Randomized Trial

Ultrasound-Guided Greater Occipital Nerve Block: An Efficient Technique in Chronic Refractory Migraine Without Aura?

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Background: The effectiveness of greater occipital nerve block (GONB) in patients with primary headache syndromes is controversial. Few studies have been evaluated the usefulness of GONB in patients with migraine without aura (MWOA).

Objective: To compare the effectiveness of ultrasound-guided GONB using bupivacaine 0.5% and placebo on clinical improvement in patients with refractory MWOA in a randomized, double-blinded clinical trial.

Study Design: A prospective, randomized, placebo-controlled, double-blind pilot trial.

Setting: Physical medicine and rehabilitation and neurology departments of a University Hospital.

Methods: Thirty-two patients with a diagnosis of MWOA according to the International Classification of Headache Disorders-II criteria were included in the study. Twenty-three patients (2 men, 21 women) completed the study. They were randomly assigned to receive either GONB with local anesthetic (bupivacaine 0.5% 1.5 mL) or greater occipital nerve (GON) injection with normal saline (0.9% 1.5 mL). Ultrasound-guided GONB was performed to more accurately locate the nerve. All procedures were performed using a 7 – 13 MHz high-resolution linear ultrasound transducer. The treatment group was comprised of 11 patients and the placebo group was comprised of 12 patients. The primary outcome measure was the change in the headache severity score during the one-month post-intervention period. Headache severity was assessed with a visual analogue scale (VAS) from 0 (no pain) to 10 (intense pain).

Results: In both groups, a decrease in headache intensity on the injection side was observed during the first post-injection week and continued until the second week. After the second week, the improvement continued in the treatment group, and the VAS score reached 0.97 at the end of the fourth week. In the placebo group after the second week, the VAS values increased again and nearly reached the pre-injection levels. The decrease in the monthly average pain intensity score on the injected side was statistically significant in the treatment group ($P = 0.003$), but not in the placebo group ($P = 0.110$). No statistically significant difference in the monthly average pain intensity score was observed on the uninjected side in either group (treatment group, $P = 0.994$; placebo group, $P = 0.987$). No serious side effect was observed after the treatment in either group. Only one patient had a self-limited vaso-vagal syncope during the procedure.

Limitations: This trial included a relatively small sample. This may have been the result of the inclusion of only those patients who correctly completed their pain diaries. Another major limitation is the short follow-up duration. Patients were followed for one month after the injection, thus relatively long-term effects of the injection have not been observed.

Conclusions: Ultrasound guided GONB with 1.5 mL of 0.5% bupivacaine for the treatment of migraine patients is a safe, simple, and effective technique without severe adverse effects. To increase the effectiveness of the injection, and to implement the isolated GONB, ultrasonography guidance could be suggested.

Key words: Migraine, greater occipital nerve, occipital nerve block, ultrasound-guided

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Primary headache disorders, particularly migraine and tension-type headache (TTH), are common worldwide, and commonly result in widespread and substantial disability (1). The prevalence of migraine headaches varies widely from one society to another, and may show changes over time within the same community. Men and women are equally affected during childhood; however, the prevalence of migraine increases more rapidly in girls after puberty (2,3). The prevalence of migraine is similar between European countries and United States (4) with rates of 17.6% in women and 5.7% in men (5). One trial demonstrated a 16.4% migraine prevalence rate in Turkey, which is similar to, or even higher than, the well-established prevalence of migraine in many other countries worldwide (6).

Migraine headaches might become quite severe and incapacitating for patients, and management can be challenging even in experienced clinics. Migraine headaches have a high economic impact due to high treatment costs and workforce loss, which are likely secondary to the severity of pain during migraine attacks (7).

Once the headaches become refractory to conventional pharmacologic management, minimally invasive techniques such as peripheral nerve blocks are feasible for pain relief, and help to decrease the frequency of the attacks. Various studies have demonstrated that peripheral nerve blocks are safe and effective for the treatment of a variety of headache disorders. These techniques not only provide adequate analgesia but can also help to decrease systemic side effects of pharmacologic therapy (8). Greater occipital nerve block (GONB) has been used for both the diagnosis and treatment of primary headaches (9-15). Various studies have reported conflicting results regarding the efficacy of GONB in the treatment of headache (10,13,14,16-23). The effectiveness of this technique in the treatment of primary headache syndromes remains controversial (24). The ultrasound-guided greater occipital nerve (GON) injection technique has been previously described. This technique has a higher success rate and might allow a more precise block of the nerve (25-27).

Considering the controversial results in the literature, we investigated the efficacy of ultrasound guided GONB in the treatment of patients with refractory migraine without aura (MWOA).

Methods

A prospective randomized, double blind, placebo-controlled pilot trial was performed in patients with refractory MWOA who were followed up by the headache specialists in the neurology department of our university hospital. The trial was approved by the ethics committee of our university and all patients provided written informed consent prior to enrollment.

We included 32 cases with a diagnosis of chronic MWOA according to the International Classification of Headache Disorders-II criteria (28) who had been under regular follow-up for at least one year. Patients with medication overuse were excluded. All patients included in the trial had refractory migraine headaches. Patients with refractory migraine are those who fail to respond adequately to preventive medication with established efficacy, alone or in combination, including more than 2 of 4 drug classes such as beta-blockers, anticonvulsants, tricyclics, and calcium channel blockers (29).

All patients underwent a clinical interview and detailed neurological examination by the same neurologist. Six patients in this sample group did not correctly fill out their pain diaries, one refused to undergo the intervention, and 2 changed their migraine treatments. Twenty-three patients (2 men, 21 women) completed the trial including a treatment group of 11 cases and a placebo group of 12 cases.

An experienced physiatrist engaged in pain management performed the detailed questioning and the GON injection of the patients. Another physiatrist performed the randomization using a block randomization method. The exclusion criteria for the randomization were as follows: patients younger than 18 years old or above 70 years; a history of occipital nerve injection or occipital nerve stimulation; a history of surgical procedures in the occipital region; a history of allergic reaction to the substance to be applied as local anesthetic; pregnancy or lactation; currently active psychiatric disease, uncontrolled hypertension, uncontrolled diabetes mellitus, uncompensated congestive heart failure, chronic renal failure, chronic liver disease, tumor and/or vascular disease, inflammatory and/or infectious diseases; and anticoagulant or antiagregant (antiplatelet) medication use that may interfere with the injection procedure.

All patients had failed to respond to prophylactic medications from several different classes, including combination pharmacotherapy, and no patients appeared be suffering from rebound headaches. They

were allowed to use previously administered headache preventive drugs during the trial period. No medical treatment change was made one month prior, during, or one month after the procedure.

The patients were randomly assigned to 2 groups. In the treatment group GONB was performed with a local anesthetic (bupivacaine 0.5% 1.5 mL) and in the placebo group occipital nerve injection of normal saline (0.9% 1.5 mL) was performed. One of the physiatrists prepared the bupivacaine and placebo solutions, and the other physiatrist examined the patients and performed the injections. The latter physiatrist was blind to the treatments, as were the patients. All patients were asked to complete a headache diary for one month prior to and one month following the injection. They recorded the number of days of headache, the headache location, the pain duration and severity, the occurrence of accompanying symptoms (e.g., nausea, vomiting, photophobia, and phonophobia), and analgesic consumption. Headache severity was assessed with visual analogue scale (VAS) from 0 (no pain) to 10 (intense pain). On the day of the injection the patients reported any tenderness in the region of the GON, the medications they were taking, and particularly any medication overuse. The medical treatment strategy of the patients did not change for at least one month prior to the injection and during the follow-up period.

The ultrasound-guided GONB was performed to more accurately locate the nerve. All procedures were performed using a portable ultrasound system with a 7 – 13 MHz multifrequency transducer (LOGIQ P5; GE Healthcare). The patient was asked to lie prone on the table. To locate the nerve we searched for the occipital artery in the medial one-third of the superior nuchal line between the occipital tubercle and mastoid process (Fig. 1). The scalp was cleaned with iodine; GONB was performed by applying the injection to the medial of the artery (Fig. 2). A 22-gauge needle was advanced beneath the lateral border of the probe using real-time ultrasound guidance and an in-plane technique. In all patients the occipital nerve was seen medial to the artery. The injected side was determined by the patients' clinical symptoms and according to the painful side reported in their headache diaries. The patients were required to lie down for 30 minutes after the injection to avoid dizziness.

Statistical Analysis

Statistical analyses were conducted using SPSS Version 11.0. Baseline characteristics were given as
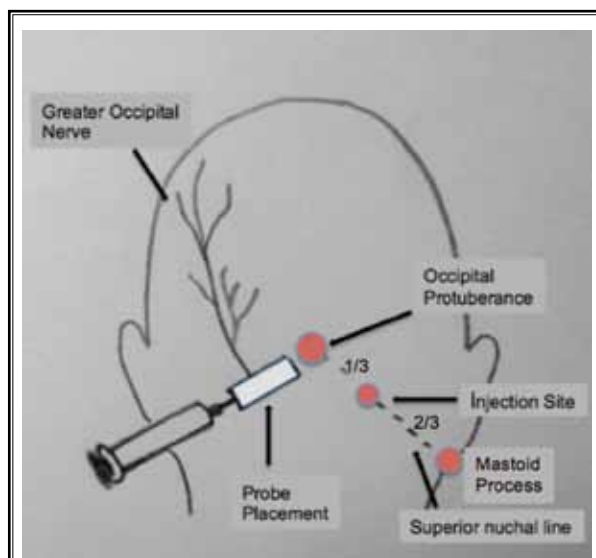

Fig. 1. *The injection site and the probe placement to perform ultrasound-guided GONB.*

mean ± standard deviation for quantitative variables. Explorative, 2-sided group comparisons for baseline characteristics between active treatment and controls were performed using 2 independent samples t-test for quantitative data and Fisher's exact test for binary data. Medians for the primary and secondary outcomes were compared using the Mann-Whitney U-test. Bonferroni correction was used for 2-sided group comparisons. A *P* value < 0.05 was accepted to be statistically significant. The expected values to calculate the sample size were 4 and 6, the standard deviation was assumed to be 1.5 and the power was determined to be 0.84 at an alpha level of 0.05 with a sample size of 11. All dropouts occurred prior to data collection; i.e., no dropouts occurred while the trial was being carried out, eliminating the need for an intention-to-treat analysis.

RESULTS

In total, 32 patients under treatment for MWOA and who fulfilled the inclusion criteria were evaluated after providing informed consent; 23 patients (2 men, 21 women) completed the trial (Fig. 3). Eight point seven percent of the patients were men and 91.3% were women. Eleven patients underwent injections of 1.5 mL 0.5% bupivacaine (treatment group) and 12 underwent injection of 1.5 mL 0.9% normal saline (placebo group). The mean age was 39.00 ± 9.67 years in the treatment group and 39.08 ± 11.42 years in the placebo group. The mean body mass index was 26.65 ± 6.67 in
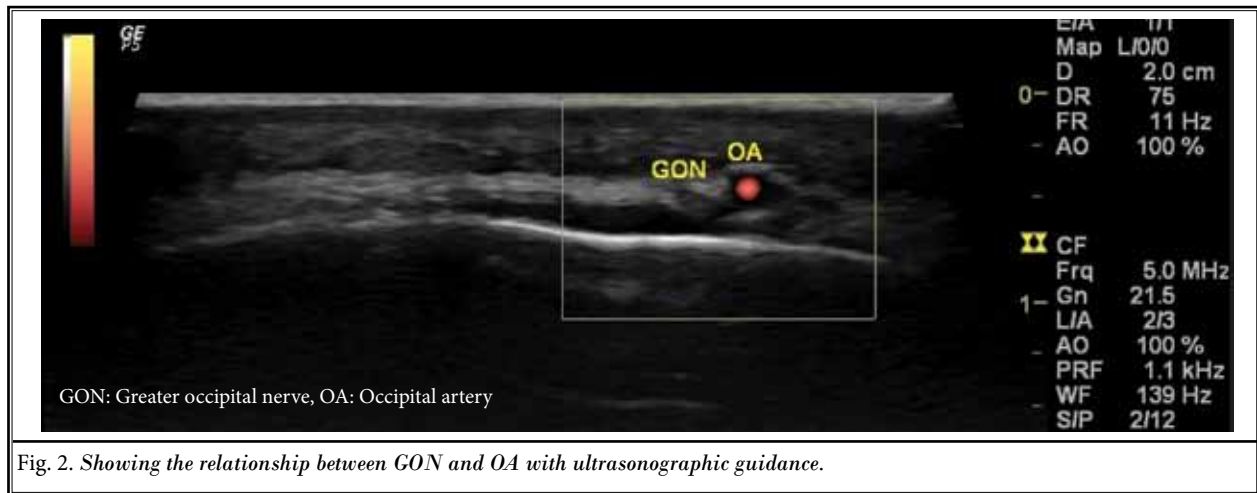
GON: Greater occipital nerve, OA: Occipital artery

Fig. 2. *Showing the relationship between GON and OA with ultrasonographic guidance.*
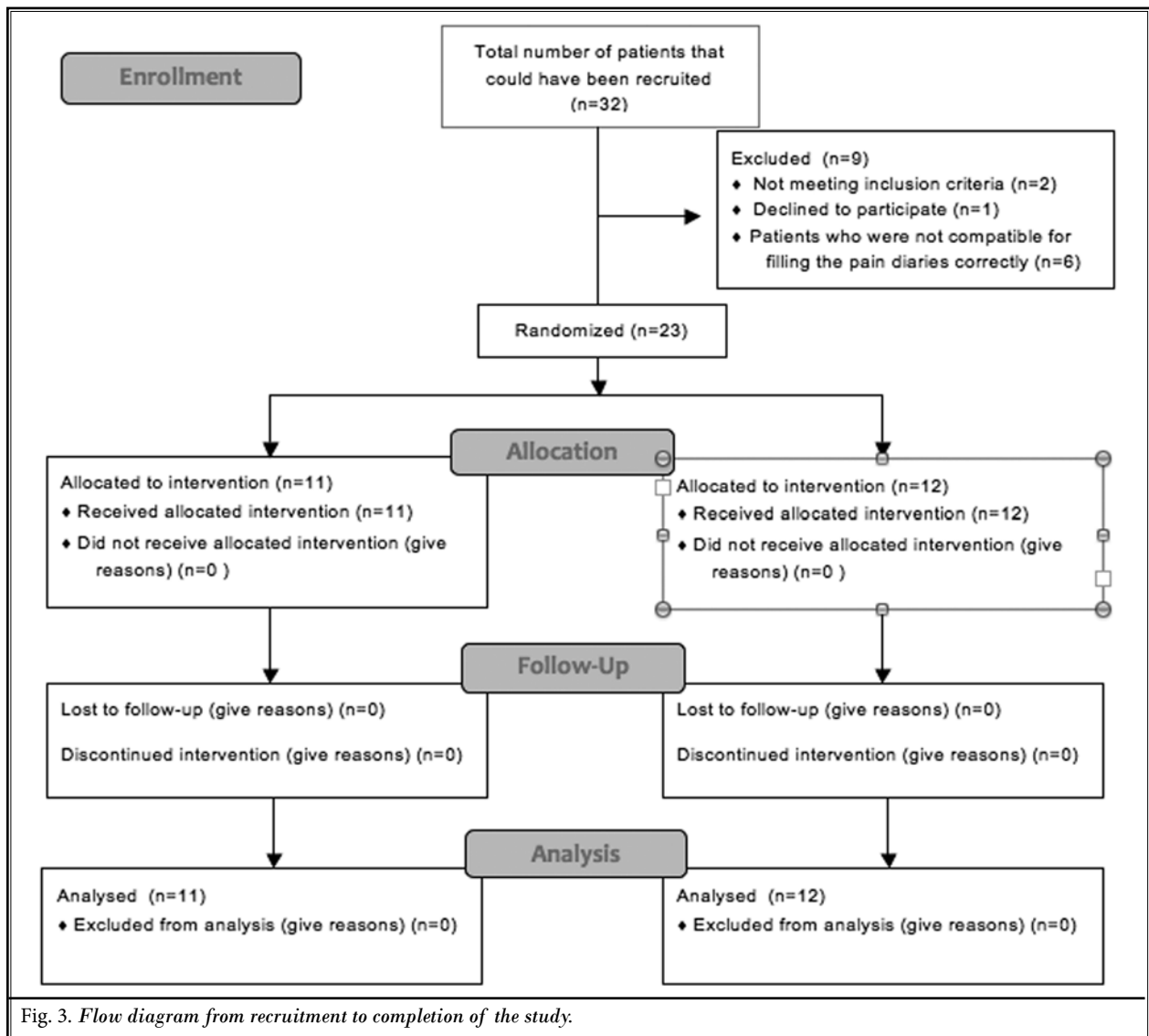

Fig. 3. *Flow diagram from recruitment to completion of the study.*

the treatment group and 25.75 ± 5.67 in the placebo group. There was no significant difference in age (*P* = 0.985), height (*P* = 0.317), weight (*P* = 0.732), body mass index (*P* = 0.73) (Table 1), or distributions or duration of symptoms (*P* = 0.413) between the 2 groups. There was no statistically significant differences in the weekly or monthly averages of headache severity on the injected side (*P* = 0.874) or uninjected side (0.583) prior to injection between the 2 groups (Table 2).

The pre- and post-injection VAS scores in both groups on the injection side were compared. In the first week, the average post-injection headache severity on the injection side was lower than the average pre-injection headache severity according to the VAS scores in both groups. This gradual decrease continued until the second week. After the second week in the treatment group, this reduction continued and VAS score reached 0.97 at the end of the fourth week. After the second week, in the placebo group, VAS score increased again and nearly reached the pre-injection levels (Fig. 4).

The pre-injection and post-injection headache severity on the uninjected side was also compared in both groups. After injection, a slight decrease in pain intensity was observed in both groups but this decline did not continue throughout the month and remained close to the pre-injection levels (Fig. 5) (*P* = 0.994 in the treatment group, *P* = 0.987 in the placebo group). On

the injection side in the treatment group, the monthly average pain intensity before the injection was 3.93 and after the injection this value decreased to 1.55. This decrease on the injected side in the treatment group was found to be statistically significant (*P* = 0.003) (Table 2). The pain intensity decreased to 2.16 in the first week after the injection, and this decline continued during the subsequent weeks.

On the uninjected side in the treatment group, the monthly average pain intensity before the injection was 2.37 and after the injection this value was close to the pre-injection level and remained at 2.38. No change in these monthly follow-up values was observed on the uninjected side (*P* = 0.994) (Table 2).

On the injection side in the placebo group, the monthly average pain intensity before the injection was 4.07 and, after the injection, this value was decreased to 2.68. The decrease at the injection side of the placebo group was not statistically significant (*P* = 0.110) (Table 2). During the second week of the injection, the pain intensity decreased to 2.27; and later, the severity of the pain started to increase and reached 3.03 in the fourth week. On the opposite of the injection side in the placebo group, the monthly average pain intensity before the injection was 1.95 and remained at 1.94 after the injection. Eventually, on the opposite side of the injection no change was observed at the monthly

Table 1. *Demographic data of the groups.*

	Treatment Group	Placebo Group	P
	mean±SD	mean±SD	
Age (yr)	39.00±9.67	39.08±11.42	0.985
Gender (M/F)	1/10	1/11	
Height (cm)	157.64±10.79	161.58±7.50	0.317
Weight (kg)	65.00±11.37	66.83±13.75	0.732
BMI	26.65±6.67	25.75±5.67	0.73

The values are reported as the mean±SD. Treatment group (n = 11) defined as patients who received the GONB with local anesthetic and placebo group (n = 12) as patients who received the GON injection with normal saline.

Table 2. *The average monthly VAS values in both groups.*

Group	Injection side			Opposite side		
	Pre-injection	Post-injection	P	Pre-injection	Post-injection	P
	VAS	VAS		VAS	VAS	
Treatment	3.93±1.80	1.55±1.42	0.003*	2.37±1.84	2.38±2.30	0.994
Placebo	4.07±2.38	2.68±1.64	0.110	1.95±1.75	1.94±1.91	0.987
P	0.874	0.095		0.583	0.625	

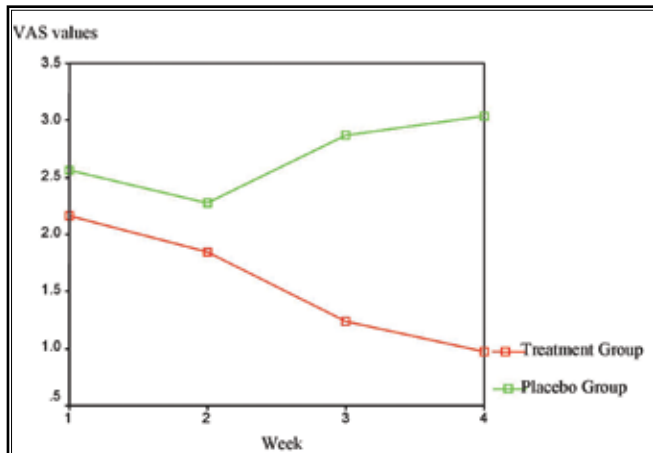*Significant change at the injection side of the treatment group.

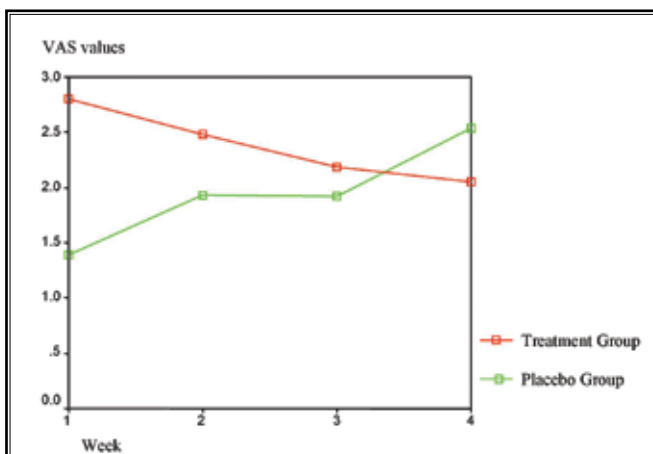Fig. 4. *Post-injection weekly average VAS values at the injection side.*

Fig. 5. *Post-injection weekly average VAS values at the opposite of the injection side.*

values (*P* = 0.987) (Table 2).

The headache course throughout the full 2-month follow-up period in each group is shown in Figs. 6 and 7. No serious side effects were observed after the treatment in either group. Only one patient had a self-limiting vasovagal syncope during the procedure.

Discussion

Chronic refractory migraine pain is reported to be a reason for substantial personal and social burden worldwide, and individuals with the greatest disability from their migraines incur and create the greatest associated costs (30-31). Once headaches become refractory to pharmacologic

management, the use of an interventional technique might be a feasible choice in the treatment of chronic migraine. Both peripheral nerve blocks (9,10,12-19,21-23) and stimulations and radiofrequency treatment, highlighted in recent years (32-35), have been found to be safe and effective modalities for the treatment of a variety of headache disorders. To date many scientific studies reported conflicting results regarding the efficacy of GONB in patients with migraine (10,13,14,16,17,22,23). These conflicting results may be due to different methodologies used in these studies.

There is little evidence in the literature regarding the impact of GONB in the treatment of migraine (13,14,16,17,23). Additionally, few placebo-controlled clinical trials have been performed to investigate its efficacy (13). Bovim and Sand (10) studied therapeutic blockage of GON and supraorbital nerve in patients with cervicogenic headache, MWOA and tension-type headache. They suggest that the pain reduction after GONB was significantly more marked in the cervicogenic headache than in patients with other types of headaches. In the present study, we investigated the efficacy of ultrasound-guided GONB in the treatment of patients with refractory MWOA.

Although easily performed, the classic method of blind injection just medial to the palpated occipital artery at the level of the superior nuchal line is not target-specific (36). Imprecise use of higher volumes could lead to additional blocks of other nerves nearby, such as the lesser or the third occipital nerve, as well as to intramuscular spread with unspecific analgesic effects. A successfully targeted block of the GON with minimum amount of local anesthetic and confirmed sensory changes to its distribution is necessary to make a specific diagnosis. To the best of our knowledge, until recent years, no selective approach for the GON was available in the literature. High-resolution ultrasound has the potential to visualize small peripheral nerves and to facilitate real-time local anesthetic blocks with high precision (37). Studies on the ultrasound-guided GON injection technique have emphasized that this technique has a higher success rate and should allow for a more precise block of the nerve (25-27). Accurate needle localization is also important for the diagnostic injections, false localization may lead to unnecessary interventions (38). Hence, the ultrasound-guided
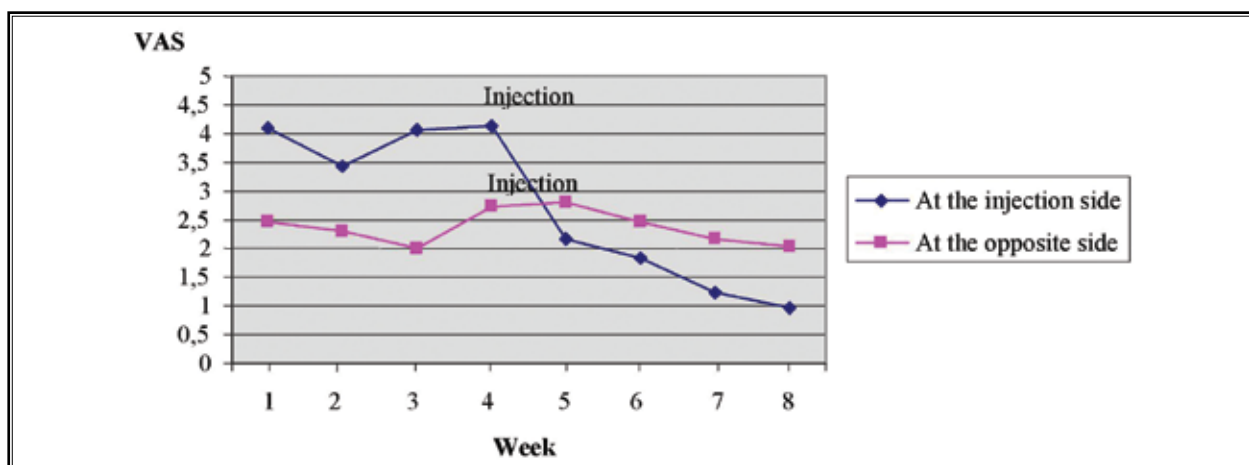
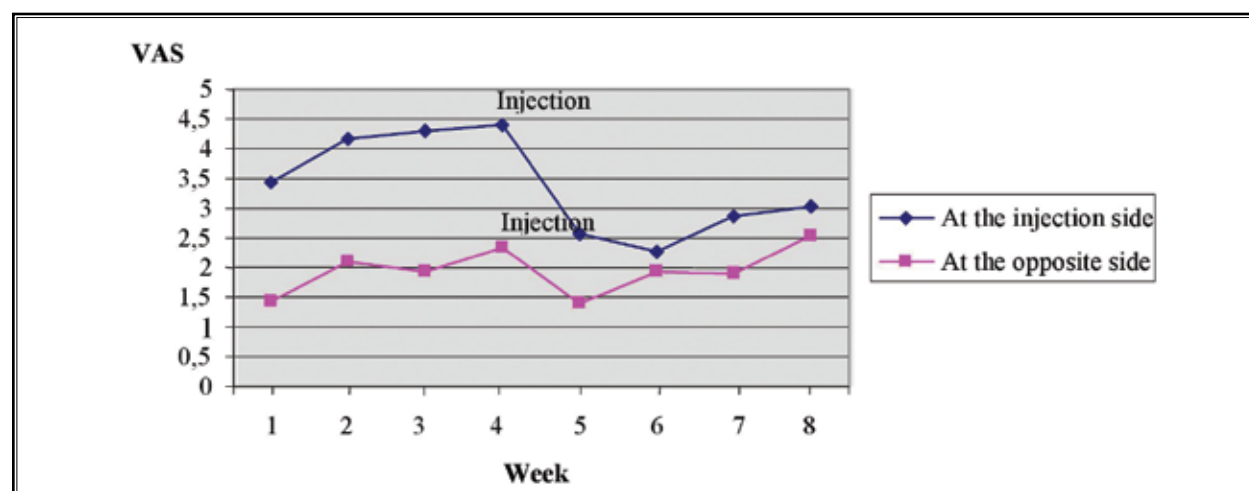Fig. 6. *The course of the headache in the treatment group.*

Fig. 7. *The course of the headache in the placebo group.*

GONB enables exact localization of the nerve, and may well increase the success rate with only small amount of the drug. The article by Greher et al (25) describes 2 different injection sites. First, classic block site medial to the occipital artery at the superior nuchal line; second, new block site over the obliquus capitis inferior muscle at C2. In the first technique, the ultrasound probe was initially placed in a transverse plane over the classical block site, at the level of the superior nuchal line, with the center of the probe 2 – 3 cm lateral to the external occipital protuberance that we have used. In the second technique that Greher et al (25) described, the ultrasound probe was moved down the neck, the spinous process of C2 was located, and then the probe was moved laterally identifying the obliquus capitis inferior muscle of the neck, and the GON was found superficial to the obliquus capitis inferior muscle at this level. We have used the classic block site that Greher et al (25) described in the first technique. Prior to injection, hair at the superior nuchal line was separated from the injection site, and abundant sterile ultrasound gel was applied in order to obtain the best image.

In contrast to the indirect methods of GON localization, which may be based on arterial palpation (36), the use of a Doppler flow probe (39), or sensory nerve stimulation (40), ultrasound allows for real-time identification of the nerve and recognition of anatomical variability in its course, divisions, and relationships with surrounding structures. Loukas et al (41) found high variability (1.5 – 7.5 cm) in the distance from the GON to the midline at a horizontal level between the external occipital protuberance and the mastoid process in

100 cadavers. Based on these data and taking into consideration of the anatomic variations, we believe that visualizing the nerve and then performing the injection is more accurate than detecting the artery with Doppler ultrasonography and performing the injection just medial to the artery.

We observed a gradual decrease up to the second week following an increase in the VAS scores, which became close to the pre-injection values in the placebo group. On the other hand the ongoing reduction in the treatment group can be interpreted as blocking of the afferent pathways that trigger migraine headache via the GON, resulting in the reduction of pain transmission via the trigeminocervical system.

The decrease in pain on the injected side in the treatment group was statistically significant ($P = 0.003$), whereas that in the placebo group was not statistically significant ($P = 0.110$). These data seem to support the idea that local anesthetic is superior to placebo in headache treatment on the injection side. In concordance with our results Takmaz et al (23) also found a significant pain reduction after GON block in patients with MWOA.

Our results show that GONB with 1.5 mL of 0.5% bupivacaine reduces the severity of the migraine headache. All patients gave a positive response to the block without any severe adverse effect. Only one patient had a vaso-vagal syncope during the procedure. Afiridi et al (16) performed a total of 116 GON injections in 101 patients with primary headache syndromes. Relatively few adverse effects, including one vaso-vagal syncopal attack during the procedure, 3 cases of transient dizziness following the injection, 2 cases of alopecia around the injection site, and 3 typical headaches triggered immediately by the injection, were reported in this study. The authors suggested that alopecia developed due to steroid use. Increased complications could be seen in association with the use of corticosteroids, which we did not use with GONB in the present study. We suggest that the side effects due to local anesthetics are extremely low and it is a reliable application, while the risk-benefit assessment should be made before corticosteroid is used for headache treatment with GONB.

GONB could be performed in conjunction with corticosteroids. In previous studies lidocaine with or without corticosteroids have been used (42). Considering the possible side effects of steroids, we wished to determine the efficacy of only local anesthetic injection of the GON. Ashkenazi et al (22) reported that adding triamcinolone to local anesthetics when performing GONB and trigger point injections was not associated with improved outcome in their sample of patients with transformed migraine. Four weeks post-treatment, they found no significant differences in symptom relief between the 2 groups, although the response to treatment of patients who received triamcinolone tended to be shorter than that of patients who received local anesthetics alone. The relief of headache may be prolonged with corticosteroid (42).

This trial has some limitations. First, it included a small sample of patients, in part because only those patients who correctly filled out their pain diaries were included. Another major limitation of this trial is the short duration of the follow-up. The patients were followed for only one month after the injection; thus, the long-term effects of the injection were not observed. We propose that further studies with larger samples of patients and a more extended observation period should be performed.

Conclusion

Although obtained from a limited number of patients, our results show that the ultrasound-guided GONB with a local anesthetic for the treatment of migraine may be a safe, simple, and effective technique. Ultrasound guidance may be recommended to improve procedural accuracy targeting the GON. Since a significant reduction in pain severity was seen on the injection side in this study, bilateral GONB could be considered for some patients.

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