RESEARCH ARTICLE / *Araştırma Makalesi*

Long-Term Effects of Ultrasound-Guided Genicular Nerve Pulsed Radiofrequency on Pain and Knee Functions in Patients with Gonarthrosis.

Gonartroz Hastalarında Ultrason Eşliğinde Uygulanan Geniküler Sinir Pulsed Radyofrekans Tedavisinin Ağrı ve Diz Fonksiyonlarına Uzun Dönem Etkisi

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Abstract

Objective Osteoarthritis of the knee is the most common musculoskeletal disease in older adults which causes chronic knee pain. Pulsed radiofrequency (PRF) on genicular nerves (GN) has become increasingly popular in the treatment of chronic knee pain due to its long duration of action and non-destructive therapy. This study aimed to reveal the effects of ultrasound-guided PRF therapy on GN in patients with knee osteoarthritis (KOA). **(Sakarya Med J 2019, 9(1):52-58)**

Materials and Methods This longitudinal study included patients, who were diagnosed with grade 3 to 4 gonarthrosis according to the Kellgren-Lawrence classification which patients suffered from intractable knee pain, at least for six months despite conservative treatment. The ultrasound-guided PRF on GN (GPRF) was performed in those patients with a reduction of 50% or more visual analog scale (VAS) score after the diagnostic GN block (GNB). VAS and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were evaluated before, and 1, 3, 6 and 12 months after the procedure.

Results Of the 293 patients included in the criteria, ultrasound-guided GPRF was administered to 232 patients who responded to GNB. While the mean VAS score of the patients before the GPRF was 6.77 ± 1.24, the mean VAS scores at the 1st, 3rd, 6th and 12th months of the GPRF were 2.76 ± 1.14, 2.94 ± 1.08, 3.53 ± 0.64, and 4.58 ± 0.75, respectively. The mean WOMAC score of the patients before GPRF was 65.75 ± 14.15, while the mean WOMAC score of the 1st, 3rd, 6th and 12th months after GPRF was 36.14 ± 13, 36.52 ± 11.06, 37.88 ± 10.86, and 41.67 ± 10.84, respectively.

Conclusion Ultrasound-guided GPRF therapy in chronic knee pain which does not respond to conservative treatments reduces pain for at least 12 months and is effective improving knee functions.

Keywords Gonarthrosis; pulsed radiofrequency; genicular nerve; knee pain

Öz

Amaç *Gonatroz, yetişkinlerde kronik diz eklem ağrısına neden olan en yaygın kas-iskelet sistemi hastalığıdır. Geniküler sinirlere radyofrekans uygulanması, uzun etki süresi ve dokuda destrüsyona yol açmaması nedeniyle kronik diz ağrısının tedavisinde giderek popüler hale gelmiştir. Çalışmamızda, konservatif tedavilere yanıt vermeyen, kronik diz ağrılı gonartroz hastalarında, geniküler sinirlere ultrason eşliğinde uygulanan pulsed radyofrekans tedavisinin (GPRF) uzun dönem ağrı ve diz fonksiyonlarına olan etkisini incelemeyi amaçladık.* ***(Sakarya Tıp Dergisi 2019, 9(1):52-58)****.*

Gereç ve Yöntemler *Çalışmaya, Kellgren-Lawrence sınıflamasına göre evre 3-4 gonartroz tanısı almış olan, en az 6 ay boyunca uygulanan konservatif tedavilere rağmen ağrıları geçmeyen hastalar dahil edildi. Geniküler sinirlere ultrason eşliğinde gerçekleştirilen tanısal blok ile VAS skoru %50 ve daha fazla azalan hastalara GPRF uygulandı. Hastaların VAS ve Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) skorları işlem öncesi, işlem sonrası 1, 3, 6 ve 12. ayda değerlendirildi.*

Bulgular *Kriterleri karşılayan 293 hastadan, geniküler sinirlere ultrason eşliğinde uygulanan tanısal bloğa yanıt veren 232 hastaya GPRF uygulandı. Hastaların GPRF öncesi VAS skoru ortalaması 6.77±1.24 iken GPRF sonrası 1, 3, 6 ve 12.ay VAS skoru ortalamaları sırasıyla 2.76±1.14, 2.94±1.08, 3.53±0.64, 4.58±0.75 bulundu. Hastaların GPRF öncesi WOMAC skoru ortalaması 65.75±14.15 iken GPRF sonrası 1, 3, 6 ve 12.ay WOMAC skoru ortalamaları sırasıyla 36.14±13, 36.52±11.06, 37.88±10.86, 41.67±10.84 bulundu.*

Sonuç *Konservatif tedavilere yanıt vermeyen gonartroza bağlı kronik diz eklem ağrısında, ultrason eşliğinde uygulanan GPRF tedavisi, en az 12 ay boyunca ağrıyı azaltmakta ve diz fonksiyonlarını iyileştirmekde etkilidir.*

Anahtar Kelimeler *Gonartroz; pulsed radyofrekans; geniküler sinir; diz ağrısı*

INTRODUCTION

Osteoarthritis of the knee is the most common musculoskeletal disease in older adults, and it often causes disability due to treatment difficulties. Chronic knee pain can negatively effect on quality of life by joint stiffness, functional limitations, and disturbance in sleep.[1]

The treatment of knee osteoarthritis (KOA) requires an all-around approach, including noninvasive methods (nonsteroidal anti-inflammatory drugs, physical therapy, and rehabilitation), minimally invasive methods (intra-articular corticosteroid or hyaluronate injections and genicular nerve procedures) and surgical procedures. Nonsteroidal anti-inflammatory (NSAI) drugs are often ineffective and may lead to serious adverse effects in the elderly population aged.[2] Corticosteroids administration into the joint space, provide pain control for 3-4 weeks. Hyaluronate, at best, may be as effective as NSAI drugs, and, in comparison with intra-articular corticosteroids, it has a delayed onset of effects and a longer-lasting benefit.[3] Surgery should be considered for patients with advanced stage of KOA, but this may not be possible because of many fragile patients who are at high risk during surgery. The pulsed radiofrequency (PRF) of genicular nerves (GN), which are becoming increasingly popular in these patients or in patients who are not willing to undergo surgery, may be a good option. The PRF is a variation of conventional radiofrequency (CRF), which does not cause harmful effect on to the targeted tissue and it has neuromodulatory role with long duration of action.

The aim of this study was to investigate the effects of ultrasound-guided GPRF in patients with KOA, on both chronic pain and function of the knee.

MATERIALS and METHODS

Patient Selection

This longitudinal study included 293 patients 18 years of age or older who were diagnosed with grade 3 to 4 gonarthrosis (M17) according to the Kellgren-Lawrence classification between November 2014 and March 2017.4 These patients suffered from intractable knee pain (Visual Analog Scale score ≥5) at least six months despite other treatments including, physiotherapy, systemic analgesics, and intra-articular injection (hyaluronic acids, corticosteroids). The information of patients was obtained from the hospital's electronic database after approval of the Sakarya University Faculty of Medicine Ethical Committee (71522473/050.01.04/61). The exclusion criteria was acute knee pain, prior knee surgery, rheumatologic diseases affecting the knee, progressive neurological disorders, intra-articular injection during the previous 3 months, radicular pain, anticoagulant treatments, pacemakers, and Implantable Cardioverter Defibrillator (ICD).

Diagnostic Genicular Nerve Block Technique

All procedures were performed in the operating room. The patient was placed in a supine position, and vital signs were monitored (electrocardiogram, noninvasive blood pressure, and peripheral oxygen saturation). The diagnostic genicular nerve block (GNB) was applied after the skin disinfection with ultrasound guidance (M5 Color Diagnostic Ultrasound System; Mindray, Shenzhen, China) using a 12 MHz linear transducer. The targets for diagnostic GNB included the superior lateral, the superior medial, and the inferior medial genicular nerves. To perform a superior medial genicular nerve block, a linear 12 MHz high-frequency ultrasound transducer was placed over the medial joint space in a sagittal orientation. The ultrasound transducer was moved proximally following the medial hyperechoic margin of the femur to identify the transition point of the medial femoral condyle for visualizing the superior medial genicular artery because of the superior medial genicular nerve close to the superior medial genicular artery. Color Doppler was then utilized to find the superior medial genicular artery. If the superior medial genicular artery cannot be visualized the ultrasound transducer was turned 90 degrees to provide a transversal view, perpendicular to the longitudinal femur axis.

This same procedure was repeated at the medial tibia and the lateral femur to target the inferior medial genicular artery and superior lateral genicular artery, respectively (Figure 1, 2). The ultrasound-guided GNB performed with 0.5% bupivacaine 3 ml each of the genicular nerve.

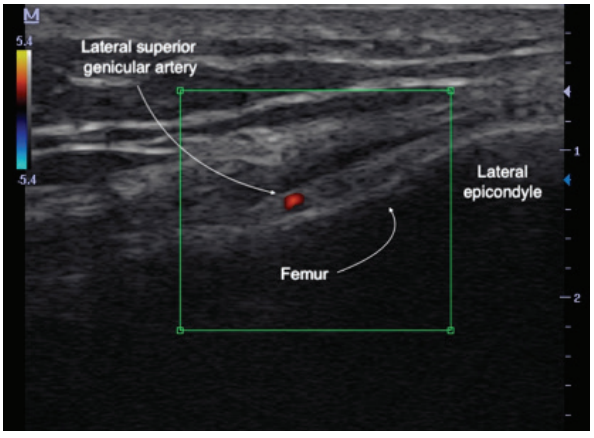

Figure 1. Color Doppler image demonstrating the superior lateral genicular artery (sagittal plane).

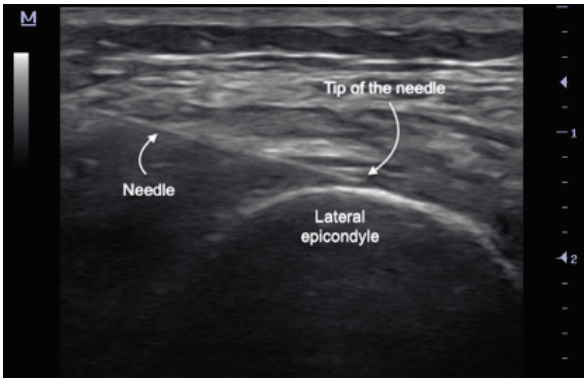

Figure 2. Ultrasound guided superior lateral genicular nerve block (axial plane)

Pulsed Radiofrequency Application Technique

The genicular nerve pulsed radiofrequency (GPRF) was performed in those patients with a reduction of 50% or more Visual Analog Scale (VAS) score after the diagnostic GNB. The ultrasound-guided GPRF was administered under operating room conditions while the patient was monitored in a supine position.

After the genicular arteries were visualized using the aforementioned ultrasound technique the 22 G 5-mm active-tip 100-mm radiofrequency needle (SC-K; Top Neuropole, Tokyo, Japan) was advanced to each nerve sequentially using the in-plane approach under real-time ultrasound guidance. After proper needle tip placement was confirmed, sensorial stimulation was given at 50 Hz for 1 ms to identify the nerve position. With the sensory stimulation, paresthesia, pain, or discomfort at the knee was required to be less than 0.5 volts. In addition, the motor stimulus applied at 2 Hz for 1 ms and at least 1 volt to determine the absence of fasciculation. The GPRF treatment was applied for three cycles at 42 °C, 45 V, 2 Hz, and 20 ms, with a wide wave for 120 s (NeuroTherm, Middleton, MA, USA). VAS and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) assessments of those patients that underwent the GPRF treatments were conducted postoperatively at the 1st month, 3rd month, 6th month, and 12th month follow-ups.[5]

Assessment of Pain and Functional Status

Before and after the GNB and GPRF applications, pain assessments were done using a VAS. The knee joint function and improvement of the quality of life was evaluated using the WOMAC. The WOMAC consists of three parts, pain, stiffness, and physical function, with a total of 24 questions. The WOMAC test has been proven validity in the Turkish language before.[5,6], The test questions are scored on a scale of 0-4, which correspond to: None (0), Mild (1), Moderate (2), Severe (3), and Extreme (4). In the first part of the questionnaire, the patient is asked to rate the severity of the pain during different physical activities (during walking, using stairs, in bed, sitting or lying, and standing upright). The severity of joint stiffness is assessed in the second part based on the patient's perceived difficulty when walking after first waking and later in the day. The third part of questionnaire assesses to physical function with 17 items. Higher scores on the WOMAC indicate worse pain, stiffness, and functional limitations.

Statistical Analysis

In the data analysis, SPSS for Mac version 23.0 was used. The values were given as the mean±standard deviation (SD) in the statistical analysis. The demographic variables were compared using a t-test or chi-squared test for the continuous and categorical variables, respectively. The difference between the repeated measurements in the group was assessed using the Repeated Measures-ANOVA (RM-ANOVA). A p level of <0.05 was accepted for the statistical significance.

RESULTS

Between November 2014 and March 2017, diagnostic GNB was performed on 293 patients. A total of 259 patients had a positive response (at least 50% reduction in VAS score) to the diagnostic GNB. Of 259 patients with positive diagnostic GNB, 12 had on-going pain relief, and 247 had recurrent pain when they were assessed for GPRF, 6 had refused GPRF. Of 241 patients with scheduled GPRF treatment, 9 had decided to surgery in wating for GPRF treatment, 232 had received GPRF treatment. The flowchart of the study is presented in Figure 3.

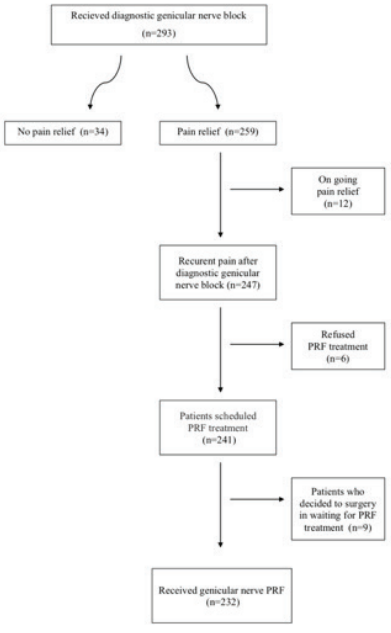

Figure 3. Flowchart of the study

The mean age of the patients was 61.97±10.49 years. The mean value of Body Mass Index (BMI) was 33.55±6.8. The number of patients with grade 3 according to Kellgren-Lawrence score was 177, and the number of patients with grade 4 was 116. The number of patients with affected right and left knee was 185, and 108 respectively. Demographic data and characteristics of these patients are shown in Table 1.

Table 1. Age, Sex, Body Mass Index, Side of The Affected Knee, and Grade of The Gonarthrosis in Patients

	Patients (n=293)
Age (years)	61.97±10.49
Sex (Male/female, n)	112/181
BMI (kg/m2)	33.55±6.8
Kellgren Lawrence (grade 3/4)	177/116
Side (Right/left)	185/108
Age and BMI (Body Mass Index) values are given by mean average ± standard deviation and percentiles.	

The VAS and WOMAC total scores were measured before therapy and at the 1st, 3rd, 6th, and 12th months following treatment. While the mean VAS score of the patients before the GPRF was 6.77 ± 1.24, the mean VAS scores at the 1st, 3rd, 6th and 12th months of the GPRF were 2.76 ± 1.14, 2.94 ± 1.08, 3.53 ± 0.64, and 4.58 ± 0.75, respectively. The mean WOMAC score of the patients before GPRF was 65.75 ± 14.15, while the mean WOMAC score of the 1st, 3rd, 6th and 12th months after GPRF was 36.14 ± 13, 36.52 ± 11.06, 37.88 ± 10.86, and 41.67 ± 10.84, respectively. A significant improvement was seen in pain and physical functions at the 1st, 3rd, 6th, and 12th months after the GPRF procedure compared to the pre-treatment scores (Figure 4, 5). The VAS scores and WOMAC scores are shown in Table 2. No adverse event or complications such as hemorrhage, thermal wound, infection, sensory or motor loss in the procedure area were observed in the follow-up GPRF.

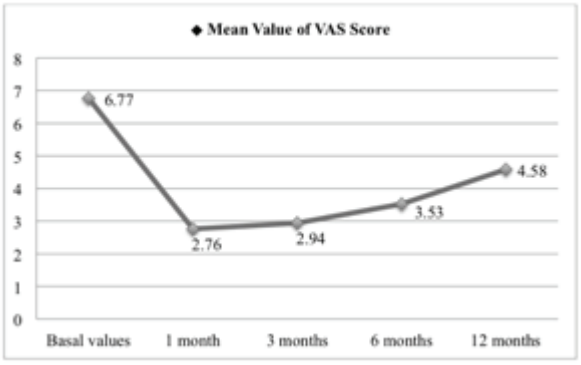

Figure 4. Mean Value of VAS Score

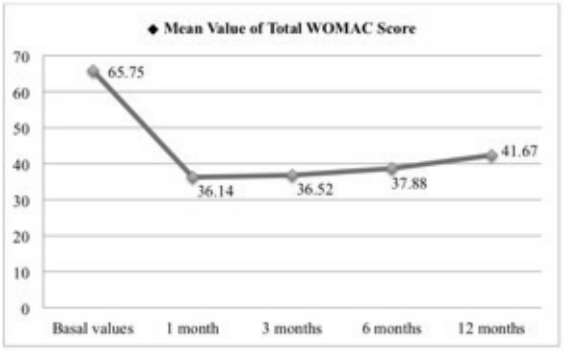

Figure 5. Mean Value of Total WOMAC Score

DISCUSSION

To the best of our knowledge, this is the most extensive study showing the clinical efficacy of ultrasound-guided GPRF in KOA. In this study, we found that ultrasound-guided GPRF can reduce osteoarthritis-related knee pain and knee function in patients with Kellgren-Lawrence classification grade 3 to 4. The patients experienced significant pain relief and functional improvement in the knee during the 12 month follow-up period. Furthermore, ultrasound-guided GPRF is a minimally invasive procedure for relieved the knee pain without any adverse effect. The procedure was performed with ultrasound guidance as it was safe in experienced hands, cost-effective, and reduced complications. With ultrasound guidance, vessels, periosteum, ligaments, tendons, and other structures can be visualized. Thanks to real-time imaging with ultrasound, the accuracy of the needle placement may increase. In contrast to the other radiological imaging techniques, ultrasound does not use or produce ionizing radiation.

The radiofrequency (RF) is used in different clinical conditions such as trigeminal neuralgia, cervicogenic headaches, and spinal pain.[7,8] Recently, PRF has been applied in the pain management of knee osteoarthritis as a relatively new intervention. Both PRF and conventional radiofrequency (CRF) have been demonstrated to have similar effects on neuronal conduction. The advantages of PRF compared to CRF are that PRF tends to be less neuro-destructive and PRF does not cause irreversible tissue damage or long-lasting structural effects, neuritis-like reactions, motor deficits and the risk of deafferentation syndrome.[9-11] PRF therapy provides an analgesic effect on neuropathic pain by suppressing the nociception-induced release of excitatory

Table 2. Distribution of Visual Analog Scale, and Western Ontario and McMaster Universities Osteoarthritis Index in Patients According to Months

	Pretreatment	1 st month	3 rd month	6 st month	12 th month
VAS	6.77±1.24*	2.76±1.14	2.94±1.08†	3.53±0.64	4.58±0.75
WOMAC Pain	13.09±4.55*	6.97±4.19	7.21±3.60†	7.89±3.01	9.84±3.15
WOMAC Stiffnes	4.79±1.73*	3.88±1.95	3.86±1.47	3.88±1.09	4.03±1.62
WOMAC Function	45.24±8.64*	23.85±10.17	23.98±9.33	24.61±9.36	26.12±7.73
WOMAC Total	65.75±14.15*	36.14±13	36.52±11.06†	37.88±10.86	41.67±10.84

VAS: Visual Analog Scale.
WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.
*Differences compared with 1, 3, 6, and 12 months ($p<0.001$).
Differences compared with 3, 6, and 12 months ($p<0.001$).
†Differences compared with 6, and 12 months ($p<0.001$).

neurotransmitters.[12] Chronic knee pain in osteoarthritis is considered nociceptive pain. However, the neuropathic mechanism may also play a role in the pain of osteoarthritis.[13] Hochman et al. reported that 34% of patients with osteoarthritis have a neuropathic symptom including burning, tingling, numbness, and pins and needles.[14] Placebo-controlled studies showing that PRF is effective were performed in neuropathic pain.[15,16] For all these reasons, PRF was preferred in our study.

Knowledge of knee joint innervation is essential for a successful RF treatment. The knee joint is innervated by the articular branches of the femoral, common peroneal, saphenous, tibial and obturator nerves1. These articular branches are known as genicular nerves. They provide innervation to the capsule of the knee joint, as well as to the intra-articular and extra-articular ligaments.[17]

Genicular nerve RF could contribute to analgesia and muscle relaxation at the chronic knee pain. Choi et al. investigated fluoroscopic guided CRF of the genicular nerves. Their studies have shown that the CRF of the genicular nerves provided more than 50% relief in pain intensity in more than 50% of patients for 12 weeks and improvement in the knee function.[18] Protzman et al. reported that the CRF of the genicular nerves branches provided the improvement in chronic knee pain after total knee replacement.[19] In the reports of Choi et al. and Protzman et al. CRF was implemented three genicular nerves (superior-lateral, superior-medial, inferior-medial). Kesikburun et al. reported a significant reduction in VAS and WOMAC scores over time in their study of the efficacy of PRF treatment on nine patients with medial knee osteoarthritis.[20] In the report of Kesikburun et al. GPRF was implemented two genicular nerves (superior-medial, inferior-medial) because of the authors was the thought that these are the only two nerves clinically relevant in pain from KOA of the medial compartment.[20] Ahmed applied ultrasound-guided GPRF to three branches of genicular nerve on one patient with OA and reported a significant reduction of pain for six months also improvement in neuropathic features.[21] In our study, we applied GPRF to three branches of genicular nerve, and we found a significant decrease in the mean score of VAS and improvement in total WOMAC score in our one year follow-up.

The relatively high volume of local anesthetic administered for diagnostic GNB could have compromised selectivity of the block. Therefore, in this study, no more than 3 cc bupivacaine were applied to each nerve for the diagnostic GNB. This study has some limitations. The invasive pseudo interventional procedure was an ethical problem to the control group. Therefore, the main limitation of this study is the lack of a control group. The second limitation is a lack of assessment of knee joint proprioception after GPRF besides, although psychological factors may contribute to the perception of pain they were not evaluated in this study. The third limitation is the range of motion was not assessed in our study and there was no electrodiagnostics assessment as electromyography (EMG) for defining or excluding unwanted side effects of PRF.

CONCLUSION

This study has shown that chronic knee pain can be controlled for a long period of time, using ultrasound-guided GPRF in gonarthrosis. There was significant pain relief, along with a significant improvement in the knee joint function. Ultrasound-guided GPRF therapy in patients with gonarthrosis can be applied safely as a nondestructive method, and that it can be repeated, if necessary. There is a need for large series, long-term, randomized controlled trials to confirm our results.

Conflicts of Interest

The authors declare no conflicts of interest.

This study was presented as a oral presentation at the 5th Pain Congress with International Participation, November 15 - 18 2018, Antalya, Turkey.

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