Research Article

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Comparison of single and repeated blockade of the greater occipital nerve in migraine treatment

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Abstract

Objective: Migraine is a neurovascular syndrome that can be triggered by several conditions such as increased stress levels, sleep disorders, some foods, hormonal abnormalities, and weather changes. In this study, the efficacy of single and repetitive greater occipital nerve blockade on patients with migraine were investigated.

Methods: Forty migraineurs were divided into 2 groups randomly. Group 1 (n=20) received 1 session of blockade and group 2 (n=20) received 3 sessions of blockade per week with 2.5 cc 1% lidocaine. The number of attacks monthly, duration of attacks (in hours), and pain severity using a visual analogue scale (VAS) were recorded, then compared with the pretreatment values and at the 6th and 12th weeks after treatment.

Results: Group 1 showed a statistically significant decrease for all parameters compared with the 6th week values ($p<0.05$). Group 2 also showed a statistically significant decrease both at the 6th and 12th weeks for all parameters ($p<0.05$). The decrease in the frequency of pain at the 6th week between group 1 and 2 was statistically significant. The decrease in pain intensity (VAS) at the 12th week in group 2 was more significant ($p<0.05$).

Conclusion: Greater occipital nerve blockade seems to be effective in the treatment of migraine and repeated blockade can be more effective in migraine treatment.

Keywords: Migraine, greater occipital nerve, occipital nerve blockade, headache, local anesthetic

INTRODUCTION

Migraine is a group of syndromes that develop from a neurovascular disorder caused by primary disease of the central nervous system and a secondary neurovascular disorder due to vascular changes. Migraine is a kind of trigeminovascular pain that effects daily life activities negatively. Migraine is frequent in the first three decades. It is regarded as "chronic" when the frequency of pain is more than 15 days per month. Before puberty, migraine is more frequent in men, but it is more frequent in women after puberty. In adulthood, the female/male ratio can rise up to 3:1. The reason for this difference is based upon hormonal changes and an increasing number of studies about the pathophysiologic mechanisms are available (1-4).

In the prophylactic treatment of migraine, there are medical and non-medical treatment methods. Psychotherapeutics, biofeedback, regular lifestyle, exercises for relief, and non-medical treatment methods such as acupuncture and hypnosis can be added to treatment or used alone when medical treatment methods are ineffective. However, more data and studies are needed to show the efficacy of these methods. Pharmacologic treatment can be used both for acute attack treatment and prophylactic treatment. Simple analgesics, non-steroidal anti-inflammatory agents, ergot alkaloids, triptans, and opioids are used in the treatment of acute attacks. Propranolol, metoprolol, amitriptyline, flunarizine, valproic acid, and topiramate are the most common medicines in use. Medicines for migraine acute attack and prophylactic treatment may have adverse effects. There are medicines that can interact and increase their adverse effect potentials, in addition to their own adverse effects, so new and effective treatment methods with fewer adverse effects are needed (4-7).

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In recent years, nerve blockades using local anesthetics for the treatment of primary headaches have become more common. In clinical practice, trigger point injections, nerve blockades (greater occipital nerve [GON], supraorbital nerve, infraorbital nerve), ganglion blockades (superior cervical ganglion, sphenopalatine ganglion) can be used successfully. Recent studies of GON blockade showed the efficacy and safety (7-10). Inan et al. reported a double-blind, multicenter, randomized, placebo-controlled GON blockade study in patients with chronic migraine. In their study, GON blockade using bupivacaine was found to be effective in the treatment of chronic migraine (11).

The aim of the current study was to compare both the efficacy of single and repeated sessions of local GON lidocaine injections in migraine.

METHODS

Our prospective randomized clinical study was approved by the local ethics institution and approval forms were signed by all of participants (GATA local ethics committee 13.07.2009-1491\780\09\1539). Patients with migraine without aura (classified in accordance with 2004 International Headache Classification) were included in this study. Patients with migraine aged 18-60 years who were having 4 or more migraine attacks per month with normal neurologic examination were randomly included in the study by the same neurologist. Patients used any kind of prophylactic treatment for headache in the last month, patients who had medication-overuse headache according to the Revised International Classification of Headache Disorders-2R (ICHD-2R), pregnant or lactating women, patients with anemia or bleeding diathesis, patients with uncontrolled blood pressure or diabetes mellitus, chronic liver, kidney or congestive heart failure, those with hypophyseal and hypothalamic dysfunction, patients with known allergies against local anesthetics, patients who had a history of malignancy or cervical or cranial surgery, patients who had received caffeine more than 500 mg/day during last month, patients who had received non-pharmacological therapy for the last 6 months, patients with major psychiatric disorders (e.g., major depression), patients who used antipsychotic, antidepressant, and antiepileptic drugs within the previous 3 months, patients with neuromuscular dysfunction, patients using agents that affect neuromuscular functions similar to curare or antibiotics such as aminoglycoside, patients with hypo-hyperthyroidism, patients who had a history of primary headaches other than chronic migraine, and patients who received GON blockade or botulinum toxin type A (BoNT-A) therapy were excluded from the study.

Forty patients (9 males and 31 females) were included in the study. Written informed consents were obtained from all patients. All patients were monitored before starting GON blockade treatment and the number of attacks, duration of attacks (in hours), and visual analogue scale (VAS) scores for the intensity of pain were recorded per month. Patients were divided into two groups randomly: GON blockade was applied to group 1 in 1 session, and in 3 sessions (once a week for three weeks) in group 2 with 1% and 2.5 mL of lidocaine. All injections were applied by the same specialist. Injections were made 2 cm lateral and 2 cm inferior of the external occipital protuberance and to the GON area. Patients were laid on their fronts on the examination couch. The GON area was cleaned using anti-septic solutions. A 26-G 0.45x13 mm pin was used, avoiding touching the periosteum; three directional aspiration following lidocaine injections were made. All patients had a history of one-sided headache but these headaches were sometimes on the right and sometimes on the left. Accordingly, 2.5 mL injections were made to both sides and after injection, local pressure was applied for approximately 1 minute to the injection area. To follow the probable adverse effects after the application, patients were kept under observation for 30 minutes. Patients were requested to note their headaches in a diary: every headache day, highest level of pain and adverse effects, if any. During the follow-up period, all examinations were performed by a different researcher who was blinded to the treatment groups. After treatment, 6th and 12th week examinations were made and the number of attacks, duration of attacks, and pain severity were recorded using VAS scales.

All statistical analyses were made using Statistical Packages for the Social Sciences version 15.0 (SPSS Inc.; Chicago, IL, USA) statistical software. Repeated measures of ANOVA were used for parametric data for the analysis of differences between dependent groups. One-way analysis of variance (ANOVA) was used to analyze parametric data of differences between dependent groups. Pearson's correlation analysis was used to examine correlations between the groups.

RESULTS

There was a statistically significant decrease in the 6th week values after treatment, both according to the frequency and duration of pain in group 1 ($p<0.05$); however, there was no significant decrease in the 12th week values ($p>0.05$). When the VAS values were compared between the 6th and 12th week after treatment, there was a statistically significant decrease ($p<0.001$ and $p<0.05$, respectively) (Table 1).

For group 2, there was a statistically significant decrease both in the 6th week and 12th week for the frequency of pain, duration of pain, and VAS values ($p<0.05$) (Table 2). Figure 1 shows the differences between groups for all parameters.

When group 1 and group 2 was compared, the decrease in pain severity was only significant in the 6th week in group 1. The decrease in pain frequency was not statistically significant in the 12th week in group 1 when compared with group 2 ($p>0.05$). When compared with pretreatment values, the decrease in the duration of pain at the 6th and 12th week were not

Table 1. Comparison of data from group 1, which received one session GON blockade treatment with 2.5 mL 1% lidocaine

	Pretreatment (I)	6 weeks post-treatment (II)	12 weeks post-treatment (III)		Comparisons		
	Mean±SD	Mean±SD	Mean±SD	p	I-II	I-III	II-III
n (F/M)		20 (15/5)		-			
Age, year		35.7±11.1		-			
BMI, kg/m^2		25.7±2.1		-			
The frequency of attacks	6.1±1.7	5.1±1.7	5.5±1.9	0.035[a]	<0.05	>0.05	>0.05
Duration of pain (hours)	28.9±22.1	22.1±16.8	26.1±20.8	0.027[a]	<0.05	>0.05	>0.05
VAS	91.3	69.8±19.4	81.8±15.7	<0.001[a]	<0.001	<0.05	<0.01

F/M: female/male; SD: standard deviation; VAS: visual analogue scale for severity of pain
If p value obtained by ANOVA is 0.05, p values between groups (I, II and III) are compared.
[a]p value for repeated measures ANOVA with post-test.

Table 2. Comparison of data from patient group 2, which received three sessions of GON block treatment with 2.5 mL 1% lidocaine

	Pretreatment (I)	6 weeks post-treatment (II)	12 weeks post-treatment (III)		Comparisons		
	Mean±SD	Mean±SD	Mean±SD	p	I-II	I-III	II-III
n (F/M)		20 (16/4)		-			
Age, year		36.5±10.2		-			
BMI, kg/m^2		25.5±1.6		-			
The frequency of attacks	6.0±1.8	3.8±1.7	4.7±1.6	<0.001[a]	<0.001	<0.05	>0.05
Duration of pain (hours)	30.1±21.9	18.7±10.5	23.1±12.7	<0.001[a]	<0.001	<0.05	>0.05
VAS	90.5±8.4	56.8±17.9	63.3±19.0	<0.001[a]	<0.001	<0.001	>0.05

F/M: female/male; SD: standard deviation; VAS: visual analogue scale for severity of pain
If p value obtained by ANOVA is 0.05. p values between groups (I. II and III) are compared.
[a]p value for repeated measures ANOVA with post-test.

Table 3. Comparison of group 1 and group 2 according to the mean change rate for frequency of attacks, duration of pain, and VAS

	6 weeks post-treatment			12 weeks post-treatment		
	Group 1	Group 2	p	Group 1	Group 2	p
The mean change rate for frequency of attacks	0.13±0.29	0.34±0.32	0.034*	0.07±0.26	0.18±0.29	0.227*
The mean change rate for duration of pain	0.12±0.36	0.23±0.38	0.367*	0.04±0.33	0.10±0.28	0.516*
The mean change rate for VAS	0.24±0.21	0.36±0.25	0.107*	0.10±0.16	0.28±0.26	0.012*

VAS: visual analogue scale for severity of pain; *Unpaired t test
The mean change rate was found by estimating the rate of change from baseline to 6 weeks and 12 weeks post-treatment

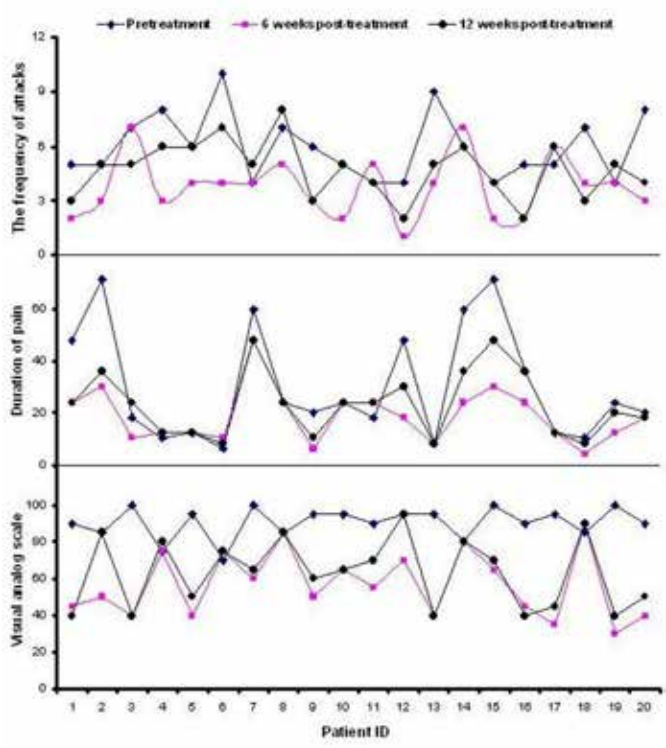
statistically significant even though they seemed more severe (p>0.05). At the 12th week, the decrease in pain severity (VAS) was more significant in group 2 when compared with group 1 (p<0.05) (Table 3).

DISCUSSION

In accordance with the findings of this study, one session of GON blockade with a lidocaine injection and 3 sessions of GON blockades were found to be effective in the decrease of attack duration and pain intensity. The efficacy of repeated GON blockade is similar but lightly superior to one session of GON blockade. Studies in recent years showed the importance of the GON in many painful conditions such as primary headaches, and researchers are working on new treatment strategies that affect this region. Stimulation and blockade applications related with the GON are the most commonly used methods.

Inan et al. reported a multi-center, randomized, double-blind, and placebo controlled GON blockade study

Figure 1. The frequency of attacks, duration of pain and VAS scores of pretreatment, 6 weeks post-treatment and 12 weeks post-treatment groups



with 72 patients (11). In the treatment group, bupivacaine was used for GON blockade and repeated GON applications were made in the placebo group using saline. Three months of treatment were evaluated by comparing them with the pre-treatment period. Repeated GON blockade with bupivacaine was reported as being more effective than placebo in migraine treatment. Bupivacaine was also applied to the placebo group after blinding was removed and then efficacy was also observed in the placebo group. There were no serious adverse effects reported that would stop the sessions in the study. In our study, lidocaine injections were applied in a single session and 3 sessions and we found that repeated GON blockade was more effective in migraine treatment.

Dilli et al. also used GON blockade in migraine treatment (12). Their randomized, double-blind, placebo controlled study was completed with 63 patients. The patients were randomly divided into 2 groups. One session of blockade was applied to two groups; 3 mL of solution was applied to the treatment group (2.5 mL 0.5% bupivacaine plus 0.5 mL (20mg) methyl prednisolone). Three milliliters of solution (2.75 mL normal saline plus 0.25 mL 1% lidocaine) were administered to the placebo group. Efficacy was defined as a 50% or more decrease in the number of days with headache. Four weeks of evaluation was made before treatment and after treatment. As a result of this study, GON blockade was not found to be more effective then placebo. Different from our study, short-term results were evaluated and a single session was performed to both groups. There was also a local anesthetic in the placebo group in low doses.

In a study conducted by Palamar et al., patients with chronic migraine were divided into 2 groups (13). A single session of GON blockade with bupivacaine was given to the treatment group, GON was administered with saline to the placebo group, and applications were given to both groups using ultrasound guidance in one session. For migraine treatment, it is reported that treatment group responded better than the placebo group.

Caputi and Firetto applied GON and supra-orbital nerve blockades with local bupivacaine in their study (14). Applications were made at least 5 and a maximum 10 times. Patients were followed starting 1 month before the injections and up to 6 months after the injections. During all periods, the patients did not take any pharmacologic treatment. The efficacy of the treatment was tracked by recording the number of monthly attacks, monthly analgesics use, and total pain index (multiplication of monthly pain hours with pain level). Eighty-five percent of the patients had a positive response to treatment. The total pain index was lowered to one third at the end of the month, and the total monthly attacks and use of analgesics were decreased during the 6 months. In addition, the number of attacks per month was decreased compared with the previous month. In that study, it was shown that repeated local anesthetic injections were effective. In our study, it was observed that repeated local lidocaine application at the GON areas responded better.

Cranium-based pain senses are conducted by trigeminal nerves. Pain is conducted to the trigeminal ganglion by the trigeminal nerve and after that to trigeminocervical complex. The trigeminocervical complex, which is related with the upper centers, has connections with the nucleus salivatorius superior and upper cervical nerves (15). An experimental study conducted by Piovesan et al. stated that applications to the greater occipital nerve and ipsilateral trigeminal nerve were found to effect 1st branch (V1). These results showed that cervical nociceptive neurons make synapses with trigeminal nucleuses (16). In our study, migraine attacks were one-sided (some on the right and some on the left). Therefore, GON blockade was applied bilaterally.

When the half-lives of local anesthetics are considered, it is observed that clinical recovery lasts longer than GON blockade. This could be a result of regulation connected with upper cervical nerves with the trigemino-cervical complex, which is related with nociceptive ways. Repetitive GON blockade injections, just like in our study, can increase these effects and longer responses can be possible.

In conclusion it is found that GON blockade with local lidocaine application is an effective treatment in migraine. Local lidocaine with repeated GON blockade application is found to be more effective then single session blockade application of GON. Also

during injection applications, no serious adverse effects were observed that could take patients out of the study. This shows the reliability and tolerability of repeating GON blockade injections in the preventive treatment of migraine.

The efficacy of local anesthetic injections for primary headache treatment are found different from each other in many studies. This could be because of factors including the local anesthetic type, the local anesthetic dose, the pharmacologic combination, study design, the application method, and the number of applications. To prove the efficacy and the power of local anesthetic injections in migraine treatment, more randomized, double-blind, placebo controlled and long-term studies are needed using different doses of local anesthetics, and combinations of local anesthetics with each other or steroids, and studies consisting of repeated injections.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of GATA local ethics committee (13.07.2009-1491\780\09\1539).

Informed Consent: Written informed consent was obtained from patients who participated in this study.

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REFERENCES

1. Ferrari MD. Migraine. Lancet 1998; 351: 1043-1051. [CrossRef]
2. Silberstein SD, Sapel JR, Freitag FG. Migraine: diagnosis and treatment. Silberstein SD, Lipton RB, Dalessio DJ, editors. Wolff's headache. 7th ed. Oxford University Press; 2001.p.201-273. [CrossRef]
3. Martin VT. Behbehani M. Ovarian hormones and migraine headache: Understanding mechanisms and pathogenesis-part 1. Headache 2006; 46: 3-23. [CrossRef]
4. Karadaş Ö. Odabaşı Z. An Open-Label Clinical Study on the Efficacy of Melatonin Prophylaxis in Migraine: A Preliminary Report. Arch Neuropsychiatry 2012; 49 : 44-47.
5. Linde M. Migraine: a review and future directions for treatment. Acta Neurol Scand 2006; 114: 71-83. [CrossRef]
6. Silberstein SD, Lipton RB. Overview of diagnosis and treatment of migraine. Neurology 1994; 44: 6-16.
7. Loder E, Biondi D. General principles of migraine management: the changing role of prevention. Headache 2005; 45(Suppl 1): S33-47. [CrossRef]
8. Karadaş Ö, Inan LE, Ulaş Ü, Odabaşi Z. Efficacy of local lidocaine application on anxiety and depression and its curative effect on patients with chronic tension-type headache. Eur Neurol 2013; 70: 95-101. [CrossRef]
9. Levin M. Nerve blocks and nerve stimulation in headache disorders. McGeeney BE, ed.Techniques in Regional Anesthesia and Pain Management. 2009; 13: 42-49. [CrossRef]
10. Ashkenazi A, Matro R, Shaw JW, Abbas MA, Silberstein SD. Greater occipital nerve block using local anaesthetics alone or with triamcinolone for transformed migraine: a randomised comparative study. J Neurol Neurosurg Psychiatry 2008; 79: 415-417. [CrossRef]
11. Inan LE, Inan N, Karadaş Ö, et al. Greater occipital nerve blockade for the treatment of chronic migraine: a randomized, multicenter, double-blind and placebo-controlled study. Acta Neurol Scand 2015; 132: 270-277. [CrossRef]
12. Dilli E, Halker R, Vargas B, et al. Occipital nerve block for the short-term preventive treatment of migraine: A randomized, double-blinded, placebo-controlled study. Cephalalgia 2015; 35: 959-968. [CrossRef]
13. Palamar D, Uluduz D, Saip S, et al. Ultrasound guided greater occipital nerve block: an efficient technique in chronic refractory migraine without aura? Pain Physician 2015; 18: 153-162.
14. Caputi CA, Firetto V. Therapeutic blockade of greater occipital and supraorbital nerves in migraine patients. Headache 1997; 37: 174-179. [CrossRef]
15. Goadsby PJ, Lipton RB, Ferrari MD. Migraine-current understanding and treatment. N Engl J Med 2002; 346: 257-270. [CrossRef]
16. Piovesan EJ, Kowacs PA, Tatsui CE, Lange MC. Ribas LC. Werneck LC. Referred pain after painful stimulation of the greater occipital nerve in humans: evidence of convergence of cervical afferences on trigeminal nuclei. Cephalalgia 2001; 21: 107-109. [CrossRef]