

# EFFECTIVENESS OF ULTRASOUND GUIDED INTRA ARTICULAR OZONE GAS INJECTION IN PATIENTS WITH KNEE OSTEOARTHRITIS FOLLOWED BY CLINICAL AND RADIOLOGICAL EVALUATION

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## ABSTRACT

**BACKGROUND:** Osteoarthritis has been known since long as the degenerative disease of elderly and can lead to debilitation resulting in compromised life style and routines, so for effective management the new conservative and therapeutic measures are discovered and practically implemented in order to improve quality of life.

**OBJECTIVE:** To determine the therapeutic efficacy of intra articular Ozone gas injection in patients with knee joint osteoarthritis, based on the clinical and radiological assessment. **DESIGN:** Quasi Experimental Prospective study.

**PATIENTS AND METHODS:** Total 60 patients were included suffering from knee joint osteoarthritis, with Numeric pain rating scale (NPRS) of 2 or more. The procedure comprised of ultrasound guided intra-articular administration of a medical mixture of Oxygen-Ozone (95% - 5%) 20 mL, with concentration 5 to 10ug / mL, given in 8 to 12 sessions (once in a week). The effect on clinical symptoms were assessed, intensity of pain was evaluated by NPRS while radiological assessment was acquired by X-ray knee joint, before and after the provided ozone treatment. **RESULTS:** The degree of OA recorded according to Numeric pain scale rating was 2 to 10. Pain intensity evaluated by NPRS significantly declined ( $P < 0.0001$ ) from the score 10 to 2 and 2 to 0 with remarkable improvement in knee joint space on follow up radiographs. **CONCLUSIONS:** Oxygen-ozone therapy is a safe and effective medical procedure that can help patients with knee joint osteoarthritis in relieving pain, discomfort, and improve functions.

**Keywords:** Ultrasound, Intra Articular, Ozone Gas, Knee Osteoarthritis, Quality of Life, NPRS, ROM

## Introduction

Osteoarthritis (OA) is a degenerative disease that worsens over time.<sup>1</sup> Knee osteoarthritis is a common degenerative joint disease that primarily affects the elderly, obese and the female population.

OA is the most common type of arthritis, which can cause significant disability and limited joint movement

in the affected joint. It has significant effect on patient's sufferings and overall quality of life with respect to their physical, psychological and social prospects.<sup>2</sup> Furthermore, osteoarthritis is one of the most debilitating diseases in the elderly population, affecting about 30% of those over the age of 70 in Spain.<sup>3</sup> The

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disease is so common that approximately 70% of people above 50 years of age have positive signs of the disease in X-rays.<sup>4</sup>

The composition of a normal knee joint is subchondral bone, synovial tissue, and articular cartilage.<sup>5</sup> In case of knee joint osteoarthritis, the pathophysiology is the tibiofemoral articular cartilage destruction resulting in reduced joint space, along with marginal osteophytosis, subchondral geodes and sclerosis.<sup>6</sup>

The predisposing factors that may lead to the development and progression of OA are obesity (raised BMI), positive family history, and frequent traumas. However, these are not the only causes.<sup>6</sup> The disease is not only a mechanical issue, but also a long-term inflammatory process in which cellular and biochemical changes occur, necessitating medical treatment and requiring Ozone therapy as a replacement.<sup>7-10</sup>

At present, there is no conservative treatment option that can completely cure osteoarthritis. The main goal is to decrease the symptoms and severity like pain, rigidity, and inflammation, and to give wide range of joint movement, while the long term goal is to prevent further joint destruction.<sup>11,5,7</sup>

Many treatment options for knee joint osteoarthritis are now available, including surgical reconstruction, physiotherapy, and conservative management with medications, but these options are mostly focused on improving symptoms. Physiotherapy consists of exercises and certain electrical applications like transcutaneous electrical nerve stimulation (TENS), while oral and topical NSAIDs, and intra articular corticosteroids are used in pharmacological care. In obese patients, weight loss is also a choice for disease management.<sup>12</sup> Total knee arthroplasty is not suitable as well as affordable to all patients.

The diagnosis of knee joint osteoarthritis is primarily based on patient symptoms, such as increased pain severity during weight bearing functions, knee joint stiffness, and loss of flexibility, which results in restricted joint mobility.<sup>13</sup> Imaging modalities such as X-rays and magnetic resonance imaging (MRI) are useful in diagnosing knee osteoarthritis.<sup>12</sup>

Apart from the above mentioned treatment options, intra-articular ozone injection is one of the highly effective treatment of choice for knee osteoarthritis. Ozone is a highly reactive and unstable gas because of three oxygen atom. Based on the effective therapeutic outcomes, nowadays ozone treatment is being

vastly provided for osteoarthritis. Apart from decreasing osteoarthritic symptoms, Ozone treatment also has antibacterial and antiviral properties and it is widely used to control different bacterial, fungal and viral pathogens. Intra articular ozone administration is highly effective in decreasing pain intensity, provides wide range of mobility in the joint and hence improves the quality of life in patients suffering from knee osteoarthritis.<sup>14</sup>

The mechanism of action of intra articular ozone treatment consists of activation of cell metabolism, helps in production of antioxidant enzymes, decreasing the production of prostaglandins and vasodilatation which enhances oxygenation to the tissues.<sup>15</sup>

At cellular level, during normal aerobic metabolism free radicles are produced which are helpful in physiological processes within the cell when these are low or average in concentration. But when these exceeds the normal level, can produce oxidative stress due to an imbalance between free radicals and antioxidant system, and this is the basic process in the degeneration of joint or OA.<sup>16</sup> Ozone gas has targeted action against oxidative stress and hence an effective therapy in OA.<sup>17</sup>

Regardless of limited clinical trial Ozone therapeutic effects on knee OA, in a recent publication, Fernández Cuadros et.al.; proved that Ozone therapy can decrease pain intensity and inflammatory reaction and hence improve the joint function in the affected patients.<sup>18</sup> In addition, they have stated that numerous therapeutic targets can be achieved by ozone.<sup>18</sup> Ozone therapy for knee OA has no universally acceptable criteria for treatment protocol (i.e., number of doses, dose concentration, volume and the frequency at which the dose should be given).<sup>18</sup>

Our purpose to conduct this study is to assess the effectiveness of Ozone treatment related to its efficacy in decreasing pain and inflammatory process and overall betterment in the quality of patient's life suffering from OA and meanwhile to assess the radiological outcomes in follow up radiographs after the ozone treatment.

## Material and Methods

A prospective quasi-experimental before-after study was conducted on 60 patients suffering from knee

OA, with Numeric pain scale rating (NPRS) of 2 or more. These 60 patients were referred to the National Institute of Rehabilitation Medicine having clinical symptoms, required conservative management, and had previously failed symptomatic medical therapy. The study was conducted from June 2020 to February 2021. The patients were referred to Radiology department from the Orthopedic and Rheumatology departments. The research was accepted by the hospital's ethics committee, and the patient gave his or her informed consent. The patients included in the study were diagnosed case of knee OA with positive findings on X-rays, having NPRS 2 or more, with previously unresponsive conservative treatment (like NSAIDs, rehabilitation or physiotherapy) and were unsuitable candidate or not willing for total knee replacement. The patients excluded from the study were those who had contraindications for Ozone therapy (such as pregnancy, patients on angiotensin converting enzyme inhibitors, those who had hyperthyroidism, thrombocytopenia, life threatening cardiovascular disorders, glucose 6-phosphate dehydrogenase enzyme deficiency and allergic to Ozone) and the uncooperative patients who did not complete the entire Ozone treatment protocols.

The given treatment protocol comprised of real time ultrasound guided intra-articular injection of Oxygen-Ozone (95%-5%) mixture at a concentration of 5 to 10 ug/mL (therapeutic dosage ranges from 10 to 80 ug/mL),<sup>18</sup> in volume of 20 ml volume administered in 8 sessions in patients with NPRS 2 to 8, while 10 sessions with NPRS 10, and 12 Sessions with NPRS 10. One session was given per week. The Medical ozone synthesizer LEPSE "OZON" 5-04. The injection was given in the knee joint keeping the patient in sitting or supine position with slight knee flexion and mild lateral displacement of patella (Fig.1). When it was not possible, mixture was given in flexed 90° knee position and ultrasound guided puncture was made in the anterior external / anterior internal patellar recess.

1% chlorhexidine solution was used as an antiseptic to clean the puncture site, and a cold topical spray solution of ethylchloride (100g) was applied to anesthetize the area.

After the administration of the ultrasound guided ozone mixture, patients were assessed for 1 - 2 months for the effects of Ozone gas injections, to

evaluate the NPRS scale, and to assess the radiological improvement by follow up X-ray knee joint in Anteroposterior (standing weight bearing position) and lateral views. The side effects were also noted.

The pain intensity was taken by Numeric pain scale rating NPRS (0-10), taken score 10 as the maximum pain experienced by the patients, and 0 as the absence of pain. Knee joint range of motion (ROM) was calculated. Radiological classification scale named Kellgren-Lawrence is the widely used scale in osteoarthritis. The scale classify the radiological changes from 0 to 4 (0= noradiological findings; 1=doubtfull joint space narrowing or possible osteophytes, 2=definite osteophytes and possible joint space narrowing; 3=definite joints pace narrowing and possible deformity of joint contour; and 4=impingement + subchondral sclerosis + sub chondral geodes + large osteophytes + definite deformity of joint contour).<sup>19</sup>

SPSS statistical package, version 20.0, was used for statistical analysis. Frequencies, averages, and percentages were used in the analysis of quantitative and qualitative variables. For comparison before and after the given therapy, the statistical Student t test was used, which evaluated paired quantitative variables. The level of statistical significance was 99% (P<0.01).

## Results

The patients between 45-51 years of age were n=10 (16.6%), 52-58 years were n=15 (25%), 59-65 years were n=25 (41.6%) and 66-72 years were n=10 (16.6%), including n=20 (33.3%) males and n=40 (66.6%) females.

		Mean	Std. Deviation	T-test	p-value
NPRS	Pre	3.000	.00000	28.146	0.000
	Post	.32	.476		
ROM	Pre	3.32	.476	-7.141	0.000
	Post	4.00	.000		
	Post	2.000 <sup>a</sup>	.00000		

Table 1: Changes in NPRS and ROM after Ozone therapy

The results revealed that the mean for pre ozone and post ozone therapy NPRS reading declined from 3 to 0.32 and p value is less than 0.005, proving that

the pain intensity was decreased after the ozone therapy, mean for pre session ROM was 3.32 which increased to 4 in post session ROM reading, revealed that range of motion in knee joint significantly improved after 8 to 12 sessions of ozone therapy (Tab.1). Follow up weight bearing X-ray knee joint in standing



**Figure 1:** Sitting and supine position of two different patients for Ozone Gas injection

demonstrated increase tibiofemoral joint space predominantly in the medial compartment.

In (Fig.2), weight bearing X-rays of both knee joints in an osteoarthritic patient before the ozone therapy shows markedly reduced joint space predominantly in the right knee joint with subchondral sclerosis. However, the radiograph after ozone therapy shows significant improvement in joint spaces bilaterally. The side effects recorded was mild pain and erythema in 13.3% of cases (08 patients) which was resolved within a few minutes.



**Figure 2:** X-ray knee joint showing interval improvement in joint space after Ozone therapy

## Discussion

Osteoarthritis is a degenerative disease of joints. Joint pain and stiffness are the usual symptoms of the disease. Other symptoms experienced by the patients are limited range of motion and swelling around the joint. According to one study, 28 percent of the popu-

lation in Pakistan suffers from knee osteoarthritis in the rural areas and 25 percent in the urban areas.<sup>20</sup>

Based on the evidences, the mechanism of degenerative diseases like osteoarthritis involves oxidative stress which is the imbalance between antioxidant system and reactive oxygen specie (ROS). By controlling antioxidant enzymes, ozone therapy is successful in preventing oxidative stress.<sup>21</sup>

The outcomes of our study proved that intra-articular ozone injection in patients suffering from knee osteoarthritis greatly improves the quality of life by reducing pain severity and providing wide range of motion in the knee joint. A prospective study similar to ours, conducted by Al-Jaziri and colleagues with 220 patients, found that ozone injections were effective in decreasing the pain severity.<sup>22</sup>

Mishra et al. concluded in a randomized control trial that the ozone therapy helps in relieving symptoms of knee osteoarthritis, showing effective results in decreasing pain and rigidity. Hence, proved that intra-articular ozone treatment is an effective conservative treatment option for knee OA.<sup>23</sup>

Lopes de Jesus et al. conducted a double blind, randomized control trial, consisted of 98 patients with knee OA, who received intra-articular ozone injection for 08 weeks. The results of this study showed that intra-articular ozone therapy improves functional movements and reduces pain intensity.<sup>24</sup>

According to another randomized control trial conducted by Feng and beiping in which two groups with knee OA were included. Patients in group A received ozone injections along with oral celecoxib and glucosamine hydrochloride for 6 weeks, while patients in group B only received glucosamine hydrochloride and celecoxib. The outcomes of study revealed that symptoms in group A patients were significantly improved with substantial decrease in pain intensity and improved functions in the joint. All of the above mentioned study results supports the results of our study.<sup>25</sup>

## Conclusion

Ozone therapy is a safe, affordable and highly effective treatment option in patients suffering from knee osteoarthritis by providing symptomatic relief as calculated by NPRS and ROM scales. The results

were supported by the radiological evidences which demonstrated increase in joint space on follow up knee joint X-rays. The outcome of our study presented significant evidence and a high recommendation, allowing us to use Ozone therapy as a conservative treatment option for knee joint osteoarthritis.

**Conflict of Interest:** None

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