▪ Headache Medicine 2023, 14(1): 7-12 ▪ p-ISSN 2178-7468, e-ISSN 2763-6178

Headache Medicine

▪ DOI: 10.48208/HeadacheMed.2023.3

Review

The effectiveness and safety of cranial nerve block in migraine: a critical review

Annelise Akemi Higa Lee, Renan Barros Domingues

Santa Casa de Misericórdia de Sao Paulo, Sao Paulo, Sao Paulo, Brazil.

Annelise Akemi Higa Lee
a.higalee@gmail.com

Edited by:
Marcelo Moraes Valença

Keywords:
Migraine
Episodic migraine
Chronic migraine
Cranial nerve block
Greater occipital nerve block
Lesser occipital nerve block

Abstract

Cranial nerve blocks (CNBs) have been used for the acute and preventive treatment of a variety of headaches, including migraine. The effectiveness of CNBs in migraine is usually observed beyond the duration of the nerve block, possibly due to central pain modulation. The most used target is the greater occipital nerve. Other commonly targeted nerves are the lesser occipital nerve and various branches of the trigeminal nerve, including the supratrochlear, supraorbital, and auriculotemporal nerves. CNBs are generally safe and well-tolerated procedures that can be performed in either emergency or outpatient settings. There is currently no guideline standardizing CNBs in migraine. In clinical practice, as well as the few published studies, the results are encouraging, justifying further studies in the area. In the present study we critically review the literature about the safety and efficacy of CNBs in the treatment of migraine attacks and in the preventive treatment of migraine.

Submitted: February 10, 2023
Accepted: March 30, 2023
Published online: March 31, 2023

Introduction

Migraine is a chronic disease that affects more than one billion people around the world.[1] In Brazil, approximately one seventh of the adult population is affected by migraine.[2,3] One of the proposed pathophysiologic mechanisms of migraine involves activation of the trigeminovascular system, which consists of small-caliber pseudounipolar sensory neurons that originate from the trigeminal ganglion and dorsal superior cervical roots.[4]

Cranial nerve blocks (CNBs) have been usedin thetreatment ofmigraine. The rationale is the anesthetic blockade of sensitive fibers of dorsal superior cervical roots or branches of the trigeminal nerve, thus leading to inhibition of the trigeminovascular system. CNBs can be used for acute treatment of migraine in patients who have severe and prolonged attacks, as well as for patients who are refractory or have contraindications to standard symptomatic treatments. Repeated blocks have been usedas an alternative for prophylactic migraine treatment.[5,6]

The CNBs technique and procedures have not yet been definitively standardized. Greater or lesser occipitalnerves block, as well as blocking trigeminal nerve branches, such as the supraorbital nerve (SON), supratrochlear nerve (STN), and auriculotemporal nerve (ATN) have been reported.The greater occipital nerve (GON) block it is the most performed and reported procedure. There is also variation in relation to the type of anesthetic used and the association or not of corticosteroids.[5-7]

The aim of the present study was to review and discuss the current literature on the use of CNBs in the treatment of migraine.

Methodology

The process of collection and selection of published papers was carried out through a search in the main online libraries of medical literature available: PubMed and LILACS, and was executed in two stages. First with a combination of descriptors, including “migraine” OR “episodic migraine” OR “chronic migraine”, and then a second search with its relation to “nerve block” OR “cranial nerve block” OR “greater occipital nerve block” OR “lesser occipital nerve block” OR “supratrochlear nerve block” OR “supraorbital nerve block” OR “auriculotemporal nerve block”, from Jan, 2012 to Jan, 2022. The two researchers searched for articles for comparison and verification of the articles found and included in the study. The screening of articles for inclusion and exclusion considered only the title and abstract of the article.

It was included articles with a population over 18 years old and we excluded publications older than 10 years, articles not written in English, duplicated articles and review articles. The type of study, studied population, blockade indication (attack or prophylactic treatment), and the results obtained in terms of efficacy, safety and adverse effects were recorded. The references were consulted and other references from the articles that were identified in the initial search were also selected and reviewed for extraction of additional information or points of view.

Results

Using the above-mentioned descriptors, the described search identified 81 articles. After applying the inclusion and exclusion criteria, 34 articles were selected, three of which were excluded due to duplicity. Of the selected articles, 13 studies were eligible based on the "abstract" analysis (Figure 1).

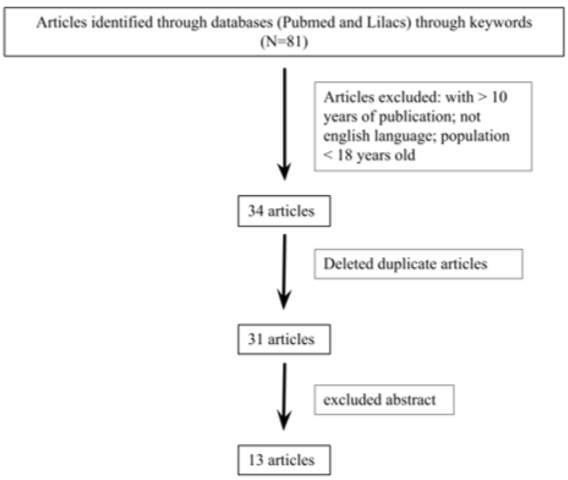

Figure 1. Article selection flowchart

Of the total of 13 articles selected, five were clinical trials and eight were observational studies. The migraine type, the clinical indication of CNBs, whether for acute or prophylactic treatment, the blocked nerve, the medication used, the dosage scheme, as well as the results found in each of the studies are shown in Table 1.

Table 1. Summary of the main findings of the selected studies on the efficacy and safety of CNBs in migraine.

Citation	Setting	Study type	Intervention (n)	Placebo (n)	Migraine type	Adverse effects	Results
Friedman et al.[8]	Acute	RCT	13	15	Migraine attack refractory to intravenous metoclopramide	Mild (3)	Headache freedom with intervention superior to placebo
Allen et al.[9]	Acute	Retrospective	562	0	Acute migraine	Mild (35 patients)	Most patients with good response
Ebied et al.[10]	Acute	Retrospective	190	0	Attack of migraine with or without aura	Mild (3%)	42% with reduced pain scores
Cuadrado et al.[11]	Acute	Observational	18	0	Migraine with aura attack	No	Pain reduction and significant aura resolution
Inan et al.[12]	Preventive	RCT	39	33	Chronic migraine without prophylactic medication and analgesic overuse	Mild (10 patients)	Intervention superior to placebo
Kashipazha et al.[13]	Preventive	RCT	24 with and 24 without triamcinolone	0	Migraine with MIDAS score > 11	No	No significant differences with and without triamcinolone
Dilli et al.[14]	Preventive	RCT	33	30	Episodic or chronic migraine	Mild (21%)	No significant differences between intervention and placebo
Palamar et al.[15]	Preventive	RCT	11	12	Refractory chronic migraine	Mild (1 patient)	Superiority of treatment over placebo
Unal-Artık et al. [16]	Preventive	Retrospective	28 unilateral 18 bilateral	0	Chronic migraine	Not reported	Reduction in pain frequency with unilateral and bilateral GON block
Inan et al.[17]	Preventive	Retrospective	78	0	Migraine without aura	Not reported	Reduction on migraine frequency for 3 months.
Okmen et al.[18]	Preventive	Uncontrolled cohort	60	0	Migraine without other prophylactic treatments	No	Reduction in MIDAS
Schwarz et al.[19]	Preventive	Observational	71	0	Chronic migraine	Mild (10 patients)	Significant reduction in headache frequency
Fernandes et al.[20]	Preventive	Uncontrolled cohort	64	0	Chronic migraine with or without aura	Mild (8%)	Reduction in pain intensity and frequency, Reduction in HIT6. No differences between GON block and MNCBs

CNBs – cranial nerve blocks RCT – randomized clinical trial; GON – great occipital nerve; MIDAS –migraine disability assessment; HIT-6 –headache impact test.; MNCBs –multiple cranial nerve blocks

Four studies assessed CNBs for acute migraine treatment, one was a randomized clinical trial (RCT)[8], two were retrospective[9,10], and one was observational[11]. A total of 783 patients were included in these four studies. Most patients obtained relief of the migraine attack with the blockade. In the only placebo-controlled study for migraine attack treatment the percentages of headache freedom at 30 minutes and sustained headache relief for 48 hours were 31% and 23%, respectively. In this study no patients in the placebo arm obtained complete headache relief. The uncontrolled studies evaluating the abortive effect of CNBs in migraine attacks showed results considered satisfactory, with symptoms relief ranging from 42% to 82% of cases.

Nine of the selected studies assessed CNBs for migraine preventive treatment. Three of them were RCT comparing CNBs with anesthetic drug against placebo. These three studies included 83 patients treated with CNBs and 65 in the placebo group.[12,14,15] In one of these three studies bupivacaine was associated with methylprednisolone and in two this anesthetic drug was given alone. Two of these three controlled studies reported superiority of blockage with bupivacaine over placebo. In one of these two studies the number of headache days had decreased from 18.1±5.3 to 8.8±4.8 during the first month after GON block and this reduction was significantly higher than with placebo12. The other study showed significant reduction in average monthly visual analogue scale from 3.93±1.80 to 1.55±1.42in the first month after injection and this reduction was significantly higher than with placebo[15].One of the three controlled studiesshowed no significant differences between blockage with anesthetic drug and placebo. In this last study it was found that the percentage of patients with at least a 50% reduction in the frequency of moderate or severe headache days was 30% both for intervention and placebo groups.[14]

One study evaluated the association or not of the anesthetic with triamcinolone and found no differences in the results in the group with and without association with this corticosteroid.[13] The other five studies evaluating CNBs for migraine prophylactic treatment were retrospective or observational and they includedoverall 339 patients. All these studies showed reduction in the number of days with pain and headache intensity when pre-treatment and post-treatment periods were compared. The frequency of reported adverse effects was very low, and only mild adverse events were recorded, the most frequent being local pain. Of the 1,205 patients treated with the block in all these 13 studies, none experienced serious adverse effects due to the procedure.

Table 1. Summary of the main findings of the selected studies on the efficacy and safety of CNBs in migraine.

Author, year	Drug used
Friedman, et al.[8]	Acute. Bilateral, GON block, 3 mL of 0.5% bupivacaine
Allen et al.[9]	Acute. Unilateral, GON block, 6.3 mL of 0.25% bupivacaine, 2.5 mL of 0.5% bupivacaine, 2.4 mL of 0.5%lidocaine
Ebied et al.[10]	Acute. Unilateral or Bilateral*, GON block, Lidocaine with dexamethasone**, bupivacaine with methylprednisolone**
Cuadrado et al.[11]	Acute. Bilateral, GON block, 2 mL of 0.5% bupivacaine
Inan et al.[12]	Preventive, Unilateral, GON block once a week. 1.5 mL of 0.5% bupivacaine
Kashipazha et al.[13]	Preventive, Bilateral, one GON block, 1 ml of 2% lidocaine with or without tramcinolone
Dilli et al.[14]	Preventive, Unilateral or Bilateral***, one GON block,0.25 mL of 0.5% bupivacaine + 0.5 mL of 20 mg methylprednisolone and 0,25 mL 1% lidocaine without epinephrine
Palamar et al.[15]	Preventive. Unilateral,USG guided one GON block. 1.5 mL of 0.5% bupivacaine
Unal-Artık et al.[16]	Preventive. Unilateral or Bilateral*, GON block once a week for the first month, after once month , 1.5 mL of 0.5% bupivacaine
Inan et al[17]	Preventive, Unilateral, GON block once a week, 2 mL of 0.25% bupivacaine
Okmen et al[18]	Preventive, Unilateral, GON block once a week, 2 mL of 0.5% bupivacaine
Schwarz et al[19]	Preventive. Bilateral, one GON block, 4 mg of Fortecortin and 4 mL of 1% lidocaine
Fernandes et al[20]	Preventive. Bilateral, one GON block or one MNCBs 2ml of 40 mg methylprednisolone, 1ml of 2% lidocaine, 1ml of 0.5% bupivacaine, 0.5ml of 2% lidocaine and 0.5 ml of 0.5% bupivacaine

*random **uninformed dose ***depending on the headache complaint

GON – great occipital USG - ultrasound MNCB –multiple cranial nerve blocks

Discussion

The present review shows that GON block is a potential effective treatment for migraine, either for symptomatic relief in attacks as for prophylactic treatment. Regarding safety, there was uniformity in the results of the studies indicating that adverse effects are rare and, when present, mild. No cases of serious adverse effects were reported in any of the reviewed studies.

Regarding CNBs in the treatment of migraine attacks, only one study was a placebo-controlled RCT.[8] It was a small study that showed significant blockade superiority, but with small percentages of complete headache remission, both after 30 minutes and 48 hours. Uncontrolled studies also showed apparently moderate results in the control of migraine attacks. The techniques used, whether with unilateral or bilateral blocks, as well as the anesthetic used and the eventual association with corticoids was not uniform across studies. Thus, the CNBs seems to be an alternative in the treatment of the migraine crisis, but its precise role remains unclear. As an advantage, its safety can be highlighted. As a disadvantage, the need of the availability of a professional trained in performing CNBs in the emergency unit stands out, which is not the case in most emergency services.

The knowledge about the effectiveness of using CNBs in the preventive treatment of migraine has also been compromised by the small size of the studies, the rarity of adequately controlled studies, the heterogeneity of the therapeutic schemes used, the non-uniformity of the evaluated outcomes, and the short follow-up time adopted in the studies. Two controlled studies showed a reduction in the number and intensity of attacks in the first 30 days after the blockade, however, another controlled study failed to demonstrate a higher percentage of treated patients reaching a 50% reduction in attacks in the first month after the intervention.[12,14,15] In this study, the rate of patients achieving this outcome was quite low in both groups. Uncontrolled studies have shown a reduction in the frequency of attacks and a reduction in the impact of migraine up to 3 months after the blockade, in comparison with the pre-blockade period. However, these results must be interpreted with caution, as it is known that treatment modality (injection vs pill) may play a role in the presence and magnitude of placebo response, since it is associated with patients' expectations.[21]

CNBs are an easy and low-cost procedure.The American Headache Society (AHS) suggests injection one third of the distance between the external occipital protuberance and the mastoid process for GON block. In one study it is suggested that there is benefit in using the ultrasound device to detect the exact location of the GON for effective blockade. Although this seems reasonable, it should be kept in mind that the need for ultrasound equipment makes the procedure more expensive and therefore reducing the availability of professionals and services qualified to perform the procedure[15]. There is no evidence to indicate superiority in performing unilateral or bilateral blocks, GON blocks or multiple cranial nerves blocks.[20] The decisions regarding the procedure in clinical practice rely much more on the physician's experience than on clear evidence.

Despite the low level of evidence, CNBs have their place in the treatment of migraine, for instance, in patients with unavoidable adverse effects with other treatments, whether for attacks or prophylactic treatment[5]. In addition, CNBs may be an alternative when conventional treatments are contraindicated as for the treatmentof migraine during pregnancy, considering the safety in this group of patients.[5,6] CNBs can also be used as an alternative for washout or bridging therapy when discontinuing analgesics in patients with analgesic overuse headache, although there is still no robust evidence in this regard.[10] CNBs can also be used as an adjunctive therapy in patients who are already on prophylactic treatment, especially if insufficient response has been achieved with conventional preventive treatment.[12] CNBs contraindications are rare and include infection and malformation at the injection site and allergy to anesthetics. CNBs should not be performed in patients using anticoagulants, or in those with coagulation disorders and bleeding risk.[5] Adverse effects are rare and mild and include pain at the application site, momentary dizziness during the procedure, vasovagal symptoms, cervical and lumbar pain after the blockade, facial edema, and facial redness.

In conclusion, the use of CNBs in the treatment of migraine is an alternative for selected cases and when theattending physician has expertise in performing it. The low level of evidence of CNBs for migraine makes it necessary to carry out well-designed controlled studies. Only with them it will be possible to define a precise role for CNBs in the treatment of migraine. Until then, the CNBs will remain as an additional resource that will be used in a non-standard way, depending on the experience of the physician, and the individual protocols of each headache service.

Conflict of interest: No conflict of interest
Financing: No funding
Authors' contribution: All the authors gave substantial contributions to manuscript.

Annelise Akemi Higa Lee
https://orcid.org/0000-0002-0796-7156
Renan Barros Domingues
https://orcid.org/0000-0002-6058-7937

References

1. Ashina M, Buse DC, Ashina H, Pozo-Rosich P, Peres MFP, Lee MJ, . . . Dodick DW. **Migraine: integrated approaches to clinical management and emerging treatments.** *The Lancet* 2021;397(10283):1505-1518 Doi: 10.1016/s0140-6736(20)32342-4
2. Ashina M, Katsarava Z, Do TP, Buse DC, Pozo-Rosich P, Ozge A, . . . Lipton RB. **Migraine: epidemiology and systems of care.** *Lancet* 2021;397(10283):1485-1495 Doi: 10.1016/S0140-6736(20)32160-7

3. Headache Classification Committee of the International Headache S. **The International Classification of Headache Disorders, 3rd edition (beta version).** *Cephalalgia* 2013;33(9):629-808 Doi: 10.1177/0333102413485658
4. Cutrer FM. **Pathophysiology of migraine.** *Semin Neurol* 2006;26(2):171-180 Doi: 10.1055/s-2006-939917
5. Özge A and Uluduz D (2019) **Introduction to interventional procedures; timing and patient selection.** In: Ozge A, Uluduz D, Karadas O, Bolay H (eds) *Peripheral interventional management in headache*. Springer, pp 7–16. Doi: 10.1007/978-3-030- 10853-3
6. Ashkenazi A, Blumenfeld A, Napchan U, Narouze S, Grosberg B, Nett R, . . . Lipton RB. **Peripheral Nerve Blocks and Trigger Point Injections in Headache Management - A Systematic Review and Suggestions for Future Research.** *Headache: The Journal of Head and Face Pain* 2010;50(6):943-952 Doi: 10.1111/j.1526-4610.2010.01675.x
7. Caputi CA and Firetto V. **Therapeutic Blockade of Greater Occipital and Supraorbital Nerves in Migraine Patients.** *Headache: The Journal of Head and Face Pain* 1997;37(3):174-179 Doi: 10.1046/j.1526-4610.1997.3703174.x
8. Friedman BW, Mohamed S, Robbins MS, Irizarry E, Tarsia V, Pearlman S and John Gallagher E. **A Randomized, Sham-Controlled Trial of Bilateral Greater Occipital Nerve Blocks With Bupivacaine for Acute Migraine Patients Refractory to Standard Emergency Department Treatment With Metoclopramide.** *Headache: The Journal of Head and Face Pain* 2018;58(9):1427-1434 Doi: 10.1111/head.13395
9. Allen SM, Mookadam F, Cha SS, Freeman JA, Starling AJ and Mookadam M. **Greater Occipital Nerve Block for Acute Treatment of Migraine Headache: A Large Retrospective Cohort Study.** *The Journal of the American Board of Family Medicine* 2018;31(2):211-218 Doi: 10.3122/jabfm.2018.02.170188
10. Ebied AM, Nguyen DT and Dang T. **Evaluation of Occipital Nerve Blocks for Acute Pain Relief of Migraines.** *The Journal of Clinical Pharmacology* 2019;60(3):378-383 Doi: 10.1002/jcph.1528
11. Cuadrado ML, Aledo-Serrano Á, López-Ruiz P, Gutiérrez-Viedma Á, Fernández C, Orviz A and Arias JA. **Greater occipital nerve block for the acute treatment of prolonged or persistent migraine aura.** *Cephalalgia* 2016;37(8):812-818 Doi: 10.1177/0333102416655160
12. Inan LE, Inan N, Karadaş Ö, Gül HL, Erdemoğlu AK, Türkel Y and Akyol A. **Greater occipital nerve blockade for the treatment of chronic migraine: a randomized, multicenter, double-blind, and placebo-controlled study.** *Acta Neurologica Scandinavica* 2015;132(4):270-277 Doi: 10.1111/ane.12393
13. Kashipazha D, Nakhostin-Mortazavi A, Mohammadianinejad SE, Bahadoram M, Zandifar S and Tarahomi S. **Preventive Effect of Greater Occipital Nerve Block on Severity and Frequency of Migraine Headache.** *Global Journal of Health Science* 2014;6(6):Doi: 10.5539/gjhs.v6n6p209
14. Dilli E, Halker R, Vargas B, Hentz J, Radam T, Rogers R and Dodick D. **Occipital nerve block for the short-term preventive treatment of migraine: A randomized, double-blinded, placebo-controlled study.** *Cephalalgia* 2014;35(11):959-968 Doi: 10.1177/0333102414561872
15. Palamar D, Uluduz D, Saip S, Erden G, Unalan H and Akarirmak U. **Ultrasound-guided greater occipital nerve block: an efficient technique in chronic refractory migraine without aura?** *Pain Physician* 2015;18(2):153-162
16. Ünal-Artık HA, İnan LE, Ataç-Uçar C and Yoldaş TK. **Do bilateral and unilateral greater occipital nerve block effectiveness differ in chronic migraine patients?** *Neurological Sciences* 2017;38(6):949-954 Doi: 10.1007/s10072-017-2861-5
17. Inan N, Inan LE, Coskun O, Tunc T and Ilhan M. **Effectiveness of Greater Occipital Nerve Blocks in Migraine Prophylaxis.** *Noro Psikiyatr Ars* 2016;53(1):45-48 Doi: 10.5152/npa.2015.10003
18. Okmen K, Dagistan Y, Dagistan E, Kaplan N and Cancan E. **Efficacy of the greater occipital nerve block in recurrent migraine type headaches.** *Neurol Neurochir Pol* 2016;50(3):151-154 Doi: 10.1016/j.pjnns.2016.01.015
19. Schwarz A, Ziegeler C, Daneshkhah S, May A and Luedtke K. **Predicting the outcome of the greater occipital nerve block - an observational study on migraine patients with and without musculoskeletal cervical impairment.** *Cephalalgia* 2021;41(1):78-89 Doi: 10.1177/0333102420954518
20. Fernandes L, Khan N, Dobson J, Randall M and Idrovo L. **Multiple Cranial Nerve Blocks as an Alternative Preventative Therapy for Chronic Migraine.** *Headache* 2020;60(5):981-987 Doi: 10.1111/head.13792
21. Anderson S, Stebbins GT. **Determinants of placebo effects.** *Int Rev Neurobiol*. 2020;153:27-47. Doi: 10.1016/bs.irn.2020.03.029