± 4.84	49.46 ± 4.24	0.78
Weight (kg)	74.66 ± 7.47	75.53 ± 3.77	0.69
Height (cm)	169.66 ± 7.95	170.73 ± 3.8	0.64
BMI kg/ m^2	26.06 ± 0.96	25.93 ± 0.96	0.7
Sex distribution (%)			
	Group A	**Group B**	**P-value**
Female	6 (40%)	10 (67%)	0.14
Male	9 (60%)	5 (33%)	
Affected side, n (%)			
	Group A	**Group B**	
Right	4 (27%)	5 (33%)	0.69
Left	11 (73%)	10 (67%)	
Dominant hand, n (%)			
	Group A	**Group B**	
Right	14 (93%)	14 (93%)	1
Left	1 (7%)	1 (7%)	

SD, standard deviation; p-value, level of significance

Effect of Treatment on Knee Pain and Range of Motion:

A) Within Groups Comparison:

There was a significant decrease in VAS post treatment compared with that pretreatment in the group A and B (p < 0.001). Also, there was a significant increase in flexion and extension ROM post treatment compared with that pretreatment in the group A and B (p < 0.001). The percent of decrease in VAS in the group A were 23.66%, while that in the group B were 52.22. The percent of increase in flexion and extension ROM in group A were 9.84 and 36.64% respectively. The percent of increase in flexion and extension ROM in group B were 20.7 and 68% respectively (table 2).

B) Between Groups Comparison:

There was no significant difference in VAS, flexion and extension ROM between both groups pre-treatment ($p > 0.05$). Comparison between both groups post treatment revealed a significant increase in flexion and extension ROM and a significant decrease in VAS in favor of group B ($p > 0.001$)(table 2).

Table 2. Mean VAS, flexion and extension ROM pre and post treatment of the group A and B:

VAS					
	Group A	**Group B**			
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	MD	t- value	p value
Pre treatment	7.86 ± 1.35	7.66 ± 1.54	-0.2	-0.37	0.7
Post treatment	6 ± 1.6	3.66 ± 1.44	-2.33	-4.18	0.001*
MD	١,٨٦	٤			
% of change	23.66%	52.22%			
t- value	9.72	28.98			
	p = 0.001*	p = 0.001*			
Flexion ROM (degrees)					
	Group A	**Group B**			
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	MD	t- value	p value
Pre treatment	102.93 ± 6.8	103.73 ± 7.04	0.8	0.31	0.75
Post treatment	113.06 ± 8.66	125.2 ± 5.51	12.13	4.57	0.001*
MD	-10.13	-21.47			
% of change	9.84%	20.7%			
t- value	-12.16	-18.6			
	p = 0.001*	p = 0.001*			
Extension ROM (degrees)					
	Group A	**Group B**			
	$\bar{x} \pm SD$	$\bar{x} \pm SD$	MD	t- value	p value
Pre treatment	22.73 ± 4.71	23.13 ± 3.75	0.4	0.25	0.79
Post treatment	14.4 ± 3.64	7.4 ± 2.32	7	6.22	0.001*
MD	8.33	15.73			
% of change	36.64%	68%			
t- value	5.38	18.31			
	p = 0.001*	p = 0.001*			

$\bar{x}$, mean; SD, standard deviation; MD, mean difference; p-value, probability value; *, significant

DISCUSSION

In this study the effectiveness of combined treatment of intra-articular ozone injections added to traditional physical therapy program was compared to that of the traditional physical therapy program alone on knee pain and ROM in mild and moderate knee OA.

To the authors` knowledge, there are limited studies examined that combined treatment in patients with knee OA.

This study showed a significant improvement ($P<0.05$) in knee pain intensity level and ROM when adding intra-articular ozone injection to physical therapy program in patients with osteoarthritic knee more than using the traditional physical therapy alone.

These results confirmed the effective role of physical therapy program in decreasing knee pain intensity level and improve knee ROM.

Roddy E., et al., (2005) in an evidence-based recommendation for exercise in knee OA reported that both strengthening and aerobic exercise can reduce pain and improve function and health status (25).

Kim L., et al., (2011) conducted a systematic review of 32 randomized clinical trials (RCTs) founded that exercises (quadriceps muscle strengthening, aerobic walking programs) are key component of the management of OA symptoms and have been shown to be beneficial for individuals with OA disease of all severities, their opinion came into agreement with our study results (26).

Page C. J. et al., (2011) reported in there systematic review of 37 RCTs that physiotherapy treatments as different exercises of quadriceps muscle strengthening aimed to dissipate knee joint load, alter lower limb alignment, improve ROM and restore normal neuromuscular function, and it is likely that a combination of treatments is most effective (27), which came into agreement with our results.

Fernandes L., et al., (2013) reported in there systematic review of 11 RCTs that exercise therapy reduced pain and improved physical function, that specific quadriceps strengthening exercise or strength training for the lower limb reduced pain efficiently and improved physical function (28), which came into agreement with our results .

Sedhom G.M., et al., (2015) conducted a RCT of 60 patients, aged from 40 to 60 years, diagnosed as grade II knee OA. The patients were randomly assigned into 4 equal groups; group A received joint mobilization, group B received KT, group C received joint mobilization and KT and group D was control

group. All groups received conventional physical therapy program of Infrared (IR) and exercise (hamstring muscle stretch, SLR, quadriceps setting, isometric strengthening of quadriceps muscle) (29).

They concluded that all treatment groups showed successful outcomes, as knee extension shows increase in ROM (29), so their results came into agreement with the current study results

Fransen M., et al (2015) reported in there systematic review of 54 RCTs that land-based therapeutic exercise provides benefit in terms of reduced knee pain and improved quality of life and moderate-quality evidence of improved physical function among people with knee OA (30).

They concluded that any type of exercise program that is performed regularly and is closely monitored can improve pain, physical function and quality of life related to knee OA (30).

Nguyen C., et al., (2016) conducted a systematic review of 35 RCTs ad they concluded that aerobic exercise as sport, walking, swimming, cycling and any physical activity the patient particularly enjoys, quadriceps and hamstring muscle strengthening and specific strengthening exercise or strength training for the lower limb may improve joint stability reduce pain and improve physical function in knee OA (31).

Lanfeng H., et al., (2018) conducted a RCT done on 250 patients with the average age was 67.8 years ,of moderate to severe knee OA, the patients were randomly divided into an exercise treatment test group (128 patients) and a traditional treatment control group (122 patients). Quadriceps isometric contraction exercise was used in the test group, and local physiotherapy and oral nonsteroidal anti-inflammatory drugs were used in the control group, knee pain was evaluated with a VAS before treatment and 1 and 3 months after treatment (32).

They found that joint pain was effectively relieved and knee joint function was improved with quadriceps isometric contraction exercise. (32), so their results came into agreement with the current study results.

Abdel-aziem A., et al., (2018) examined the effect of physiotherapy rehabilitation program on moderate knee osteoarthritis in patients with different pain intensities, on 60 patients with age between 45 and 62 years and ≤grade 2 knee OA. They were classified into three groups according to pain intensity: mild, moderate, and severe pain groups. All groups underwent a standard set of pulsed electromagnetic field, US,

stretching exercises, and isometric quadriceps strength. Pain intensity, knee ROM, were evaluated using the VAS, universal goniometer (33).

They concluded that pain intensity is one of the prominent factors that are responsible for the improvement of knee osteoarthritis, all groups showed significant decreased in the pain intensity and improved the knee flexion ROM, and level of functional performance in knee OA (33), so their results came into agreement with the current study results.

Omar R. A., et al., (2018) reported in there RCT that done on 45 subjects suffering from unilateral primary knee OA, with the age between 40 to 50 years. The finding of this study revealed that conventional physical therapy program (US, TENS and quadriceps set exercise) had a significant effect on pain and active ROM of flexion and extension (34), so their results came into agreement with the current study results.

The current study results reported a significant improvement of adding intra-articular ozone injections to traditional physical therapy program on osteoarthritic knee pain intensity level and ROM.

The effects of physical therapy rehabilitation program were discussed in details in the previous section and now we will discuss the ozone results.

The first author who had the idea to inject small volumes of ozone in patients affected by tendinitis and myofascial pain was Dr. Alexander Balkany in Zurich in the 1970s. Ozone in the form of an O2-O3 gas mix has been recommended for many years as a treatment for many diseases (41, 42). Initially, its application was limited to the positive nutritional effects on tissues due to the improvement the gas induces on the circulation (43, 44, 45, 46, 47, 48).

Medical ozone appears to behave as a bioregulator when it comes into contact with a biological liquid, releasing factors from human endothelial cells and normalizing the cellular redox balance (10).

Madrigal (2007) reported that ozone in osteoarticular diseases produces: better vascularization on bones and cartilage, accelerating anabolism and recovery. Anti-inflammatory effect by ozone activation over prostaglandins; immunomodulatory effect on autoimmune and inflammatory diseases (such as OA); has a trophic effects on bone and cartilage, ozone improves the cell permeability and diminishes articular effusion (40).

Mishra SK., et al., (2011) in a RCT evaluate the role of intra-articular ozone injection and methylprednisolone intra-articular injection in patients with knee OA, 46 patients in two study groups, with

main aged 42±4years and with grade II knee OA. Both groups received baseline conservative management like lifestyle modification, therapeutic exercise program, superficial heat and orthosis (in case of mediolateral instability) (35).

They concluded that the group that received ozone had a better result in the relief of pain stiffness and physical disability in relation to the group that received methylprednisolone (35).

So their results came into agreement with the current study results as they selected a range of patients' age which was near to the current study selected criteria.

Camelia C., et al (2014) studied the role of ozone therapy in maintaining the articular function and in relieving the pain for patients with knee OA (36).

This study included 100 patients aged between 50 and 65 years old, with grade II and III knee OA. They were randomly classified into 2 groups first group followed physiotherapy treatment program of 18 sessions (with hydro thermotherapy, electrotherapy and kinethotherapy procedures applied in the medical gym or/and in the swimming pool), and 12 sessions intra-articular ozone injection to the second group (36).

They concluded that ozone therapy had a significant improvement for the patients with contraindications for physiotherapy, also they had shown great response in relief of pain, stiffness and physical disability without any significant adverse effect when they had tried ozone therapy only compared to physiotherapy. Also they found similar improvement of the knee ROM, on average with 10-12 degrees in knee flexion (36).

So their results came into agreement with our study results they selected the moderate grade of knee OA which was near to the current study selected criteria.

Hamza M H., et al (2016) they assesed functional improvement in patients suffering from knee osteoarthritis treated by physical therapy alone, compared to those treated by physical therapy combined with ozone therapy. This study included 50 patients aged between 45 and 55 years old, with grade I, II and III knee OA (37).

They were randomly divided into two groups; each one of 25 patients, the first group followed physical-therapy treatment settings including Infrared, Interferential, exercise focused on general fitness, balance, coordination, stretching, and lower extremity muscle strength, and included a daily home exercise program over a three times/ week

protocol. The second group followed 20 ozone therapy settings (three times/ week; periarticular injection) combined with the same physical – therapy treatment protocol for 7 weeks (37).

They concluded that ozone therapy had a significant improvement of pain on VAS scale was more noticeable to patients who were applied in group 2 than that in group 1 (median VAS was 4, 1 respectively). And significant improvement of the knee ROM; flexion was 115 degree and that increased along with treatment up to 125 degree (37).

These conclusions can explain and support our findings.

Gaballa M N., et al., (2019) they investigate the efficiency of intra-articular injection of platelet-rich plasma (PRP) and ozone therapy in the treatment of patients with primary knee OA compared to a basic rehabilitation program (38).

This study included 60 knee OA patients with mean age of 55 ± 4.5 years They were randomly classified into 3 equal groups according to their treatment; group I (platelet-rich plasma group), group II (ozone group) and group III (rehabilitation group). The basic rehabilitation program included IR, TENS, quadriceps muscle strengthening exercises (quadriceps setting and SLR), hamstring stretch and gluteus strengthening at a frequency of 3 sessions/week for 1 month (considered as a control group) (38).

All patients were assessed by VAS and 6-min walk test at baseline and after 1 and 3 months (38).

They concluded that PRP is superior to ozone in the treatment of knee OA and is an encouraging treatment option. PRP injection alone was effective for achieving at least 3 months of pain-free daily activity (38).

So these study disagreed with our results may be due to different mechanism of action between PRP and ozone..

CONCLUSION

Adding intra-articular ozone injection to physical therapy program can soothe pain and increase ROM in patients with osteoarthritic knee more than using the traditional physical therapy alone.

Disclosure Statement

No author has any financial interest or received any financial benefit from this research.

Conflict of Interest

The authors state no conflict of interest.

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