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Addition of lesser occipital nerve blockade to greater occipital nerve blockade in patients with chronic migraine

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Abstract

Objectives: The aim of this study was to compare greater occipital nerve blockade (GONB) alone and GONB combined with lesser occipital nerve blockade (LONB) in chronic migraine patients. *Methods:* Patients were randomly divided into two groups: Group A consisted of 22 patients who received only GONB; while Group B consisted of 20 patients who underwent GONB and LONB. The demographics and clinical characteristics of the patients were evaluated. The injections were given unilaterally and to the side where the subjects experienced greater pain. GONB with or without LONB was performed on each patient once a week for 4 weeks and then two more times a month apart; 6 times in total. The number of headache days, severity of attacks and duration of headache episodes was recorded from headache diaries before treatment and the on the first, second and third month following the start of treatment. Treatment efficiencies were evaluated within and between the groups. *Results:* The duration of pretreatment headaches was significantly longer in Group B (p=0.032). There were no differences between the groups in terms of other demographic and clinical characteristics. When the treatments applied in group A and group B were evaluated separately compared to the control group, there was a statistically significant decrease in the number of headache days, VAS scores and headache duration ($p < 0.05$). When the results of treatment between groups were compared, there was no difference in terms of the number of headache days and VAS scores. Although the duration of headache was longer in the pretreatment period in group B, this difference disappeared on posttreatment follow-up ($p > 0.05$). *Conclusions:* This study suggests that there is no difference in the number of headache days or headache intensity between GONB alone or in combination with LONB in chronic migraine patients. GONB combined with LONB in patients may be more effective than GONB alone when headaches of longer duration are present.

Keywords: Greater occipital nerve, lesser occipital nerve, blockade, chronic migraine

INTRODUCTION

Chronic migraine is a type of primary headache that significantly impairs quality of life. It affects approximately 1-2% of the general population and 8% of migraine patients.[1] Chronic headache leads to multifarious outcomes such as limitations in social life, work and financial losses, psychiatric comorbidities, decreased productivity and excessive drug use. Therefore, it is crucial to break this vicious circle with early treatment.

Currently, in addition to pharmacological treatments and botulinum neurotoxin applications, neuromodulation also plays an important role in the treatment of chronic migraine. Biofeedback, cognitive behavioral therapies and stress management are known non-pharmacological neuromodulation methods. Peripheral nerve blockade with anesthetic agents, occipital, supraorbital and vagal nerve stimulation as well as central neuromodulation techniques are also alternative treatment modalities.[2-9]

It has been shown that peripheral nerve blockades are effective in the acute and chronic treatment of some primary headaches including migraine and cluster headache.[10-13] It is also known that local anaesthetics with a longer duration of action are useful in the treatment of pain when used in peripheral nerve blockade.[14,15] However, the mechanism of action on pain control remains

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unclear. It has been suggested that beyond the peripheral mechanisms, there may be changes in the nociceptive pathways of the brain with consequent central pain modulation.[16,17]

The greater occipital nerve alone or in combination with the lesser occipital nerve or branches of the trigeminal nerve (such as the supraorbital and supratrochlear nerves) can be a target for nerve blockade. It has been reported that multiple cranial nerve blocks can be performed in primary headaches that do not respond to greater occipital nerve blockade (GONB).[18] There are few studies concerning which nerve blocks are more effective in pain control in particular patient groups. The aim of this study was to compare GONB with the combination of GONB with LONB in patients with chronic migraine.

METHODS

Study population

This retrospective observational study included 42 patients aged between 20 and 65 years who were admitted to the neurology outpatient clinic with the diagnosis of chronic migraine between July 2018 and July 2019. The diagnosis of chronic migraine was made according to the 2013 beta version of the International Headache Classification (ICHD-3 Beta version).[19]

GONB alone or GONB combined with LONB was performed sequentially. GONB alone was performed in two consecutive patients, and GONB combined with LONB was performed in the next two patients. The patients were divided into two groups. Group A consisted of 22 patients who underwent GONB alone; Group B consisted of 20 patients who underwent GONB and LONB. Clinical characteristics of the patients such as age, gender, BMI, duration of education, disease duration, duration of attack, severity of attack (using VAS score), nausea, phonophobia, photophobia, osmophobia, and aura were obtained from medical file records.

The number of headache days as well as severity and duration of attacks were recorded before intervention and in the first, second and third months post treatment. Data was collected using monthly headache diaries for each patient.

Patients included in the study were those who did not want to use any prophylactic medication for headache because of side effects or other medical disorders. Those with a history of analgesic overuse were excluded. Patients with known neurological disorders other than migraine, arrhythmia or any known cardiac disease, alcohol or substance abuse, and pregnant women were excluded from the study.

The study was conducted in accordance with the rules of the Helsinki Declaration with the approval of the Institutional Ethics Committee.

Nerve blockade procedure

Surface marking of the injection site was determined as 1/3 medial to the midline along the line between the occipital protuberance and the mastoid protrusion for the GONB, and a corresponding point 2/3 lateral to the same line for the LONB. 1.5 ml of bupivacaine was diluted with 1 mL isotonic saline in a 5 ml syringe and injected subcutaneously with an insulin needle [26-G (0.45x13 mm)] at a single point. These injection sites were determined according to practices documented by the American Headache Society.[20] The injections were done unilaterally and to the side where subjects experienced greater pain.

Nerve blockades were administered once a week for 4 weeks, then at the end of the 2nd and 3rd months from the start of treatment, 6 times in total. The number of headache days, severity and duration of attacks before the procedure and 1 month, 2 months and 3 months after the blockade were recorded for each patient using monthly headache diaries.

Statistical analysis

Statistical analysis was performed using SPSS Statistics 17 software (IBM Corporation, Armonk, NY, USA). Descriptive statistics are shown as median (25-75 percentile), frequency distribution and percentage. Categorical variables were analyzed using Fisher's exact test and Yates-corrected Chi-square test. Shapiro-Wilk test was used to determine the distribution normality of the data. Friedman test was used to determine the statistical significance of the difference between ≥3 dependent groups for non-normally distributed variables, and the Mann-Whitney U test was used for two independent groups. Post-hoc Bonferroni correction and Wilcoxon signed-rank tests were used for pair-wise comparison to determine the statistical significance of the difference between dependent groups. $P<0.05$ was considered statistically significant.

RESULTS

The demographic and clinical characteristics of groups A and B are summarized in Table 1. There was no statistically significant difference between the groups in terms of age, gender, BMI and duration of education ($p>0.05$). The pre-treatment duration of headache episodes in Group

Table 1: Demographic and clinical characteristics of Group A and B

	Group A (n=22)	Group B (n=20)	*p*
Age (years)	39.5 (32-49.25)	39 (32.5-48)	0.821
Gender (female/male)	19/3	17/3	0.900
BMI (kg/m²)	26.75 (22.92-31.62)	28.1 (24.76-33.11)	0.392
Education (years)	10.5 (8-11.25)	8 (5-11)	0.355
Attack duration (hours)*	24 (12.45-39)	36 (24-48)	**0.032**
VAS*	8 (6.85-9)	8.25 (8-9.37)	0.217
Attack frequency*	18 (15-26)	19 (15-26.25)	0.816
Disease duration (years)	10 (5-20)	10 (7.7-14.75)	0.759
Aura	7/15	7/13	0.829
Nausea	21/1	18/2	0.493
Photophobia	22/0	20/0	1
Phonophobia	20/2	20/0	0.512
Osmophobia	18/3	16/4	0.881

Group A: The patients with chronic migraine undergoing only greater occipital nerve blockage. Group B: The patients with chronic migraine undergoing greater and lesser occipital nerve blockage. BMI: Body Mass Index; VAS: Visual Analog Scale. All comparison were considered statistically significant at $p<0.05$. Data are expressed as median (25th, 75th percentile).

B was significantly longer (p=0.032); however, there were no differences between the groups with regard to number of headache days, VAS scores , disease duration, nausea, photophobia, phonophobia, osmophobia and aura.

Table 2 shows the treatment response of the individual groups in terms of number of headache days, VAS scores and duration of headache in posttreatment at the end of first, second and third months. There was a statistically significant decrease in the number of headache days, duration of headache and VAS scores at the end of first, second and third months ($p<0.05$). It was determined that both treatment groups (GONB and GONB combined with LONB) experienced statistically significant benefit.

When the GONB and GONB combined with LONB groups were compared pretreatment, and at the first, second and third months posttreatment, no statistically significant differences were found in the number of headache days and VAS ($p>0.05$) (Table 3). The pre-treatment duration of headaches was significantly longer in Group B, but there was was no significant difference in the headache duration between the groups post-treatment ($p>0.05$).

The number of headache days for both groups pretreatment, and in the first, second and third months after the treatment is shown in Figure 1, VAS values in Figure 2 and the duration of headache in Figure 3.

Table 2: Comparisons of treatment response of the groups seperately in terms of number of headache days, VAS scores and headache duration in posttreatment at the end of first, second and third months

	I-II	I-III	I-IV
Group A			
Headache days	p<0.001	p<0.001	p<0.001
VAS	p<0.001	p<0.001	p<0.001
Headache duration (hours)	p<0.001	p<0.001	p<0.001
Group B			
Headache days	p<0.001	p<0.001	p<0.001
VAS	p<0.001	p<0.001	p<0.001
Headache duration (hours)	p<0.001	p=0.001	p=0.002

I: Pretreatment, II: Posttreatment 1st month, III: Posttreatment 2nd month, IV: Posttreatment 3rd month. BMI All comparison were considered statistically significant at $p<0.05$. p value for Friedman test (nonparametric repeated measures ANOVA) with Wilcoxon test for two groups comparison.

Table 3: Comparisons of the number of headache days, VAS scores and headache duration values in pretreatment, posttreatment first, second and third months in the groups

	Group A (n=22)	Group B (n=20)	*p*
Headache days			
Pretreatment	18 (15-26)	19 (15-26.25)	0.816
Posttreatment 1st month	6 (4-8.25)	5.5 (4-10.5)	0.859
Posttreatment 2nd month	3 (1-6)	4 (2-9)	0.751
Posttreatment 3rd month	3 (0.75-6)	3 (1-4)	0.905
VAS			
Pretreatment	8 (6.85-9)	8.25 (8-9.37)	0.217
Posttreatment 1st month	6 (4.22-6.92)	6.55 (4.7-7.25)	0.398
Posttreatment 2nd month	5 (4.37-7.02)	5.55 (3.32-7)	0.940
Posttreatment 3rd month	4.5 (1.5-5.81)	5 (3-6.5)	0.693
Headache duration (hours)			
Pretreatment	24 (12.4-39)	36 (24-36)	**0,032**
Posttreatment 1st month	10,5 (5.30-16.51)	12 (5.5-24)	0.494
Posttreatment 2nd month	5.5 (3.75-10.5)	15 (5-24)	0.096
Posttreatment 3rd month	6 (0.75-12.91)	18 (5.5-24)	0.055

VAS: Visual Analog Scale. All comparison were considered statistically significant at $p<0.05$. Data are expressed as median (25th, 75th percentile).

DISCUSSION

The results of this study suggests that GONB alone and the combination of GONB with LONB were similar each other in terms of improving headache days and intensity of headache episodes in patients with chronic migraine. A combination of GONB and LONB may be more beneficial in patients who suffer from more prolonged migraine attacks. The benefits of combined GONB with LONB on headache duration was observed within a month of treatment.

Activation of the trigeminovascular system is known to lead to migraine headache. Excitation of trigeminal sensory afferent nerves surrounding the cranial vessels results in nociceptive stimulation of the trigeminal ganglion in the trigeminocervical complex. From there, signals are transmitted to the thalamus and other regions associated with pain modulation such as the periaquaductal gray matter and locus coeruleus.[21] The mechanism by which occipital nerve blockade affects pain control remains unclear. It has been suggested that GONB may alleviate migraine headache because of alterations in the activity of the trigeminal-cervical complex.[22] GONB may reduce entry to the trigeminal caudal nucleus and thus diminish central sensitization.[23] In a study in which GONB was performed on chronic migraine patients, it was found that it increased the pain threshold in the trigeminal regions on algometry, and might have an effect on central sensitization in the trigeminal caudalis nucleus.[24]

The GON arises from the medial branch of the second cervical dorsal ramus and may also receive some fibers from the third cervical nerve. The LON contains fibers from the ventral rami of the second and third cervical nerve. The combination of GONB with LONB anatomically affects the ventral and dorsal rami of the second and third cervical nerve. In our study, the addition of LONB to GONB showed an additional contribution on subjects with longer headache duration. Although our data suggest this result, more comprehensive studies are needed.

In a recent review, it was reported that GONB reduced the number of headache days and pain intensity over a 4-week period when compared to the control group, however it had no significant effect on the duration of the attack.[25] In the meta-analysis of Zhang *et al*., it was concluded that GONB had no significant effect on headache duration.[26] Inan and colleagues in their randomized, double-blind placebo-controlled study in patients with chronic migraine showed that GONB is effective in reducing the number of headache days, VAS score and headache duration.[11]

In our clinic, GONB with bupivacaine is applied unilaterally since bilateral administration is not shown to be superior to unilateral administration.[27] Bupivacaine is preferred in peripheral cranial nerve blockades because of its long duration of action. We applied GONB and LONB several times in order to increase the effectiveness of treatment.

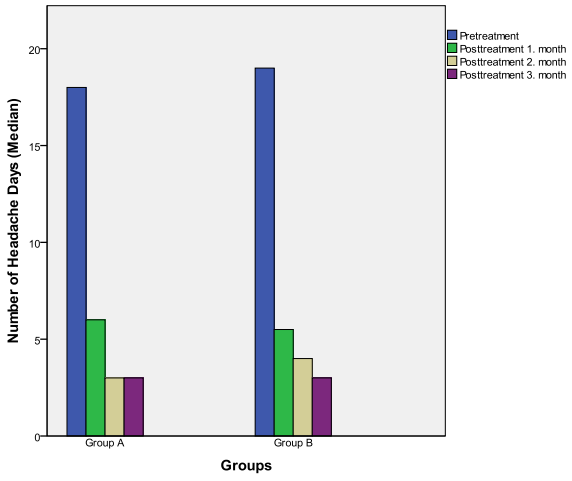

Figure 1. Number of headache days in the groups in pretreatment, posttreatment first, second and third months. Group A: The patients with chronic migraine undergoing only greater occipital nerve blockage. Group B: The patients with chronic migraine undergoing greater and lesser occipital nerve blockage.

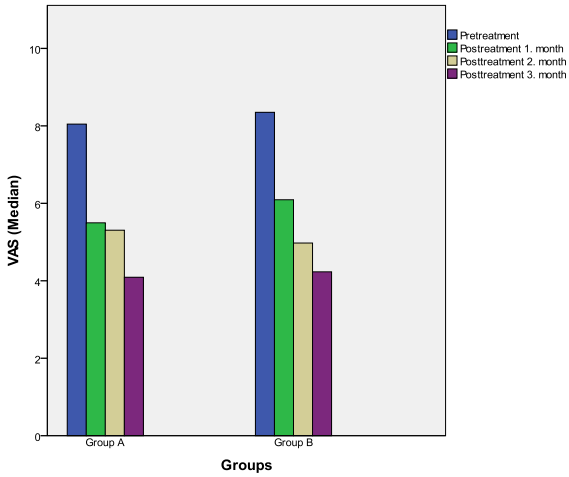

Figure 2. VAS values of the groups in pretreatment, posttreatment at the end of first, second and third months.

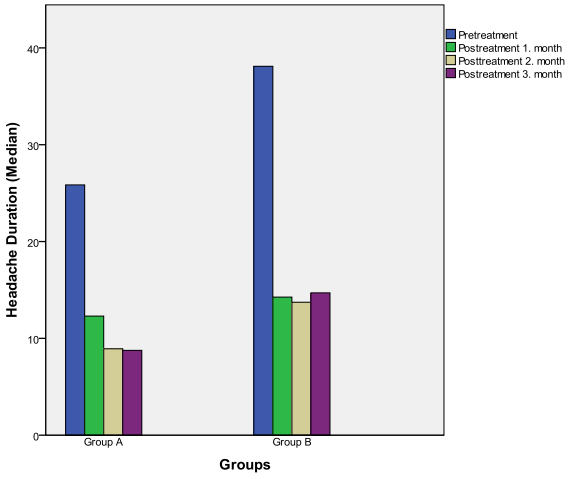

Figure 3. Headache duration of the groups in pretreatment, posttreatment at the end of first, second and third months.

The limitations of the study were the relatively low number of the patients, the low number of the male cases, and the retrospective design. In addition, the effects of occipital nerve blockade on headache were followed up for 3 months. Further studies with larger patient numbers and prospective long-term follow-up may show different results.

This study is the first study to compare the efficacy of greater and lesser occipital nerve blockade in patients with chronic migraine. Addition of LONB to GONB may provide benefit in chronic migraine patients with headaches of longer duration.

DISCLOSURE

Financial support: None

Conflicts of interest: None

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