Original Article/*Özgün Araştırma*

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Ultrasound-Guided Genicular Nerve Alcohol Neurolysis for the Management of Knee Osteoarthritis Pain

Diz Osteoartriti Ağrısının Tedavisinde Ultrason Kılavuzluğunda Geniküler Sinir Alkol Nörolizi

Gokhan Yildiz, Gevher Rabia Genc Perdecioglu

Ankara Etlik City Hospital, Clinic of Algology, Ankara, Türkiye

ABSTRACT

Objective: Chemical neurolysis of genicular nerves is an increasingly common procedure for knee osteoarthritis (KOA) pain. This study aimed to evaluate the efficacy of alcohol neurolysis of the genicular nerves in KOA pain.

Methods: Patients with KOA underwent superior medial, superior lateral and inferior medial genicular nerves alcohol neurolysis after ≥ 50% pain relief following diagnostic genicular nerve blocks. Numeric rating scale (NRS) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scores were evaluated at baseline, 1 and 3 months after the procedure. Our primary outcome was pain relief, as revealed by the change in NRS scores. Secondary outcomes were changes in WOMAC score and the incidence of procedure-related adverse events.

Results: Fifty-one patients who met the inclusion criteria were included. The median baseline NRS score was 8, and the 1st and 3rd month scores were 3. The median WOMAC score at the baseline was 68. It was 30.25 at month 1 and 30 at month 3. The reduction in NRS and WOMAC scores was significant at both times compared with baseline ($p<0.001$). Genicular alcohol neurolysis provided 50% or more pain relief in 64.7% of the patients at the 3rd month follow-up. Paresthesia was observed in five (9.8%) patients and hypoesthesia in two (3.9%) patients, but these adverse events resolved within one month without treatment.

Conclusion: Genicular nerve alcohol neurolysis may be a good alternative to more expensive methods, such as radiofrequency, with low cost, and high efficacy. Further studies are needed to determine the ideal alcohol dose.

Keywords: Osteoarthritis, knee, denervation, paresthesia, hypoesthesia, ultrasonography

ÖZ

Amaç: Geniküler sinirlerin kimyasal nörolizi, diz osteoartriti (DOA) ağrısında giderek yaygınlaşan bir prosedürdür. Bu çalışmanın amacı, DOA ağrısında geniküler sinirlerin alkol nörolizinin etkinliğini değerlendirmektir.

Yöntem: Diz osteoartritli hastalara, tanısal geniküler sinir bloklarını takiben ≥%50 ağrı rahatlamasından sonra superior medial, superior lateral ve inferior medial geniküler sinirlere alkol nörolizi uygulandı. Sayısal derecelendirme ölçeği (NRS) ve Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) skorları başlangıçta, işlemden 1 ve 3 ay sonra değerlendirilmiştir. Birincil amacımız NRS skorlarında ortaya çıkacak değişim ile ağrı düzeyinde oluşacak değişikliğin gösterilmesiydi. İkincil amacımız ise WOMAC skorundaki değişiklikler ve prosedürle ilişkili advers olayların insidansıydı.

Bulgular: Dahil edilme kriterlerini karşılayan elli bir hasta çalışmaya dahil edildi. Medyan başlangıç NRS skoru 8, 1. ve 3. ay skorları ise 3 idi. Başlangıçtaki medyan WOMAC skoru 68 idi. Birinci ayda 30,25 ve üçüncü ayda 30 idi. Sayısal derecelendirme ölçeği ve WOMAC skorlarındaki azalma her iki dönemde de başlangıca kıyasla anlamlıydı ($p<0,001$). Geniküler alkol nörolizi sonrası 3. ay takibinde hastaların %64,7'sinde %50 veya daha fazla ağrı sağlandığı saptandı. Beş hastada (%9,8) parestezi ve iki hastada (%3,9) hipoestezi gözlendi, ancak bu advers olaylar tedavi olmaksızın bir ay içinde düzeldi.

Sonuç: Geniküler sinir alkol nörolizi, düşük maliyet ve yüksek etkinlik ile radyofrekans gibi daha pahalı yöntemlere iyi bir alternatif olabilir. İdeal alkol dozunu belirlemek için daha fazla çalışmaya ihtiyaç vardır.

Anahtar sözcükler: Osteoartrit, diz, denervasyon, parestezi, hipoestezi, ultrasonografi

INTRODUCTION

The management of knee osteoarthritis (KOA) pain is a complex and severe public health problem, especially in the elderly population. Genicular ablation procedures are becoming increasingly important in the treatment of chronic KOA pain when conservative therapies have failed (1). These methods involve partial sensory denervation of the joint capsule by

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***Corresponding author:** Gokhan Yildiz • gkoyldz@gmail.com

Gokhan Yildiz 0000-0001-5905-938X / Gevher Rabia Genc Perdecioglu 0000-0002-5174-9500

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applying chemical neurolytics or radiofrequency energy to the genicular nerves responsible for transmitting pain signals from the knee. Patients with advanced KOA often have severe comorbidities, which may interfere with the surgical operation due to surgical and anesthesia-related risks. Less invasive methods than surgery (such as intra-articular injection) may be limited in providing prolonged pain relief (2). In addition to the fact that genicular radiofrequency ablation, which is widely used, requires trained personnel and high-cost equipment, treatment failure rates have been reported to be over 25% (3).

Chemical neurolytics, such as alcohol or phenol, have come to the fore because of their low cost and ease of application compared to radiofrequency ablation (4). These methods can be easily applied with ultrasound (US) guidance, which allows precise targeting of the relevant nerves. However, there is a lack of literature on appropriate agents and dose selection issues. While there are more randomized studies on the efficacy of phenol for genicular neurolysis, there are only case reports on neurolysis with alcohol (4-8).

Alcohol damages or destroys nerve tissue and disrupts nerve conduction by directly applying high concentrations of ethyl alcohol to the nerve. Alcohol neurolysis is typically performed at 45% and 100% concentrations, with lower concentrations having only a local anesthetic effect. Alcohol neurolysis is similar to phenol neurolysis, which uses carbolic acid as the chemical agent. Both alcohol and phenol mediate their effects by non-selective denaturation of proteins when applied to the nerves (9).

The primary objective of this study was to evaluate the analgesic efficacy of US-guided alcohol neurolysis of the genicular nerves in the treatment of chronic KOA pain. Second, we aimed to assess the effect of this method on functionality and identify procedure-related adverse events.

MATERIAL and METHODS

The local ethics committee approved this retrospective observational study, number 2023-417. The inclusion criteria were as follows: 1) male and female patients older than 18 years; 2) Kellgren-Lawrence grade III or IV KOA; 3) knee pain with a score of ≥ 6 on the Numeric Rating Scale (NRS), unresponsive to conservative treatments, and persisting for more than six months; 4) knee pain caused solely by osteoarthritis (excluding causes such as inflammatory arthritis, meniscopathy or sciatica). Exclusion criteria were 1) history of intra-articular injection within three months before or after the procedure; 2) coagulopathy and anti-aggregant or anticoagulant use; 3) hepatic-renal-psychiatric disease; 4) previous knee surgery.

Diagnostic Genicular Block

Asepsis conditions were provided for all interventions. Vascular access was established for all patients. All interventions were performed by pain physicians with at least five years of experience and were well-trained in US. No sedation was provided during the procedures.

The patient was positioned supine, with the knee slightly flexed and a 12 MHz linear transducer (LOGIQ P9, GE Ultrasound, Sunhwan-ro, Jungwon-gu, Seongnam-si, Gyeonggi-do, Korea) was used for all procedures. The genicular nerves are not directly visible by US. However, they can be localized using anatomical landmarks at the junction of the shaft and condyle of the femur and tibia and the proximity of the genicular arteries. To locate the genicular arteries, the transducer was placed on the femur for the superomedial (SMGN) and superolateral genicular nerves (SLGN) and on the tibia for the inferomedial genicular nerve (IMGN). The probe was then moved up and down, and the genicular arteries close to the periosteum were detected using the Doppler function of US (Figure 1). The needle entry site was anesthetized with 1 mL of 2% prilocaine. A spinal needle was inserted near the genicular artery using the in-plane technique and 1 mL of 0.5% bupivacaine was injected for each genicular nerve after negative aspiration.

Alcohol Neurolytic Blockade

Patients who reported a 50% or greater pain relief for at least 2 hours after diagnostic blockade underwent neurolytic blockade using the same technique one week later. Before alcohol neurolysis, 1 mL of 2% lidocaine was administered per genicular nerve to prevent injection pain after reaching the vicinity of the genicular artery. Neurolysis was performed by administering 1 mL of 99% alcohol per genicular nerve. The patients were observed for adverse events for at least 2 hours after both diagnostic and neurolytic blockade.

Measured Variables and Follow-up

Baseline measurements were taken before the procedure and final measurements were taken 1 and 3 months after the procedure. Patient characteristics were collected through medical history, physical examination, and imaging. Pain intensity was assessed using an 11-point numerical rating scale (NRS-11), where 0 indicated no pain and 10 represented the worst pain imaginable. Knee function was assessed using the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), which includes five questions about pain, two about stiffness, and 17 about functional limitations. Each question was scored from 0 to 4 (10).

A decrease of ≥ 50% in the NRS score at the measurement times was considered significant. The primary outcome of

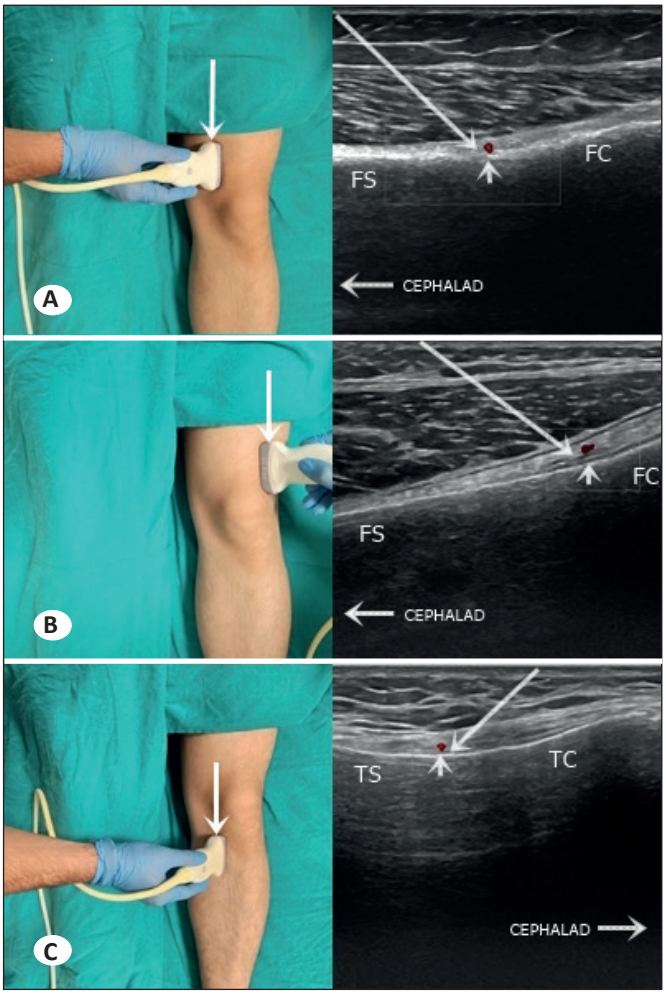

Figure 1: Transducer placement and ultrasound view for the superior medial genicular nerve **(A)**, superior lateral genicular nerve **(B)**, and inferior medial genicular nerve **(C)**. **FS:** Femoral shaft, **FC:** Femoral condyle, **TS:** Tibial shaft, **TC:** Tibial condyle, short arrows indicate genicular arteries, long arrows indicate the trajectory of the needle.

this study was the change in knee pain assessed using NRS before and 1 and 3 months after genicular nerve alcohol neurolysis. The secondary outcomes were the change in knee functionality at the measurement times assessed by WOMAC and the incidence of procedure-related adverse events.

Statistical Analysis

All analyses were performed using the Jamovi project (2022, Jamovi version 2.3, computer software). The results are expressed as frequencies and percentages. Normality analysis was performed using the Shapiro-Wilk test, skewness-kurtosis, and histograms. Variables are presented as mean ± standard deviation (SD) and median (minimum-maximum). The main effect of time on the NRS and WOMAC scores was analyzed using the Friedman test. The difference between the NRS and WOMAC scores was evaluated using Bonferroni correction. Statistical significance was set at $p<0.05$.

RESULTS

Seventy patients were screened for eligibility for this study. Eight patients did not respond to the diagnostic genicular blockade, and seven were lost to follow-up. Two patients underwent intraarticular injection, and two patients underwent radiofrequency ablation during the follow-up period. The study was completed with 51 patients (Figure 2). The baseline patient characteristics are presented in Table I.

The change in NRS score over time was significant (Friedman, $p<0.001$). The median baseline NRS score was 8, and the 1st and 3rd month scores were 3. When analyzing the change over time, the difference between the baseline-1st month and baseline-3rd month change was statistically significant (Bonferroni correction; $p<0.001$, both times). The change between 1st and 3rd months was not significant (Table II).

The change in the WOMAC score over time was significant (Friedman, $p<0.001$). While the median WOMAC score at baseline was 68, it was 30.25 at month 1 and 30 at month 3. When analyzing the change between time points, the baseline-1st month and baseline-3rd month decrease were statistically significant (Bonferroni correction, $p<0.001$, both times). The difference between 1st and 3rd months was not statistically significant (Table II).

Paresthesia was observed in five (9.8%) patients and hypoesthesia in two (3.9%) patients, with the most prolonged duration of approximately one month. Both adverse events resolved spontaneously without treatment. No motor weakness was observed in any of the patients.

DISCUSSION

In this study, alcohol neurolysis for genicular nerve ablation provided significantly adequate analgesia at 1 and 3 months after treatment compared to baseline and improved patients' functionality. Only case reports have been published on the use of genicular alcohol neurolysis for the treatment of chronic knee pain (6-8). In these three case reports, adequate analgesia was achieved with genicular alcohol neurolysis in all ten patients. Our study is the first large-scale study on this subject, and pain relief of 50% or more was observed in 64.7% of the patients at 3 months.

Radiofrequency ablation (RFA) is the most commonly used method for ablation of genicular nerves. The success rate of RFA for KOA has been reported to be as low as 49% (1). There are few studies on the increasingly popular genicular phenol neurolysis. Risso et al. evaluated the efficacy of genicular phe-

Table I. Characteristics of the Patients

Characteristics	Mean±SD	Median (min-max)
Age (years)	59.5 ± 6.4	59 (47-75)
BMI (kg m^{-2})	30.9 ± 3.3	31.10 (23.4-38.2)
Pain Duration (months)	16.8 ± 2.2	16 (13-21)
Gender (F/M), n(%)	40 (78)/11 (22)	
KL grade (3/4), n(%)	29 (56.8)/22 (43.2)	
Comorbidity (DM/HT), n(%)	7 (13.7)/6 (11.7)	
Temporal variation of values		
NRS-baseline	8 ± 0.84	8 (7-9)
NRS-1st month	3.71 ± 2.75	3 (1-9)
NRS-3rd month	4.04 ± 2.4	3 (1-8)
WOMAC-baseline	68.13 ± 8.02	68 (56-82)
WOMAC-1st month	36.87 ± 19.56	30.25 (10-76)
WOMAC-3rd month	37.15 ± 19.35	30 (12-78)

BMI: Body mass index, **KL:** Kellgren-Lawrence, **DM:** Diabetes mellitus, **HT:** Hypertension, **NRS:** Numeric rating scale, **WOMAC:** Western Ontario and McMaster Universities Osteoarthritis Index, **SD:** Standard deviation.

Table II: Temporal Variation of Numeric Rating Scale and Western Ontario and McMaster Universities Osteoarthritis Index

	NRS				WOMAC			
	Median	Mean rank	Test st	p	Median	Mean rank	Test st	p
Baseline	8 (7-9)	2.69	49.22	<0.001	68 (56-82)	2.85	66.28	<0.001
1st month	3 (1-9)*	1.54			30.25 (10-76)*	1.48		
3rd month	3 (1-8)*	1.77			30 (12-78)*	1.67		

*: Significant difference from baseline Friedman, **NRS:** Numeric rating scale, **WOMAC:** Western Ontario and McMaster Universities Osteoarthritis Index.

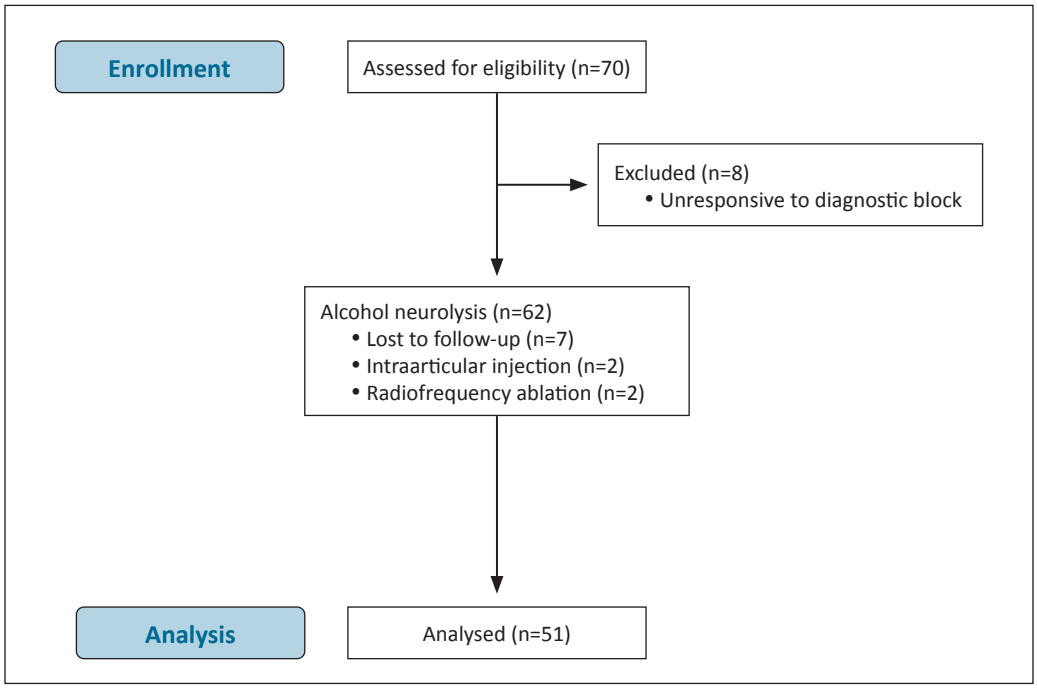

Figure 2: Patient flow chart.

nol treatment for KOA pain and reported a success rate of 46% (5). Another prospective study compared genicular phenol and RFA treatments and found that 53.1% of patients had a 50% or greater reduction in pain three months after genicular phenol treatment compared to 50% in the RFA group (4). In addition, paresthesia around the knee is observed in 34.4% of patients in the phenol group, while this rate was 6.3% in the genicular RFA group. After genicular alcohol treatment, the paresthesia rate was 9.8% in our study, lasted approximately one month, and regressed without treatment. We also observed hypoesthesia in two patients within the first month, and this side effect was resolved without treatment. No adverse events have been reported in case reports related to genicular alcohol treatment in the literature.

The lesion size produced by RFA depends on tissue characteristics and electrode position. In addition, less clinical improvement may be observed because of variations in the localization of the genicular nerves (11,12). Repeated RFA applications can overcome this, but may increase the risk of complications. Liquid chemical neurolytics administered for genicular nerve neurolysis can cover genicular nerve variations by spreading over a much larger area with a low volume (13). In our study, we used approximately 1 mL of 99% alcohol per genicular nerve, as in previous case reports, with successful results using alcohol neurolysis. Ahmed et al. applied alcohol neurolysis to the middle genicular nerve, inferior lateral genicular nerve, and lateral retinacular nerve in addition to the SMGN, SLGN, and IMGN in their study with four patients (6). Because of the limited number of studies in the literature and the risk of possible motor weakness due to the strong neurolytic effect of alcohol, we targeted three well-known primary nerves (SMGN, SLGN, and IMGN) for genicular alcohol neurolysis.

The literature on chemically induced geniculate neurolysis is limited. There is no consensus on the ideal agent and dose. Alcohol and phenol are two neurolytic agents commonly used for the treatment of chronic pain. They cause non-selective destruction of nerve tissue by precipitating cell membrane proteins, extracting lipid compounds, demyelinating nerve fibers, and inducing Wallerian degeneration. However, they also have potential adverse effects, such as alcoholic neuropathy, hypoesthesia, neuritis, deafferentation pain, motor deficits, and damage to non-targeted tissues. Phenol is a highly viscous and dense liquid that is difficult to inject except in 6-8% solutions. Alcohol is less dense than phenol, and is more likely to spread from the injection site. Alcohol may cause severe burning and injection pain when injected at high concentrations. In our study, 1 mL of 2% lidocaine was administered to each genicular nerve before alcohol injection to prevent injection pain, and this actually reduced the alcohol concentration in the target neuronal tissue.

Although no clinical difference in efficacy has been demonstrated between US and fluoroscopy as imaging modalities for genicular nerve block, it may be advantageous to use US to avoid risks such as genicular artery injury and damage to the surrounding tissues (14). This is because the genicular artery (GA) and nerve (GN) are close (15,16). In addition, the GN often cannot be visualized by US, and variations in nerve localization can be better observed according to the GA position determined by the Doppler function of US. The risk of vascular injury can be reduced by using the in-plane technique and Doppler function, as in our study. In addition, damage to other surrounding structures by neurolytic agents can be avoided. The fact that the patient and the performing physician are not exposed to radiation is another advantage of US (17).

Our study had several limitations. First, due to the design of our study, we did not have a control group. The second limitation was that the follow-up period was limited to three months. Another limitation was that the effect of the interventions on analgesic consumption could not be evaluated due to incomplete medical records.

CONCLUSION

Alcohol neurolysis of the genicular nerves should be considered as an option for patients with chronic knee pain who have failed conservative treatment and are not candidates for surgery. Although this is not a cost-effectiveness study, alcohol neurolysis is a low-cost alternative to more expensive procedures, such as RFA. Procedure-related adverse events occurred within a short period and did not require treatment. Further studies are required to determine the appropriate agents and doses.

AUTHOR CONTRIBUTIONS

Conception or design of the work: GY
Data collection: GY
Data analysis and interpretation: GRGP
Drafting the article: GY
Critical revision of the article: GRGP
The author (GY, GRGP) reviewed the results and approved the final version of the manuscript.

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