Neurology Asia 2024; 29(3) : 673 – 679

Ultrasound-guided pulsed radiofrequency of the greater occipital nerve in chronic migraine; proximal approach versus distal approach, a single-blind, randomized controlled trial

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Abstract

Background & Objective: Ultrasound-guided pulsed radiofrequency treatment of the greater occipital nerve can be used at distal and proximal levels of the greater occipital nerve in patients with chronic migraine. We aimed to evaluate the treatment efficacy, procedure duration, and pain experienced during the procedure for both methods. *Methods:* In the study, 60 chronic migraine patients randomly divided into two groups using a computer programme were evaluated. In the proximal group, the greater occipital nerve was accessed at the level of the 2nd cervical vertebra, while in the distal group it was accessed at the level of the protuberencia occipitalis. Patients completed the Migraine Disability Rating Scale, Visual Analogue Scale and a headache diary before treatment as well as at 1 month and 3 months afterwards. The time from the beginning of the intervention to the spread of the stimulus to the C2 dermatome during the sensory stimulation test was recorded. Patients were asked to rate their pain during the procedure using a Visual Analogue Scale. *Results:* The Visual Analog Scale scores and headache frequencies were significantly decreased in both the proximal group and distal group ($p<0.001$). The procedure time was shorter ($p<0.001$) and was less painful in the distal group ($p<0.001$). *Conclusions:* In this study, we observed that pulsed radiofrequency of both distal and proximal levels of the greater occipital nerves effectively treated migraine. A shorter procedure time and superior patient tolerability make the distal stimulation the procedure of choice.

Keywords: Chronic migraine, greater occipital nerve, radiofrequency, ultrasound-guided, pulsed radiofrequency, headache

INTRODUCTION

Chronic migraine (CM) is a neurological disease that causes severe disability and impaired quality of life. It has an annual incidence of 2.5-3.1%.[1-3] Greater occipital nerve (GON) block and pulsed radiofrequency (pRF) are used in the treatment of acute and chronic refractory migraine, occipital neuralgia, intracranial hypotension headache, and cervicogenic headache.[4-11] The effects of these treatments are based on the connections between the sensory neurons of the upper cervical spinal cord and the trigeminal nucleus caudalis.[12]

Neuromodulation methods such as pRF were included among the new migraine treatments in the consensus statement published by the American Headache Society in 2021.[13] Because the temperature of the RF cannula tips does not exceed 42°C, the procedure does not cause permanent nerve damage. The main effect occurs through change in the neuronal substructures from electric fields.[14,15] Dorsal horn, A-delta, and C-fibers are selectively affected.[16,17] As a result, pRF suppresses inflammatory cytokines, increases endogenous opioids, and decreases the response of the central nervous system to painful stimuli.[14-18]

US (ultrasound)-guided GON pRF can be performed in two ways: by targeting the proximal portion of the GON at the level of the C2 vertebra or by targeting the distal portion of the GON at the level of the occiput. Blockade or pRF of the distal extension of the GON is usually performed using a blind technique. However, the diameter and location of the GON are variable, and the nerve

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Date of Submission: 5 January 2024; Date of Acceptance: 26 June 2024

https://doi.org/10.54029/2024thj

runs adjacent to the occipital artery. Therefore, US guidance reduces the risk of complications.[19-21]

This is the first study to compare US-guided pRF applied at proximal and distal GON sites. In this study, we aimed to compare the efficacy, advantages, and disadvantages of both methods in the treatment of chronic migraine.

METHODS

Study design

This study was designed as a single-blind, randomized controlled trial. Ethical approval was obtained from the ethics committee (20.06.2022, Decision Number:140/20) and subsequently registered in the Clinical Trials Protocol Registration and Results System (NCT05888298). This trial was designed according to the CONSORT guidelines, and written informed consent was obtained from all patients. The design and process of this study are illustrated in Figure 1. Literature analyses were performed using the PubMed database, searching for the keywords ''greater occipital nerve'', ''radiofrequency'', ''nerve block'', ''chronic migraine'', ''migraine treatment'', ''neuromodulation''.

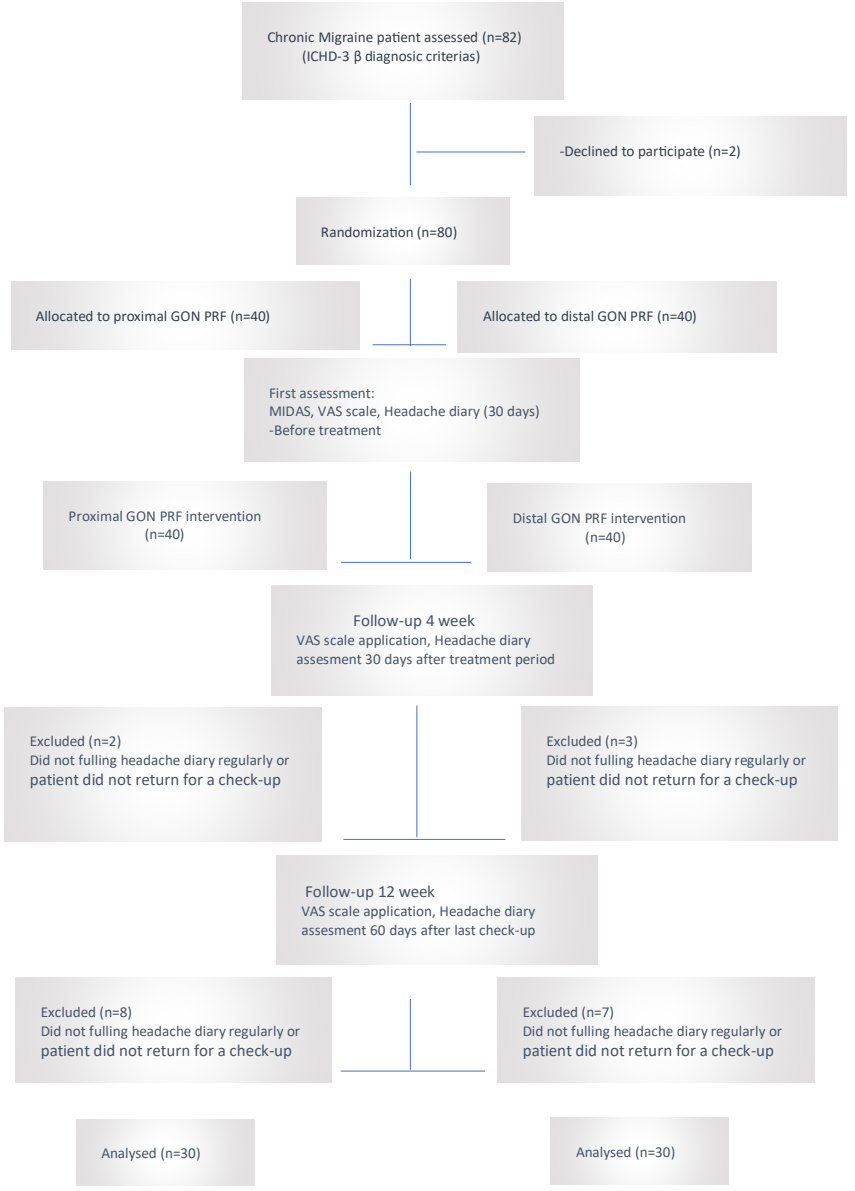

Figure 1. Flowchart diagram

Patients

Participants diagnosed with chronic migraine according to the ICHD-3 β diagnostic criteria were evaluated between September 2022 and January 2023. Between February 2023 and May 2023, participants underwent two treatments at the Algology Department.

The inclusion criteria for this study were as follows:1) age between 18-60 years; 2) Migraine Disability Assessment Score (MIDAS) > 2; 3) despite prophylactic treatment, more than 3 attacks per month or headache more than 10 days per month. Exclusion criteria were: 1) presence of uncontrolled hypertension, fibromyalgia, intracranial lesions, other primary headaches, dementia, and psychiatric disorders; 2) use of migraine prophylaxis medication within the last three months; and 3) interventional procedures such as GON blockade, botulinum toxin injection, and sphenopalatine ganglion blockade within the last six months.

Randomization and blinding

The participants were randomly divided into two groups: proximal and distal using a computer-assisted randomization program. In the proximal group, the GON was accessed at the level of the 2nd cervical vertebra, while in the distal group it was accessed at the level of the protuberencia occipitalis. The evaluation forms were completed by a single observer who was blinded to the intervention groups before treatment and at Week 4.

Outcome measurements

Our primary outcome was improvement in the severity of migraine attacks as assessed using Visual Analog Scale (VAS) scores before and after treatment. Our secondary outcomes were improvements in headache frequency, time to C2 dermatome stimulation during RF sensory stimulation, and VAS scores during the procedure. We assessed the change in headache frequency using headache diaries before and after the treatment. To compare the procedure times between distal and proximal applications, we recorded the time for the sensory stimulus to spread to the C2 dermatome in each patient. After placing the RF cannula in the target area, we recorded the time in seconds from the moment we started to deliver stimulation until the patient experienced symptoms radiating to the C2 dermatome such as numbness and tingling. The pain felt during the procedure was rated by each patient using the VAS scale, and this value was labelled as the procedural VAS.

Intervention: The intervention was performed on the side where the patient had the most attacks, either the right or left GON.

Identification of GON at the C2 level (proximal): A linear ultrasound probe (GE Healthcare Ultrasound LOGIQ P9) was placed transversely at the level of the second cervical vertebra, with the patient in the prone position. After visualizing the bifid spinous process of C2, the linear probe was shifted laterally and the fascia between the semispinalis capitis and obliquus capitis inferior muscles was detected. Occipital artery pulsations were visualized in the same plane. The GON was visualized lateral to the vascular pulsation.

Identifying GON at the occiput level (distal): The superior nuchal line was visualized by placing a linear ultrasound probe transversely to the occiput level, with the patient in the prone position. The probe was shifted laterally, and occipital artery pulsation was visualized. The GON was located medial to the vascular pulsation.

Pulsed radiofrequency therapy application: Once the GON was identified, an RF cannula (22-gauge 6 cm 5 mm active-tip hybrid electrode) was inserted laterally to medially using an in-plane technique. After visualizing the electrode tip close to the GON, a sensory stimulation test was performed by using an RF generator (TOP TLG-10 STP TOP Corporation, Inc.). When we obtained dysesthesia and a tingling sensation in the occipital region with a voltage lower than 0.2 V, we applied pRF treatment (5 Hz at 45 V, 5 ms at a temperature of 42 °C). After 4 min of pRF treatment, 3 mL 0.5% bupivacaine and 2 ml of saline solution were injected after negative inspiration.

Sample size determination

Using the G*Power software program, a sample size of 34 individuals per group was determined with an effect size of 0.639, α=0.05, and power (1-β)=0.80. The VAS scores (mean and standard deviation) was used as the basis for the analysis.[22]

Statistical analysis

All analyses were performed using Jamovi Project (2022, Jamovi Version 2.3, Computer Software).

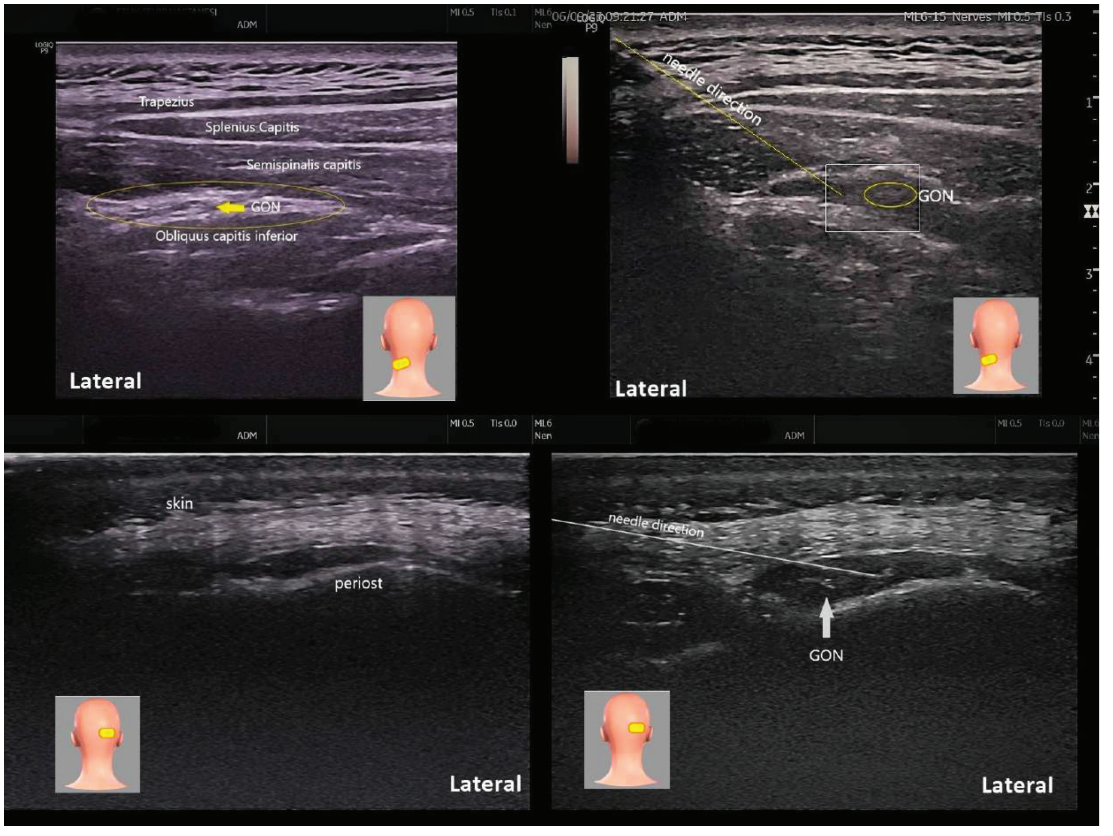

Figure 2. Proximal and distal approaches of the US-guided GON pRF
Upper images: GON pRF at the C2 level (proximal approach), Left: Pre-procedure, Right: During-procedure after injection
Bottom images: GON pRF at the occiput level (distal approach); Left: Pre-procedure; Right: During-procedure after injection

The findings of this study are expressed as frequencies and percentages. Normality analysis was performed using the Shapiro-Wilk test, skewness kurtosis, and histograms. normally distributed variables were presented as mean ± standard deviation (SD) and median (minimum-maximum). Categorical variables were compared using the chi-squared test. Numerical dependent variables were compared between the groups using an independent sample t-test and the Mann-Whitney U test. The VAS score and frequency of headache were analyzed using the Friedman test. Statistical significance was set at $P < 0.05$.

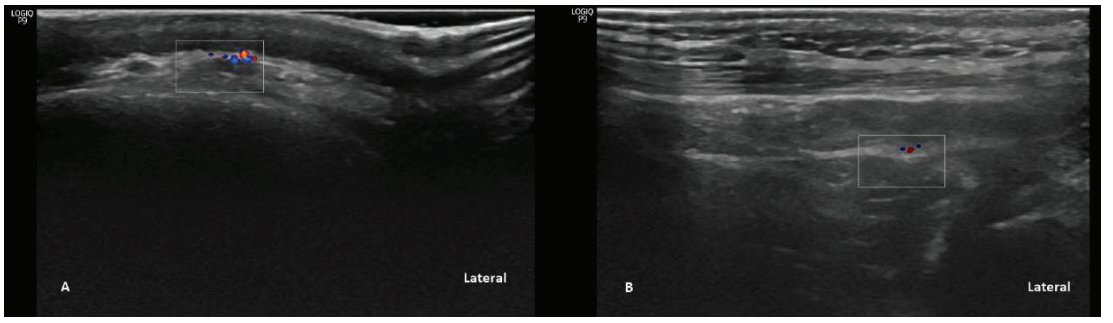

Figure 3. Occipital artery Doppler image at proximal and distal levels
A: Distal approach, B: Proximal approach

Table 1: Demographic data and intergroup comparisons

	Distal Group		Proximal Group		Levene		Test st.	p-value
	Mean±Std. Dev.	Med(min-max)	Mean±Std. Dev.	Med(min-max)	F	Sig.		
Age	41.27±10.61	40(23-60)	39.13±11.06	40.50(20-60)	0.09	0.762	0.762	0.449[a]
Gender n(%) Female	22(73.3)		20(66.7)					0.779[b]
Male	8(26.7)		10(33.3)					
MIDAS n(%) 3	10(33.3)		11(36.7)					1.000[b]
4	20(66.7)		19(63.3)					
VAS basal	8.33±1.42	8.5(2-10)/33.65*	8±1.23	8(6-10)/25.35*			355.5	0.145[c]
VAS 1month	2.67±1.78	2(0-6)/27.08*	3.73±2.53	3(1-10)/33.92*			552.5	0.123[c]
VAS 3month	5.33±2.20	5(1-10)/33.08*	4.67±2.87	4.5(1-10)/27.92*			372.5	0.248[c]
Frequency basal	24.50±3.59	24.5(19-30)/32.32*	23.6±4.57	24.5(12-30)/28.68*			395.5	0.418[c]
Frequency 1month	7.80±4.91	7(1-24)/26.22*	11.60±7.37	10(2-27)734.78*			578.5	0.057[c]
Frequency 3month	15.03±8.09	15.5(2-30)/24.62*	20.30±6.66	21(5-30)/36.38*			626.5	**0.009**[c]
Time to C2 dermatome stimulation (sec)	50±19.43	45(30-90)/16.88*	248.50±1.5.2	240(30-42)/44.12*			858.5	**<0.001**[c]
VAS procedure	3.12±1.24	3(2-7)/20.6*	4.67±1.22	3(2-7)/40.4*			747	**<0.001**[c]

a: Independent Samples T-Test, b: Chi-Square Test, c: Mann–Whitney U test, * Mean rank.

RESULTS

A total of 60 patients completed the study. No side effects were observed in any of the patients. No significant differences were observed between groups in terms of age or sex. The baseline MIDAS scores were similar in both groups (Table 1).

The VAS scores were similar between the groups at all time points (Table 1). The temporal change in the VAS score was significantly decreased in both groups (Mann Whitney U Test; both $p<0.001$). When the change between time points was analyzed using Bonferroni correction, the change between all time points was statistically significant in the distal group, whereas the change between baseline month 1 and baseline month 3 was significant in the proximal group (Table 2).

The headache frequency was similar before and 1 month after treatment. At 3 months post-treatment, the headache frequency was lower in the proximal group than in the distal group

Table 2: Temporal change of VAS and headache frequency

		VAS				Frequency of Headache			
		Median (min-max)	**Mean Rank**	**Test St.**	**p-value**	**Median (min-max)**	**Mean Rank**	**Test St.**	**p-value**
Distal Approach	Time 1 (basal)	9(2-10)	2.87			24.5(19-30)	2.9		
	Time 2 (4 week)	2(0-6)*	1.12	50.58	**<0.001**	7(1-24)*	1.28	41.05	**<0.001**
	Time 3 (12 weeks)	5(1-10)*	2.02			15.5(2-30)*	1.82		
Proximal Approach	Time 1 (basal)	8(6-10)	2.85			24.5(12-30)	2.55		
	Time 2 (4 week)	3(1-10)*	1.38	40.84	**<0.001**	10(2-27)*	1.18	33.15	**<0.001**
	Time 3 (12 weeks)	4.50(1-10)*	1.77			21(5-30)	2.27		

Friedman test, *; Statistically significant decrease compared to baseline; Bonferroni correction

(Mann-Whitney U test; p=0.009) (Table 1). The decrease in headache frequency over time from baseline was statistically significant in both groups (Friedman test, p<0.001 for both). The change between time points was analyzed using Bonferroni correction. In the distal group, changes at all times were statistically significant. In the proximal group, the change between baseline-1 and 1-3 months was significant (Table 2).

For each patient, the time from the start of the procedure until sensory stimulation of the C2 dermatome was obtained was recorded in seconds.. This time was significantly shorter in the distal group than in the proximal group (Mann-Whitney U-test; <0.001) (Table 1).

Procedural VAS scores, which assessed the pain experienced during the procedure, were analyzed between the groups. Procedural VAS scores were significantly lower in the distal group (Mann–Whitney U test; p<0.001).

DISCUSSION

In this study, we found that US-guided GON pRF treatment at both the proximal and distal levels improved pain severity and frequency during the three-month follow-up period. In addition, the distal procedure group had a shorter procedure time and fewer painful procedures. Karaoğlan and Flamer compared GON blocks applied distally and proximally. They found that proximal application was more effective.[21,22] Until this study, we are unaware of any published data comparing pRF procedures at different levels of the GON.

Güner *et al*. reported that GON pRF treatment at C2 at the proximal level is an effective and safe treatment for headaches for up to 12 weeks.[10] Cohen *et al*. reported that GON pRF treatment applied blindly at the occiput at the distal level was effective for 12 weeks in migraine and occipital neuralgia patients with occipital nerve sensitivity.[4] Another study by Karaoğlan *et al*. on the results of GON pRF applied with a blind technique at the occiput level showed that the treatment was effective for up to six months.[11] Our results are consistent with previous data. However, unlike our study, these studies performed unguided distal GON blocks.

The most notable finding of our study was that the distal application was faster and less painful than the proximal application. To the best of our knowledge, these two procedures have not been compared in terms of procedure time and tolerability.

The time taken to stimulate the C2 dermatome was three times longer in the proximal group than in the distal group (mean rank proximal: 44.12, distal: 16.88). At the distal level, the RF cannula passes only through the skin and subcutaneous fat. Therefore, it is quicker to receive C2 dermatomal stimulation of the occipital fossa. At the proximal level, the RF cannula crosses the trapezius, splenius capitis, and semispinalis capitis muscles between the skin and nerves. In addition, the area is rich in muscles and fascia, and anatomical variations in the position of the GON make it difficult to reach the target nerve.

According to procedural VAS scores, patients in the proximal group experienced 2 times more pain during the procedure as those in the distal group (Mean Rank proximal 40.4, distal 20.6). GON pRF applied at the distal level was better tolerated by patients. This is an important finding of our study, and these two applications have not been compared in this regard.

With proximal-level application we often had to change the direction of the RF cannula several times to get closer to the GON or to obtain stimulation of the C2 dermatome. On occasion we had to re-enter the skin with the needle. As a result, the procedure time was longerand pain sensation was greater in the proximal stinulation group.

The limitations of our study are that we did not evaluate the effect of treatment on analgesic use and the follow-up period was limited to 3 months.

In conclusion, US-guided GON pRF at the proximal and distal levels is an effective treatment for chronic migraine. Distal stimulation seems to be more advantageous because of a shorter procedure time and less procedure-related pain.

DISCLOSURE

Financial support: None

Conflict of interest: None

REFERENCES

1. Schwedt TJ. Chronic migraine. *BMJ* 2014; 24(348):g1416. https://doi.org/10.1136/bmj.g1416
2. Xu J, Kong F, Buse DC. Predictors of episodic migraine transformation to chronic migraine: a systematic review and meta-analysis of observational cohort studies. *Cephalalgia* 2020; 40(5):503-16. doi: 10.1177/0333102419883355.
3. Headache Classifcation Committee of the International Headache Society (IHS) The International Classification of HeadacheDisorders, 3rd ed. *Cephalalgia* 2018;38(1):1–211. doi: https://doi.org/10.1177/0333102417738202.

4. Cohen SP, Peterlin BL, Fulton L, *et al*. Randomized, double-blind, comparative-effectiveness study comparing pulsed radiofrequency to steroid injections for occipital neuralgia or migraine with occipital nerve tenderness. *Pain* 2015; 156(12):2585-94. doi: 10.1097/j.pain.0000000000000373.
5. Huang JHY, Galvagno Jr SM, Hameed M, *et al*. Occipital nerve pulsed radiofrequency treatment: A multi-center study evaluating predictors of outcome. *Pain Med* 2012; 13(4):489-97. doi: 10.1111/j.1526-4637.2012.01348.x.
6. Niraj G, Critchley P, Kodivalasa M, Dorgham M. Greater occipital nerve treatment in the management of spontaneous intracranial hypotension headache: A case report. *Headache* 2017;57(6): 952-5. doi: 10.1111/head.13095.
7. Vanderhoek MD, Hoang HT, Goff B. Ultrasound guided greater occipital nerve blocks and pulsed radiofrequency ablation for diagnosis and treatment of occipital neuralgia. *Anesth Pain Med* 2013; 3(2):256-9. doi: 10.5812/aapm.10985.
8. Manolitsis N, Elahi F. Pulsed radiofrequency for occipital neuralgia. *Pain Physician* 2014;17(6):E709-17.
9. Kwak S, Chang MC. Management of refractory chronic migraine using ultrasound-guided pulsed radiofrequency of greater occipital nerve: Two case reports. *Medicine* (Baltimore). 2018; 97(45):e13127. doi: 10.1097/MD.0000000000013127.
10. Guner D, Eyigor C. Efficacy of ultrasound-guided greater occipital nerve pulsed radiofrequency therapy in chronic refractory migraine. *Acta Neurol Belg* 2023; 123(1):191-8. doi: 10.1007/s13760-022-01972-7.
11. Karaoğlan M, Küçükçay B. Using GON block as a diagnostic block: Investigation of clinical efficacy of GON radiofrequency treatment for migraine patients. *Neurol Asia* 2022; 27(4) : 991-9. doi: 10.54029/2022sxa.
12. Viganò A, Torrieri MC, Toscano M, Neurophysiological correlates of clinical improvement after greater occipital nerve (GON) block in chronic migraine: relevance for chronic migraine pathophysiology. *J Headache Pain* 2018;19(1):73. doi: 10.1186/s10194-018-0901-z.
13. Ailani J, Burch RC, Robbins MS; Board of Directors of the American Headache Society. The American Headache Society Consensus Statement: Update on integrating new migraine treatments into clinical practice. *Headache* 2021; 61(7):1021-39. doi: 10.1111/head.14153.
14. Cosman ER Jr, Cosman ER Sr. Electric and thermal field effects in tissue around radiofrequency electrodes. *Pain Med* 2005; 6(6):405-24. doi: 10.1111/j.1526-4637.2005.00076.x.
15. Fernandez MI, Watson PJ, Rowbotham DJ. Effect of pulsed magnetic field therapy on pain reported by human volunteers in a laboratory model of acute pain. *Br J Anaesthesia* 2007;99(2):266–69. doi: 10.1093/bja/aem129.
16. Hamann W, Abou-Sherif S, Thompson S, Hall S. Pulsed radiofrequency applied to dorsal root ganglia causes a selective increase in ATF3 in small neurons. *Eur J Pain* 2006;10:171-6. doi: 10.1016/j.ejpain.2005.03.001.
17. Sam J, Catapano M, Sahni S, Ma F, Abd-Elsayed A, Visnjevac O. Pulsed radiofrequency in interventional pain management: Cellular and molecular mechanisms of action - An update and review. *Pain Physician* 2021;24(8):525-32.
18. Lin FY, Huang KF, Chen JC, Lai MF, Ma KH, Yeh CC. The Clinical application of pulsed radiofrequency induces inflammatory pain via MAPKs activation: A novel hint for pulsed radiofrequency treatment. *Int J Mol Sci* 2021;22(21):11865. doi: 10.3390/ijms222111865.
19. Güvençer M, Akyer P, Sayhan S, Tetik S. The importance of the greater occipital nerve in the occipital and the suboccipital region for nerve blockade and surgical approaches--an anatomic study on cadavers. *Clin Neurol Neurosurg* 2011;113(4):289-94. doi:10.1016/j.clineuro.2010.11.021
20. Huanmanop T, Issara I, Agthong S, Chentanez V. Evaluation of the greater occipital nerve location regarding its relation to intermastoid and external occipital protuberance to mastoid process lines. *Folia Morphol (Warsz)* 2021;80(3):533-41. doi:10.5603/FM.a2020.0099
21. Karaoğlan M, İnan LE. A comparison of the clinical efficacy of GON block at the C2 level and GON block at the classical distal occipital level in the treatment of migraine. *Clin Neurol Neurosurg* 2022; 215:107190. doi: 10.1016/j.clineuro.2022.107190.
22. Flamer D, Alakkad H, Soneji N, *et al*. Comparison of two ultrasound-guided techniques for greater occipital nerve injections in chronic migraine: a double-blind, randomized, controlled trial. *Reg Anesth Pain Med* 2019;44(5):595-603. doi: 10.1136/rapm-2018-100306.