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Original Article

Intra-articularly applied pulsed radiofrequency can reduce chronic knee pain in patients with osteoarthritis

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Abstract

Background: Osteoarthritis (OA) is the most widespread chronic joint disease worldwide. Symptomatic knee OA is observed in approximately 12% of individuals more than 60 years of age. Conservative treatments models may not be effective always, and that some of them have serious adverse effects that prompted the researchers to research different treatment methods. In this study, we investigated short- and mid-term effectiveness of intra-articular pulsed radiofrequency (PRF) applied in patients with chronic knee pain due to OA.
Methods: This study was carried out in the pain management center of a university hospital between January 2009 and June 2009. The patient record files of 31 patients who received intra-articular PRF were retrospectively reviewed. The antero-lateral area of the knee, where the intervention would be applied, was anesthetized with 1% lidocaine. An introducer needle was placed intra-articularly. PRF was started as 42°C at 2 Hz for 15 minutes. The pain of the patients was evaluated by 10 cm Visual Analog Scale (VAS). Furthermore, the ages, the gender, the symptom duration of the patients, the side of the knee on which the intervention was applied, and the complications were collected for statistical evaluation.
Results: Although the mean initial VAS scores of the patients were 6.1 ± 0.9 cm, it was found, respectively, to be 3.9 ± 1.9 cm and 4.1 ± 1.9 cm at the first- and sixth-month follow-ups. In general, a decrease of 32.8% in mean in the VAS scores was achieved in the last follow-up; whereas the rate of patients reporting a minimum decrease of 2 points in the VAS scores was 64.5% and the rate of patients reporting a decrease of ≥50% in their pain was calculated as 35.5%.
Conclusion: PRF applied to the knee joint appears to be an effective and safe method.

Keywords: Knee; Osteoarthritis; Pain; Pulsed radiofrequency; Radiofrequency

1. Introduction

Osteoarthritis (OA) is the most widespread chronic joint disease worldwide. Its primary symptoms are pain, stiffness, loss of function in the joints, and muscle atrophy.[1–3] One of the most incurred joints in OA is the knee joint, which carries the heavy burden of the body.[4] Knee OA is closely related with increasing age and obesity. Symptomatic knee OA is observed in approximately 12% of individuals aged more than 60 years.[5] The conservative treatment of OA usually includes physical therapy, analgesics including nonsteroidal anti-inflammatory drugs (NSAIDs) and intra-articular steroid and hyaluronan injections.[6] Although conservative management is effective in most OA patients, these treatments are not effective in a small percentage of patients, and some of them

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have serious adverse effects, prompting the investigators to research different treatment methods.

Minor and major surgical methods are also applied for treatment of knee OA. The place of arthroscopy, which is one of these methods, is controversial. It was reported that arthroscopy would not be useful in cases where findings of a meniscal rupture or a recent trauma do not exist.[7] Another method that can be applied for surgical treatment of OA is total knee replacement. Despite the successful results achieved by total knee replacement, which is an option considered for end-stage knee diseases, a significant percent of the patients continue suffering from pain despite total knee replacement.[8]

As a general concept, pain treatment by radiofrequency (RF) energy has had wide coverage in the pain management practice for the past 30 years.[9] In conventional radiofrequency thermocoagulation (CRFT) applications, an electrode emitting RF currents is placed on the target nerve and the destruction of the nerve tissue is ensured by the heat produced.[10] CRFT has many fields of application such as "denervation of the medial branch innerving the zygapophycial joint", "dorsal root ganglionotomy", "intradiscal applications", "percutaneous cordotomy for treatment of malign pain", and "trigeminal radiofrequency ganglionotomy for treatment of trigeminal neuralgia".[10]

Pulsed RF (PRF) application is a relatively new method that has been developed as an alternative to CRFT. PRF has much less (if any) neurodestructive characteristic. In PRF, the RF energy is applied at high voltage (typically 45 V) and with 20 millisecond bursts followed by 480 millisecond silent phases.[11] Thus, because of the long silent phase, the tissue temperature will be spread and will not exceed 42°C. So, no tissue damage will develop because the tissue temperature will remain below 45−50°C, which is considered as the irreversible tissue damage threshold.[12] PRF, which can be applied in a similar manner to CRFT applications (such as facet medial nerve or trigeminal nerve applications), is distinguished mainly by peripheral applications where CRFT is never applied. PRF has been reported to be used successfully in treatment of disorders such as myofascial trigger points,[11] phantom limb pain,[13] occipital neuralgia,[14] meralgia paresthetica,[15] and premature ejaculation.[16] One of the fields where PRF was claimed to be effective is that of intra-articular applications.[17,18]

Based on a study published by Sluijter et al[17] in 2008, we have been applying intra-articular PRF for treatment of chronic pain developing due to knee OA in our pain management center. In this study, we intended to survey retrospectively the cases where we applied intra-articular PRF, and to study the effectiveness of this method.

2. Methods

2.1. Study design and setting

This study was carried out with the approval of the Institutional Review Board and in a retrospective, noncontrolled manner. All patients who participated in the study were informed in written and verbal on the intervention to be applied before application, and their written consents accepting the intervention were obtained. The study and all interventions were carried out in the pain treatment center of a university hospital. The files of the patients, on whose knee joints PRF was applied between January 2009 and June 2009, were reviewed independently by a physician who was not involved in the study.

2.2. Participants

The following were used as the criteria for being included in the study: (1) patients with a diagnosis of knee OA according to The American College of Rheumatology criteria[19]; (2) patients between Stage 1 and Stage 3 radiologically, according to the Kellgren-Lawrence classification[20]; (3) patients who had continued to conservative treatment such as physical therapy, analgesic drugs including NSAIDs or opioids, for at least six months, but could not respond to the treatment sufficiently [<2-point improvement in pain severity by Visual Analog Scale(VAS)].

The following were used as the exclusion criteria for the study: (1) patients at Stage 4 radiologically, according to the Kellgren-Lawrence classification; (2) existence of general contraindications against application of invasive intervention (such as hemorrhagic diathesis, systemic infection, or local infection at the area to be intervened); (3) excessive use of opioid; (4)psychiatric disorders.

2.3. Procedures

All procedures were carried out under local anesthesia, with blind technique, in the intervention room of the pain treatment center. After the patients who would be intervened were prepared according to the standard hunger protocol (6−8 hours of hunger), all of them had vascular access and were given isotonic solution of 0.9%. Following the standard monitorization (3-lead ECG, TA, pulsoxymetry), the patients were seated in a chair. After the area to be intervened was wiped with an iodine-based antiseptic solution, it was draped according to the rules of sterility. The antero-lateral part of the knee was palpated, and the entry point was anesthetized with 1% lidocaine. An introducer needle with 22 G 100-mm length and 10-mm active tip (Baylis Medical Inc., Montreal, Canada) was placed intra-articularly through the predefined area. After satisfactory placement, the stylet in the introducer was removed and RF probe (Baylis Medical Inc., Montreal, Canada) was placed through the introducer needle. Then, PRF was applied with 42°C temperature and a pulse width of 20 milliseconds, at 2 Hz for 15 minutes. Because the application was not painful, sedoanalgesia was not applied to any patients during the intervention. After the intervention was completed, a plaster was applied to the entry point and the patients were transferred to the recovery room. The patients who stayed in this room for 30 minutes were monitored by the clinic nurse for early complications and then discharged from hospital with

suggestions to rest for the 1st day and then engage in their normal life in the following days.

2.4. Outcome measurements

The pain of the patients was evaluated by a 10-cm VAS. In this scale, "0" identifies the situation where no pain exists and "10" identifies the most severe pain that can be imagined. Because most of our patients did not experience pain unless movement, pain severity was assessed on motion.

Furthermore, the ages, the gender, the duration of symptom, and the side of the knee on which the intervention was applied (right or left) were collected for statistical evaluation.

Additionally, if early or late complications developed, these were also recorded for evaluation.

2.5. Follow-up period

From all patients who received knee PRF between January 2009 and June 2009, only those who received PRF due to OA and the follow-up notes of whom existed for the 1st month and 6th month after the intervention were included in the study.

The successful result criteria were determined as achievement of a decrease of at least 2 points in VAS scores when the latest follow-ups were compared with the baseline.[21,22]

2.6. Statistical analysis

All data were analyzed using the Medcalc Version 10.3.0.0 (MedCalc Software, Mariakerke, Belgium) for Windows. We used the paired samples *t* test with Bonferonni's correction to perform pairwise comparisons. We also used Spearman correlation coefficients to assess the effects of various factors on the outcomes. $p < 0.05$ was considered statistically significant in all analyses. The values are given as mean ± standard deviation.

3. Results

3.1. Demographic characteristics

The knee PRF application was performed on a total of 49 patients between January 2009 and June 2009. From these patients, those who received knee PRF for reasons other than OA and those whose follow-up data are missing were excluded from the study. Thus, the remaining 31 patients were taken into statistical evaluation. The mean age of the patients was 62.8 ± 9.3 years, and 71% of them were women. The mean symptom duration was 78.8 ± 64.3 months. Twenty-three patients had bilateral knee OA, all of them underwent PRF application made bilaterally whereas 16.1% of the patients took only analgesic drugs (NSAIDs and/or opioids) and 35.5% of them had been treated with analgesic drugs (NSAIDs and/or opioids) + physical therapy + intra-articular injection (steroid or hyaluronan) before PRF applications. (Table 1).

Table 1
Demographic characteristics of study patients

Age (y)	Mean ± SD	62.8 ± 9.3
	Range	36–78
Gender	Women *n* (%)	22 (71)
	Men *n* (%)	9 (29)
Duration of symptom (mo)	Mean ± SD	78.8 ± 64.3
	Range	6–240
Symptomatic knee side	Right *n* (%)	2 (6.4)
	Left *n* (%)	6 (19.4)
	Bilateral *n* (%)	23 (74.2)
Treatment forms applied before	Analgesic drugs (NSAIDs and/or opioids)	5 (16.1)
	Analgesic drugs (NSAIDs and/or opioids) + physical therapy	15 (48.4)
	Analgesic drugs (NSAIDs and/or opioids) + physical therapy + intra-articular injection (steroid or hyaluronan)	11 (35.5)

NSAID = nonsteroidal anti-inflammatory drugs; SD = standard deviation.

3.2. Outcome data

Although the mean of the initial VAS scores of the patients was 6.1 ± 0.9 cm, these values were found, respectively, to be 3.9 ± 1.9 cm and 4.1 ± 1.9 cm at the 1st month and 6th month follow-ups (Fig. 1). Thus, a decrease of 2.0 ± 1.4 cm in mean was achieved when the latest follow-up scores were taken as reference in comparison with the baseline scores. Although this decrease in VAS scores was found as a statistically significant difference, no statistically significant differences were found between the follow-up periods themselves (Table 2). In general, a decrease of 32.8% in mean of the VAS scores was achieved at the last follow-up when compared with the baseline.

The rate of the patients reporting at least 2 cm of decrease in VAS scores in comparison with the baseline scores, which we considered as success criteria, was found to be 64.5%. The

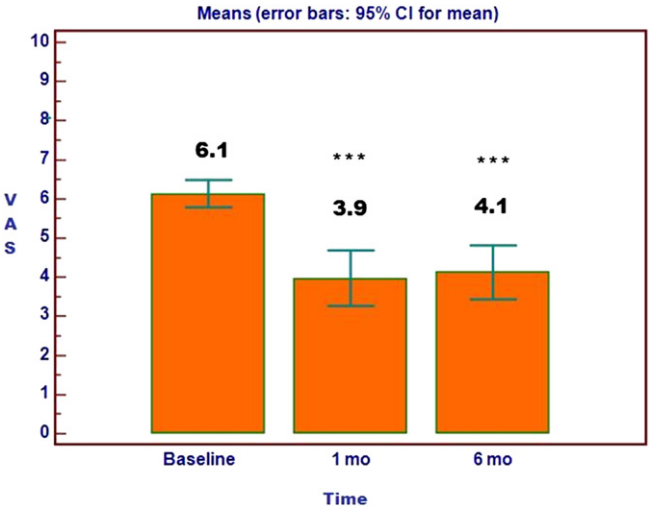

Fig. 1. Agraphic showing the change in time in VAS scores. ***$p < 0.0001$, statistically significant difference when comparing the baseline scores. CI = confidence interval; VAS = Visual Analog Scale.

Table 2
Pairwise comparisons of all-time VAS scores

Factors		Mean difference	Standard error	p[a]	95% CI[a]
$VAS_{baseline}$	$VAS_{1\ mo}$	2.161	0.286	<0.0001	1.435 to 2.887
	$VAS_{6\ mo}$	2.000	0.254	<0.0001	1.356 to 2.644
$VAS_{1\ mo}$	$VAS_{6\ mo}$	−0.161	0.192	1.0000	−0.648 to 0.325

[a] Bonferroni-corrected.
CI = confidence interval; VAS = Visual Analog Scale.

rate of the patients reporting ≥50% decrease in their pain in comparison with that of the last follow-up was calculated as 35.5%.

The possible effects of various factors such as age, duration of symptom and gender on the final outcomes were studied by using Spearman's coefficient of rank correlation (Table 3). Although there is no correlation between gender ($p = 0.9643$) and age ($p = 0.1878$) and the outcomes, an inverse correlation was found between the pain duration of the patients ($p = 0.0338$) and amount of decrease in VAS scores.

3.3. Safety

In none of the patients, on whom the application was performed, were found any major or minor complications in the early or late period. In other words, no patients developed hemorrhage, infection, increase in their existing complaints, or thermal injury.

4. Discussion

Although it is still not understood completely how PRF takes effect,[17,18,23] laboratory reports suggest a genuine neurobiological phenomenon altering the pain signaling, which has been described as neuromodulatory.[13] Sluijter et al[17] suggested the hypothesis that PRF may have dual effect in intra-articular applications. In the first effect on the nervous system, PRF causes suppression of the excitatory C-fiber response and inhibition of the synaptic transmission.[17,18] This effect explains the immediate pain relief effect of PRF particularly observed in small joint applications. It is suggested that PRF shows its second effect (which explains the effectiveness observed particularly in large joint applications such as knee and shoulder joints, and emerging gradually) over the immune cells. According to this suggestion, the electric field affects the immune cells and thus affects production of proinflammatory cytokines such as interleukin-1β, tumor necrosis factor-α, and interleukin-6. Therefore, it is suggested that PRF affects the inter-cell communication by intermediary of these cytokines and triggers, rather than a limited effect, formation of possibly more generalized response.[17]

Table 3
Effect of various factors on the outcome

Variable Y	Decrease in VAS score	Decrease in VAS score	Decrease in VAS score
Variable X	Sex	Duration of pain	Age
Sample size	31	31	31
Spearman's coefficient of rank correlation	−0.00817	−0.3823	0.240
Significance level	0.9643	0.0338*	0.1878
95% confidence Interval for Spearman's coefficient of rank correlation	−0.361 to 0.347	−0.6487 to −0.03228	−0.124 to 0.548

*Correlation is significant at the 0.05 level.
VAS = Visual Analog Scale.

Unlike CRFT, PRF can be applied to peripheral nerves because it does not cause neuronal damage, and to inside joints because it does not cause tissue damage. However, studies on intra-articular application of PRF are scarce and, as far as we know, there are only two articles in the literature in English. In a series of cases published by Sluijter et al[17] in 2008, PRF was applied to various joints (cervical facet, knee, shoulder, sacroiliac, atlanto-axial, and radiocarpal joints) of six different patients who had arthrogenic pain. The authors have reported that they have obtained excellent results from all application in mid and long term. In another study,[18] Halim et al applied intra-articular PRF to atlanto-axial joints of 86 patients with cervicogenic headache. In this retrospective study, the long-term effectiveness of PRF was studied, and the rate of patients reporting ≥50% decrease in their pain scores 1 year after the application was reported as 44.2%.

The most important weakness of the present study is that it was not a randomized controlled study, but only a study designed, retrospectively. Hence, generalization of the outcomes of our study to the society may not be very accurate. However, though our study was a retrospective one, it gives an encouraging view on the effectiveness of intra-articular PRF application. The placebo-controlled, randomized, and double-blind studies to be planned in future may provide more objective information on effectiveness of intra-articular PRF application. One shortcoming of our study is that it did not have a long follow-up period. We do not know whether or not this effectiveness observed in PRF application in the short- to mid-term follow-up period will also continue in the long term. To find the answer to this question, studies with long follow-up periods should be carried out.

In conclusion, PRF, applied to knee joint of patients who suffer from chronic knee pain due to OA and do not respond to the conservative treatment methods sufficiently, seems to be an effective and safe method. To discriminate it from placebo response, prospective, randomized, and placebo-controlled studies with long follow-up period are needed.

References

1. Altman RD, Rosen JE, Bloch DA, Hatoum HT, Korner P. A double-blind, randomized, saline-controlled study of the efficacy and safety of EUFLEXXA for treatment of painful osteoarthritis of the knee, with an open-label safety extension (the FLEXX trial). *Semin Arthritis Rheum* 2009;**39**:1–9.
2. Ay S, Evcik D. The effects of pulsed electromagnetic fields in the treatment of knee osteoarthritis: a randomized, placebo-controlled trial. *Rheumatol Int* 2009;**29**:663–6.

3. McCarthy CJ, Callaghan MJ, Oldham JA. Pulsed electromagnetic energy treatment offers no clinical benefit in reducing the pain of knee osteoarthritis: a systematic review. *BMC Musculoskelet Disord* 2006;**7**.
4. Englund M. The role of biomechanics in the initiation and progression of OA of the knee. *Best Pract Res Clin Rheumatol* 2010;**24**:39−46.
5. Losina E, Walensky RP, Kessler CL, Emrani PS, Reichmann WM, Wright EA, et al. Cost-effectiveness of total knee arthroplasty in the United States: patient risk and hospital volume. *Arch Intern Med* 2009; **169**:1102−3.
6. Karlsson J, Sjögren LS, Lohmander LS. Comparison of two hyaluronan drugs and placebo in patients with knee osteoarthritis: a controlled, randomized, double-blind, parallel-design multicentre study. *Rheumatology* 2002;**41**:1240−8.
7. Felson DT. Arthroscopy as a treatment for knee osteoarthritis. *Best Pract Res Clin Rheumatol* 2010;**24**:47−50.
8. Lowry AM, Simopoulos TT. Spinal cord stimulation for the treatment of chronic knee pain following total knee replacement. *Pain Physician* 2010; **13**:251−6.
9. Van Zundert J, Raj P, Erdine S, van Kleef M. Application of radiofrequency treatment in practical pain management: state of the art. *Pain Pract* 2002;**2**:269−78.
10. Bogduk N. Pulsed radiofrequency. *Pain Med* 2006;**7**:396−407.
11. Tamimi MA, McCeney MH, Krutsch J. A case series of pulsed radiofrequency treatment of myofascial trigger points and scar neuromas. *Pain Med* 2009;**10**:1140−3.
12. Erdine S, Bilir A, Cosman ER, Cosman Jr ER. Ultrastructural changes in axons following exposure to pulsed radiofrequency fields. *Pain Pract* 2009;**9**:407−17.
13. West M, Wu H. Pulsed radiofrequency ablation for residual and phantom limb pain: a case series. *Pain Pract* 2010;**10**:485−91.
14. Vanelderen P, Rouwette T, De Vooght P, Puylaert M, Heylen R, Vissers K, et al. Pulsed radiofrequency for the treatment of occipital neuralgia: a prospective study with 6 months of follow-up. *Reg Anesth Pain Med* 2010;**35**:148−51.
15. Philip CN, Candido KD, Joseph NJ, Crystal GJ. Successful treatment of meralgia paresthetica with pulsed radiofrequency of the lateral femoral cutaneous nerve. *Pain Physician* 2009;**12**:881−5.
16. Basal S, Goktas S, Ergin A, Yildirim I, Atim A, Tahmaz L, et al. A novel treatment modality in patients with premature ejaculation resistant to conventional methods: the neuromodulation of dorsal penile nerves by pulsed radiofrequency. *J Androl* 2010;**31**:126−30.
17. Sluijter ME, Teixeira A, Serra V, Balogh S, Schianchi P. Intra-articular application of pulsed radiofrequency for arthrogenic pain: report of six cases. *Pain Pract* 2008;**8**:57−61.
18. Halim W, Chua NH, Vissers KC. Long-term pain relief in patients with cervicogenic headaches after pulsed radiofrequency application into the lateral atlantoaxial (C1−2) joint using an anterolateral approach. *Pain Pract* 2010;**10**:267−71.
19. Altman R, Asch E, Bloch D, Bole G, Borenstein D, Brandt K, et al. Development of criteria for the classification and reporting of osteoarthritis. Classification of osteoarthritis of the knee. Diagnostic and Therapeutic Criteria Committee of the American Rheumatism Association. *Arthritis Rheum* 1986;**29**:1039−49.
20. Kellgren JH, Lawrence JS. Radiological assessment of osteo−arthrosis. *Ann Rheum Dis* 1957;**16**:494−502.
21. Freeman BJ, Fraser RD, Cain CM, Hall DJ, Chapple DC. A randomized, double-blind, controlled trial: intradiscal electrothermal therapy versus placebo for the treatment of chronic discogenic low back pain. *Spine* 2005;**30**:2369−77.
22. Maurer P, Block JE, Squillante D. Intradiscal electrothermal therapy (IDET) provides effective symptom relief in patients with discogenic low back pain. *J Spinal Disord Tech* 2008;**21**:55−62.
23. Tekin I, Mirzai H, Ok G, Erbuyun K, Vatansever D. A comparison of conventional and pulsed radiofrequency denervation in the treatment of chronic facet joint pain. *Clin J Pain* 2007;**23**:524−9.