





Effectiveness of Combined Peripheral Nerve Blocks Versus Isolated Greater Occipital Nerve Block in the Management of Cluster Headache

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ABSTRACT

Introduction: Cluster headache (CH) is a primary headache disorder classified under trigeminal autonomic cephalalgias, characterized by severe, disabling pain attacks. In treatment-resistant cases, where pharmacological interventions are insufficient, peripheral nerve blocks have emerged as a promising interventional option. This study aimed to compare the efficacy of isolated greater occipital nerve (GON) block with combined GON, supraorbital nerve (SON), and sphenopalatine ganglion (SPG) blocks in reducing attack frequency, pain intensity, and treatment response in patients with CH.

Methods: This retrospective study included 44 patients diagnosed with CH according to the The International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria, who were treated at Ankara Bilkent City Hospital Neurology Clinics between August 2021 and December 2024. Patients were divided into two groups: those who received GON block alone (n=18) and those who underwent combined GON+SON+SPG blocks (n=26). Demographic and clinical data were collected. Attack frequency, pain duration, and Barrow Neurological

Institute Pain Scale (BNI-PS) scores were evaluated at baseline, and at the 1st week and 1st month following intervention.

Results: Compared to the GON-only group, patients in the combined block group showed significantly greater reductions in both attack frequency and BNI-PS scores at both follow-up points (p<0.05). Moreover, the duration of pain resolution was significantly shorter in the combined block group (8.96 ± 6.13 days vs. 18.28 ± 17.89 days; p=0.046). No significant differences were found between the groups in terms of baseline demographic or other clinical variables.

Conclusion: Our findings suggest that combined peripheral nerve blocks involving the GON, SON, and SPG are more effective than GON block alone in reducing attack burden and pain duration in patients with CH. This interventional approach may offer a valuable alternative for patients who are unresponsive to conventional medical therapies.

Keywords: Cluster headache; pain management; peripheral nerve block

Cite this article as: Yön Mİ, Ulusoy EK, Baraz B, Yoldaş TK. Effectiveness of Combined Peripheral Nerve Blocks Versus Isolated Greater Occipital Nerve Block in the Management of Cluster Headache. Arch Neuropsychiatry 2026;63:258–262. doi: 10.29399/npa.29145

INTRODUCTION

CH is a primary headache disorder within the group of trigeminal autonomic cephalalgias, characterized by severe, unilateral, periorbital pain attacks. These attacks typically begin abruptly, last between 15 and 180 minutes, and often recur daily. During an attack, ipsilateral cranial autonomic features—such as conjunctival injection, lacrimation, rhinorrhea, nasal congestion, ptosis, and facial sweating—are frequently observed (1, 2). CH is especially challenging to manage in cases that significantly impair quality of life or prove refractory to pharmacological therapies.

The pathophysiology of CH is thought to involve activation of the trigeminovascular system, hypothalamic dysfunction, and hyperactivation of the cranial parasympathetic pathways. Functional imaging studies have repeatedly demonstrated activation of the posterior hypothalamus during attacks, suggesting a central role for this structure in attack generation (3, 4). Activation of trigeminal afferents stimulates the parasympathetic outflow via the sphenopalatine ganglion (SPG), contributing both to the characteristic pain and to the accompanying autonomic symptoms (5).

Although pharmacological treatments are effective for many CH patients, alternative interventional approaches are considered for those who do not respond, develop intolerance, or are otherwise unsuitable for prophylactic medication. In this context, peripheral nerve blockades have emerged as an effective option for both acute attack management and prophylaxis (6).

Peripheral nerve blockades generally involve injecting a local anesthetic agent and/or corticosteroid around the target nerve. Greater occipital nerve (GON) blockade is performed at a point just above the nuchal line near the occipital protuberance, where the GON emerges; sphenopalatine ganglion (SPG) blockade may be administered intranasally or via a percutaneous approach; and supraorbital nerve (SON) blockade is carried out at the level of the supraorbital notch in the frontal region (6, 7). Injection frequency is typically tailored to clinical response, most commonly on a weekly or biweekly schedule. A single injection can provide relief for several weeks, and some patients experience even longer periods of remission (8).

Highlights

- **Combined nerve blockades significantly reduced attack frequency.**
- **Combined nerve blockades shortened the duration of pain resolution.**
- **Pain scores were lower in the combined blockade group.**

Both European Federation of Neurological Societies (EFNS) and American Headache Society (AHS) guidelines recommend peripheral nerve blockades for CH patients who are resistant to medical therapy or develop medication intolerance (1, 9). Randomized controlled trials of GON blockade have documented significant reductions in attack frequency and pain intensity, along with a favorable safety profile (10). SPG blockade has also been evaluated as an effective interventional method—particularly in refractory cases—for acute attack relief and as a preventive measure (11). Collectively, these data indicate that peripheral nerve blockades are assuming an increasingly important role in CH treatment algorithms.

However, there remains a paucity of literature comparing the efficacy of combined peripheral nerve blockades versus GON blockade alone, particularly with regard to pain control and attack frequency in medically refractory CH. In this study, we aimed to compare patients who received only GON blockade with those who underwent combined GON, SON, and SPG blockades, in order to evaluate the effects of multimodal nerve blockade on attack frequency, pain severity, and overall treatment response in CH.

METHODS

This study retrospectively reviewed the clinical data of 44 patients who presented to the Headache Outpatient Clinic of the Neurology Department at Ankara Bilkent City Hospital between August 2021 and December 2024 and were diagnosed with CH according to ICHD-3 criteria (12). Ethical approval was obtained from the Ankara Yıldırım Beyazıt University Institute of Health Sciences Ethics Committee, and all procedures were conducted in accordance with the Declaration of Helsinki.

Patients were divided into two groups based on the type of peripheral nerve blockade received:

Group 1: Patients who underwent unilateral greater occipital nerve (GON) blockade only

Group 2: Patients who received unilateral GON blockade in addition to ipsilateral supraorbital nerve (SON) and sphenopalatine ganglion (SPG) blockades

Blockades were administered on a weekly basis on the same side as the CH. For each patient, the following demographic and clinical variables were recorded: age, sex, headache lateralization, presence of autonomic signs, use of short- and long-term medical prophylaxis, the number of cluster attack periods per year, and the total number of blockade sessions performed.

Peripheral Nerve Blockade Procedures

- **GON Blockade:** After cleaning the intervention area on the painful side with an antiseptic solution, an imaginary line was drawn between

the external occipital protuberance and the mastoid process. At the medial one-third point of this line, a mixture of 1.5 mL of 0.5% bupivacaine and 0.5 mL of saline was injected subcutaneously to achieve blockade of the greater occipital nerve.

- **SON Blockade:** On the painful side, the supraorbital notch was palpated and marked. The intervention site was disinfected, and a 1% lidocaine solution was injected approximately 1 cm medial to the notch to blockade the supraorbital nerve.
- **SPG Blockade:** With the patient in the supine position and the head slightly extended, a cotton swab soaked in 10% lidocaine was inserted through the nostril on the painful side, advanced into the nasal cavity, and positioned to contact the sphenopalatine fossa for approximately 30 minutes.

Clinical Evaluation

To assess treatment efficacy, the following parameters were recorded at three time points—baseline (pre-blockade), 1 week post-blockade, and 1 month post-blockade:

- Attack frequency
- Pain severity (measured by the Barrow Neurological Institute Pain Scale, BNI-PS)
- Time to pain resolution (days)

Pain severity was evaluated using the BNI-PS, a five-point scale defined as follows (13):

- **I:** No pain, no treatment required
- **II:** Occasional pain, no treatment required
- **III:** Mild pain controlled with medication
- **IV:** Mild pain not controlled with medication
- **V:** Severe pain or treatment-refractory pain

Statistical Analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). The Shapiro–Wilk test was used to assess the normality of continuous variables. For comparisons of continuous variables between groups, either the independent-samples t-test or the Mann–Whitney U test was applied, depending on normality. For within-group comparisons over time, either the paired t-test or the Wilcoxon signed-rank test was used. Categorical variables were compared using the chi-square test or Fisher’s exact test as appropriate. Continuous variables are presented as mean \pm standard deviation (SD), and categorical variables are presented as frequency and percentage (%). A two-tailed p-value < 0.05 was considered statistically significant for all analyses.

RESULTS

In this study, patients receiving only greater occipital nerve (GON) blockade were compared to those who underwent combined blockade of the GON, supraorbital nerve (SON), and sphenopalatine ganglion (SPG), in terms of various clinical and demographic characteristics. A total of 44 patients were included: 18 patients underwent only GON blockade, and 26 patients received all three types of blockade. There was no statistically significant difference between the groups regarding gender distribution, with a male predominance observed in both groups (16 males, 2 females vs. 20 males, 6 females; $p = 0.539$). Mean ages were similar between groups (43.7 ± 11.61 vs. 39.2 ± 11.89 years), with no statistically significant difference ($p = 0.219$). Similarly, there were no significant differences

between groups in terms of headache lateralization (right/left), cluster type (episodic/chronic), presence of autonomic symptoms, annual number of cluster headache days, response to medical treatment, use of acute treatments, or use of short- and long-term prophylactic treatments ($p > 0.05$ for all comparisons) (Table 1).

The mean number of blockade sessions administered was not significantly different between patients receiving only GON blockade (2.83 ± 1.79) and those undergoing all three blockades (3.58 ± 2.61) ($p = 0.269$). However, the duration until pain resolution after blockade was significantly shorter in the group receiving combined blockades (8.96 ± 6.13 days) compared to the GON-only group (18.28 ± 17.89 days) ($p = 0.046$).

Pre-treatment BNI-PS scores were comparable between patients receiving only GON blockade and those receiving all three blockades (4.50 ± 0.51 vs. 4.77 ± 0.51 , respectively; $p = 0.096$). Both groups demonstrated significant reductions in BNI-PS scores at one week and one month post-blockade (Figure 1). Specifically, in the GON-only group, significant differences were observed between baseline and week 1 ($p < 0.001$), week 1 and month 1 ($p = 0.0018$), and baseline and month 1 ($p < 0.001$). Comparisons between groups showed significantly lower BNI-PS scores at both one week (3.28 ± 0.75 in GON-only vs. 2.77 ± 0.82 in combined blockade; $p = 0.040$) and one month (2.61 ± 1.24 in GON-only vs. 1.77 ± 0.95 in combined blockade; $p = 0.022$).

Baseline attack frequency was not significantly different between the two groups (8.78 ± 9.80 in GON-only vs. 7.35 ± 6.21 in combined blockade; $p = 0.558$). Both groups showed significant reductions in attack frequency following blockade therapy (Figure 2). In the GON-only group, statistically

significant reductions were observed from baseline to week 1 ($p = 0.006$), week 1 to month 1 ($p = 0.003$), and baseline to month 1 ($p = 0.004$). Similarly, the combined-blockade group showed significant reductions in attack frequency from baseline to both week 1 ($p < 0.001$) and month 1 ($p < 0.001$), though no significant difference was noted between week 1 and month 1 ($p = 0.327$). Comparisons between groups revealed significantly fewer attacks in the combined-blockade group compared to the GON-only group at week 1 (0.92 ± 0.74 vs. 2.06 ± 1.55 ; $p = 0.009$) and at month 1 (0.69 ± 1.09 vs. 1.56 ± 1.42 ; $p = 0.038$).

DISCUSSION

GON blockade is one of the most commonly applied peripheral nerve blockade techniques in cluster headache (CH) treatment and has been demonstrated to be particularly effective in reducing the frequency and severity of acute attacks. Ambrosini et al. reported that GON blockade significantly reduced attack frequency and provided prophylactic effects in some patients (10). Bartsch and Goadsby emphasized that, due to its connections between cervicogenic and trigeminal systems, the GON plays a pivotal role in modulating headache circuits (14). However, in some refractory cases, as observed in our study, isolated GON blockade may be insufficient for suppressing autonomic symptoms and modulating complex pain propagation pathways.

In our study, patients who underwent triple nerve blockade exhibited a statistically significant greater reduction in attack frequency compared to those receiving only GON blockade. This finding indicates that multiple nerve blockades may be more effective not only in decreasing pain intensity but also in modulating attack frequency and altering

Table 1. Demographic and clinical characteristics of patients with cluster headache

	GON Blockade Only (n=18)	Combined Blockades (GON, SON, SPG) (n=26)	p-value
Age (Mean \pm SD)	43.72 \pm 11.61	39.23 \pm 11.89	0.219
Male (%)	16 (88.9%)	20 (76.9%)	0.539
Side of Cluster Headache (Right/Left)	8/10	19/7	0.109
Cluster Type (Episodic/Chronic)	14/4	15/11	0.290
Cluster Headache Days per Year (Mean \pm SD)	11.67 \pm 11.25	6.54 \pm 6.48	0.093
Poor or Partial Response to Medical Treatment (%)	17 (94.4%)	26 (100.0%)	0.852
Use of Acute Attack Treatment (%)	10 (55.6%)	16 (61.5%)	0.932
Use of Short-Term Prophylaxis (%)	11 (61.1%)	13 (50.0%)	0.675
Use of Long-Term Prophylaxis (%)	16 (88.9%)	22 (84.6%)	1.000
Presence of Autonomic Symptoms (%)	18 (100%)	26 (100%)	1.000
Lacrimation (%)	17 (94.4%)	21 (80.8%)	-
Conjunctival Injection (%)	16 (88.9%)	20 (76.9%)	-
Edema (%)	8 (44.4%)	19 (73.1%)	-
Rhinorrhea (%)	14 (77.8%)	15 (57.7%)	-
Miosis (%)	0 (0.0%)	1 (3.8%)	-
Ptosis (%)	1 (5.6%)	0 (0.0%)	-
Forehead Flushing (%)	10 (55.6%)	16 (61.5%)	-
Ear Fullness (%)	11 (61.1%)	13 (50.0%)	-

GON: Greater Occipital Nerve; SON: Supraorbital Nerve; SPG: Sphenopalatine Ganglion

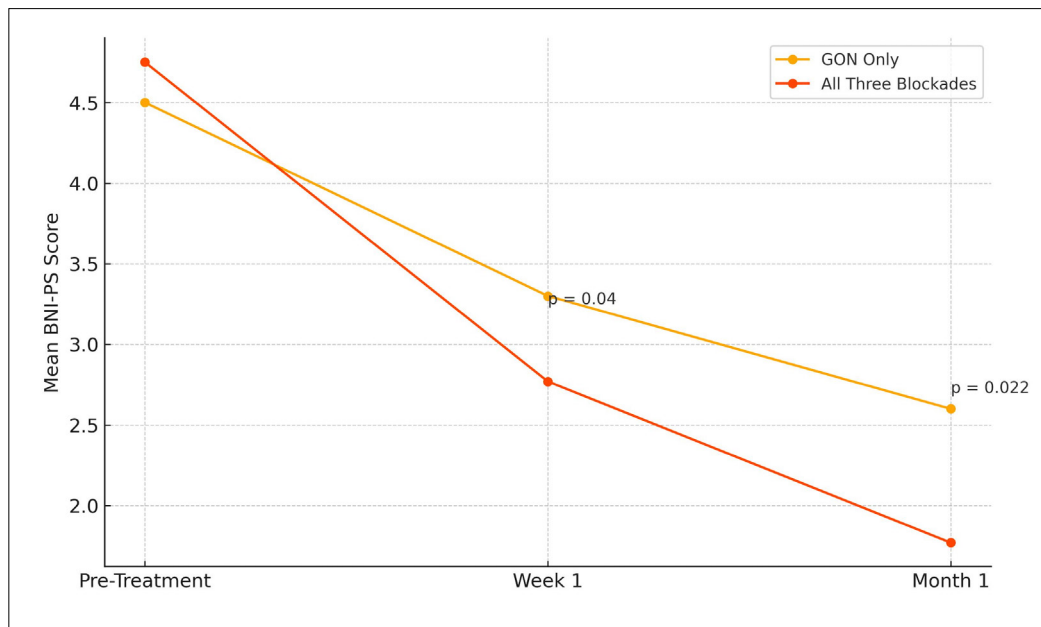


Figure 1. Change in BNI-PS Scores at Baseline, Week 1, and Month 1

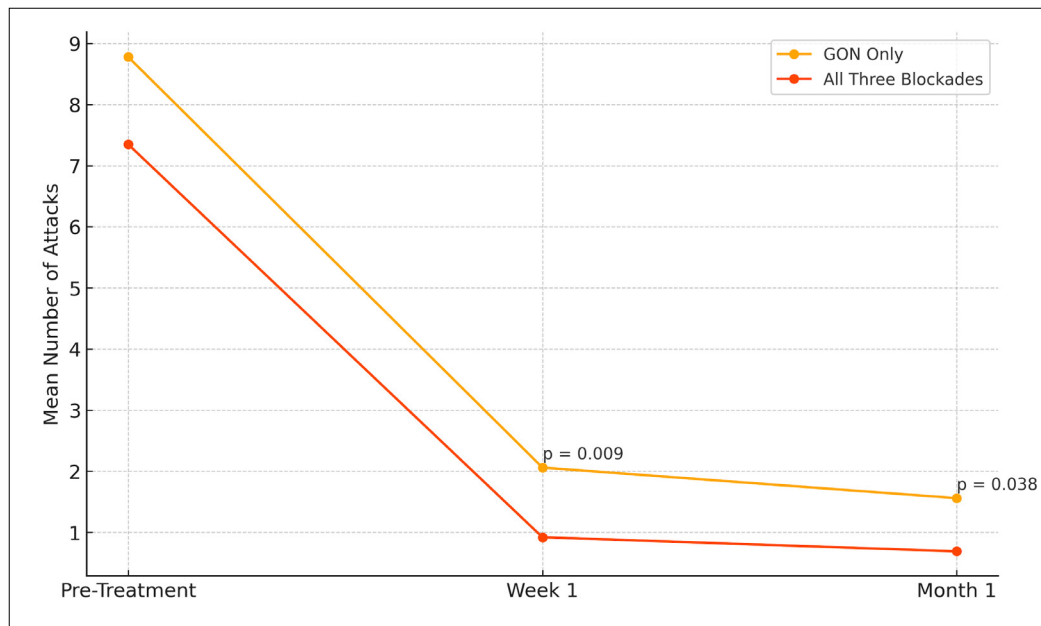


Figure 2. Change in Attack Frequency at Baseline, Week 1, and Month 1

neurophysiological thresholds. Similarly, Miller et al. reported that combined cranial nerve blocks achieved superior outcomes compared to isolated GON blockade in reducing both attack frequency and duration (15). Jürgens et al. similarly noted that SPG blockade effectively suppressed the episodic nature of CH, achieving long-term attack control (16). This effectiveness is thought to result from simultaneous inhibition of both central and peripheral components of the trigeminal-autonomic reflex (7). At the pathophysiological level, this effect is attributed to multidirectional modulation of neural activity in the hypothalamic-trigeminal-autonomic pathway (17). While GON and SON blockades inhibit sensitization of the trigeminovascular system via trigeminal afferent pathways, SPG blockade interrupts the triggering cycle of attacks by suppressing parasympathetic hyperactivity associated with hypothalamic activation.

Regarding pain scores, our study demonstrated significantly lower BNI-PS scores in patients undergoing triple nerve blockade compared to those receiving only GON blockade. This result suggests that combined

blockades are superior in managing not only attack frequency but also pain intensity. Similar findings have been reported in the literature. Láinez and Marti noted a marked reduction in pain scores following SPG blockade, especially in refractory headache cases (11). Miller et al. similarly found that multiple peripheral nerve blockades reduced pain more rapidly and intensely in patients unresponsive to conventional treatments (15).

The observed effectiveness may largely result from simultaneously targeting neuropeptide release and central sensitization mechanisms at multiple points. GON blockade primarily reduces CGRP and substance P levels at the cervical dorsal root, while SPG blockade inhibits both nitric oxide and vasoactive intestinal peptide (VIP) release, thus decreasing parasympathetic tone (5). SON blockade reduces cortical pain perception by interrupting nociceptive inputs from the supraorbital region (7). This synergistic effect may explain the stronger impact of multiple nerve blockades on pain scores.

In our study, the duration to pain resolution in the triple blockade group was significantly shorter compared to the GON-only group. This finding suggests that combined nerve blockades may provide stronger and faster analgesic effects. Miller et al. reported similar outcomes, observing that multiple cranial nerve blockades significantly shortened pain duration as well as attack frequency in refractory headache patients (15). Consequently, simultaneous blockade of multiple nerves may inhibit pain transmission pathways at several levels, reducing the duration of acute attacks.

This study has several limitations. Primarily, the relatively small sample size may limit statistical power, especially when performing subgroup comparisons. Furthermore, the observational and retrospective design prevents the establishment of direct causality. Variability in blockade technique standardization and differences among practitioners could also potentially influence outcomes. Additionally, patient follow-up was limited to one month, restricting assessments of long-term efficacy and recurrence rates. Finally, reliance on subjective patient-reported outcomes, such as pain and attack frequency, introduces a risk of reporting bias. Therefore, multicenter, randomized studies with longer follow-up periods are warranted.

In conclusion, our findings suggest that combined nerve blockades provide a more effective, rapid, and potent treatment alternative compared to isolated GON blockade in patients with CH. This combined approach may be particularly beneficial as an adjunct therapy for patients refractory to medical treatment.

Ethics Committee Approval: Ethical approval was taken from Ankara Yıldırım Beyazıt University Institute of Health Sciences Ethics Committee (Approval No:04/1233 and 17.04.2025).

Peer-review: Externally peer-reviewed.

Author Contributions: Concept- EKU; Design- MİY; Supervision- TKY; Resource- MİY; Materials- BB; Data Collection and/or Processing- BB; Analysis and/or Interpretation- MİY; Literature Search- TKY; Writing- MİY; Critical Reviews- EKU.

Conflict of Interest: The authors declared that there is no conflict of interest.

Financial Disclosure: None

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