

The effectiveness of greater occipital nerve blockade in treating acute migraine-related headaches in emergency departments

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Objective: This study aimed to evaluate the effectiveness of a greater occipital nerve (GON) blockade against a placebo and classical treatments (non-steroidal anti-inflammatory drugs + metoclopramide) among patients who were admitted to the emergency department (ED) with acute migraine headaches.

Method: This prospective-randomized controlled study was conducted on patients with acute migraine headaches. The patients were randomly assigned to 3 treatment groups: the GON blockade group (nerve blockade with bupivacaine), the placebo group (injection of normal saline into the GON area), and the intravenous (IV) treatment group (IV dexametoprolfen and metoclopramide). Sixty acute migraine attack patients were assigned to 3 groups of 20 patients each. The pain severity was assessed at 5, 15, 30, and 45 minutes with a 10-point pain scale score (PSS).

Results: The mean decreases in the 5-, 15-, 30-, and 45-minutes PSS scores were greater in the GON blockade group than in the dexametoprolfen and placebo groups. When comparing the 30- and 45-minutes PSS changes, a statistically significant difference was found among the 3 groups ($P = .03$ and $P = .03$, respectively).

Conclusion: A GON blockade was as effective as an IV dexametoprolfen + metoclopramide treatment and superior to a placebo in patients with acute migraine headaches. Despite being an invasive procedure, a GON blockade might be an effective option for acute migraine treatment in the ED due to its rapid, easy, and safe application.

KEYWORDS

acute migraine, emergency medicine, greater occipital nerve blockade, headache

1 | INTRODUCTION

Primary headache (migraine headaches, tension headaches, cluster headaches, etc.) is common symptom presenting to the emergency department (ED) in the worldwide. Migraine is a primary cause of headaches and has episodic and variable prognoses; the lifetime incidence is 43% among females and 18% among males.¹ In acute attacks affecting the quality of life, the first resort of migraine patients is often EDs.² However, no precise standard treatment has yet been defined to end acute attacks in the ED, and the rates of response to non-specific drugs (non-steroidal anti-inflammatory drugs [NSAIDs], combined analgesics, antiemetics, triptans, etc.) are quite variable.³⁻⁸

Peripheral nerve blocks are an alternative to drugs for primary headaches. Local anesthetics and/or steroidal injections are used for this purpose. The procedure is fast, easy, generally safe, and painless enough to be tolerated at a very high level, making nerve blocks attractive for clinicians and patients, especially for resistant headaches.^{9,10} In recent studies, the use of nerve blocks, especially greater occipital nerve (GON) blockades, has gradually become popular for migraine prophylaxis.^{11,12} A limited number of publications have reported the effectiveness of GON blockades in reducing the pain in the acute phase.¹³⁻¹⁵ On the other hand, to our knowledge, there has been no randomized controlled study in the literature that investigated the utility

of GON blockades for the treatment of acute migraine attacks in the ED.

Our study aimed to evaluate the effectiveness of a GON blockade against a placebo and a classical treatment (NSAIDs+metoclopramide) among patients who were admitted to the ED due to acute migraine headaches.

2 | MATERIALS AND METHODS

2.1 | Study design and setting

Our prospective-randomized controlled study was conducted between January and December 2016 at an ED that admits about 250 000 patients annually. Prior to the study, the approval of the local ethical council and the Ministry of Health Drugs General Directorate for Pharmaceuticals and Pharmacy (number 2016-AKD-3) was received.

2.2 | Selection of participants

All the patients aged 18-65 years who had been admitted to the ED for headaches were assessed by emergency physicians according to the International Classification of Headache Disorders—3rd edition. Then, the patients thought to have migraines (with or without auras) were reevaluated by a neurologist for this study. The patients who were considered to have had acute migraine attacks were included in the study.¹⁶ The written consent of all the participating patients was received by the same neurologist after a briefing. Exclusion criteria for this study were as following; patients who had previously had GON blockades for migraine treatment, patients had taken any analgesic drugs or drugs for migraine prophylaxis in the last 6 hours, patients had an active infection/skull defect/hemangioma in the injection area, patients had a history of allergy to any of the drugs used in our study, patients used any anticoagulant-agents, patients had bleeding diathesis, patients had hemodynamic instability, patients were pregnant, and patients were breastfeeding mothers.

2.3 | Randomization and interventions

The patients were randomly divided into 3 groups using Random Allocation Software 1.0.¹⁷ After setting the number of groups, the name of each group (GON blockade, IV treatment, or placebo), and the sample size (20 patients each) in the option window, a random sequence was generated by the program. The patients in the first group received 50 mg of dexketoprofen trometamol (Arveles, IE Ulagay-Menarini İlaç San., Turkey) and 10 mg of metoclopramide (Metpamid, Sifar İlaç San., Turkey) in 100 mL of normal saline intravenously. A GON blockade with 1 mL of 0.5% bupivacaine (Marcaine, AstraZeneca Türkiye İlaç San., Turkey) and 1 mL of normal saline was applied to the second group around the GON (totally 2 mL: 1 mL normal saline plus 1 mL bupivacaine); 2 mL of normal saline was applied to the third group in the same area, as a placebo. The reason for we prefer low volume (2 mL) rather than high volume (3 mL or

more) for local anesthetic agent was using low volume cause less side effects according to our previous clinical experience. The injection area for the second and third groups was the medial one-third of the distance between the occipital process and the mastoid process. The patients were asked to sit down and bend over a table for these procedures. The injection area between the hairs was disinfected with iodine, and a single injection (if the headache was on one side) or a double injection (if the headache was on both sides—2 mL injections (placebo or bupivacaine) were applied each side; totally 4 mL) was applied subcutaneously with a 26-gauge (0.45 × 13-mm) needle. The treatments used in the second and third groups were prepared in a different room before the procedure by another researcher in the study; the practitioner performing the procedure did so without being informed of the selected treatment. As the prepared injections had the same color and appearance, the practitioner and the patient were both blind for only GON blockade and placebo groups.

2.4 | Methods of measurement

The patients' pretreatment (0-minutes) headache scores on a scale of 0-10 points (with 10 being the maximum) were recorded using the pain scale score (PSS), which is a numeric rating scale (NRS). The post-treatment headache evaluation was performed by the same practitioner recording the PSS at 5, 15, 30, and 45 minutes.

2.5 | Statistical analyses

The statistical analyses were carried out using SPSS 15.0 (Chicago, IL, USA). The Shapiro-Wilk test was used to evaluate the normality of all the parameters related to the subjects. Parametric data were expressed as mean values and standard deviations (SD). Nonparametric data were expressed as numbers, percentages, median values, and interquartile ranges (IQR; 25%-75%). Nonparametric data were analyzed using the Kruskal-Wallis test. The 95% confidence intervals (CIs) were calculated whenever appropriate, and a *P* value <.05 was considered to be statistically significant. The sample size was estimated with G-Power for Mac OS X (version 3.1.9.2; Universität Dusseldorf, Germany). Our goal was to achieve the power to detect a 2-point difference on the PSS among the treatment groups. Also, we considered a standard deviation as 2 points, in accordance with methods from previous studies.^{18,19} Thus, assuming a two-sided $\alpha = .05$, we anticipated a sample size of 16 patients for each group to achieve 80% power. An additional 12 patients (4 in each group) were included to account for potential protocol violations.

3 | RESULTS

During the study, 534 patients were admitted to the ED with a complaint of headache, and 85 of those were considered to have had an acute migraine attack. Twenty-five patients meeting the exclusion criteria were not included in the study, and the remaining 60 acute migraine-attack patients were randomly placed in the 3 groups

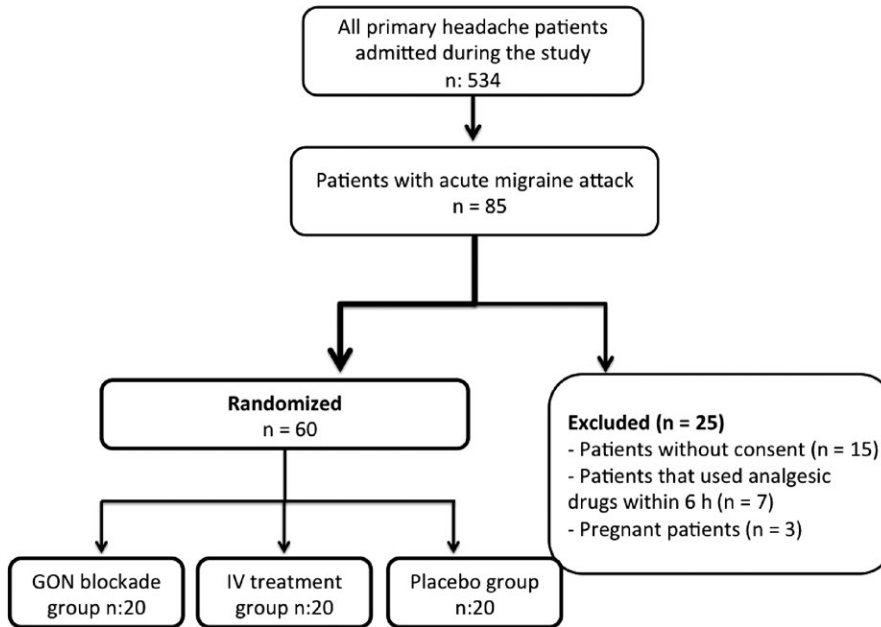


FIGURE 1 Patient flowchart

(Figure 1). There were no statistically significant differences in the demographics or baseline characteristics of the patients in the treatment groups (Table 1).

For each of the 3 groups, there was no statistical and clinical significant difference between the pretreatment baseline PSS. While no clear difference was observed between the 5- and 15-minutes PSS following the treatment, at 30 minutes, the median PSSs were observed to be 3 (IQR: 0-4.75) for the GON blockade group, 1 (IQR: 0-4) for the IV treatment group, and 4.5 (IQR: 1-6) for the placebo group (Table 2).

The changes in the PSSs from the pretreatment baseline values are shown in Table 3 and Figure 2. Although the median decreases in the 5-, 15-, 30-, and 45-minutes PSSs were greater in the GON blockade group than in the IV and placebo groups, there was no statistically significant difference among the groups. A statistically significant difference was found in between the 30-minutes score and the 45-minutes score in each of the 3 groups and then

compared those 3 numbers ($P = .02$ and $P = .02$, respectively). According to the pairwise comparisons of the treatment groups, the reason for this difference seemed to be the statistically significant decrease in the PSS score in the GON blockade group compared with the placebo group ($P = .012$ for 30 minutes; $P = .016$ for 45 minutes; Table 4).

No severe adverse systemic effects such as hypotension, bradycardia, or anaphylaxis or local adverse effects such as pain or hematoma in the injection area were observed in any of the patients during the treatment or follow-up.

4 | DISCUSSION

The most important result in our study was that the GON blockade was as effective as an IV treatment of dexketoprofen+metoclopramide and superior to a placebo.

	GON blockade group (n = 20)	IV treatment group (n = 20)	Placebo group (n = 20)	P
Sex [n (%)] Male	2 (10)	5 (25)	2 (10)	.3
Age [median (IQR 25%-75%)]	40 (33-45)	35 (30-41)	40 (29-43)	.3
Accompanying symptoms [n (%)]				
Aura	1 (5)	4 (20)	5 (25)	.2
Photophobia	18 (90)	15 (75)	14 (70)	.2
Phonophobia	13 (65)	10 (50)	13 (65)	.5
Nausea and/or vomiting	16 (80)	18 (90)	18 (90)	.5
Pain onset (h) [median (IQR 25%-75%)]	8.5 (4.5-11.5)	9 (5-15)	12 (6-20)	.3

TABLE 1 Baseline characteristics of the study population

GON, greater occipital nerve; IV, intravenous; IQR, interquartile range.

TABLE 2 Pain scale score of patients throughout time according to groups

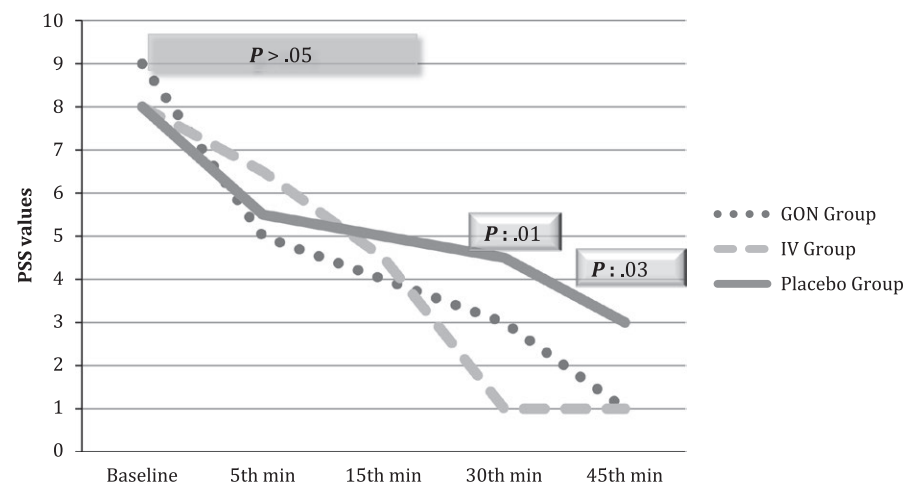
PSS [median (IQR 25%-75%)]	GON blockade group (n = 20)	IV treatment group (n = 20)	Placebo group (n = 20)	P
Baseline	9 (7.25-9.75)	8 (7-9)	8 (7-9.5)	.2
5th min	5 (3.25-8)	6.5 (5-7)	5.5 (5-7)	.7
15th min	4 (0-6.5)	4.5 (2.3-5)	5 (3-6)	.3
30th min	3 (0-4.75)	1 (0-4)	4.5 (1-6)	.01
45th min	1 (0-3)	1 (0-2)	3 (1-5.75)	.03

PSS, pain scale score; IQR, interquartile range; GON, greater occipital nerve; IV, intravenous.

TABLE 3 Median value decrease in baseline pain scale score based on the duration in the treatment groups

Change from baseline PSS [median (IQR 25%-75%)]	GON blockade group (n = 20)	IV treatment group (n = 20)	Placebo group (n = 20)	P
0-5 min	3 (1-4.75)	1 (0.25-2)	2 (1-3)	.07
0-15 min	5 (2.25-7)	4 (2-5)	3 (2-4.75)	.18
0-30 min	6 (4-4.75)	5 (4-7)	4 (2-5.75)	.02
0-45 min	7 (5-9)	7 (5-8)	5 (2.25-7)	.02

PSS, pain scale score; IQR, interquartile range; GON, greater occipital nerve; IV, intravenous.

**FIGURE 2** Pain scale score (PSS) change in patients throughout time according to groups

A limited number of publications have evaluated the effectiveness of a GON blockade for the treatment of acute migraines and the reduction in headaches. In a study conducted by Young et al¹⁵ with 25 patients, the mean VAS score was 5.85 before the GON blockade, and a decrease of 64% was reported in the mean 5-minutes VAS score. In our study, the median pre-GON blockade PSS was 9, and we saw a decrease of 44.4% in the 5-minutes PSS after the treatment. Unlike Young et al.'s study group, which included patients who had responded to a GON blockade treatment before, ours excluded those patients; this might have caused us to find a lower recovery rate in the 5-minutes PSS. Another reason why we found a lower 5-minutes PSS response might have been the higher median baseline PSS—that is, the fact that our GON blockade was applied to patients with more severe headaches. Nevertheless, a GON blockade was the treatment that achieved the greatest decrease in the 5-minutes

PSS score compared with the other groups in our study (IV group: 18.8%; placebo group: 31.2%). A study by Dilli et al²⁰ which investigated the short-term preventive effects of a GON blockade in episodic and chronic migraine patients, reported that there was no significant difference between a GON blockade and a placebo in the second minute post-injection. Similarly, in our study, though no significant difference was found between the GON blockade and the placebo in the 5-minutes PSSs, we observed that the GON blockade was statistically superior to the placebo after 30 and 45 minutes. In the light of these findings, we think that the partial results achieved in the short term after the GON blockade or the normal saline injection (placebo) are related to the placebo effect, and the actual effectiveness of the GON blockade emerges upon the completion of the central inhibition process. Other studies support this idea; Cuadrado et al²¹ found that the maximum response to the GON blockade was

TABLE 4 Comparison of the treatment groups by the changes in pain scale score based on duration

	P value*
0-30 min	
GON vs placebo	.012
IV treatment vs placebo	.03
GON vs IV treatment	.56
0-45 min	
GON vs placebo	.016
IV treatment vs placebo	.03
GON vs IV treatment	.39

PSS, pain scale score; CI, confidence interval; GON, greater occipital nerve; IV, intravenous.

*New *P* value was calculated as .0169 using Bonferroni correction.

achieved after a median of 22.5 minutes in all patients and 35 minutes in fully responsive patients. Ashkenazi et al¹³ reported a statistically significant decrease in the headache severity 20 minutes after the GON blockade, compared to the baseline (mean score of 3.2 points out of 11).

The mechanism of the GON blockade effect in migraine treatment has yet to be clearly elucidated. However, activity changes in the trigeminal-cervical complex secondary to the blockade have been reported.²² The fact that the effect of the GON blockade remained even after the effect time of the injected drug ended was associated with these changes, and how the migraine prophylaxis was achieved with repeated GON blockade treatments was explained in an effort.^{12,23} Yet, it is obvious that the effectiveness of a GON blockade in the acute period after a single application, which is associated with complex central inhibition mechanisms, cannot be related only to the anesthetic effect of the applied drug. The modulation of the nociceptive fibers arriving at the trigeminal caudal nucleus has also been reported, along with other associated mechanisms.^{22,24} In a recent study, Cuadrado et al²³ investigated the short-term effects of a GON blockade in chronic migraines and used the pressure-pain threshold (PPT) as the evaluation criterion. The PPT is defined as the minimum pressure that causes pain.²⁵ In that study, Cuadrado et al found significant increases in the PPT values in the supraorbital and infraorbital regions 1 hour after the GON blockade, compared to the placebo ($P = .022$ for the supraorbital region, $P = .013$ for the infraorbital). This result was interpreted by the authors as supporting the idea that the GON blockade inhibits the nociceptive stimuli arriving at the trigeminal-cervical nucleus during the acute period.²³ In accordance with this information, the most probable mechanism that makes a GON blockade useful in the treatment of acute migraine headaches seems to be the above-mentioned trigeminal nucleus-nociceptive stimulus modulation.

To our knowledge, the only publication in the literature involving the use of a GON blockade in migraine treatments in EDs is the study performed by Cuadrado et al in which they

used a GON blockade in the acute treatment of extant or persistent migraine auras. Some of the 20 patients in the study were treated at the ED, while the blockade was applied to the others in the headache unit of the neurology clinic. The main purpose of that randomized uncontrolled study was to investigate the efficiency of a GON blockade for visual or sensorial auras. According to the secondary results of the study, the total rate of response to the GON blockade was 16 of 20 cases (80%), and a full response was achieved in 11 cases (55%).²¹ Our study is the first to evaluate the effectiveness of a GON blockade in acute migraine treatment at an ED in a randomized and controlled manner. All of our patients were evaluated at the ED, and the GON blockades were applied there, too. This is also the first study to compare the effectiveness of a GON blockade to both a classical treatment and a placebo. We think that, in light of our findings, a GON blockade is a good treatment of choice that can be safely applied for acute migraine treatment at EDs, both because it is as effective as the classical NSAID+metoclopramide treatment and superior to a placebo and because no adverse effects were observed.

We did not observe any systemic or local side effects during the study period. Similar to our results, many studies and a meta-analysis showed that there is no serious adverse event due to GON blockade. However, the same studies showed not serious but several side effects such as facial edema, sleeping disturbances, and local/neck pain.²⁶⁻²⁹ We believe that possible cause of this difference may be the agents used for GON blockade were different from each other. For example, in a study, Gantenbein et al have reported that several side effects were developed in 14.2% of all patients after applied GON blockade.²⁹ While, in this study, all patients were injected 3 mL betamethasone and 2 mL 2% lignocaine, and in our study, we used 1 mL bupivacaine (0.5%) and 1 mL normal saline. This lower dosage could be the reason for not seeing any side effects.

5 | LIMITATIONS

There are certain limitations to our study. First, as our study took place in a single ED, the results cannot be generalized to all other EDs. Second, it is known that the injections have placebo effects.³⁰ Hence, when evaluating our study results, one should not ignore the placebo effects caused by the applications of both the GON blockade and the saline placebo. Moreover, whereas both the doctor and patient were blind in the GON blockade group and the placebo group, they were not blind in the IV treatment group, to which dextropropofol and metoclopramide were applied intravenously. Another limitation is that the effectiveness of the GON blockade was not evaluated according to the migraine subtypes; it might not be accurate to generalize the results from a heterogeneous study group to individual subtypes. Also, our study results were based on subjective information provided by the patients, which must be considered when evaluating our study. Finally, the relatively small

number of patients in the study might have prevented us from identifying clear correlations among the parameters; further studies with higher numbers of patients could provide clearer evaluations of the effectiveness.

6 | CONCLUSION

A GON blockade was as effective as an IV dexketoprofen and metoclopramide treatment and superior to a placebo (saline injection into the GON area) among patients who were admitted to the ED due to acute migraine headaches. Despite being an invasive procedure, a GON blockade might be an effective option for acute migraine treatment in the ED due to its rapid, easy, and safe application.

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The authors have no acknowledgment to declare.

CONFLICT OF INTERESTS

The authors declare no potential conflict of interest.

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