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Does Bupivacaine Concentration Matter? A Comparative Study of 0.25% and 0.5% Bupivacaine in Greater Occipital Nerve Blocks

Burcu Karpuz Seren[1], Esra Aciman Demirel[2], Sibel Cekic[3], Huseyin Tugrul Atasoy[2]

1 Tekirdağ Namık Kemal University, Faculty of Medicine, Department of Neurology, Tekirdağ, Türkiye

2 Zongudak Bulent Ecevit University, Faculty Of Medicine, Department of Neurology, Zonguldak, Türkiye

3 Ayten Bozkaya Spastik Children's Hospital and Rehabilitation Center Department of Neurology, Zonguldak, Türkiye

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Abstract

Objective: This study aimed to assess the effectiveness of two concentrations of bupivacaine (0.25% and 0.5%) in greater occipital nerve (GON) blocks in patients with chronic migraine.

Method: In this retrospective analysis, 72 patients with chronic migraine, treated between 2019 and 2021, were divided into two groups: Group 1 (0.25% bupivacaine) and Group 2 (0.5% bupivacaine). Patients received weekly GON blocks for four weeks, followed by monthly sessions for six months. Pain levels were measured using the Visual Analogue Scale (VAS) at the initial visit (VAS-1), after the first month (VAS-2), and at six months (VAS-3).

Results: Both bupivacaine concentrations significantly reduced VAS scores over time. In Group 1, the mean VAS score decreased from 8.49 at baseline to 4.80 at the first month and 4.21 at six months. In Group 2, the VAS scores decreased from 8.65 to 4.35 at the first month and 3.2 at six months. The reductions within each group were statistically significant ($p<0.01$); however, no significant differences were found between the groups at any time point (VAS-1, $p=0.588$; VAS-2, $p=0.329$; VAS-3, $p=0.144$). The differences in pain reduction between the two groups (VAS-1 to VAS-2 and VAS-1 to VAS-3) were also not statistically significant ($p=0.218$ and $p=0.271$, respectively).

Conclusion: The findings suggest that both 0.25% and 0.5% bupivacaine are effective in reducing pain in patients with migraine, with no added benefit from the higher concentration. Future studies with larger samples and different methodologies are recommended to further refine GON block protocols.

Keywords: Migraine, Headache, Greater Occipital Nerve Block, Preventive Treatment

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Correspondence / Yazışma Adresi: *Burcu Karpuz Seren, Tekirdağ Namık Kemal University, Faculty of Medicine, Department of Neurology, Tekirdağ, Türkiye e-mail: burcukarpuz@outlook.com*

Bupivakain Konsantrasyonu önemli midir? Büyük Oksipital Sinir Blokajlarında %0,25 ve %0,5 Bupivakainin karşılaştırmalı bir çalışması

Öz

Amaç: Bu çalışmada, kronik migren hastalarında büyük oksipital sinir (BOS) bloklarında iki farklı bupivakain konsantrasyonunun (%0,25 ve %0,5) etkinliğini değerlendirme amaçlandı.

Yöntemler: Bu retrospektif analizde, 2019-2021 yılları arasında tedavi edilen 72 kronik migren hastası iki gruba ayrıldı: Grup 1 (%0,25 bupivakain) ve Grup 2 (%0,5 bupivakain). Hastalara dört hafta boyunca haftada bir BOS blok tedavisi, ardından altı ay boyunca aylık seanslar uygulandı. Ağrı düzeyleri, ilk başvuru (VAS-1), birinci ay (VAS-2) ve altıncı ay (VAS-3) ölçümleriyle Görsel Analog Skala (VAS) kullanılarak değerlendirildi.

Bulgular: Her iki bupivakain konsantrasyonu da zaman içinde VAS skorlarını anlamlı şekilde azalttı. Grup 1'de ortalama VAS skoru başlangıçta 8,49 iken, birinci ayda 4,80'e ve altıncı ayda 4,21'e düştü. Grup 2'de ise VAS skorları 8,65'ten birinci ayda 4,35'e ve altıncı ayda 3,2'ye geriledi. Her iki gruptaki azalmalar istatistiksel olarak anlamlıydı ($p < 0,01$); ancak hiçbir zaman noktasında gruplar arasında anlamlı fark bulunmadı (VAS-1, $p=0,588$; VAS-2, $p=0,329$; VAS-3, $p=0,144$). Ağrı azalmasındaki grup farkları da (VAS-1'den VAS-2'ye ve VAS-1'den VAS-3'e) istatistiksel olarak anlamlı değildi (sırasıyla $p=0,218$ ve $p=0,271$).

Sonuç: Bulgular, hem %0,25 hem de %0,5 bupivakainin migren hastalarında ağrıyı azaltmada etkili olduğunu, ancak daha yüksek konsantrasyonun ek bir fayda sağlamadığını göstermektedir. Daha büyük örneklemler ve farklı metodolojilerle yapılacak gelecekteki çalışmalar, BOS blok protokollerinin daha da netleştirilmesine katkı sağlayabilir.

Anahtar kelimeler: Migren, Baş ağrısı, Büyük Oksipital Sinir Bloğu, Önleyici Tedaviler.

INTRODUCTION

Migraine is the most common reason for seeking medical attention among all headache disorders and is considered by the World Health Organization (WHO) to be one of the most disabling conditions globally. The International Headache Society (IHS), in the third edition of the International Classification of Headache Disorders (ICHD-3), defines chronic migraine as 'headaches occurring on 15 or more days per month for more than 3 months, with at least 8 of those days having the features of a migraine headache'[1]. Numerous pharmacological treatments are available for migraine, including beta-blockers, calcium channel blockers, newer-generation antidepressants, and certain anticonvulsants. However, in cases where medical therapy is insufficient (most notably the greater occipital nerve (GON) block), are utilized. GON blocks are regarded as safe and effective interventions that can provide long-term pain relief.

The pathophysiology of primary headaches involves the activation of the trigeminovascular system. The trigeminovascular system is composed of neurons with cell bodies located in the trigeminal ganglion, which innervates the cerebral vessels. It is believed that afferent sensory fibers from the dorsal roots of C2 and C3 are connected through the trigeminal nucleus caudalis transmission[2]. The trigeminovascular system is also thought to play a role in the effectiveness of the greater occipital nerve (GON) block[3].

The GON is the largest purely afferent nerve, originating from the medial branch of the dorsal ramus of the C2 spinal nerve[4]. The GON continues by receiving fibers from the C1 spinal nerve, follows an oblique course, and then crosses the inferior oblique and rectus capitis posterior major muscles, eventually piercing the semispinalis capitis muscle. Near the attachment point of the trapezius muscle to the occipital bone, the GON pierces this muscle and

travels subcutaneously. After passing beneath the skin, it courses medial to the occipital artery[4]. The point of subcutaneous entry is located one-third medial to an imaginary line drawn between the external occipital protuberance and the mastoid process, which serves as the site for GON block administration. The patient is seated and tilted forward to facilitate optimal blocking. For convenience, some clinicians perform the block 2 cm lateral and 2 cm inferior to the external occipital protuberance. Clinicians commonly use local anesthetics and/or steroids in GON blocks.

Studies on primary and secondary headaches, including migraine, cluster headaches, drug overuse headaches, and post-dural puncture headaches, have shown that the GON block is effective for pain modulation[5,6].

Although numerous studies have been published on greater occipital nerve (GON) blocks exist in the literature, there is no consensus regarding the optimal choice of local anesthetic agent, its combination with steroids, the frequency and duration of administration, whether the block should be applied unilaterally or bilaterally, or whether trigger point injections should be performed.

This study aimed to determine the effectiveness of different doses of bupivacaine (0.25% and 0.5%) used in GON blocks. This study hypothesized that higher concentrations of bupivacaine (0.5%) would result in superior pain reduction compared with lower concentrations (0.25%)

METHOD

This study retrospectively evaluated patients who presented to the neurology departments of a state hospital and a university research hospital between 2019 and 2021 and underwent GON block. Ethical approval was obtained from the institutional review board (No. 2022/02, dated January 26, 2022). The study included the patients diagnosed with chronic migraine according to the criteria of the ICHD-3, who did not respond to medical prophylaxis and therefore had GON block. When the hospital records were examined, we found that 0.25% Bupivacaine was used for GON block at the university research hospital and 0.5% Bupivacaine was used for the GON block at the state hospital. The patients were thus divided into two groups. Group-1 includes the patients who received 0.25% Bupivacaine and Group-2 included the patients who received 0.5% Bupivacaine. Patients received GON block once a week for the first month and then once a month for six months (patients received a total of ten doses of GON block). Figure 1 shows the progression of patient selection and the number of patients at each step. Patients with a history of occipital region surgery, anesthetic allergy, cutaneous infections or dermatological disease were excluded from the study. GON block was applied once a week for four weeks and then once a month for six months at one-third of the distance medially along the imaginary line between the external occipital protuberance and the mastoid process. A total of 2 mL of bupivacaine was diluted with 2 mL of saline, and 2 mL of the resulting solution was injected on each side. Patients were observed for 30 minutes for possible side effects after treatment and no side effects were observed.

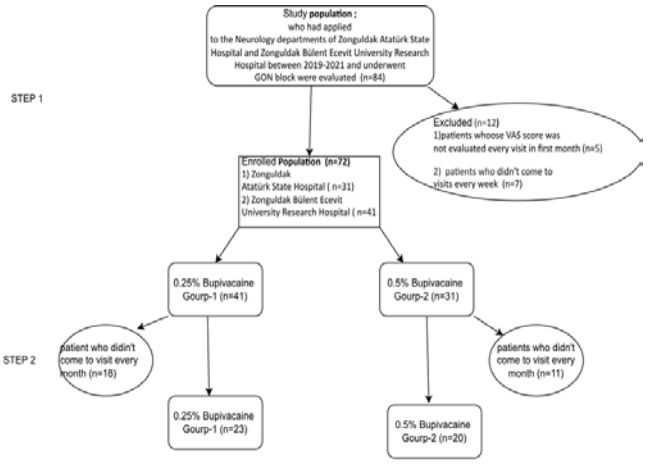

Figure. 1Flow chart

The Visual Analogue Scale (VAS) is a one-dimensional scale that is frequently used to measure of subjective parameters such as pain severity and is often used to assess pain severity in headache patients and to monitor treatment response. To evaluate treatment benefit and determine whether to continue therapy, VAS scores were assessed at each visit. This study included patients whose VAS scores were assessed before the first GON block and after each block. Patients whose VAS scores were not assessed or who did not attend regular visits every week were excluded. Patients' initial VAS score was recorded as VAS-1, first month (fourth dose) assessment was recorded as VAS-2 and the final assessment (tenth dose) was recorded as VAS-3. Due to the COVID-19 pandemic restrictions, 29 patients were unable to attend their final 6-month assessment (VAS-3). These patients were therefore excluded from the analyses involving the VAS-3 time point".

Statistical Analysis

The data obtained in the study were analyzed using Jamovi 2.3.2.0 program. Descriptive statistical methods were used, and data were expressed as numbers, percentages, means, and standard deviations. The conformity of the data to normal distribution was evaluated using the Kolmogorov-Smirnov tests and Shapiro-Wilk tests. Independent groups t-test (Student t-test), and dependent groups t-test (Paired sample t-test) was used to meet the data. To manage the missing data from 29 patients at the VAS-3 time point, all within-group (longitudinal) and between-group comparisons involving VAS-3 were conducted using a completer-only (per-protocol) analysis, which included only the 43 patients who completed all study visits. The statistical alpha level of significance was considered $p<0.05$.

RESULTS

In this study, 84 patients were evaluated who had undergone GON block. Twelve patients were excluded from the study: seven who did not attend regular weekly visits and five who were not evaluated by a clinician for VAS score assessment. After the fourth-dose evaluation, 72 patients were included in the analysis. In all, 65 of 72 patients were women and 7 of them were men. Group-1 had 37 women, 4 men, and Group-2 had 28 women, 3 men, and there was no statistically significant difference between the groups in terms of gender (p= 0,991). The mean age for Group-1 patients was 40.0, the mean age for Group-2 patients was 44.7 (p=0.072) (table 1).

Tablel: Baseline characteristics of participants and operations

	Group 1 (n=41)	**Group 2** (n=31)	**p**
Average age	40	44.7	0.072
F/M	37/4	28/3	0.991

The mean VAS-1 score of all patients was 8.56, and mean VAS-2 score was 4.61; this reduction was statistically significant ($p<0.01$). The mean VAS-1 score for group-1 patients was 8.49, the mean VAS-2 score was 4.80, and the difference between VAS scores was statistically significant ($p<0.01$). The mean VAS-1 score for group-2 patients was 8.65, the mean VAS-2 score was 4.35, and the difference between VAS scores was statistically significant ($p<0.01$) (table 2). The values of the mean VAS-1, VAS-2 and VAS-3 scores of both groups were not significantly different (p=0,588, p=0,329, respectively) (table 3). To address the potential for selection bias from the 29 patients lost to follow-up at 6 months, we compared the baseline and early treatment characteristics of the completers (n=43) who attended the final visit and the dropouts (n=29) who did not. There were no statistically significant differences between these two groups in terms of gender (p=0.968), mean age (p=0.222), baseline VAS-1 score (p=0.870), or 1-month VAS-2 score (p=0.866). These findings suggest that the patient attrition

due to the COVID-19 pandemic was random and not related to baseline patient characteristics or early treatment response, thus minimizing the risk of selection bias in the 6-month (VAS-3) data.

Table II: Comparison of the VAS-1, VAS-2 and VAS-3 scoresof the groups

	VAS-1	VAS-2	VAS-3	p
Group-1	8.49± 1.31	4.80±1.57	4.21±1.75	<0.01
Grou-2	8.65± 1.08	4.35±2.32	3.2±2.68	<0.01

**VAS: Visual Analogue Scale*

Table III: Comparing VAS scores between Group-1 and Group-2

	Group-1	Group-2	p
VAS-1	8.49± 1.31	8.65 ± 1.08	0.588
VAS-2	4.80±1.57	4.35 ±2.32	0.329
VAS-3	4.21±1.75	3.2±2.68	0.144

**VAS: Visual Analogue Scale*

The differences between the VAS-1 scores and the VAS-2 scores of both groups were compared, and no significant difference was found between the two groups (p=0,218). The differences between the VAS-1 scores and the VAS-3 scores of both groups were compared, and no significant difference was found between the two groups (p=0,271) (table 4).

Table IV: Comparing VAS scores differences of both groups.

	p	Mean difference	SE difference
VAS-1-VAS-2 dif	0.218	-0.6074	0.4888
VAS-1–VAS-3 dif	0.271	-0.8587	0.7688

**VAS: Visual Analogue Scale*

DISCUSSION

The peripheral nerve blocks are commonly used with local anaesthetics and/or steroids. Local anaesthetics work by blocking the sodium channels in the neuronal membrane. The C and A-delta fibres that transmit pain are the first to be blocked fibres due to their small diameter, so the first pain sensation disappears after treatment[7]. Local anaesthetic agents are divided into two groups, esters, and amides. Ester local anaesthesia is associated with higher allergic reaction incidence due to para-aminobenzoic acid (PABA), one of their metabolites. Amid local anaesthetics are not metabolised to the PABA, and therefore excessive sensitivity to amid local anaesthetics is rare[8]. Therefore, amid local anaesthesia is used in the GON block and is commonly referred to 0.5% bupivacaine, 0.25% bupivacaine, 0.5% lidocaine. Due to the long-acting nature of bupivacaine, most studies have used 2 ml of 0.5% bupivacaine and all anaesthetics used have been found to be effective.

Cvetkovic et al. conducted a double blind, randomized, placebo controlled, crossover trial comparing GON blocks with lidocaine + betamethasone versus lidocaine + saline in patients with treatment resistant chronic migraine, and found that the addition of corticosteroid (betamethasone) did not result in a statistically significant reduction in monthly migraine days (p = 0.147) compared with local anesthetic alone[9]. It has been reported that there are side effects such as alopecia, Cushing's syndrome, and cutaneous atrophy occur in blocks with steroid combinations such as triamcinolone, betamethasone, metiprednizolon, etc[10]. In the narrative review of İnan et al., it has also been mentions that adding steroids to the treatment does not provide any additional benefit[11]. Since the combination of steroids and local anesthetics offers no additional benefit and may cause more visible side effects, it is generally not preferred.

In our study, it has been found that GON block is beneficial in patients with migraine. In both the 0.5% and 0.25% use of bupivacaine doses, a significant decrease in VAS pain scores was observed during the 4-week observation period and also 6-month of observation period. When the decreases in VAS scores were compared, no significant difference was found between the

two groups. According to our results, bupivacaine is an effective anaesthetic in GON block, but bupivacaine doses do not provide an advantage over each other.

In two separate studies between Inan et al. and Gul et al., patients were divided into two groups and one group received bupivacaine ant the other received saline as a placebo. Both studies showed that bupivacaine was superior to placebo[12,13].

In the study conducted by Korucu et al., patients admitted to the emergency department with acute migraine attacks into three groups. They applied 0.5% bupivacaine for GON block in the first group, intravenous (IV) treatment containing Dexketoprofen and Metoclopramide in the second group, and saline in the third group to the GON area. The GON block was found to be as effective as IV treatment for acute migraine headache and superior to placebo (the group with saline applied)[14].

In our study, since no difference in treatment efficacy was observed between 0.5% and 0.25% bupivacaine, our findings suggest that the concentration of bupivacaine is not a significant determinant when selecting it as a local anesthetic. Given the lack of significant differences, the routine use of higher concentrations may not be justified.

The primary limitation of this study was the significant patient attrition, with 29 of 72 patients (40.3%) lost to follow-up before the 6-month VAS-3 assessment. This attrition further complicated a key methodological weakness: low statistical power. In addition because the study was retrospective study, only VAS scoress were available for pain assessment. The relatively small cohort size remains another limitation, highlighting the need for future large-scale prospective studies to explore additional factors influencing migraine outcomes.

Ethical approval: Ethical approval was obtained from the institutional review board (No. 2022/02, dated January 26, 2022).

Conflict of Interest: The authors declared no conflicts of interest.

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