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Comparison of efficacy of radiofrequency alone or steroid or ozone intra-articular after radiofrequency ablation of genicular nerves in patients with chronic pain due to knee osteoarthritis: A prospective, randomized, controlled clinical trial

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Abstract

Although the exact cause of osteoarthritis (OA) is unknown, it is believed to be a collection of related but distinct diseases that can occur due to a variety of biological and mechanical factors, such as metabolic predisposition, genetic or hereditary predisposition, age, and physical factors like obesity. Slowly progressing articular disease, osteoarthritis causes joint pain, stiffness, and a loss of mobility. Anti-inflammatory characteristics of corticosteroids make them popular in pain management. Adrenal corticosteroids are commonly utilised in epidural, joint, peripheral nerve, and soft tissue injections. They are produced in the adrenal cortex. It was the goal of this study to assess the effectiveness of ozone, steroid, and a placebo in patients with osteoarthritis of the knee following radiofrequency ablation of the genicular nerves. It was conducted at the Benha university hospital and comprised 75 patients with osteoarthritis of the knee joint who were randomly assigned to receive either a placebo or an active treatment. No differences were found between the study groups in age, gender, BMI, pain duration, or Kellgren-Lawrence grade, according to the research. The median VAS score revealed a considerable disparity among the three study groups. Results showed it was substantially higher in group I (7 points) than in groups II (six points) and III (4 points) (5). At the beginning of the research, there were no significant differences between the study groups in terms of VAS. In terms of the oxford knee score (OKS), there was no significant difference between the study groups at the beginning. There was no discernible difference in overall patient satisfaction across the trial groups. Patients with osteoarthritis of the knee had their genicular nerves ablate using radiofrequency.

Keywords: radiofrequency, steroid, ozone intra, articular, radiofrequency ablation, genicular nerves, knee osteoarthritis.

1. Introduction

A prevalent kind of arthritis and a major contributor to disability is osteoarthritis (OA). Around 250 million people around the world and over 27 million people in the United States are affected by this degenerative and progressive joint condition. Over 65-year-old women, obese patients, and African-Americans have the highest chance of getting OA (about 35 percent). As the population continues to live longer and as obesity rates rise across the board in the United States, the number of people with diabetes is only going to grow in the coming years. Given the functional damage and handicap this ailment causes, as well as the detrimental impact it has on our society's social and economic components, this is cause for worry [1].

There are three bones in the knee (the femur at the back, the tibia at front, and the patella at the front), two kinds of cartilage (the menisci and hyaline cartilage), and a synovial membrane that make up the knee's largest synovial joint. Avascular cartilage receives lubrication and nourishment from the synovium, which produces synovial fluid. Since this joint is frequently used and stressed, painful conditions like OA occur frequently there [2].

Osteoarthritis of the knee discomfort is difficult to treat pharmacologically and can have unpleasant side effects. Knee arthroplasty may be an option, but there may be a long wait list, or some patients may not be candidates for surgery, or the patient may refuse to have a total knee replacement performed.. As a result, an effective alternative pain therapy with few side effects that may provide pain relief to individuals who are difficult to control would be a valuable addition to the therapeutic alternatives available [3].

For almost three decades, radiofrequency thermocoagulation (RFTC) has been employed as a less invasive and target-selective modality technique. This has been shown to be effective in the treatment of several chronic pain syndromes for the reduction of pain. In order to cause coagulative necrosis in the target tissue, continuous radiofrequency ablation (CRF) employs a high-frequency alternating current [4].

Osteoarthritis of the knee is commonly treated with intra-articular injections of prednisolone. It has been shown in clinical studies that the benefits are quite temporary (between one and four weeks). Steroidal short-term effects found in controlled studies and in clinical practise vary. When corticosteroids work, they do so by reducing inflammation by restricting capillary dilation and vascular structural permeability. There are substances that limit polymorphonuclear leukocytes and macrophage accumulation as well as kinin release from the body. In addition, they prevent the release of tissue-destructive enzymes, which assault and destroy healthy tissue without regard for source [5].

The study's goal is to examine the effectiveness of ozone, steroid, and a placebo in patients with osteoarthritis of the knee following radiofrequency ablation of the genicular nerves.

2. Patients and Methods

A. Technical design

1-Study type and region

This Prospective, single blind randomized clinical trial was conducted at Benha university hospital.

2-Study population

This study was conducted on 75 patients suffering from pain caused by osteoarthrosis of the knee joint.

3- Sample size

The sample size calculation was performed using G.power 3.1. The sample size was calculated as N ≥19 in each group based on the following considerations:

- 95% confidence limit and 95% power of the study.
- Group ratio 1:1
- The mean (±SD) of NRS at rest at 6 month (the primary outcome of our study) was 3.31 ± 0.64 with radiofrequency ablation of genicular nerves of knee and expected 25% decrease with the other techniques.

Six cases were added to each group to overcome dropout, so the total required cases are 25 in each group.

2.1. Inclusion criteria

- patients suffering from pain caused by osteoarthrosis of the knee joint. (grade 3-4 according to the Kellgren Lawrence classification).
- pain of moderate to severe intensity (VAS≥5, on a 10-point scale) during >3 months.
- pain resistant to conservative treatments.

2.2Exclusion criteria

- Acute knee pain associated with radicular neuropathy or intermittent claudication.
- Connective tissue diseases affecting the knee.
- Serious neurologic or psychiatric disorders.
- Mental deterioration impeding adequate communication or collaboration.
- Injection with steroids or hyaluronic acids during the previous 3 months.
- Anticoagulant medications and prior electro-acupuncture treatment.
- Infection at the site of injection.
- Patient with previous total knee replacement.

2.3Groups allocations

Patients will be randomly allocated into three main groups

- **Group 1: RFP** group**:** in this group the patient will not be injected intra-articularly after radio-frequency ablation of genicular nerves and this is the placebo group.
- **Group 2: RFS** group**:** in this group the patients will be injected with steroids intra-articularly after radiofrequency ablation of genicular nerves.
- **Group 3**: **RFO** group: in this group the patients will be injected with ozone intra-articularly after radiofrequency ablation of genicular nerves

B. Operational design

All patients will be subjected for

1. Full history taking.

2. Preoperative assessment

- One day before the intervention, all the patients were interviewed to explain the procedure.
- Routine investigations as complete blood count (CBC) and coagulation profile (prothrombin time and INR), random blood sugar was fulfilled.

3. Technique

- Thirty minutes before the procedure, an IV access was inserted and 1 gm cefazoline was given by infusion.
- The patient was monitored with ECG, pulse oximeter and non-invasive blood pressure.
- 1-2 mg midazolam and 20-50 microgram fentanyl were given to the patient.
- Under sterile conditions, the patient was placed in a supine position on a fluoroscopy table with a pillow under the popliteal fossa. The true AP fluoroscopic view of the tibiofemoral joint was obtained and showed an open tibiofemoral joint space with equal width interspaces on both sides. Skin and soft tissues were anesthetized with 1 mL 1% lidocaine. A 10 cm 22-gauge RF cannula with a 10 mm active tip (epimed , USA) was employed for the technique. Under fluoroscopic guidance, the cannula was advanced percutaneously towards areas connecting the shaft to the epicondyle, the so-called ‘‘tunnel technique’’, until bone contact was made the curve if the needle tip was directed away from the bone .After reaching correct position , the needle was turned 180 degree until the curve hugs the bony surface then lateral view was done, the needle tip was inserted a point midway between anterior two third and posterior one third . Sensory stimulation at 50 Hz was performed to identify the nerve position. The sensory stimulation threshold was required to be less than 0.7 V. In order to avoid inactivating motor nerves, the nerve was tested for the absence of fasciculation in the corresponding area of the lower extremity on stimulation of 2.0 V at 2 Hz. Lidocaine (2 mL of 2%) was injected before activation of the RF generator. The RF electrode was then inserted through the canula, and the electrode tip temperature was raised to 80 C for 2 minutes thermal radiofrequency. Two RF lesion were made for each genicular nerve.
- Then, the (RFS) group were injected with 40 mg methyprednisolone dissolved in 4 ml normal saline intra-articular and this were the first group.
- The second group (RFO) were injected with 5 ml ozone intra-articular after RF.
- The third group (RFP) were not injected after RF.

4. Primary Outcome Measures:

- Pain reduction [Time Frame:1 week 1, 6 months]
- Pain intensity is measured using a 10-point VAS score.

5. Secondary Outcome Measures:

- Global patient satisfaction [Time Frame: 1week,1 and 6 months]
- Satisfaction is scored on a 4-point Likert scale: 1 (poor), 2 (average), 3 (good) and 4 (very good)
- Oxford knee score to assess knee function.

Our primary outcome was the Oxford Shoulder Score (OSS), a patient-reported measure of functional limitation following shoulder surgery. Development and validation included patients with frozen shoulder, and it had been used in the long-term follow-up of these patients.

- The OSS is a 12-item measure with five response categories and a range of scores from 0 (worst) to 48 (best). It has been validated against the professionally endorsed Constant Score and the 36-item Short Form Health Survey (SF-36) and responsiveness over a 6-month period following surgical intervention has been established.
- The OSS were be completed at the hospital at baseline (i.e. day of randomization) and posted to trial participants at 3, 6 and 12 months after randomization. The primary endpoint is 12 months after randomization. The OSS was also be collected at the hospital on the day that treatment starts (i.e. day of the operation or for patients allocated to ESP on the day when the steroid injection is given or first visit to physiotherapy, whichever is the first to be delivered) and posted to participants to complete 6 months from when treatment starts. The OSS was being collected on the day the treatment starts and 6 months later due to the variation in waiting times as to when the trial interventions start.
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3. Results

No significant differences were reported between the study groups regarding age (P-value = 0.179), gender (P-value = 0.846), body mass index (P-value = 0.281), pain duration (P-value = 0.114), and Kellgren-Lawrence grade (P-value = 0.156) (Table 1 & figure 1).

VAS at baseline and follow up

The median VAS score showed an overall significant difference between the three study groups (P -value < 0.001). Post hoc revealed that it was significantly higher in group I (7) than groups II (6) and III (5).

No significant differences were reported between the study groups regarding VAS at baseline (P-value = 0.199, one month (P-value = 0.112), and six months (P-value = 0.06) **Table (2) & figure (2).**

Table (1) General characteristics in the studied groups

		Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	P-value
Age (years)	Mean ±SD	65 ±14	63 ±12	69 ±8	0.179
Gender	Males	9 (36.0)	11 (44.0)	10 (40.0)	0.846
	Females	16 (64.0)	14 (56.0)	15 (60.0)	
Body mass index	Mean ±SD	33 ±7	33 ±7	30 ±4	0.281
Pain duration (months)	Median (range)	60 (24 - 120)	60 (24 - 120)	72 (36 - 120)	0.114
Kellgren-Lawrence grade	Grade III	12 (48.0)	7 (28.0)	6 (24.0)	0.156
	Grade IV	13 (52.0)	18 (72.0)	19 (76.0)	

One-way ANOVA was used for age and BMI. Kruskal Wallis test was used for pain duration. Chi-square test was used for categorical data

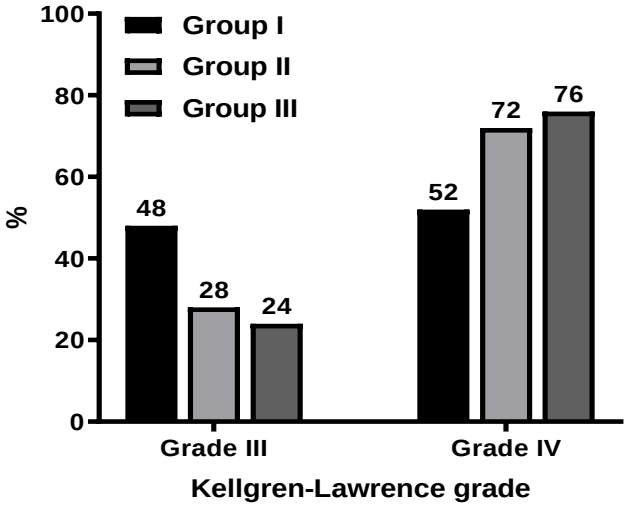

Fig. (1) Kellgren-Lawrence grade in the studied groups

Table (2) VAS at baseline and follow up in the studied groups

VAS		Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	P-value
Baseline	Median (range)	9 (7 - 10)	9 (6 - 10)	9 (7 - 10)	0.199
One week	Median (range)	7 (4 - 9) [a]	6 (3 - 9) [b]	5 (3 - 8) [b]	**<0.001**
One month	Median (range)	3 (1 - 10)	3 (1 - 10)	2 (1 - 9)	0.112
Six months	Median (range)	3 (1 - 10)	3 (1 - 10)	2 (1 - 9)	0.06

Kruskal Wallis test was used. Post hoc was done using Bonferroni's method. Different letters indicate significant pair

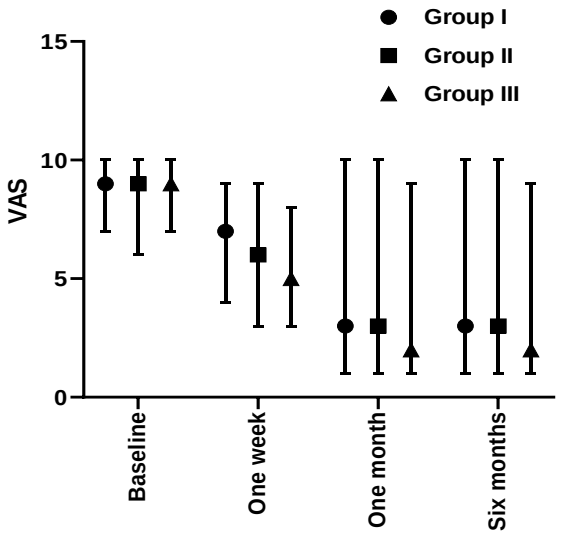

Fig. (2) VAS at baseline and follow up in the studied groups

❖ **Oxford knee score (OKS) at baseline and follow up**

No significant difference was reported between the study groups regarding oxford knee score (OKS) at baseline (P-value = 0.305), one week (P-value = 0.520), one month (P-value = 0.483), and six months (P-value = 0.350) **(figure 3). Oxford knee score (OKS) at baseline and follow up in the studied patients**

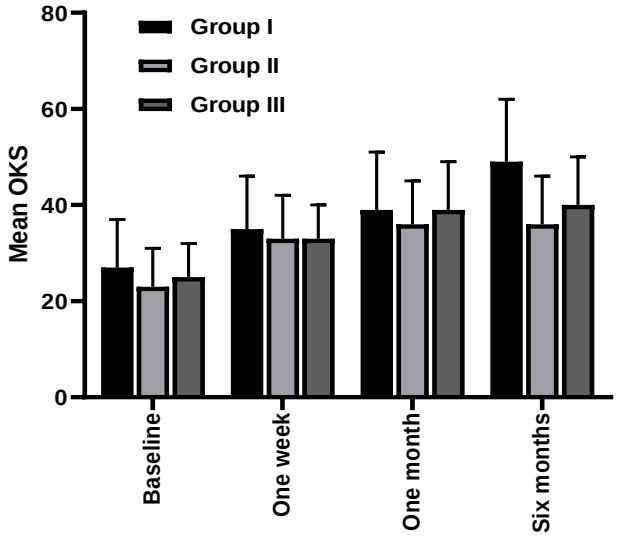

Fig. (3) Oxford knee score (OKS) at baseline and follow up in the studied patients

❖ **Patient satisfaction**

No significant difference was reported between the study groups regarding global patient satisfaction at one week (P-value = 0.758), one month (P-value = 0.778), and at six months (P-value = 0.637) **(Table 3).**

Table (3) Patient satisfaction in the studied groups at different follow-up times.

Patient satisfaction		Group I (n = 25)	Group II (n = 25)	Group III (n = 25)	P-value
One week	**Poor to average**	23 (92.0)	21 (84.0)	21 (84.0)	0.758
	Good to very good	2 (8.0)	4 (16.0)	4 (16.0)	
One month	**Poor to average**	9 (36.0)	7 (28.0)	7 (28.0)	0.778
	Good to very good	16 (64.0)	18 (72.0)	18 (72.0)	
Six months	**Poor to average**	9 (36.0)	6 (24.0)	7 (28.0)	0.637
	Good to very good	16 (64.0)	19 (76.0)	18 (72.0)	

Chi-square or Fisher's exact test was used

4. Discussion

Age (P-value = 0.179), gender (P-value = 0.846), BMI (P-value = 0.281), pain duration (P-value = 0.114), and the Kellgren-Lawrence scale grade (P-value = 0.156) were all found to be non-significant across the research groups.

According to our findings, the study by Hashemi et al. [5] found that a total of 72 patients (aged 51-78 years) were included in the study, half of whom were female, of the same age, and had a similar BMI (Body Mass Index). The mean BMI of participants in the Ozone and RF groups was 28.64 4.98 and 26.13 3.03 (p= 0.06), respectively. Aside from that, the average age was 66.69 years old for men and 68.33 years old for women (p= 0.459). In the ozone group, there were 20 patients over the age of 65, while in the RF group, there were 32 patients over the age of 65. In terms of gender distribution, ladies made up 86.1% of mention group contributors while males made up 77.8% of mention group contributors

According to the results of this investigation, there was a significant difference between the three study groups' median VAS scores at baseline and follow-up (P -value 0.001). Results showed it was substantially higher in group I (7 points) than in groups II (six points) and III (4 points) [5]. Neither the baseline (P-value = 0.299) nor the month-and-six-month (P-value = 0.06) VAS scores differed significantly across the study groups.

According to Erdem & Sir's [6] study, pulsed radiofrequency of the genicular nerves greatly improved the majority of patients' perceived pain and impairment. Our findings corroborated this. 14 of 17 patients (82%) and 15 of 17 patients (88%) in Group 1 showed improvement in pretreatment VAS ratings of 50% at 3 weeks and 3 months after therapy, while 4 of 6 patients (67%) and 4 of 6 patients (67%) in Group 2 did the same. Osteoarthritis patients were separated into two groups: those who had arthroplasty, and those who experienced osteoarthritis-related knee discomfort.

At 2 (P 0.001) and 4 (P 0.001) weeks following GNB, Kim et al. [7] found that VAS scores were considerably lower in the lidocaine plus TA group than in the lidocaine alone group. To meet the criteria for a minimally clinically meaningful improvement, patients in the lidocaine with TA group reported relief from acute pain that persisted for at least two weeks after the treatment was completed.

According to Konya et al. [8], retrospective evaluations were performed on 48 patients who had genicular nerves ablated using radiofrequency (RF). In comparison to preoperative values, the mean VAS scores were significantly lower at 1 and 3 months, as well as at 6 months (P 0.001). The WOMAC index was found to be significantly lower postoperatively than preoperatively (P 0.001). Sixty-seven percent of opiate users and 56 percent of NSAID users had quit taking their medications, according to the research. Neither during the procedure nor afterward, there were any major complications.

In addition, Kamel [9] noted that the trial included 60 individuals with osteoarthritis of the knee that had been diagnosed with chronic. Twenty-five of the patients (Group A) received only conventional analgesics after radiofrequency neurotomy of the genicular nerves. The VAS was significantly different between the two groups in the second week, third month, and sixth month. When comparing pretreatment VAS levels with VAS values over the course of the entire follow-up period, substantial shifts were observed.

The VAS and GPM were used to measure the endpoint pain reduction in the study by Lopes de Jesus et al. [10]. (Geriatric Pain Measure). These tests revealed statistically significant differences in the follow-up behaviour of the groups, with p 0.001 indicating a significant difference. P 0.001 showed that values fell precipitously after the second treatment stage. There were statistically significant differences in the results between the two groups, with patients treated with ozone reporting less discomfort shortly after the intervention began (p 0.001).

According to the findings of Anzolin & Bertol [11], using ozone on individuals with osteoarthrosis has clinically significant benefits. Due to its low cost and effectiveness, ozone therapy for osteoarthrosis should be incorporated in the country's Public Health system, given the disease's prevalence.

There was no significant difference found between the study groups in terms of Oxford knee score (OKS) at baseline, one week, one month, and six months (P-value = 0.350), according to the results of the current research.

The study of Fonkoue [12] backed up our findings, which showed that group allocation had no significant impact on OKS mean changes. The passage of time has a profound impact on each group. There was no connection between the passage of time and the distribution of participants into groups. At 4 and 12 weeks, the OKS improved in both groups when compared to the initial value. To test the effectiveness of a GNB, the researchers randomly assigned 55 patients with chronic knee osteoarthritis pain to either the CT (traditional) or RT (updated) groups (n = 28 each). The patients were given a fluid mixture of 2 mL: lidocaine 1 percent + 20 mg triamcinolone.

At baseline, the OKS was 7.75 1.25. After the procedure, the OKS was 28.88 2.53 (p value 0.05) and 28.13 1.80 (p value 0.05) at 1 and 6 months. Patients with osteoarthritis of the knee joint in grades III and IV, with severe pain (NRS > 7) who had failed conservative management and intra-articular injections after a positive genicular nerve block with local anaesthetics underwent ultrasound-guided radiofrequency ablation (RFA) of all genicular nerves of the knee joint.

However, Ragab et al. [14] have shown that when comparing the mean change in VAS and OKS at 2, 4 and 8 weeks from baseline values for both groups, the GNB group showed significantly improved pain and functional ability at all follow-up periods in comparison to the IACSI group.

It was reported that both groups in the Hashemi et al. [5] trial reacted effectively to treatment and the degree of pain decreased significantly after 12 weeks compared to the baseline. Even though VAS and OKS showed greater reduction of pain in the RF group, the difference was not statistically significant ($p>0.05$). According to the OKS, RF provided better pain reduction for those who were older ($p=0.0001$) than those who were younger ($p=0.0001$).

At one week (P-value = 0.758), one month (P-value = 0.778), and six months (P-value = 0.637), no significant difference was seen between the study groups in terms of global patient satisfaction when looking at the data we have.

There were statistically significant differences only at 1-hour post intervention in the Fonkoue [12] trial between the RT and control groups for patients who achieved pain reduction of more than 50% in the knee (82.1% [95 percent CI = 63.1–93.9] vs. 100 percent [95 percent CI = 97.2–100] P =.02). Up to 12 weeks after intervention, both procedures significantly reduced pain and improved joint function.

All evaluation metrics improved significantly in the IACSI and IACSI + GNB groups, according to Yilmaz et al. [15]. All evaluation parameters except QMA (quadriceps muscle cross-sectional area) (0.10 0.18 and 0.11 0.22, respectively) and NHP (Nottingham Health Profile) scores in the 1st month evaluation (- 3.11 6.99 versus - 3.54 1.74, respectively) showed better improvement in the IACSI + GNB group than the IACSI group.

A 2-month follow-up research conducted by Giombini et al. [16] found that patients with osteoarthritis (OA) of the knee who received O2O3 and HA together had a better outcome than those who received HA and O2O3 alone.

5. Conclusion

After radiofrequency ablation of genicular nerves in knee osteoarthritis patients, there was no statistically significant difference in the efficacy of ozone, steroid, and placebo.

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