Original Article

Ultrasound-Guided Combined Greater Occipital Nerve Block at the C2 Level with Trapezius Trigger Point Injection and Supraorbital-Supratrochlear Nerve Block: More Effective on Allodynia and Disability in Chronic Migraine

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Abstract

Background: Chronic migraine (CM) patients with cutaneous allodynia (CA) show a poor response to treatment. Long-term studies have yet to be conducted to demonstrate the efficacy of blocks on CA. This study evaluated the improvement in allodynia and disability in CM treated with ultrasound (US)-guided blocks. **Methods:** In this prospective, non-randomized comparative study, 60 CM patients with CA were evaluated for the clinical effectiveness of the therapy using the numeric rating scale (NRS), headache impact test-6 (HIT-6), brush allodynia test, and allodynia symptom checklist (ASC-12). At the first visit, tenderness in the nerve or trapezius muscle was confirmed in the intervention group. US-guided greater occipital nerve block (GONB), GONB, and trapezius muscle injection (TPI), or GONB, TPI, and peripheral trigeminal nerve block (PTNB), respectively, were performed four times once a week for a month. Initial and third-month assessments were performed. **Results:** The ASC-12 scores decreased in the GONB+TPI+PTNB and GONB groups more than the GONB+TPI group (mean rank, respectively, 26.86, 27.40, 38.39; $P = 0.018$). The decrease in HIT-6 scores was greater in the GONB+TPI+PTNB group than in the GONB group (mean rank, respectively, 21.98, 39.95, $P < 0.017$) in the first month. In the third month, the GONB+TPI+PTNB group scored HIT-6 significantly lower than GONB and GONB+TPI (mean rank: 18.84, 38.73, 35.61; $P < 0.001$). **Conclusions:** GONB+TPI+PTNB was more successful in alleviating allodynia and disability.

Keywords: Allodynia, migraine, nerve block, proximal GONB, trapezius muscle

Introduction

Cutaneous allodynia (CA) refers to the sensation of pain experienced by the normal skin when exposed to a non-noxious stimulus.[1,2] Population-based studies[3] have shown that CA affects between 40 and 70% of people with migraines. The increased number of headaches, inability to work, and longer duration of illness indicate that CA is a symptom of a more severe migraine disorder or that repeated attacks can lead to CA.[1-4]

CA reduced the effectiveness of migraine treatment. Compared to patients without CA, patients with CA are more likely to experience poor responses to triptans, non-steroidal anti-inflammatory drugs (NSAIDs), opioids, and barbiturates.[5] Trigger point injections (TPIs), supraorbital and supratrochlear nerve blocks (SONB, STNB), and greater occipital nerve block (GONB), which are all effective migraine treatments, can be used when medical therapy fails.[6-19] Myofascial discomfort can cause or contribute to headache syndromes by generating trigger points, which are areas of concentrated allodynia. The trapezius muscle, the most typical headache trigger point location, can induce pain in the temporal, jaw, occiput, and upper neck regions.[19] Several studies have been conducted on the early effects of blocking the peripheral nerve and trigger sites on CA using blind, landmark-based methodologies. In addition, studies have compared the groups based on early evaluations of brush allodynia, headache attacks, and numerical pain levels.[20-22] Ultrasound (US)-guided nerve blocks appear relatively safe, effective, and easy to perform. Compared to proximal (C2 level) and distal US-guided block approaches, C2-level blocks have a greater definitive block impact and are more successful in the long term.[23-25]

This prospective, non-randomized comparative study was conducted to determine the clinical efficacy of repetitive

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GONB at the C2 level, and TPI (regarding tenderness on the trapezius muscle), or GONB at the C2 level, peripheral trigeminal nerve block (PTNB, regarding SONB, STNB), and TPI under US guidance in chronic migraine (CM) patients with CA. We hypothesized that repetitive GONB+TPI+PTNB would provide a clinically meaningful benefit to CM patients with CA.

Methods

Design and study population

After approval by the regional ethics committee (2021-110/08.04.2021), the current prospective, non-randomized comparative study was conducted at the headache outpatient clinic of our tertiary research and practice hospital between April 2021 and April 2022. This study was conducted following the tenets of the Declaration of Helsinki.

The primary outcome was allodynia assessed by the brush allodynia test and allodynia symptom checklist (ASC-12). Secondary outcomes were the effects of blocks on headache disability assessed by headache impact disability index (HIT-6), the headache intensity determined by a numeric rating scale (NRS), migraine days per month, and rescue drugs used determined by asking the patient at each visit and data from the headache diaries.

The International Classification of Headache Disorders, third edition (ICHD-3) guidelines were used to diagnose CM.[26] Allodynia was examined using the brush allodynia test by a neurologist. Patients with CM have headaches at least 15 days per month in the past 3 months, with at least 8 days per month when their headaches and associated symptoms fulfill the migraine diagnostic criteria.[26] Patients were allowed to take preventive headache medication orally. Before the initial intervention session, the dosage and schedule of oral prophylaxis must be maintained for at least 4 weeks. The dosage was not changed until week 12. CM individuals with CA older than 18 years who provided written informed consent, had no psychiatric issues, had no other primary headache diagnosis, had no infection at the injection site, had no coagulation abnormalities, were not pregnant, and had not undergone surgery at the injection site were given blocking intervention.

In our usual headache outpatient clinical practice, we conducted nerve blocks and TPI without anesthesia in the local operating room using a Hitachi Aloka-ProSound F37 ultrasonography system with a linear (UST-568) 13-5 MHz probe four times a month, once a week. We selected the nerves or muscles based on the region of maximum tenderness and area of sensitization. After 5 min, numbness along the nerve's dermatomal distribution indicated nerve block success.

Patients who satisfied the inclusion criteria were invited to participate in the study. The current study's follow-up consisted of five visits with blocks repeatedly performed during the first four sessions.

Every time a patient attended, surveys were administered, and a pain specialist performed a brush allodynia test 20 min before and after each intervention. The same physician performed each block once a week in the first month. The type and side of the block to be performed were determined based on more palpable tenderness during the initial visit.[15] Both sides were blocked in cases of tenderness except GONB. GONB was performed unilaterally as the previous studies recommended.[25] With 1–5 mL of 0.5% bupivacaine administered to each block, the same blocks on the same side were repeated in the other weeks.[6] The instructions are detailed below. Follow-up assessments were conducted in the first and third months using the brush allodynia test and surveys.

We divided the patients according to the tenderness of the nerve and/or trapezius muscle tenderness in the initial visit:

Group 1: GON tenderness only, so we blocked GON unilaterally where there was the most tender.

Group 2: Tenderness in the GON and trapezius muscle; unilateral GONB and unilateral/bilateral TPI.

Group 3: Tenderness in the GON, SON, STN, and trapezius muscle; unilateral GONB, unilateral/bilateral PTNB, and unilateral/bilateral TPI.

Initially, 90 CM patients with CA were selected. Twenty-two patients did not meet the inclusion criteria, two became pregnant during the study, and six were dropped in the follow-up. Finally, 60 patients treated with GONB, GONB+TPI, or GONB+TPI+PTNB were analyzed [Figure 1]. The primary data measurement was determined *a priori*, with secondary data measured *post hoc*; the data have not been previously published.

Demographic and disease characteristics

Headache features and demographic data were also discussed. Patients were questioned in detail during the initial assessment about their headache symptoms and demographic information. As suggested by the Turkish National Headache and Pain Research Association, patients were required to keep headache diaries beginning 4 weeks prior to the treatment and continuing for 3 months. The number of migraine days in a month and the usage of rescue medicine, including triptans and NSAIDs, were calculated from the diaries and were questioned by the patient at each appointment.

Evaluation parameters

Numeric rating scale

In every session, both before and after the intervention, patients rated the intensity of their pain at the present time using the NRS, where the left side of the 10 cm long line denoted "no pain" and the right side was "intolerable terrible pain".[27] The highest NRS scores in the first and third months were also recorded from the headache diaries.

Headache impact test-6

HIT-6 was used to evaluate headache-related disabilities. The final score ranged from 36 to 78 points: minimal influence (49 points), considerable impact (50–55 points), significant

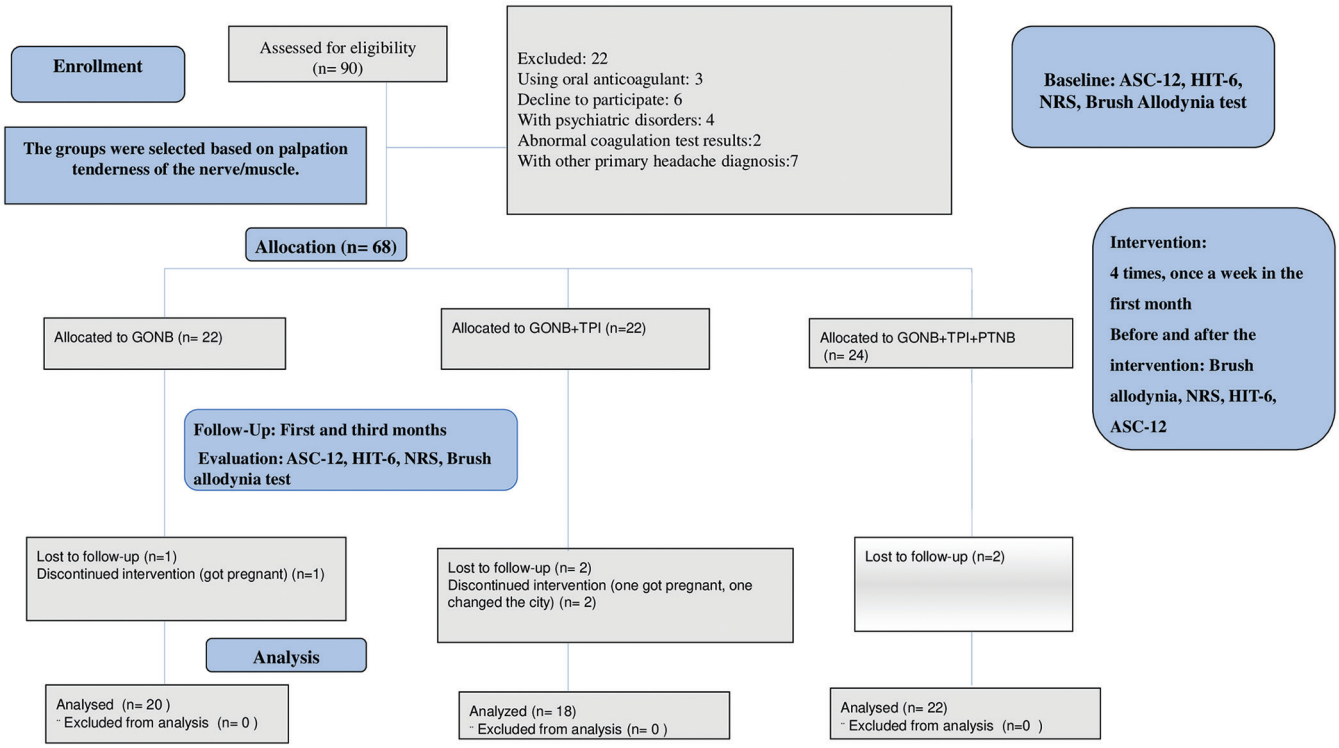

Figure 1: Flowchart diagram of the study (GON: Greater Occipital nerve, SON: Supraorbital nerve, STN: Supratrochlear nerve, The GONB Group: The Greater Occipital Nerve Block Group, The GONB+TPI Group: The Greater Occipital Nerve Block and Trigger Point Injection group GONB+TPI+PTNB: The Greater Occipital Nerve and Peripheral Trigeminal Nerve Block and Trigger Point Injection Group, HIT-6: Headache Impact Test-6, ASC-12: Allodynia Symptom Checklist-12, NRS: Numeric Rating Scale)

impact (56–59 points), and severe impact (60 points or more). The scale was previously verified in Turkish with a Cronbach alpha of 0.87.[28]

Allodynia symptom checklist-12

ASC-12 was verified in Turkish (Cronbach's alpha = 0.76), and its range was 0–24: non-allodynia 0–2, mild allodynia 3–5, moderate allodynia 6–8, and severe allodynia >9.[29]

Brush allodynia test

Brush allodynia (BA) was also evaluated by applying a 4 × 4-inch gauze pad 10 times at a rate of 2/s to certain dermatomes in the trigeminal (V1, V2, and V3) and cervical (C2, C5, and C8) regions recommended as in the literature.[20] Each dermatome's allodynia score was calculated 20 min before and after therapy using the following formulas: zero for no pain and one for pain.[20]

Interventional technique

GON block at the C2 level

The patient was prone to neck flexion. The linear probe was initially positioned transversely on the occipital protuberance and then progressed caudally, demonstrating that the C2 spinous process resembled the two horns. By moving the probe laterally, the semispinalis capitis and obliquus capitis inferior muscles were identified. The GON was found at this level, deeper than the semispinalis capitis muscle and superior to the inferior oblique capitis muscle [Figure 2a].[23-28] A 22-gauge spinal needle and 3 ccs of 0.5% bupivacaine were used to perform GON blocking from this location.[24]

Trigger point injection

A linear US transducer was used to scan the sagittal plane after the most painful part of the trapezius muscle was identified by touch [Figure 2b]. Using the in-plane approach, a 5 cm, 22-gauge needle was introduced into the most tender site of the muscle, passing through the skin, fat, and muscle tissue. Then, 5 ccs of 0.5% bupivacaine was injected to fulfil the entire muscle.[30,31]

Supraorbital and supratrochlear nerve blocks

The patient was placed in a supine position. Across the medial third of the supraorbital boundary lies the supraorbital notch, supraorbital nerve (SON), and right above its medial limit, the supratrochlear nerve (STN) [Figure 2c and d]. 1 cc of 0.5% bupivacaine was injected into the target using a 5 cm, 22-gauge needle and the in-plane technique.[32]

Statistical analysis

Statistical analysis was performed using the Statistical Package for Social Sciences (SPSS 23.0 IBM SPSS Inc., Chicago, IL, USA). The conformance of the variables to a normal distribution was assessed visually (using histograms and probability graphs) and using the Kolmogorov–Smirnov method. It was determined that the data were suitable for non-parametric distribution for all comparisons. The demographic information is displayed as numbers (%) and the median (min-max). For categorical data, Pearson's Chi-squared test was applied. Comparisons between the

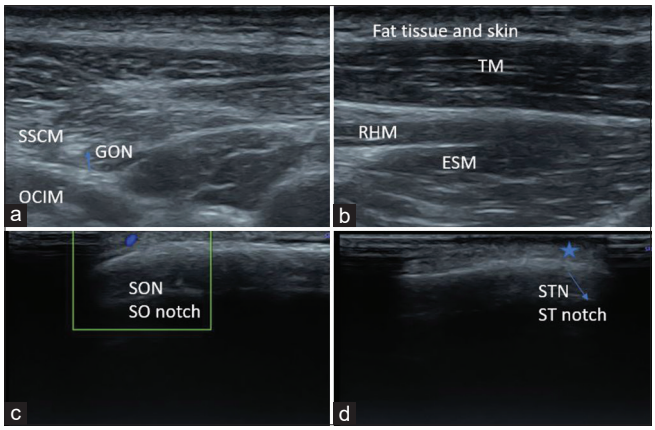

Figure 2: Sonoanatomy of Interventions: (a) Greater Occipital Nerve (GON) at C2 level, Semispinalis capitis muscle (SSCM), Obliquus capitis inferior muscle (OCIM) (b) Trapezius Muscle (TM), rhomboid muscle (RHM), erector spina muscle (ESM) (c) Supraorbital Nerve (SON) and Supraorbital notch (SO notch), (d) Supratrochlear nerve (STN) and supratrochlear notch (ST notch)

two dependent groups before and after the visit were made using the Wilcoxon signed-rank test. Friedman's test was used to compare multiple dependent groups. The Kruskal–Wallis test was utilized to conduct numerical comparisons of interventional techniques distributed into three independent groups. Following the Kruskal–Wallis and Friedman tests, which analyzed data from more than two groups, pairwise comparisons across groups were declared significant with the *P* value applied *post hoc* Bonferroni correction. The corrected *P* value was determined using the formula (0.05/number of intra-group comparisons). The *P* value of all tests was calculated as two-tailed with a 95% confidence interval and significance at < 0.05.

The primary objective was to determine the effect of nerve blocks and TPI on CA, as measured by ASC-12. To our knowledge, no previous research has examined the effects of all blocks on allodynia. The effects of greater occipital nerve block and trigger point injection on the CA in 20 minutes were only investigated in one study.[20] The allodynia was assessed by BA in 19 patients before and 20 minutes after the blocks.[20] To reach the targeted number of patients, we conducted a sample analysis with G.Power (3.1.9.7).[33] The "Wilcoxon signed-rank test, *a priori*: Compute required sample size- given alpha, power, and effect you" approach was applied. The BA score for cervical areas was 28.42 before the block (13.55 standard deviation: SD) and 9.73 after the block (4.86 SD) from previous studies for analysis, and five patients were required to attain the cervical allodynia's target strength of 80% and correlation between groups of 0.5 (default). The BA score in the trigeminal fields was 20.08 (9.57 SD) before intervention, and the post-intervention score was 13.74 (6.55 SD); 14 patients were required to attain the trigeminal allodynia's target strength of 80% and a correlation between groups of 0.5 (default). It was decided to choose a sample size minimum of 14 numbers that were higher than needed for two distinct locations. In terms of the number of transactions to be conducted in three distinct zones and the number of inter-groups, a total of 42 individuals (3 × 14) were targeted.

Results

Socio-demographic and baseline results

The socio-demographic results and headache features are shown in Table 1. Forty of the 60 participants were female. The median age of all groups was 43.22 (22–65), and there was no difference between groups. The sociodemographic characteristics of the patients were similar. The GONB group experienced significantly more unilateral headaches (60%, $P = 0.018$) than the other groups. The prevalence of nausea (57/60, 95.0%) and phonophobia (57/60, 95.0%) were similar across all groups. In all groups, the median headache duration was 180 (10–380) months, and the median migraine attack per month was 15 (10–20) days, which did not differ between groups ($P = 0.068$, $P = 0.144$, respectively). All groups had similar monthly NSAID and triptan consumption. The prophylaxis agents used by the patients are presented in Table 1 in detail. There was no difference between groups in each drug. The most used agents were antiepileptics (31.7% sodium valproate, 26.6% topiramate) and antidepressants (28.3% serotonin and norepinephrine reuptake inhibitors, 20.0% amitriptyline).

Patients with CM were included if BA was positive in at least one dermatome. The examination results are detailed below. All groups had a similar range for V1, 63.3%; V2, 65.0%; V3, 80.0%; C2, 100%; C5, 95.0%; and C8, 55.0% [Supplementary Table 1]. No allodynia, 6.7% (4/60); mild allodynia, 10% (6/60); moderate allodynia, 18.3% (11/60); and severe allodynia, 65.0% (39/60) were the percentages in our analysis of the ASC-12 subgroups. The GONB+TPI+PTNB group had the highest ASC-12 score compared to the other groups [median = 12.5 (9.75–18), $P = 0.020$] [Table 2]. Under the HIT-6 categorization, all individuals experienced a severe impact and had similar scores [median = 76.0 (74–78)]. The median NRS score for all groups was 10.0 (9.25–10).

Clinical efficacy

Immediate effects

When analyzing the immediate effects of the block after 20 min, the ASC-12 and NRS ratings reduced significantly ($P = 0.001$). There was no difference between the groups. [Table 3].

BA effect

Pain decreased from the baseline to the first month in the V3, C2, C5, and C8 dermatomes ($P = 0.012$, $P = 0.001$, $P = 0.012$, and $P = 0.01$, respectively). In V1, V2, and V3, the C2, C5, and C8 dermatomes regressed between the first and third months ($P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.001$, $P = 0.016$) [Supplementary Table 1].

ASC-12 effect

At the beginning of the study, the ASC-12 score was substantially higher in GONB+TPI+PTNB than in the other

Table 1: Sociodemographic results and headache characteristics

	GONB (*n*=20)	GONB + TPI (*n*=18)	GONB + TPI + PTNB (*n*=22)	*P*	All groups (60)
Age	44.15 (22-63)	47.33 (27-65)	39.00 (23-55)	0.065**	43.22 (22-65)
Sex					
Female	13 (65.0)	10 (55.6)	17 (77.3)	0.343***	40 (66.7)
Male	7 (35.0)	8 (44.4)	5 (22.7)		20 (33.3)
BMI	26.18 (17.3-39.1)	28.34 (17.3-40.0)	25.76 (17.3-40.4)	0.600***	27.55 (23.1-17.3)
Smoking	15 (75.0)	14 (77.8)	17 (77.3)	>0.999***	46 (76.7)
NSAID usage count per month at first visit	10 (8-20)	10 (0-20)	10 (0-20)	0.676**	10 (0-20)
Triptan usage count per month at first visit	10 (8-20)	10 (4-20)	8 (3-20)	0.128**	10 (3-20)
Alcohol consumption	14 (70.0)	17 (94.4)	19 (86.4)	0.072***	50 (83.3)
Months with headache	180 (12-360)	200 (10-380)	120 (10-280)	0.068**	180 (10-380)
Migraine days per month	17.5 (10-20)	17.5 (11.5-20)	10 (10-15)	0.144**	15 (10-20)
Headache side (bilateral) (*n*/%)	8 (40.0)	15 (83.3)	15 (68.2)	0.018***	38 (63.3)
Photophobia	14 (70.0)	13 (72.2)	21 (95.5)	0.074***	48 (80.0)
Phonophobia	19 (95.0)	16 (88.9)	18 (100)	0.276***	57 (95.0)
Nausea	19 (95.0)	17 (94.4)	21 (95.5)	0.989***	57 (95.0)
Prophylactic Treatments:					
Topiramat	6 (30.0)	3 (16.7)	7 (31.8)	0.514***	16 (26.6)
Sodium Valproate	6 (30.0)	5 (27.8)	8 (36.4)	0.829***	19 (31.7)
SNRI	5 (25.0)	6 (33.3)	6 (27.3)	0.842***	17 (28.3)
Amitriptyline	4 (20.0%)	5 (37.8)	3 (13.6)	0.539***	12 (20.0)
Flunarizine	2 (10.0)	2 (11.1)	1 (4.5)	0.716***	5 (8.3)
Propranolol	3 (15.0)	0 (0.0)	3 (13.6)	0.237***	6 (10.0)

*Column percentage, **Kruskall Wallis test was used, ***Pearson Chi-Square test was used. GONB: greater occipital nerve block TPI: trigger point injection. PTNB: peripheral trigeminal nerve block BMI: body mass index. SNRI: Serotonin and norepinephrine reuptake inhibitors (venlafaxine, duloxetine). The demographic information is displayed as numbers (n) (%) and the median (min-max)

Table 2: Comparison of the HIT6 and ASC-12 scores between groups

	GONB (*n*=20)	GONB + TPI (*n*=18)	GONB + TPI + PTNB (*n*=22)	*P**	Pairwise differences**
HIT-6 score					
Initial	78 (74.5-78)	76 (72-78)	76 (74-78)	0.367	-
Mean rank	34.45	27.00	29.77		
1 month	70 (66-74)	68 (65-70)	63.5 (62-70)	0.005	(GONB + TPI + PTNB- GONB) (*P*<0.017***)
Mean rank	39.95	31.08	21.98		
3 month	63 (51-68)	62.5 (48-68)	60 (48-63)	<0.001	(GONB + TPI + PTNB-GONB + TP), (GONB + TPI + PTNB- GONB) (*P*<0.017***)
Mean rank	38.73	35.61	18.84		
ASC-12 Test Score					
Initial	9 (4.25-13.5)	8.5 (6.75-15)	12.5 (9.75-18)	0.020	(GONB + TPI + PTNB- GONB) (*P*<0.017***)
Mean rank	24.35	27.47	38.57		
1 month	5 (3-8)	7.5 (4.75-12)	9 (4.5-11)	0.042	no difference was found (*P*>0.017***)
Mean rank	22.58	35.39	33.70		
3 month	0 (0-5)	1 (0-16)	0 (0-9)	0.018	(GONB + TP + PTNB- GON + TP), (GONB - GON + TP)
Mean rank	27.40	38.39	26.86		

*Kruskall Wallis Test was used, **Posthoc Bonferroni correction was used; corrected P value was significant at <0.017, ***p-value significance level for the posthoc test. HIT-6: headache impact test-6. ASC-12: allodynia symptom checklist-12. HIT-6 test score category 1: no impact, 2: some impact, 3: substantial impact, 4: severe impact. ASC-12 test score category 1: no allodynia, 2: mild, 3: moderate, 4: severe. GONB: greater occipital nerve block. TPI: trigger point injection. PTNB: peripheral trigeminal nerve block. The scores were presented as median with 25%-75% and mean rank of scores were given

groups (mean rank: 38.57, $P = 0.02$), but after the intervention, the results were similar in the first month. In the third month, GONB+TPI+PTNB and GONB outperformed superior to the GONB+TPI (mean rank, respectively, 26.86, 27.40, 38.39; $P = 0.018$) [Table 2].

HIT- 6 effect

The HIT-6 scores in all groups decreased from the baseline to the third month [from a median of 76.0 (74–78) to 48.0 (46–54)]. The decrease in HIT-6 scores was greater in the GONB+TPI+PTNB group than in the GONB group (mean

Table 3: Immediate effects of blocks on the ASC-12 and NRS scores in all groups

n=60	Median (25-75%)	Ranks	Ranks Sum	*P**
ASC-12 Test scores				
1 week (before intervention)	10 (7-15.75)	after < before negative ranks: 46	1207.0	<0.001
1 week (after intervention)	6 (0-10)	before < after positive ranks: 3	18.0	
2 week (before intervention)	6 (4-9)	after < before negative ranks: 49	1357.0	<0.001
2 week (after intervention)	3 (0-6.75)	before < after positive ranks: 4	74.0	
3 week (before intervention)	3 (1-6)	after < before negative ranks: 41	911.0	<0.001
3 week (after intervention)	0 (0-1)	before < after positive ranks: 2	25.0	
4 week (before intervention)	0 (0-3)	after < before negative ranks: 28	406.0	<0.001
4 week (after intervention)	0 (0-0)	before < after positive ranks: 0	0	
NRS Scores				
1 week (before intervention)	10 (9.25-10)	after < before negative ranks: 60	1830	<0.001
1 week (after intervention)	3 (1-5.75)	before < after positive ranks: 0	0	
2 week (before intervention)	8 (7-9)	after < before negative ranks: 60	1830	<0.001
2 week (after intervention)	2 (1.25-4)	before < after positive ranks: 0	0	
3 week (before intervention)	6 (5-7)	after < before negative ranks: 59	1770	<0.001
3 week (after intervention)	2 (1.25-4)	before < after positive ranks: 0	0	
4 week (before intervention)	5 (4-6)	after < before negative ranks: 54	1530	<0.001
4 week (after intervention)	2 (1-3)	before < after positive ranks: 1	10	

*Wilcoxon signed-rank test was used. ASC-12: allodynia symptom checklist-12. NRS: Numeric Rating Scale. The scores were presented as median with 25%-75% and mean rank of scores were given.

rank, respectively: 21.98, 39.95, $P < 0.017$) in the first month. In the third month, the GONB+TPI+PTNB group scored significantly lower than GONB and GONB+TPI (mean rank: 18.84, 38.73, 35.61; $P < 0.001$) [Table 2].

NRS effect

In both groups, the NRS scores reduced from the initial to the last visit (initial NRS = 10, final NRS = 4, $P = 0.001$). No difference was found between the intervention groups [Table 4].

Rescue therapy (NSAIDs, triptan count) and migraine attacks per month

The amount of NSAID usage per month decreased in the first and third months (mean rank: 5.53, 4.50, 3.68, $P = 0.001$). Between the groups, there was no difference. Triptan use per month decreased in all groups in the first month, with a more significant decline in the GONB+TPI+PTNB group in the first month (median: 4.5, $P = 0.019$). However, in the third month, the GONB+TPI+PTNB group decreased more than the GONB group but not the GONB+TPI group. All groups experienced a statistically significant ($P = 0.005$) decrease in the frequency of migraine days per month but no difference between the groups [Table 4].

Side effects

We observed dizziness and nausea in 18 patients, but these symptoms were relieved after 15 min.

Discussion

The data showed that all blocks efficiently reduced allodynia, headache attack frequency, and intensity in patients with CM with allodynia. The effectiveness was confirmed by physical examinations and diagnostic tools, as recommended in the literature.[34] The efficacy of GONB+TPI+PTNB on the allodynia and headache disability in the third month was higher than that of GONB and GONB+TPI. Triptan consumption also declined more in the GONB+TPI+PTNB than in the other groups.

PTNB, TPI, and GONB are often used because they are safe, well-tolerated, and effective in treating migraines, allodynia, and photophobia.[6-25] In general, 48 to 100% of adult migraineurs receive full or partial relief from migraine prevention that lasts a few days to several months.[6] The combination of GONB and TPI has been found to reduce allodynia in previous studies, with 85% improvement between 5 and 20 min and 1 week after therapy.[20-22] The literature supports our findings. In contrast to our trial, previous studies used a local anesthetic (LA) and a steroid, and the blocks were administered only once. The administration of steroids for the CM block is still being discussed in the literature. In addition to the lack of evidence regarding its efficacy, steroids have been linked to several specific adverse effects, including alopecia, hypopigmentation, and cutaneous atrophy, especially when repeated blocks are administered.[6-8] Therefore, steroids were not administered.

In the current study, repetitive blocks of tender nerves (GON, SON, STN) and trapezius muscles were performed, as Ilhan *et al*.[16] did, to reduce both central sensitization (CS) and peripheral sensitization (PS). In addition to CS, PS of peri-cranial and extra-cranial peri-vascular nociceptors is regarded as a cause of CA.[35] When repetitive blockages of painful nerves obstruct the peripheral input, the central processing returns to normal. This peripheral-central connection implies that peripheral therapeutic measures also have a secondary effect on the intricate plastic modifications

Table 4: Comparison of the number of rescue drugs used (NSAIDs, triptan) and migraine days per month between groups

	GONB	GONB+TPI	GONB+TPI+PTNB	*P**	Pairwise differences**
NSAID usage per month					
Initial	10 (8.5-10)	10 (8-10)	10 (7.5-12)	0.676	-
Mean rank	33.10	28.61	29.68		
1 month	6 (4-9.5)	8 (5.5-8)	6 (2.25-8)	0.615	-
Mean rank	29.60	33.78	28.64		
3 month	5 (.25-6)	5 (0-8)	3.5 (0-6.5)	0.588	-
Mean rank	31.98	32.50	27.52		
Triptan pill usage per month					
Initial	10 (8-10)	10 (7.5-11.25)	8 (5-10)	0.128	-
Mean rank	35.03	32.31	24.91		
1 month	6 (6-8)	6 (6-8)	4.5 (2.75-6.5)	0.019	(GONB+TPI+PTNB- GONB), (GONB+TPI+PTNB-GONB+TP) (P<0.017***)
Mean rank	36.23	33.83	22.57		
3 month	6 (4-6)	6 (4-6)	3.5 (2-6)	0.010	(GONB+TPI+PTNB-GONB) (P<0.017***)
Mean rank	37.70	32.44	22.36		
Migraine days per month					
Initial	17.5 (10-20)	17.5 (11.5-20)	10 (10-15)	0.144	-
Mean rank	33.25	34.42	24.80		
1 month	12 (8.25-18)	13.5 (9-18)	8 (8-12)	0.040	no difference was found (P<0.017***)
Mean rank	34.63	35.03	23.05		
3 month	9 (6-15.75)	10 (7-16)	6 (6-10)	0.088	-
Mean rank	32.45	35.92	24.30		

*Friedman test was used, ** Bonferroni correction was used, ***P-value significance level for the posthoc test, NSAID: non-steroidal anti-inflammatory drug. GONB: greater occipital nerve block. TPI: trigger point injection. PTNB: peripheral trigeminal nerve block. The numbers of drugs and days were presented as median with 25%-75% and mean rank of the drugs and days were given.

of nociceptive transmission in the central nervous system, particularly in severe and chronic pain disorders.[24] In postherpetic neuralgia, 8% capsaicin patches have been found to successfully treat tactile allodynia by reducing the painful area in patients with neuropathic pain.[36] Our findings led us to believe that similar effects were observed. LAs are used to eliminate the focus containing active nociceptors and diminish impulses from the upper cervical spinal cord to the trigeminal nucleus caudalis complex, thereby relieving allodynia and pain.[35]

In a recent study, Derya *et al*.[37] found that adding a distal level GON block to the proximal level GON block or blocking bilaterally provides no extra benefit to patients with CM with CA. In our study, we performed unilateral proximal GONB selecting the most tender side. Nevertheless, we performed the SONB, STNB, and TPI bilateral if the tenderness was bilateral to diminish the PS. However, the comparison was not made because of the small sample size. New studies can be conducted with the effectiveness of the peripheral blocks and TPI unilateral vs. bilateral.

In the most recent meta-analysis, using the occipital nerve with SON blocks, sphenopalatine ganglion blocks, cervical spine percutaneous treatments, and implanted stimulation to prevent CM was weakly recommended. This meta-analysis found inadequate data for evaluating TPIs for migraine prophylaxis.[38] However, trigger points are believed to be focal areas of allodynia arising from myofascial pain, which can contribute to or provoke headache disorders, such as migraine.[19,35-39] There is a theory that nociceptive inputs from trigger sites with myofascial origins affect migraine pathogenesis.[35,38] We hypothesize that TPI reduces hyperalgesia and allodynia at the injection site and in referred areas that coincide with migraine pain sites. In our study, only the first visit was used to quantify tenderness, and one muscle served as the baseline for each group. The effectiveness could have been improved if we had checked each muscle for TP and placed each block according to the discomfort at each visit. To understand the impact of TPI on allodynia, TPI should be performed at all trigger sites.

US guidance is crucial for all blocks. Using the US, headache interventionists can easily target the GON at the C2 level, trapezius muscle, and superficial branches of the trigeminal nerve (such as SON and STN), avoiding collateral injury to the nearby vessels and preventing accidental nerve injury, vascular thrombosis, and post-injection hematoma.[30,32,38] US guidance may have been the reason for the fewer reported side effects in the current study.

The strength of this study is its comprehensive monitoring of the findings 3 months after the initial intervention. Using validated research methodologies and US-guided blocks has also enhanced our research.[34] Nevertheless, this study has several limitations. Although the evaluation was prospective, the patients were not randomly assigned to the block category. At the first visit, tenderness in the

nerve or trapezius muscle was confirmed in the intervention group, which increases the possibility of bias. Tenderness was not assessed during other visits. To standardize our groups, we were also required to select one muscle for TPI. Due to ethical concerns, the current study was limited by the lack of a control group and the continued use of oral prophylaxis in all patients. Although drug posology was maintained throughout the trial, we cannot completely rule out the potential that this affected our study. But the effect of prophylactic drugs on CA is conflicting in the literature whether affecting or not.[1] In a recent research with 71 CM patients, the authors found topiramate and flunarizine efficient to relieve allodynia.[39] The prophylactic drugs were similiar between the three groups, but we did not analyze the subgroups for each drug. Even if BA and ASC-12 scales are valuable and trustworthy tools for allodynia, quantitative sensory testing should be performed.

Additionally, CM or CA may be associated with depression, anxiety, and sleep disturbances, affecting the headache profile and the treatment efficacy.[23,37,39,40] We asked the patients if they had these comorbidities and reviewed their hospital records. However, we did not use validated tools or perform a comprehensive psychiatric evaluation. The small sample size was another area for improvement in the current study. We could not have evaluated the effect of blocks on allodynia in each dermatome nor unilateral vs. bilateral PTNB and TPI.

CA is prevalent in patients with migraine, showing the presence of CS and PS, and is associated with migraine progression. GONB+TPI+PTNB was found to be more successful in alleviating allodynia. Our findings should be validated further using well-designed, appropriately powered, randomized controlled trials to compare the long-term efficacy, safety, and cost-effectiveness of nerve blocks and TPI with the US in a large cohort of patients.

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Conflicts of interest

There are no conflicts of interest.

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Supplementary Table 1: Brush allodynia exam according to dermatomes

Brush Allodynia Exam ($n=60$)	Ophthalmic (V1) dermatome		Maxillary (V2) dermatome		Mandibular (V3) dermatome		Cervical 2 dermatome		Cervical 5 dermatome		Cervical 8 dermatome	
	No pain	Pain	No pain	Pain	No pain	Pain	No pain	Pain	No pain	Pain	No pain	Pain
Initial	22 (36.7)	38 (63.3)	21 (35.0)	39 (65.0)	12 (20.0)	48 (80.0)	0 (0.0)	60 (100)	3 (5.0)	57 (95.0)	27 (45.0)	33 (55.0)
P-value of initial and first month	0.180		0.180		0.012		<0.001		0.012		<0.001	
1 month	27 (45.0)	33 (55.0)	26 (43.3)	34 (56.7)	21 (35.0)	39 (65.0)	11 (18.3)	49 (81.7)	12 (20.0)	48 (80.0)	47 (78.3)	13 (21.7)
P-value of first and third months	<0.001		<0.001		<0.001		<0.001		<0.001		0.016	
3 month	47 (78.3)	13 (21.7)	46 (76.7)	14 (23.3)	44 (73.3)	16 (26.7)	37 (61.7)	23 (38.3)	37 (61.7)	23 (38.3)	54 (90.0)	6 (10.0)

The Mc Nemar test was used to compare brush allodynia between visits. Numbers and percentiles were given for each dermatome