

# Efficacy and safety of greater occipital nerve block with a small volume of lidocaine and methylprednisolone in tertiary headache center

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## ABSTRACT

**Background:** The greater occipital nerve block (GON-B) is used in clinical practice for treating different forms of headache. There is no standardized procedure to perform GON-B. This study evaluates the efficacy and feasibility of a low-volume GON-B protocol utilizing a pre-mixed solution of lidocaine (10 mg) and methylprednisolone (40 mg) across various headache disorders.

**Methods:** This observational case series included patients receiving their first GON-B from November 2019 to February 2021. Participants were diagnosed with migraine, cluster headache, cervicogenic headache, or paroxysmal hemicrania. The primary outcome was the degree of response to the GON-B.

**Results:** Thirty-nine patients with migraine underwent a first GON-B. Regarding headache frequency, 26% achieved substantial response and 33% partial response. For headache intensity, 26% reported substantial and 49% partial improvement. Migraine patients experienced a significant reduction in median monthly headache days from 25 to 13 ( $p=0.001$ ) and in headache intensity from a median of 8 to 6 on the Numerical Rating Scale (NRS) scale ( $p<0.001$ ). Of the 27 patients receiving a second GON-B, 33% had a substantial response, 48% a partial response, and 19% no response. Results from subsequent sessions were consistent with these findings. Ten patients with cluster headache underwent GON-B, showing a significant reduction in pain intensity from a median NRS score of 10 to 5 ( $p=0.008$ ). Two patients with cervicogenic headache showed a partial response to GON-B, with pain intensity decreasing from 8 to 6 and 8 to 7 over 30 monthly episodes. A patient with paroxysmal hemicrania received seven GON-B injections, reducing daily attacks from 30 to 10 and pain intensity from 7 to 6 on the NRS scale.

**Conclusions:** These outcomes affirm GON-B potential in interrupting pain pathways, even at a low dose, in a wide range of headache disorders.

**Key words:** greater occipital nerve, nerve block, migraine, cluster headache, cervicogenic headache.

## Introduction

Headache disorders are among the most prevalent causes of disability mostly in people of young age (1). Despite the advancements in pharmaceutical interventions for headache disorders, a subset of patients continues to experience challenges in finding relief through common drug treatments (2). For patients who remain unyielding to common therapeutic interventions, the search for alternative and innovative treatments becomes paramount. One such approach that has gained attention for its potential efficacy is the greater occipital nerve block (GON-B) (3,4). The greater occipital nerve is a crucial component of the trigeminocervical system, a neural network implicated in headache pathophysiology (5). In the context of headache prevention, GON-B interrupts the nociceptive signals originating from this system (6). This interference with pain signaling underscores the rationale behind utilizing GON-B as a preventive measure for those who exhibit resistance or refractoriness to other headache treatments. GON-B also has a rapid learning curve for physician and a rapid technique of administration that confers practical advantages in the transitional treatment of headache exacerbations. Studies have explored the use of GON-B across various headache types, including migraine, cluster headaches, and tension-type headaches. This widespread interest is due to GON-B's ability to modulate the trigeminocervical complex, a key player in the pathophysiology of these disorders, providing a rationale for its efficacy across different headache modalities.

To date, there is a great heterogeneity for techniques used for GON-B, which is performed with different injection points, different drugs, and different volumes and doses (3,7-10). A

pre-mixed combination of lidocaine 10 mg and methylprednisolone 40 mg, in a 1 mL volume, injected with a fine needle can ensure a quick and comfortable GON-B which is easy to implement in clinical practice. However, the effectiveness of this drug mixture for the treatment of headache disorders has not been established.

We present an observational case series of patients with several headache disorders treated with low-volume GON-B.

## Results

During the study period we included 52 patients (**Table 1**) for a total of 110 injections. The population included 39 patients with migraine (76%), 9 with cluster headache (18%), 2 with cervicogenic headache (4%) and 1 with paroxysmal hemicrania (2%).

**Migraine.** The group of patients with migraine included 32 (82%) women and 7 men (18%), with a median age of 54 years [Interquartile Range (IQR)14-88 years]; 28 (72%) had chronic and 11 (28%) episodic migraine. Three patients (8%) reported aura. The median age of migraine onset was 20 years (IQR 10-78 years); the median of years lived with migraine was 24 years (IQR 0-68 years).

Thirty-nine patients received a first GON-B. Referring to headache frequency, ten patients (26%) had a substantial response and 16 (33%) had a partial response. Referring to headache intensity, ten patients (26%) had a substantial response and 19 (49%) a partial response. Patients with migraine showed a significant reduction in median monthly headache days after the first GON-B, from 25 (IQR 12-30) to 13

(IQR 8-30;  $p=0.001$ ; **Figure 1A**). Headache intensity decreased from a median of 8 points on NRS scale (IQR 5-10) to 6 points (IQR 4-10;  $p<0.001$ ; **Figure 1B**).

Referring to consistency of response, 27 patients received a second GON-B, with 33% achieving a substantial response, 48% experiencing a partial response, and 19% showing no response. Among substantial responders, 44% discontinued treatment due to sustained benefit, while one patient ceased treatment following a syncope event. Additionally, 31% of patients with partial or no response interrupted treatment. Subsequent sessions showed similar trends, with the distribution of substantial and partial responders shown in **Figure 2**.

**Cluster headache.** Ten patients with cluster headache (9 with episodic CH, 1 with chronic CH), including 9 males and 1 female, with a median age of 33 years (IQR 15-59), underwent GON-B. The median age of CH onset was 25 years (IQR 14-51). The median frequency of daily attacks was 2 (IQR 1-4 attacks/day),

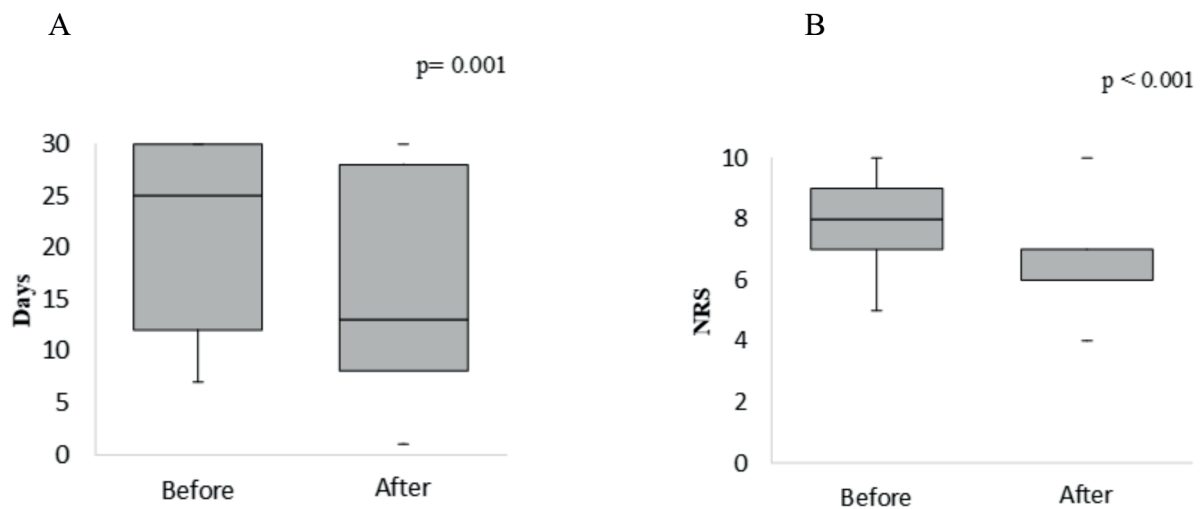
with median duration of each attack is 120 minutes (IQR 60-180 minutes) and median intensity of attack of 10 (IQR 9-10).

These patients all showed a partial response and a significant reduction in pain intensity after first GON-block from a median of 10 points on Numerical Rating Scale (NRS) scale (IQR 9-10) to 5 points (IQR 0-8;  $p=0.008$ ).

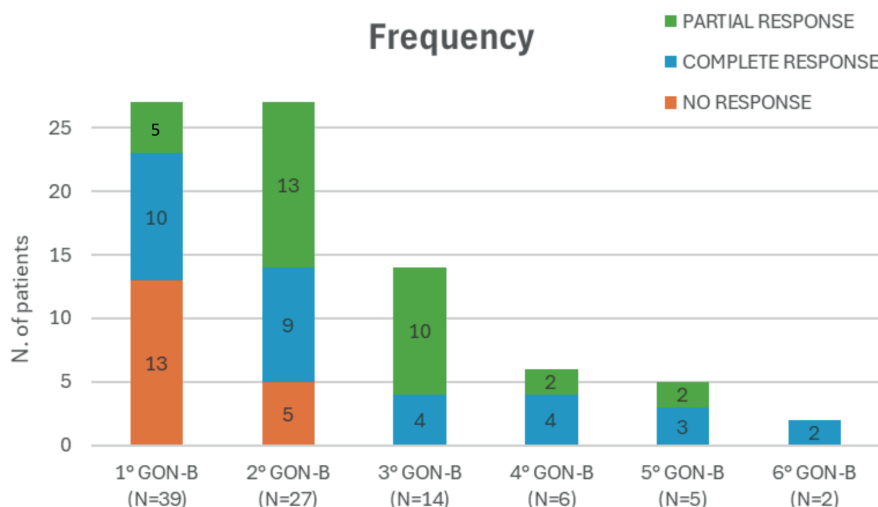
**Table 1.** Characteristics of the study sample.

	Migraine	Cluster headache
Total	39	10
Age, median (IQR)	54 (14-88)	33 (15-59)
Sex (%)	32 women	10 women
Disease duration, median years (IQR)	24 (3-30)	7.5 (3-18)

IQR, interquartile range.



**Figure 1.** Decrease in frequency of headache (A) and intensity of pain (B) after the first greater occipital nerve block in patients with migraine.



**Figure 2.** Number of patients with migraine and response on frequency of headache.

**Cervicogenic headache.** In our study, two patients with cervicogenic headache were treated. Each of them received four bilateral GON-B injections. Initially experiencing 30 episodes per month, they both reduced to 25 after the first GON-B, showing a partial response. Pain intensity decreased from 8 to 6 on the NRS scale for one patient and from 8 to 7 for the other.

**Paroxysmal hemicrania.** The patient with paroxysmal hemicrania received seven bilateral GON-B injections, reducing attacks from 30 per day to 10 after the first GON-B showing a substantial response, with pain intensity decreasing from a mean of 7 to 6 on the NRS scale.

**Adverse events.** Adverse events were reported by 4 (7.8%) patients in the overall population. Specifically, alopecia at the site of injection was reported by one patient, swelling at the site of injection by one patient, and syncope during the procedure by two patients.

## Discussion

Our study presents data on a group of patients treated with suboccipital, mostly bilateral, injections of a mixture of lidocaine (10 mg) and methylprednisolone (40 mg) for different headache disorders. We noted a marked decrease in both the frequency and intensity of pain since the first treatment, with sustained improvements over time.

Our results are consistent with prior evidence, including systematic reviews of randomized trials (11-13) and a large retrospective cohort study (4) highlighting GON-B's effectiveness in acute migraine management and its role in reducing headache frequency in chronic migraine. The efficacy of GON-B for the prophylactic treatment of cluster headache has previously been suggested by open label studies (14-16) and randomised placebo-controlled trials (17,18). In our study, we observed that GON-B is effective in stopping cluster symptoms. According to this evidence, the use of GON-B could be an effective alternative to oral steroids for the transitional treatment of cluster headache (19), with a rapid administration and onset of action and no need for titration.

About patients suffering from paroxysmal hemicrania and cervicogenic headache, an improvement in pain intensity was observed but, due to the small size of the sample studied, we could not perform a statistical analysis. The limited available evidence suggests that GON-B effectively improves pain in patients with cervicogenic headache, both as acute and as preventative treatment (9). The little evidence in the literature on paroxysmal hemicrania reported conflicting results. An Italian case report described a case of episodic paroxysmal hemicrania successfully treated with repeated unilateral suboccipital steroid injections (20).

The efficacy of steroid (triamcinolone 20 mg, or methylprednisolone 80 mg) to local anesthetic agents in GON-B remains a topic of debate. While some evidence suggests that the addition of triamcinolone does not improve outcomes (21), contrasting data from a double-blind placebo-controlled study highlight a significant role for steroids, particularly in patients with cluster headache (17). Steroids decrease inflammation by inhibiting the release and synthesis of proinflammatory substances, directly stabilize membranes, reversibly inhibit nociceptive C-fibers, and modulate nociceptive input in substantia gelatinosa. Furthermore, the choice between using anesthetics alone versus combining them with steroids (or steroids alone in some cases) introduces another layer of complexity. While local anesthetics provide immediate pain relief by blocking nerve conduction, steroids offer a more prolonged anti-inflammatory effect that could potentially extend the duration

of pain relief. The optimal strategy may vary depending on the chronicity and severity of the headache disorder being treated, highlighting the need for tailored treatment plans based on individual patient characteristics and responses. Randomized evidence suggests that steroids are the main effective component of GON-B for cluster headache, while local anesthetics are the only effective component in patients with migraine (22).

The choice between unilateral *versus* bilateral GON-B significantly influences treatment outcomes and patients' comfort. This decision is often dictated by the characteristics of the headache, such as its distribution and nature. Unilateral blocks may be adequate for patients experiencing strictly unilateral headache syndromes, whereas bilateral blocks might be necessary for achieving comprehensive relief in cases involving alternating sides or bilateral pain. However, there is no evidence base to support this statement.

Additionally, the dosages of the medications used in GON-B might play an important role in the effectiveness of the treatment. While lower doses might minimize side effects, they may not offer the same level of efficacy as higher doses. Conversely, higher doses, while potentially more effective, come with an increased risk of side effects, such as steroid-induced atrophy or systemic effects. Optimizing the dosage for both anesthetics and corticosteroids, possibly through dose-finding studies, could enhance the effectiveness of GON-B while minimizing adverse outcomes.

The observed alopecia in our study, reported in a patient treated with a mixture of lidocaine (10 mg) and methylprednisolone (40 mg), is rare. Previous studies have mainly associated this side effect with triamcinolone and, less frequently, with betamethasone (23)

Steroid-induced alopecia is usually due to the effects of these drugs on hair follicles. While methylprednisolone is less commonly linked to alopecia compared to triamcinolone, it can still cause similar adverse effects due to its pharmacological properties.

Although lidocaine is primarily used for its anesthetic properties, it might enhance the local effects of methylprednisolone. However, there is no conclusive data indicating a negative interaction between lidocaine and methylprednisolone that could explain the alopecia.

The rare occurrence of alopecia in our study suggests it might be an idiosyncratic response, potentially related to individual patient factors such as genetic predisposition or sensitivity to corticosteroids. Further research is needed to understand this adverse effect better and develop management guidelines.

Our study performed a thorough analysis of the effectiveness of a technique for GON-B using a mixture of low-dose and low-volume drugs. The low doses might have contributed to the relatively low effectiveness in the presence of a low proportion of adverse events. Our study faces limitations primarily stemming from a small patient cohort and their heterogeneous data, observational and retrospective nature. The retrospective design, without pre-specified outcomes and sample size, limits its quality compared with prospective studies.

## Conclusions

According to our study, low-volume GON-B with 10 mg lidocaine and 40 mg methylprednisolone is a safe and effective treatment for different types of headache disorders. A low-volume procedure with pre-mixed drugs can minimize patients' discomfort and improve feasibility even in emergency settings.

## Materials and Methods

**Study design.** This real-life single-center study was a retrospective and prospective observational audit conducted from November 2019 to February 2021. No changes were made to normal clinical practice. The study was approved by the Internal Review Board of the University of L'Aquila with protocol number 40/2020. Each patient signed a written informed consent.

**Inclusion and exclusion criteria.** The study included all patients referred to our center and treated with GON-B from November 2019 to February 2021, with the following International Classification diagnoses and treatment methods:

- Episodic migraine (EM) with high frequency (8-14 days/month of headache) or chronic migraine (CM), with occipital origin or with occipital tenderness, for preventive treatment in patients who had failed two or more oral treatments due to tolerability or ineffectiveness;
- Episodic cluster headache, for transitional treatment during the cluster, or chronic cluster headache, for preventive treatment;
- Cervicogenic headache and paroxysmal hemicrania for preventive treatment.

Patients will be excluded from the study if they are experiencing secondary headaches, as these may interfere with the study's focus. Additionally, individuals currently participating in another interventional research study will not be eligible, to prevent potential conflicts and ensure the integrity of the study results. Those with coexisting medical conditions that might compromise their safety or the study's objectives will also be excluded to maintain the welfare of the participants and the validity of the findings. Patients already in treatment with another preventive medication will also be excluded to avoid confounding effects on the study outcomes. Finally, pregnant women or patients known to have allergies to local anesthetics will not be included in the study.

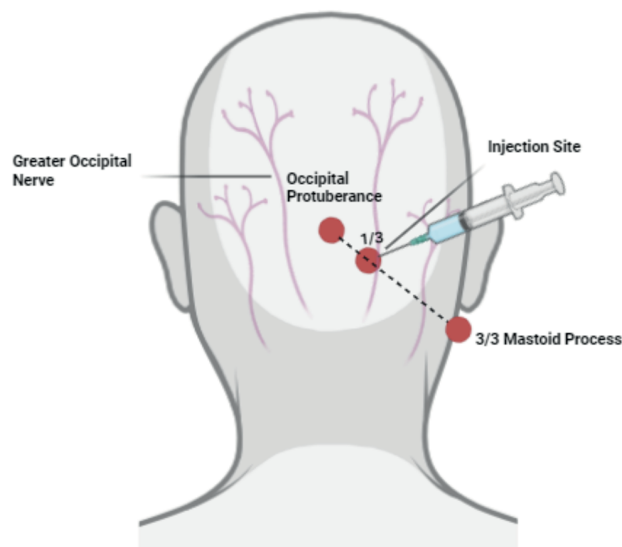
**Study procedures.** We included patients who underwent their first-ever GON-B from November 2019 up to February 2021. In line with our standard clinical practice, patients kept a headache diary, recording the frequency and severity of their attacks. Information on outcome was obtained during follow-up visits and/or by telephone interviews.

**Data collection.** The following data were collected. Personal data: age, sex, age at headache onset; history of headache related to the last month: frequency (daily for cluster headache, monthly for all other headache disorders) and intensity of acute attacks (on a 1-10 NRS). These data were collected through a paper headache diary and by monthly phone calls.

**Treatment.** Patients were treated with local injections of methylprednisolone 40 mg + lidocaine 10 mg for each nerve, unilateral in cluster headache and bilateral in migraine. As an injection site we used the point between the medial third and the middle third of a line connecting the external occipital protuberance with the mastoid process (**Figure 3**).

Injections were made by proceeding in a radial pattern around the point of the GON. The injection site was then massaged to spread the mixture. GON-B was repeated monthly if patients reported a  $\geq 30\%$  improvement in monthly headache days from baseline and willing to repeat the procedure.

**Outcomes.** The primary outcome was the degree of response to the first GON-B, which was categorized as substantial - if the patient experienced a reduction in attack frequency and/or



**Figure 3.** Injection technique for greater occipital nerve block. Injection sites are positioned at one third the length of a line traced between the external occipital protuberance and the mastoid process.

severity of  $\geq 50\%$  from baseline - or partial - if the reduction in attack frequency and/or severity was  $< 50\%$  from baseline. No response was considered if patients reported attacks worsening after the injection. This definition was also applied to patients with cluster headache, cervicogenic headache and paroxysmal hemicrania. Secondary outcomes included the decrease in headache frequency and severity. The additional outcome was the consistency of effect, defined as the persistence of effect after repeated GON-B. Outcomes were assessed during the first week after treatment in the case of cluster headache and to the first month after the treatment in the case of all other headache disorders.

**Statistical analysis.** All analyses were performed using R Statistical Software (v4.1.2; R Core Team 2021). Descriptive data was presented as number and percentage for discrete data, as means and standard deviations or median and interquartile range for continuous data. Statistical tests included chi-squared for discrete data and Wilcoxon test for continuous data. We did not perform a sample size calculation as we based upon a clinical convenience sample.

## References

1. GBD 2016 Neurology Collaborators. Global, regional, and national burden of neurological disorders, 1990-2016: a systematic analysis for the Global Burden of Disease Study 2016. *Lancet Neurol* 2019;18:459-80.
2. Sacco S, Lampl C, Amin FM, Braschinsky M, Deligianni C, Uludüz D, et al. European Headache Federation (EHF) consensus on the definition of effective treatment of a migraine attack and of triptan failure. *J Headache Pain* 2022;23:133.
3. Inan LE, Inan N, Unal-Artik HA, Atac C, Babaoglu G. Greater occipital nerve block in migraine prophylaxis: narrative review. *Cephalalgia* 2019;39:908-20.
4. Allen SM, Mookadam F, Cha SS, Freeman JA, Starling AJ, Mookadam M. Greater occipital nerve block for acute treatment of migraine headache: a large retrospective cohort study. *JABFM* 2018;31:211-8.

5. Terrier LM, Hadjikhani N, Destrieux C. The trigeminal pathways. *J Neurol* 2022;269:3443-60.
6. Hoffmann J, Mehnert J, Koo EM, May A. Greater occipital nerve block modulates nociceptive signals within the trigeminocervical complex. *J Neurol Neurosurg Psychiatry* 2021;92:1335-40.
7. Castillo-Álvarez F, Hernando de la Bárcena I, Marzo-Sola ME. Greater occipital nerve block in the treatment of headaches. Review of evidence. *Medicina Clinica* 2023;161:113-8.
8. Ornello R, Lambro G, Caponnetto V, Frattale I, Di Felice C, Pistoia F, et al. Efficacy and safety of greater occipital nerve block for the treatment of cluster headache: a systematic review and meta-analysis. *Exp Rev Neurother* 2020;20:1157-67.
9. Caponnetto V, Ornello R, Frattale I, Di Felice C, Pistoia F, Lancia L, et al. Efficacy and safety of greater occipital nerve block for the treatment of cervicogenic headache: a systematic review. *Exp Rev Neurother* 2021;21:591-7.
10. Gordon A, Roe T, Villar-Martínez MD, Moreno-Ajona D, Goadsby PJ, Hoffmann J. Effectiveness and safety profile of greater occipital nerve blockade in cluster headache: a systematic review. *J Neurol Neurosurg Psychiatry* 2023;95:73-85.
11. Velásquez-Rimachi V, Chachaima-Mar J, Cárdenas-Baltazar EC, Loayza-Vidalon A, Morán-Mariños C, Pacheco-Barrios K, et al. Greater occipital nerve block for chronic migraine patients: A meta-analysis. *Acta Neurol Scandin* 2022;146:101-14.
12. Tang Y, Kang J, Zhang Y, Zhang X. Influence of greater occipital nerve block on pain severity in migraine patients: A systematic review and meta-analysis. *Am J Emerg Med* 2017;35:1750-4.
13. Zhang H, Yang X, Lin Y, Chen L, Ye H. The efficacy of greater occipital nerve block for the treatment of migraine: A systematic review and meta-analysis. *Clin Neurol Neurosurg* 2018;165:129-33.
14. Bigo A, Delrieu F, Bousser MG. [Treatment of vascular pain of the face by methylprednisolone injection into the area of the greater occipital nerve: 16 cases]. *Revue Neurologique* 1989;145:160-2. [Article in French].
15. Peres MF, Stiles MA, Siow HC, Rozen TD, Young WB, Silberstein SD. Greater occipital nerve blockade for cluster headache. *Cephalalgia* 2002;22:520-2.
16. Afridi SK, Shields KG, Bhola R, Goadsby PJ. Greater occipital nerve injection in primary headache syndromes: prolonged effects from a single injection. *Pain* 2006;122:126-9.
17. Ambrosini A, Vandenheede M, Rossi P, Aloj F, Sauli E, Pierelli F, et al. Suboccipital injection with a mixture of rapid- and long-acting steroids in cluster headache: a double-blind placebo-controlled study. *Pain* 2005;118:92-6.
18. Holle D, Burmeister J, Scherag A, Ose C, Diener HC, Obermann M. Study protocol of Prednisone in episodic Cluster Headache (PredCH): a randomized, double-blind, placebo-controlled parallel group trial to evaluate the efficacy and safety of oral prednisone as an add-on therapy in the prophylactic treatment of episodic cluster headache with verapamil. *BMC Neurol* 2013;13:99.
19. Obermann M, Nägel S, Ose C, Sonuc N, Scherag A, Storch P, et al. Safety and efficacy of prednisone versus placebo in short-term prevention of episodic cluster headache: a multicentre, double-blind, randomised controlled trial. *Lancet Neurol* 2021;20:29-37.
20. Rossi P, Di Lorenzo G, Faroni J, Sauli E. Seasonal, extratrigeminal, episodic paroxysmal hemicrania successfully treated with single suboccipital steroid injections. *Eur J Neurol* 2005;12:903-6.
21. Ashkenazi A, Matro R, Shaw JW, Abbas MA, Silberstein SD. Greater occipital nerve block using local anaesthetics alone or with triamcinolone for transformed migraine: a randomised comparative study. *J Neurol Neurosurg Psychiatry* 2008;79:415-7.
22. Gul HL, Ozon AO, Karadas O, Koc G, Inan LE. The efficacy of greater occipital nerve blockade in chronic migraine: a placebo-controlled study. *Acta Neurol Scandin* 2017;136:138-44.
23. Lambro G, Lagrata S, Matharu MS. Cutaneous atrophy and alopecia after greater occipital nerve injection using triamcinolone. *Headache* 2012;52:1596-9.

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Contributions: CR and RO drafted the manuscript, created figures and tables and revised the manuscript for intellectual content. SS coordinated the study and revised the manuscript for intellectual content. Other authors contributed to patient inclusion and retrieval of data. All the authors have read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

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