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ORIGINAL ARTICLE

Comparison of the clinical efficacy of bilateral and unilateral GON blockade at the C2 level in chronic migraine

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Abstract

The main purpose of this study was to retrospectively compare the unilateral and bilateral application of proximal greater occipital nerve (GON) block at the C2 level in the treatment of chronic migraine disease. In chronic migraine patients who underwent GON blockade, the average number of migrainous painful days per month, the average duration of pain in attacks, the highest visual analogue scale (VAS) score in pain intensity for one month, and total analgesic use were recorded before and after the block. According to the GON block protocol applied by our clinic, the patients were treated for GON block 4 times a month, once a week. The data obtained were recorded before the treatment, in the 1st and 3rd months after the last injection, and the results were compared using the chi-square, Fisher, Mann-Whitney *U*, and Wilcoxon-signed rank tests. During the 3-month follow-up, the groups did not differ significantly in terms of the number of days with headache in 30 days, the average duration of headache, the highest VAS score in 30 days, and total analgesic use in 30 days. In both groups, the findings decreased in the 1st month and increased in the 3rd month compared to pre-treatment. However, results of both the 1st and 3rd months were significantly lower than pre-treatment ($p<0.05$), and there was a clinical benefit compared to pretreatment. While the GON block at the C2 level was effective in the treatment of chronic migraine, the superiority of bilateral application to unilateral application was not detected.

Keywords Greater occipital nerve block · C2 level · Chronic migraine · Unilateral block · Bilateral block · Cerebellar syndrome

Introduction

Although chronic migraine is a clearly clinically defined subtype of migraine that affects 1–2% of the general population, it receives little attention [1]. According to the recently published ICHD-3 criteria, the term chronic migraine is a headache occurring on 15 or more days/month for more than 3 months, which, on at least 8 days/month, has the features of migraine headache [2]. Severe, disabling, and receiving little attention, chronic migraine is a disease that significantly impairs the patient's quality of life and socioeconomic functionality [3, 4]. Each year, 3% of episodic migraine patients evolve in a chronic form [5] Considering that chronic migraine is such a serious disease and its treatment is difficult, it is of great importance to identify, treat, and eliminate risk factors. Two of the most important factors that increase the risk of conversion from episodic migraine to chronic migraine are the overuse of acute migraine medications [5, 6] and ineffective acute treatment [7]. The difficulties encountered in the treatment of chronic migraine increase the importance and necessity of interventional procedures. Recently, many studies concerning the use of GON blockade have been performed in migraine patients [8, 9].

The rationale for using GON block as a treatment for headache comes from the proximity of sensory neurons in the upper cervical spinal cord to trigeminal nucleus caudalis (TNC) and the convergence of sensory input to TNC neurons from both cervical and trigeminal fibers. The evidence for this comes from several studies [10]. In an animal

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study, stimulation of the GON was shown to increase metabolic activity in the TNC, as well as in the upper cervical dorsal horn [11]. The same neural sites are activated after mechanical or electrical stimulation of trigeminally innervated structures, such as the superior sagittal sinus [12]. This observation suggests that a convergence of sensory input from cervical and trigeminal afferents occurs at the level of the second neurons in the TNC. In further support of this hypothesis, Bartsch and Goadsby [13] demonstrated in a rat model of cranial nociception that dorsal horn neurons at the C2 level respond to dural stimulation. In accordance with these data, it has been shown in humans that GON block may result in alleviation of pain even outside of the skin territory supplied by the nerve [14].

A study by Greher et al. [15] described a more proximal block of the GON that was superficial in the obliquus capitis inferior muscle at the C2 level. Although there are several studies in the literature stating that GON blockade at the C2 level is effective in occipital neuralgia and cervicogenic headache patients [16–18], there is still not enough information about its effectiveness in migraine patients. The aim of this study was to observe the effectiveness of GON blockade at the C2 level for 3 months in chronic migraine patients. In order to determine this clinical efficacy, medication use, attack frequency, which are considered risky for chronic migraine, and maximum pain intensity (measured by VAS) were evaluated in this study. As a result, a significant reduction in all parameters was observed at 3 months after GON block compared to before treatment.

Materials and methods

This retrospective study included patients who applied to the Pain Department of the Ordu State Hospital and who were diagnosed with chronic migraine according to ICHD-3 criteria and did not receive any prophylactic treatment for at least 2 months for any reason [19]. The records of patients who underwent GON blockade between October 1, 2020, and August 1, 2021, were reviewed retrospectively.

GON blockade treatment was administered to patients who accepted this treatment with written consent, had no infection at the injection site, had no coagulation disorder in laboratory findings, had no pregnancy status, and had no history of previous surgery at the injection site.

For the GON block performed at the C2 level, the patient was asked to stand in the prone position and keep the neck flexed. The obliquus capitis inferior (OCI) muscle and the spinous process of C2 were used as anatomical markers. The 12–18 MHz linear probe was first placed transversely on the occipital protuberance. From this point on, the linear probe was lowered caudally in the sagittal plane and the spinal process of C1 was visualized as a single horn. When the probe was advanced more caudally, the spinous process of C2 in the form of two horns was visualized and stopped at this point. After that, the probe was moved laterally, and the OCI and semispinalis capitis (SSC) muscles were imaged. In order to better visualize the long axis of the muscles in this region, the lateral part of the probe was slightly inclined cephalad. As soon as this movement was completed, the lamina of C2 was seen as a boat, and the OCI muscle was prominent in it. The flat image between the OCI and SSC muscles was determined as the target point, and the medially occipital artery and lateral GON were made visible (Fig. 1). GON blockade from this point using a 22-gauge spinal needle was repeated once a week for a month on both sides using 4 ml of 0.5% bupivacaine on each side for the group (BC2) with bilateral GON blockade [20]. Unilateral GON blockade was performed using 4 ml of 0.5% bupivacaine, starting from one side of the unilaterally administered group (UC2). During the weekly blocks, the side that was not blocked in the previous week was blocked the subsequent week and the GON was blocked 2 times on each side, a total of 4 times in a 1-month period. All GON blockades were administered by the same physician, and after all blocks, the patients were hospitalized for 30 min and followed up for observation. None of the patients had previously received

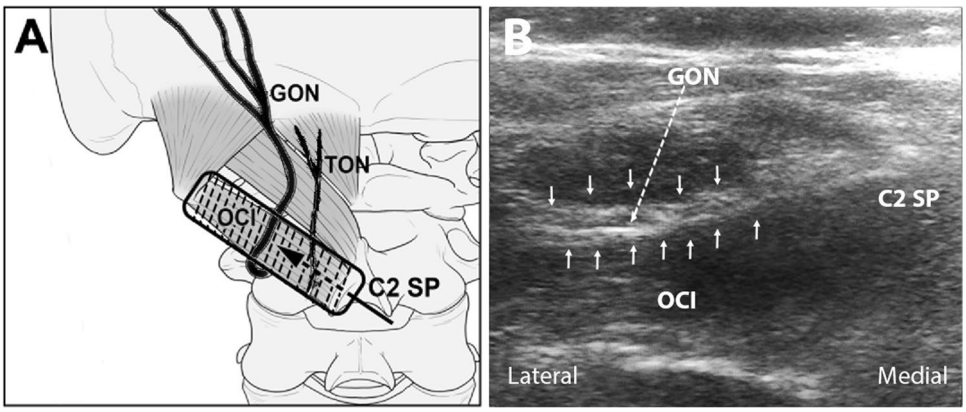

Fig. 1 **A** schematic diagram showing the probe position and needle direction for greater occipital nerve block. **B** Ultrasound image demonstrating needle placement

GON blockade treatment for any reason. By the nature of this retrospective design, treatment choices were made at the discretion of the treating physician.

Demographic data such as age, gender, height, weight, and accompanying diseases of the patients were recorded. The average number of migrainous headache days per month before (at least 1 month before treatments) and after GON blockade, the average duration of headache episodes, the highest VAS score in 1 month, and the total analgesic use were obtained from headache diaries and used to determine the effectiveness of GON blockade. Chi-square test and Mann-Whitney *U* tests were used to compare the basic demographic findings of the groups. The reason for using the Mann-Whitney *U* test was the acceptance that the relevant data could not show parametric properties since it was obtained from less than 30 patient groups. The reason why the Fisher test was used in the comparison of complications and additional disease findings was that the data showed categorical characteristics but could not meet the necessary conditions for the chi-square test. In addition, the Mann-Whitney *U* test and Wilcoxon-signed rank test were used to compare outcome data between groups before and after treatment, since they did not show parametric properties. All analyses were evaluated using a 95% confidence interval and at a $p < 0.05$ significance level.

Results

Demographic results

A total of 52 patients, 25 in the BC2 group and 27 in the UC2 group, were included in the study. Table 1 shows the basic demographic findings of the patients. Groups did not differ significantly from each other in terms of gender, age, body mass index (BMI) (kg/m^2), the average duration of migraine diagnosis (years), number of days with headache, average duration of headache (h), the highest VAS score experienced in 30 days, and total analgesic use in 30 days ($p > 0.05$). Eighty percent of the patients in the BC2 group were female and 20% were male, while 81.5% of the patients in the UC2 group were female and 18.5% were male. The mean age was 39.04 ± 6.50 in the BC2 group and 39.48 ± 6.42 in the UC2 group. BMI was 26.14 ± 4.74 in the BC2 group and 25.89 ± 4.53 in the UC2 group. The duration of migraine diagnosis was 15.12 ± 7.40 in the BC2 group and 16.07 ± 6.67 in the UC2 group. The number of days with headache in 30 days was 9.12 ± 4.88 in the BC2 group and 9.04 ± 3.80 in the UC2 group. The mean duration of headache (h) was 34.24 ± 24.03 in the BC2 group and 36.15 ± 24.32 in the UC2 group. The highest VAS score in 30 days was 8.96 ± 0.73 in the BC2 group and 9.04 ± 0.71 in the UC2 group. Total analgesic use in 30 days was 9.84 ± 5.06 in the BC2 group and 10.37 ± 4.50 in the UC2 group. Furthermore, the rate of comorbidity was 8% in the BC2 group and 18.5% in the UC2 group.

Outcomes

In Table 2, the comparison data between the groups regarding the examined parameters are given. Before treatment, the number of days with headache in 30 days, the mean duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days did not differ significantly between the groups ($p > 0.05$).

During the 1st month, the number of days with headache in 30 days, the mean duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days did not differ significantly between the groups ($p > 0.05$).

During the 3rd month, the number of days with headache in 30 days, the mean duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days did not differ significantly between the groups ($p > 0.05$).

When the findings were evaluated together, it was seen that the number of days with headache in 30 days, the mean duration of headache (h), the highest VAS score in 30 days, and the total analgesic use in 30 days did not differ significantly before the treatment, in the 1st month

Table 1 Basic demographic findings

N	BC2 25	UC2 27	*Δ*	*p*
Gender (female/male %)	%80/%20	%81.5/%18.5	% − 1.5	$x^2_{(1)} = 0.018$; $p = 0.892$
Age (years); average (std. dev.)	39.04 (6.50)	39.48 (6.42)	−0.44	$U = 324.5$; $p = 0.811$
BMI (kg/m^2); average (std. dev.)	26.14 (4.74)	25.89 (4.53)	0.25	$U = 332.5$; $p = 0.927$
Number of years with migraine (year); average (std. dev.)	15.12 (7.40)	16.07 (6.67)	−0.95	$U = 301.5$; $p = 0.509$
Number of days with headache in 30 days	9.12 (4.88)	9.04 (3.80)	0.08	$U = 329.5$; $p = 0.883$
Average duration of headache (h)	34.24 (24.03)	36.15 (24.32)	−1.91	$U = 321.5$; $p = 0.765$
Highest VAS score in 30 days	8.96 (0.73)	9.04 (0.71)	−0.08	$U = 318.0$; $p = 0.697$
Total analgesic use in 30 days	9.84 (5.06)	10.37 (4.50)	−0.53	$U = 303.5$; $p = 0.531$

Table 2 Comparison between groups

	BC2 Mean (std. dev.)	UC2 Mean (std. dev.)	Δ	U	p
Number of days with headache in 30 days					
Pre-treatment	9.12 (4.88)	9.04 (3.80)	0.08	329,500	0.883
1st month	1.04 (1.40)	1.30 (1.35)	−0.26	296,000	0.411
3rd month	1.60 (2.29)	1.67 (1.92)	−0.07	314,000	0.655
Average duration of headache (h)					
Pre-treatment	34.24 (24.03)	36.15 (24.32)	−1.91	321,500	0.765
1st month	7.84 (10.13)	7.67 (9.88)	0.17	328,500	0.868
3rd month	10.17 (13.01)	9.92 (12.59)	0.25	308,500	0.945
Highest VAS score in 30 days					
Pre-treatment	8.96 (0.73)	9.04 (0.71)	−0.08	318,000	0.697
1st month	3.16 (1.84)	3.33 (1.84)	−0.17	315,500	0.681
3rd month	4.24 (1.74)	4.26 (1.72)	−0.02	333,500	0.940
Total analgesic use in 30 days					
Pre-treatment	9.84 (5.06)	10.37 (4.50)	−0.53	303,500	0.531
1st month	1.28 (1.86)	1.67 (1.82)	−0.39	290,000	0.349
3rd month	2.16 (3.08)	2.15 (2.60)	0.01	315,500	0.676

or in the 3rd month after the treatment. However, while the mean number of days with headache in 30 days was higher in the BC2 group before treatment, it was higher in the UC2 group in the 1st and 3rd months after treatment. On the contrary, the mean duration of headache was higher in the UC2 group before treatment, while it was higher in the BC2 group in the 1st and 3rd months after treatment. The highest VAS score in 30 days was higher in the UC2 group before and after treatment. While total analgesic use in 30 days was higher in the UC2 group before and after treatment in the 1st month, it was higher in the BC2 group in the 3rd month after treatment. However, none of the differences was significant ($p > 0.05$).

In addition, when the complications seen in both groups were examined, 20% of the BC2 group members had complications, while the UC2 group had no signs of complications (Table 3). Therefore, the complication rate was higher in the BC2 group. Complications in the BC2 group were as follows: dizziness after only one injection (8%), dizziness after 2 or more injections (4%), cerebellar like syndrome (4%), and vertigo (4%). However, it was observed that all complications were temporary. The difference was not significant ($p > 0.05$).

In Table 4, the comparison data before and after treatment for the examined parameters are given according to the groups. As Table 4 reveals, in both groups, the number of days with headache in 30 days, the average duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days decreased in the 1st month compared to the pre-treatment period and increased in 3 months. However, results of both the 1st and 3rd months were significantly lower than before treatment ($p < 0.05$). Although the positive effect, which was greater in the 1st month, decreased partially in the 3rd month, it was still significant compared to the pre-treatment, and this finding showed that the clinical effect continued until the 3rd month in both groups.

Discussion

The acquired data showed that GON blockade at the C2 level is effective in the treatment of chronic migraine. There was no significant difference in clinical efficacy between the

Table 3 Complications

	BC2	UC2	Δ	p
Complication				
None	20 (%80)	27 (%100)	−7 (%20)	$\text{Fisher}_{(4)} = 5388$; $p = \mathbf{0.020}$
1 occurrence of dizziness	2 (%8)	0	2 (%8)	
2 or more occurrences of dizziness	1 (%4)	0	1 (%4)	
Cerebellar like syndrome	1 (%4)	0	1 (%4)	
Vertigo	1 (%4)	0	1 (%4)	

Table 4 Comparison before and after treatment

	BC2 Mean (std. dev.)	Δ	p	UC2 Mean (std. dev.)	Δ	p
Number of days with headache in 30 days						
Pre-treatment	9.12 (4.88)			9.04 (3.80)		
1st month	1.04 (1.40)	−8.08	▼ $p=\mathbf{0.000}$	1.30 (1.35)	−7.74	▼ $p=\mathbf{0.000}$
3rd month	1.60 (2.29)	−7.52	▼ $p=\mathbf{0.000}$	1.67 (1.92)	−7.37	▼ $p=\mathbf{0.000}$
Average duration of headache (h)						
Pre-treatment	34.24 (24.03)			36.15 (24.32)		
1st month	7.84 (10.13)	−26.4	▼ $p=\mathbf{0.000}$	7.67 (9.88)	−28.48	▼ $p=\mathbf{0.000}$
3rd month	10.17 (13.01)	−24.07	▼ $p=\mathbf{0.000}$	9.92 (12.59)	−26.23	▼ $p=\mathbf{0.000}$
Highest VAS score in 30 days						
Pre-treatment	8.96 (0.73)			9.04 (0.71)		
1st month	3.16 (1.84)	−5.8	▼ $p=\mathbf{0.000}$	3.33 (1.84)	−5.71	▼ $p=\mathbf{0.000}$
3rd month	4.24 (1.74)	−4.72	▼ $p=\mathbf{0.000}$	4.26 (1.72)	−4.78	▼ $p=\mathbf{0.000}$
Total analgesic use in 30 days						
Pre-treatment	9.84 (5.06)			10.37 (4.50)		
1st month	1.28 (1.86)	−8.56	▼ $p=\mathbf{0.000}$	1.67 (1.82)	−8.7	▼ $p=\mathbf{0.000}$
3rd month	2.16 (3.08)	−7.68	▼ $p=\mathbf{0.000}$	2.15 (2.60)	−8.22	▼ $p=\mathbf{0.000}$

*Difference values were calculated on the basis of pre-treatment and significant differences were shown with ▼(decrease) or ▲(increase) symbols

unilateral and bilateral application of this blockade. According to the data, the number of days with headache in 30 days, the average duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days decreased in the 1st month compared to the pre-treatment period and increased in 3 months in both groups. However, results of both the 1st and 3rd months were significantly lower than before treatment, and there was a benefit compared to pre-treatment. Compared to pre-treatment, the average duration of headache (h) at the end of the 3rd month decreased by 70.3% after the application of bilateral block and 72.5% after the application of unilateral block. The rates of reduction of the highest VAS score in 30 days of the application of bilateral block and unilateral block were 52.7% and 53.1%, respectively. Total analgesic use in 30 days decreased by 78% with bilateral block and 79.2% with unilateral block. The number of days with headache in 30 days decreased by 82.4% with bilateral block and 81.6% with unilateral block. As a result, it was determined that both bilateral and unilateral application of GON blockade at the C2 level had a positive effect in the treatment of migraine in chronic migraine patients.

In the literature, the effectiveness of GON blockade with the classical distal occipital approach in the treatment of chronic migraine has been shown in previous studies [9, 21]. In a prospective double-blind placebo-controlled study performed by Inan et al. [9] with the classical method from the distal occipital level, in which 72 patients completed the study, GON blockade was performed using 1.5 ml of 0.5% bupivacaine. 1.5 ml bupivacaine was repeated 4 times, once a week, to 39 patients in the chronic migraine treatment group. In this study, the number of days of headache, duration of headache, and VAS score of the group receiving bupivacaine treatment decreased significantly from the 1st month onwards, and this effect continued for 3 months. In this study, the application interval, the number of repetitions of the GON blockade, and the patients' follow-up times were all similar to those of our study. Likewise, the results were similar to ours. However, the local anesthetic doses and the application technique of the GON blockade differed.

Busch et al. [22] investigated the effect of unilateral GON blockade on the nociceptive blink reflex in 15 healthy volunteers without headache. They observed a significant reduction in the ipsilateral and contralateral nociceptive blink reflex response area and an increase in (late response) R^2 delay on the injection side. Based on the findings, the researchers hypothesized that unilateral nerve block caused bilateral inhibition. They also suggested that this inhibitor effect was subject to modulation of heterosynaptic convergent conduction of second-line neurons or interneurons in the deep layers extending from the caudal trigeminal nucleus to upper cervical segments. We hypothesized that the efficacy of a unilateral and a bilateral GON blockade might be similar [22]. The results showed that both the unilateral and the bilateral application at the C2 level have a positive effect on migraine in patients suffering from chronic migraine. There was thus no significant difference in clinical efficacy between the unilateral and the bilateral application of the GON blockade.

In a retrospective study conducted by Ünal-Artık et al. [23] in 41 patients with chronic migraine, bilateral and unilateral applications of classical GON blockade performed at

the distal occipital level were compared. In this study, GON blockade was applied 4 times, once a week, and then, GON blockade was continued monthly. The patients were followed up for 3 months, and the average VAS score, the number of days with headache in 1 month, and the average duration of headache (h) were examined. There was no significant difference between the two groups. 1.5 ml of 0.5% bupivacaine was used in this study. To the best of our knowledge, there are currently no studies on the effectiveness of a GON blockade performed at the C2 level in migraine patients. The study that comes closest to ours in terms of study design and data is that by Ünal-Artık et al. [23]. The authors examined both the efficacy of a GON blockade and the differences between the unilateral and bilateral application of the blockade in patients with chronic migraine. However, the local anesthetic doses and the GON blockade technique differed from ours. The authors found no significant difference between the bilateral and unilateral application of the GON blockade in chronic migraine patients; both applications were effective for three months. These results are similar to ours.

In the literature, no complications are discussed for the GON blockade performed at the C2 level, which has been studied for its effectiveness on cervicogenic headaches or occipital neuralgia [16–18]. However, in our study, complications such as cerebellar syndrome, vertigo, and dizziness were observed in the group that underwent the bilateral GON blockade. No complications were observed in the unilateral blockade group. Since all the complications were temporary, we did not detect a significant difference between the two groups from this point of view. However, cerebellar syndrome-like complications were an unexpected result for both the physician and the patients. Right dysmetria, dysdiadochokinesia, and right ataxic gait were observed in both patients. These complications have not been discussed before in the literature. During neuroimaging, the patients showed no pathology. The complaints regressed in about 6 h.

Ideally, a future study addressing GON block at the C2 level for chronic migraine would be a prospective, randomized, placebo/sham controlled clinical trial to better ascertain the optimal dosage and length of treatment. An optimally designed head-to-head study would be especially helpful to compare treatment response and describe both short- and long-term potential adverse events. In the absence of this data, however, our study suggests unilateral and bilateral GON blockade at the C2 level may both effective in chronic migraine treatment.

Conclusion

In our current retrospective study, we compared the effectiveness of bilateral and unilateral GON blockade at the C2 level. According to the available data, the number of days with headache in 30 days, the average duration of headache (h), the highest VAS score in 30 days, and total analgesic use in 30 days decreased significantly in both groups compared to pre-treatment, and there was no significant difference between the two groups. Complications were observed in the group with bilateral GON blockade, while no complications were observed in the group with the unilateral blockade. In conclusion, it is likely that the incidence of side effects might be reduced using unilateral block. In addition, it appears that patients tolerate unilateral block better than bilateral block. The available data were evaluated in light of the limitations of the study, which are primarily its retrospective design and the limited number of patients.

Declarations

Ethical approval The study was registered by the local ethical committee Ordu University Ethical Committe, Ordu, Turkey (Komite Etik No:07.10.2021/213).

Informed consent Not applicable.

Conflict of interest The authors declare no competing interests.

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