



Comparison between Fluoroscopy Guided Radiofrequency Ablation of Genicular Nerves and Intra Articular Injection of Methylprednisolone Acetate in Relieving Pain and Improving Function in Grade 3 and 4 Osteoarthritis of Knee: A Randomised Controlled Trial

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ABSTRACT

Background: Osteoarthritis is the second most common rheumatologic problem in India. The prevalence of osteoarthritis in India is 22% to 39% and knee osteoarthritis alone contributes to 80% of the osteoarthritis burden. Knee osteoarthritis is much more prevalent in India than in the West and accounts for as much more disability as any other chronic condition. Despite the immense impact of this disease, very few effective non-surgical options are available to handle it. In the severe stages of osteoarthritis, knee arthroplasty remains the last option. However, many cannot afford an arthroplasty surgery due to the poor socio-economic condition of the people in this part of the country. **Objective:** To compare two non-surgical options for relieving pain and function-fluoroscopy-guided radiofrequency ablation of genicular nerves and intra-articular injection of methylprednisolone acetate in patients with osteoarthritis of the knee who are candidates for knee arthroplasty. **Methods:** A randomized controlled trial was done in the Department of Physical Medicine and Rehabilitation, Regional Institute of Medical Sciences (PMR, RIMS) for 1 year on 76 patients with knee osteoarthritis Kellgren-Lawrence (KL) Grade 3 and 4. The participants were divided into two groups-study and control groups. The study group underwent Radiofrequency Ablation (RFA) of genicular nerves of the knee, while the control group received Intra-Articular (IA) knee injection with 2 ml of Methylprednisolone acetate (40 mg/ml) mixed with 2 ml of Lignocaine 2%. Assessments of Visual Analog Scale (VAS) and Western Ontario McMaster University Osteoarthritis Index (WOMAC) were done at 1 week, 4 weeks, and 12 weeks. **Results:** Study group who received RFA of genicular nerves showed a decrease in VAS score from 6.84 ± 0.64 at baseline to 2.61 ± 0.72 at 1 week and 2.97 ± 0.88 at 12 weeks. The control group receiving 80mg of Methylprednisolone also showed a decrease in VAS score from 5.82 ± 0.56 at baseline to 2.18 ± 0.39 at 1 week and 4.03 ± 0.54 at 12 weeks. Consistent improvement was also seen in the WOMAC function score in both groups. It significantly improved from 44.79 ± 7.18 at baseline to 26.79 ± 4.37 at 12 weeks in the RFA group, while in the steroid group it improved from 41.26 ± 5.31 at baseline to 24.89 ± 3.43 at 12 weeks ($p < 0.05$). **Conclusion:** RFA of the genicular nerve provides longer and sustained pain relief in Grade 3, 4 OA knee than the intra-articular steroid. It can thus be used as an effective modality for relieving pain in patients unable to undergo knee joint replacement surgery.

Keywords: Osteoarthritis, Kellgren-Lawrence Grade, Radiofrequency ablation, Relieving pain, WOMAC

INTRODUCTION

Osteoarthritis (OA) is a destructive joint failure, a condition in which all structures in the joint have undergone a pathologic change, often in concert. Osteoarthritis is the second most common rheumatologic problem in India. The prevalence of OA in India is 22% to 39% and knee OA alone contributes to 80% of osteoarthritis burden. Despite

the immense impact of this disease, very few effective non-surgical options are available to handle it [1,2]. The optimal management of knee OA requires a combination of non-pharmacologic and pharmacologic treatments such as acetaminophen, non-steroidal anti-inflammatory drugs, or selective COX-2 inhibitors (Etoricoxib 90 mg, available in India). However, these drugs are associated with potential safety concerns and short half-life [3,4]. Radiofrequency ablation of the genicular nerve is one new topic in the management of chronic OA knee pain.

The knee joint is innervated by branches from the obturator, femoral, tibial, and common fibular nerve. Genicular branches from the tibial (Superomedial, Inferomedial, and Middle genicular nerve) and common fibular nerves (Superolateral, Inferolateral, and recurrent genicular nerve) accompany the genicular arteries. Conventional Radiofrequency ablation uses a high-frequency alternating current. An electrode is placed on the target nerve and thermocoagulation induces tissue destruction by producing heat up to 60°C-80°C. Under fluoroscopic or ultrasound guidance, relying on bony landmarks, thermal RFA targets the lateral superior, medial superior, and medial inferior genicular nerves [5,6].

Intra-articular treatment is of special interest not only for pain relief and pain flares in more acute situations but also to delay any surgical intervention by improving the patients' subjective quality of life. To this date no comparison study between intra-articular knee with methylprednisolone acetate and RFA genicular nerves in chronic OA knee with Kellgren Lawrence Grade 3, 4 has been done.

MATERIALS AND METHODS

A randomized controlled trial was done in the Department of Physical Medicine and Rehabilitation, Regional Institute of Medical Sciences for 1 year starting from March 2019. Seventy-six patients diagnosed with KL Grade 3, 4 OA knee were recruited for the study from the OPD patients. Informed consent was taken from all participants before starting the study.

Persons with osteoarthritis of the knee as per 2016 revised ACR criteria for early diagnosis of osteoarthritis, radiologic tibiofemoral OA (Kellgren Lawrence Grade 3, 4) with a positive diagnostic block (>50% improvement in pain) were included in the study.

Patients with bilateral OA knee of Grade 3 or more, prior knee surgery/injury, arthritis due to other causes, serious neurologic/psychiatric disorder, injection with steroids/hyaluronan in the last 3 months, on a pacemaker, uncontrolled diabetes, coagulation disorder, VAS score <5, local or systemic infection, allergy to anesthetic medication used, uncooperative patient were excluded from the study.

The 76 participants were assigned to two groups-the study and the control group using block randomization.

The study group underwent continuous RFA of superolateral, superomedial, and inferomedial genicular nerves under fluoroscopic guidance following a successful diagnostic block (>50% improvement in pain within 2 hours-4 hours) of genicular nerves with 2% Lignocaine.

Twenty-two gauge RF cannula 10 cm in length with 10 mm active tip was inserted perpendicular to skin under fluoroscopy guidance (SIEMENS Multimobil 5E, C-Arm, manufactured by SIEMENS LTD, Goa, India) and was advanced percutaneously towards area connecting shaft to the epicondyle until bone contact was made. The stylet was removed and an RF probe was inserted. To confirm the sensory nerve position, stimulation was done with 50 Hz at (0.3-0.5) V. To avoid motor nerve ablation, it was made sure no fasciculation of lower limb muscles occur by stimulation with 2 Hz at 1.0 V.

One ml of 2% Lignocaine was given before activation of RF generator (Radiofrequency Generator INOMED RFG-1B LG2 Lesion Generator Version II (Model: LG2), made in Germany). RF lesion was performed over 90 sec with temperature raised to 70°C-75°C. One RF lesion was made for each genicular nerve [5].

Figure 1 shows the fluoroscopic image in AP view showing RF cannula placement at the junction of shaft of femur with the femoral condyles where the superomedial and superolateral genicular nerves traverse. Figure 2 shows the placement of 22G RF cannula at superolateral, superomedial, and inferomedial genicular nerves followed by insertion of RF probes to confirm needle position at the target nerves by sensory stimulation (50 Hz at 0.3 V-0.5 V) and to avoid motor nerve ablation (stimulation with 2 Hz at 1 V). Continuous RF ablation of the three genicular nerves is then done at 70 degrees Celsius for 90 minutes as shown in Figure 3.



Figure 1 Shows fluoroscopic image in AP view showing RF cannula placement at the junction of shaft of femur with the femoral condyles where the superomedial and superolateral genicular nerves traverse



Figure 2 Shows placement of 22G RF cannula at superolateral, superomedial and inferomedial genicular nerves followed by insertion of RF probes to confirm needle position at the target nerves by sensory stimulation (50 Hz at 0.3 V-0.5 V) and to avoid motor nerve ablation (stimulation with 2 Hz at 1 V)



Figure 3 Continuous RF ablation of the three genicular nerves are then done at 70 degrees Celsius for 90 minutes

The control group received intra-articular knee injection with Methylprednisolone acetate 2 ml (Depomedrol, 40 mg/ml; Manufacturer: Pfizer) mixed with 2 ml of 2% Lignocaine. The patient was placed in the sitting position with knees flexed to 90 degrees. The patellar tendon was palpated and the middle of the patellar tendon was marked. The patient was prepared in a standard aseptic and antiseptic fashion over an area large enough to allow palpation of landmarks and a sterile technique was used throughout the procedure. A 21G needle was inserted horizontally and advanced to the intercondylar notch. Aspiration was attempted until the needle has entered the synovial space. If there was an effusion of joint, the aspiration was completed. After negative aspiration or if the aspirated fluid was non-inflammatory (clear and viscous), the joint was injected with the above solution containing a mixture of methylprednisolone acetate and lignocaine [7].

Follow-up assessments were done at 1 week, 4 weeks, and 12 weeks post-procedure to see changes in pain and function using the outcome variables VAS and WOMAC respectively.

Statistical Analysis

Analysis was done using Statistical Package for the Social Sciences, SPSS 21 version. For descriptive statistics, mean and standard deviation were used. For analytical statistics, paired t-test, independent t-test, and ANOVA were used for numerical data; and chi-square test was used for categorical data. p -value < 0.05 was taken as significant.

RESULTS

Table 1 shows that there were no statistical differences in the baseline characteristics between the groups, hence we proceeded with the study. When studying the background characteristics of the patients, most of the patients were from the age group of 50-70 years, with females comprising 78.90%. Maximum numbers of patients were from the plain area of Manipur (82.90% from plains vs. 17.10% from hilly areas).

Table 1 Baseline characteristics of participants

Characteristics	Group		p-value
	Study (n, %)	Control (n, %)	
Age (years) Mean (SD)	65.26 (6.85)	58 (8.94)	0.385
41-50	3 (50)	3 (50)	
51-60	10 (37)	17 (63)	
61-70	17 (56.7)	13 (43.3)	
71-80	8 (61.5)	5 (38.5)	
Sex			
Male	7 (43.8)	9 (56.2)	0.574
Female	31 (51.7)	29 (48.3)	
Place of residence			
Plain area	33 (52.4)	30 (47.6)	0.361
Hilly area	5 (38.5)	8 (61.5)	
Side of knee OA			
Right side	28 (56.0)	22 (44.0)	0.226
Left side	10 (38.5)	16 (61.5)	
Kellgren Lawrence grading			
Grade 4	13 (44.8)	16 (55.2)	0.637
Grade 3	25 (53.2)	22 (46.8)	
Duration of knee OA			

<1 year	2 (50.0)	2 (50.0)	0.448
1-3 years	18 (43.9)	23 (56.1)	
>3-5 years	12 (52.2)	11 (47.8)	
>5 years	6 (75.0)	2 (25.0)	
VAS Score			
Mild (1-3)	4 (40.0)	6 (60.0)	0.227
Moderate (4-6)	18 (43.9)	23 (56.1)	
Severe (7-9)	16 (64.0)	9 (36.0)	
Total WOMAC score	59.47 (7.49)	47.92 (6.78)	0.138

Table 2 and Table 3 show significant improvement in both VAS and WOMAC in both groups during all follow-ups. When comparison was done between the study and control group, maximum improvement was seen in both groups at 1 week, with a mean improvement in VAS scores from (6.84 ± 0.64 vs. 5.82 ± 0.56) at baseline to (2.61 ± 0.72 vs. 2.18 ± 0.39) at 1 week. However, on comparing mean VAS scores achieved at 4 weeks with 12 weeks, it is found that at 12 weeks there was a greater improvement in the study group (2.61 ± 0.72 to 3.97 ± 0.88 vs. 2.18 ± 0.39 to 4.03 ± 0.54). Comparing WOMAC score shows functional improvement was greatest at 12 weeks in both the groups. It significantly improved from 44.79 ± 7.18 at baseline in the study group to 20.42 ± 3.36 at 12 weeks follow up; while in the control group it improved from 41.26 ± 5.31 to 25.26 ± 3.16 at 12 weeks ($p < 0.05$).

Table 2 Table showing VAS scores of participants at baseline, 1 week, 4 weeks and 12 weeks follow up (n=76)

Parameters VAS scores	Groups Mean(SD)		p-value*
	Study (n=38)	Control (n=38)	
Baseline	6.84 (0.638)	5.82 (0.563)	0.001
1 week	2.61 (0.718)	2.18 (0.393)	
4 weeks	2.61 (0.718)	2.18 (0.393)	
12 weeks	2.97 (0.885)	4.03 (0.545)	
*p-value<0.05 is taken as significant			

Table 3 Table showing total WOMAC scores of participants at baseline, 1 week, 4 weeks and 12 weeks follow up (n=76)

Parameters Total WOMAC scores	Groups Mean (SD)		p-value*
	Study (n=38)	Control (n=38)	
Baseline	59.47 (7.490)	47.92 (6.780)	0.001
1 week	33.95 (5.146)	35.58 (3.561)	
4 weeks	30.32 (3.480)	31.34 (3.257)	
12 weeks	22.13 (4.783)	28.03 (4.365)	
*p-value<0.05 is taken as significant			

DISCUSSION

To our knowledge, this is the first study comparing conventional RFA of genicular nerves to intra-articular methylprednisolone in Grade 3 and 4 osteoarthritis of the knee. Patients with Grade 3 and 4 with severe knee pain are candidates for knee replacement, however many have a recurrence of pain following the surgery, while many are physically not fit to undergo surgery. The level of evidence for intra-articular steroids in osteoarthritis knee is considered to be Level 1A+, however, its effect lasts for only 3-4 weeks [8].

Sari S, et al., first compared RFA to intraarticular injections in a trial [9]. Seventy-three patients with at least Grade 2 Kellgren-Lawrence OA were randomized to receive either RFA of the SL, SM, and IM genicular nerves at 80°C for 90 seconds or intra-articular injection of bupivacaine, morphine, and betamethasone. Patients were assessed at baseline, 1 and 3 months for pain level *via*. VAS and function *via*. the Western Ontario and McMaster Universities Osteoarthritis (WOMAC) index. Results showed statistically superior pain relief with RFA at 1 and 3 months, but superiority in the total WOMAC score with RFA only at 1 month.

Qudsi-Sinclair, et al., performed a randomized controlled trial where 28 participants with knee pain following total knee replacement were evaluated after having received traditional radiofrequency (n=14) or local anesthetic and corticosteroid block of genicular nerves in the knee (n=14) [10]. During the first 3 to 6 months an improvement in joint function and a reduction in pain was shown with the results being similar between the two arms.

Davis T, et al., conducted the largest study on RFA knee and was also the first to employ Conventional RFA (CRFA) [11]. One hundred and fifty patients with at least KL Grade 2 were randomized to receive either CRFA or Intra-Articular Steroid (IAS) injection. The primary outcome was the percentage of patients achieving at least 50% pain reduction at 6 months follow-up as measured by the Numerical Rating Scale. Secondary outcome measures included function measured on OKS, the patient's overall perception of the treatment, and analgesic usage. Pain relief with CRFA was superior to that obtained with IAS at all periods, and at 6 months follow-up 74% of the CRFA group had at least 50% relief compared to just 16% of the IAS group. Function and global perception were also superior in the CRFA cohort, although there was no statistical difference between the groups in terms of oral opioid use.

El Hakeim EH, et al., compared RFA to non-interventional therapy. Sixty patients with at least Grade 3 Kellgren-Lawrence OA were randomized to receive either RFA of the SM, SL and IM branches or conventional treatment with oral acetaminophen and diclofenac [12]. Patients were evaluated at baseline, 2 weeks, 3 months, and 6 months. Results showed statistically superior pain relief with RFA at all follow-up intervals. Function, as assessed by the WOMAC index, was improved in both groups at 6 months but was superior with RFA. Lastly, patient satisfaction as measured on a Likert scale was significantly higher at 3 and 6 months follow-up in the RFA group.

The present study found that both RFA of genicular nerves and Intra-articular steroids can result in a significant reduction of pain with improvement in function in Grade 3, 4 OA knee. However, at 12 weeks effect of steroids starts wearing off with an increase in VAS from 2.18 ± 0.39 at 4 weeks to 4.03 ± 0.54 at 12 weeks, while in the RFA group the pain relief achieved at 1 week was sustained till 12 weeks.

CONCLUSION

RFA of the genicular nerve provides longer and sustained pain relief in Grade 3, 4 OA knee than the intra-articular steroid. It can thus be used as an effective modality for managing severe pain in knee osteoarthritis in patients who are unfit for knee replacement surgery, unwilling to undergo surgery, or recurrence of pain following knee replacement surgery. Lack of larger sample size, absence of blinding, and short follow-up were some of the limitations in the study. It, therefore, necessitates that a study be done on a larger sample size with longer follow-up to substantiate the finding.

DECLARATIONS

Conflicts of Interest

The authors declared no potential conflicts of interest concerning the research, authorship, and/or publication of this article.

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