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Peripheral nerve block in patients with medication-overuse headache: systematic review and meta-analysis

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Abstract

Background Medication-overuse headache (MOH) is a disabling condition, particularly in settings with limited access to advanced preventive therapies. Peripheral nerve blocks (PNB) may offer a pragmatic option to reduce headache burden during MOH management. We aimed to assess the efficacy and safety of PNB in adults with MOH.

Methods We conducted a systematic review in January 2025 using Scopus, PubMed, Embase, Web of Science, and the Cochrane Library. Randomized clinical trials comparing PNB with standard of care or other active interventions in adults with MOH were eligible. Primary outcomes included headache frequency, headache intensity, successful detoxification, and adverse effects. Risk of bias was assessed using the Cochrane Risk of Bias Tool 2.0. Random-effects meta-analyses were conducted when appropriate, and certainty of evidence was evaluated using the GRADE approach.

Results Three randomized clinical trials involving 249 adults with MOH were included. All trials evaluated bilateral greater occipital nerve blocks, with variability in anesthetic agents, number of sessions, and use of additional nerve block sites. Standard of care consisted of medication withdrawal, hydration, and preventive therapy. Follow-up ranged from 1 to 4 months. Compared with standard of care alone, a single PNB session significantly reduced headache frequency (–4.56 days/month; 95%CI: − 7.46 to − 1.66) and monthly rescue medication use (–2.30 doses of medication/month; 95%CI: − 2.71 to − 1.89), without significant effects on headache intensity or detoxification success. Multiple PNB sessions were associated with greater reductions in headache frequency (–9.00 days/month; 95%CI: − 9.45 to − 8.55), headache intensity (–2.65 units in visual analog scale; 95%CI: − 2.77 to − 2.53), and monthly rescue medication use (–6.70 doses of medication/month; 95%CI: − 7.10 to − 6.30), with low to moderate certainty of evidence. Compared with topiramate, a single PNB session did not reduce headache frequency (+ 1.50 days/month; 95%CI: +1.21 to + 1.79), with no differences in headache intensity (very low certainty). Adverse effects were only reported by one trial, with no significant differences compared with topiramate.

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Conclusion PNB, particularly when administered in multiple sessions, may reduce headache frequency and intensity in adults with MOH when other therapies are unavailable. However, given the limited evidence and low certainty, further high-quality trials are needed to define optimal protocols and long-term effectiveness and safety.

Keywords Nerve block, Headache disorders, secondary, Systematic review, Meta-Analysis

Background

Medication-overuse headache (MOH) is a secondary form of headache that primarily affects individuals with primary headache disorders and a high burden of acute treatment use [1]. It is characterized by occurring on more than 15 days per month for at least three months in individuals who overuse analgesics or triptans to manage a pre-existing headache condition, such as migraine [2]. Its global prevalence ranges from 0.5% to 7.2%, with a higher incidence among women aged 30 to 50 years [3]. MOH is among the top 20 causes of disability worldwide and accounts for up to 50% of consultations in specialized headache clinics [4, 5] and one fifth of all headache-attributed health loss [6].

The pathophysiology of MOH involves mechanisms of both central and peripheral sensitization, as well as alterations in pain modulation. Peripheral sensitization occurs when nociceptors lower their activation threshold in response to inflammatory mediators, leading to localized hyperalgesia [7]. Central sensitization, in turn, involves neuronal hyperexcitability at both spinal and supraspinal levels, amplifying nociceptive signals and promoting pain chronification [8]. Prolonged use of medications such as triptans and/or opioids increases the expression of calcitonin gene-related peptide (CGRP) and neuronal nitric oxide synthase, thereby perpetuating the pain cycle [9]. In addition, genetic, emotional, and psychological factors may contribute to the development and persistence of this condition [5], altering brain functional connectivity [10].

Therapeutic management primarily involves patient and family education, behavioral intervention, and the prevention of medication overuse [11, 12]. Detoxification through the withdrawal of the overused medications, along with the initiation of preventive treatment for the underlying primary headache, constitutes a fundamental cornerstone of management [13]. The greater occipital nerve block have been proposed as a useful therapeutic alternative in different headache disorders [14, 15]. This minimally invasive technique is performed on an outpatient basis by infiltrating local anesthetics near specific nerves, thereby interrupting pain signaling pathways and modulating neurogenic inflammation; this approach helps to reduce central sensitization and break the cycle of chronic pain [16, 17].

The effects of peripheral nerve blocks have been studied as acute rescue and preventive treatment in patients with chronic headaches. During the first 30 min, a reduction of up to 45% in acute headache intensity has been reported, with sustained effects lasting up to six months [18]. In cases of chronic migraine, greater occipital nerve block has demonstrated efficacy in reducing attack frequency up to two months [19]. Some studies suggest benefits even in the absence of concomitant acute medication use, although rescue effectiveness appears to be lower in MOH, where failure rates of occipital nerve block reach up to 44%, compared to 16% in other headache types [20]. Thus, the final intend of this intervention could work as a transitional therapy with short-term efficacy, during detoxification, with long enough effect until preventive treatment starts its effect. However, uncertainties remain regarding the efficacy and safety of the peripheral nerve block in this specific subgroup of chronic headaches with MOH. Furthermore, there could be differences in the effects between single and multiple applications of peripheral nerve block [21].

A recent systematic review suggests that peripheral nerve block, when combined with preventive medication, may reduce the number of headache days per month in patients with MOH [22]. However, this analysis may not include all available studies, lacks the GRADE approach for assessing the certainty of evidence, and does not address potential adverse effects of the procedure, such as nerve injury, infection, hematoma, or systemic toxicity [23, 24]. In addition, the peripheral nerve block is not yet established as an only acute therapy, a disease-modifying therapy for MOH, or a transitional intervention that may facilitate medication withdrawal and support the initiation of preventive treatments for the underlying primary headache disorder. Therefore, the aim of the present study is to synthesize the available evidence evaluating the benefits and adverse effects of peripheral nerve block, compared to standard of care or other treatments, in patients with MOH.

Methods

Study design

A systematic review with meta-analysis was conducted in accordance with the PRISMA recommendations for reporting systematic reviews [25]. The protocol for the present study was registered at Universidad Científica del Sur (Registration Code: PRE-15–2025-00046) and on the PROSPERO online platform (CRD420250617669).

Population and selection criteria

We searched for primary randomized controlled trials (RCT) and observational studies involving patients with MOH, according to ICHD-3 criteria [26]. These studies assessed peripheral nerve block as either acute or chronic treatment, compared with standard of care or other therapy control groups, whether conventional or invasive, and reported outcomes related to the reduction in headache intensity and frequency, adverse effects, post-intervention quality of life, successful detoxification, and headache-related disability were included. Studies were excluded if they included patients with others chronic headache or migraine without specifying results in the MOH subpopulation. Studies with a control group using an alternative method of peripheral nerve block, those with insufficient outcome data for the population of interest, as well as reviews, conference abstracts, pre-post studies without control groups, or editorials were excluded. Case reports or series with fewer than 10 patients and those lacking full-text access were also excluded.

Search strategy and databases

A systematic search strategy was designed in Scopus using the keywords "Headache," "Overuse," and "Nerve block," which was then adapted for PubMed-Medline, Web of Science, Cochrane Central, and Embase (including Clinicaltrials.gov) (Supplementary Material 1). The search included products published until January 2nd, 2025. Additionally, references and citations of the selected studies were reviewed to include any potential additional studies not considered in the initial search, on March 5, 2025.

Study selection

The results from each database were downloaded in a format compatible with EndNote™ X8 (Clarivate, Philadelphia, USA) for import and duplicate removal. Unique records were transferred to the online software Rayyan (Rayyan Systems Inc., Cambridge, USA), where three reviewers (PAAT, CFCC, and MESS) independently reviewed a random sample of 20 records (titles and abstracts) in a pilot test to assess the agreement (≥ 80%) in the application of the selection criteria. Following this, they completed the review of the titles and abstracts for the remaining records. Each record was evaluated independently, blinded, and in triplicate by the reviewers. A fourth reviewer resolved any discrepancies when necessary (CAAR). Full-text articles of the studies included in the initial review were then assessed following the same methodology previously described, including only those studies that met the selection criteria.

Additionally, when the studies included in this systematic review were obtained, the reference lists of the full-text original studies and their citations in Google Scholar (https://scholar.google.com/) were reviewed to identify studies not detected in the first phase. This was done following the same methodology previously mentioned.

Data collection

Prior to data extraction, a table was designed in Excel to gather key information from each study: study country, population characteristics, period, inclusion/exclusion criteria, mean age and sex, intervention and control (drug, dose, frequency, route), blocking technique, standard of care, outcomes, follow-up, funding, and conflicts of interest. Quantitative outcomes, such as the number of participants, events, mean, and standard deviation, were recorded. In the event that the results were presented only in the form of graphs, without specifying absolute or relative numerical data, the online application Plot Digitizer (https://plotdigitizer.com/app; pOrbital ©) [27] was used to calculate the quantitative results and subsequently extract them in the data collection sheet. The table was validated through a pilot test with three reviewers and two randomly selected studies. The reviewers independently extracted the data, blinded and in triplicate.

Primary outcomes

Headache intensity was measured using the Visual Analog Scale for pain, as well as the frequency of headaches, expressed in the number of headache days per month. Adverse effects were determined by the presence or absence of these following the intervention. Also, successful detoxification was defined as no use of overused medication with remission to episodic headache, a decrease in symptomatic medication use to less than 15 days per month, or a significant improvement in quality of life. Originally, the disappearance of headache and headache-related disability, using the HIT-6 or MIDAS tools, were considered also as primary outcome. However, there was no RCT assessing these last outcomes.

Secondary outcomes

Rescue medication use was determined by the monthly number of doses of acute medications for headache relief that the patients reported after the intervention.

Assessment of the quality of selected studies

The selected RCTs with available full text were individually assessed using the Cochrane Risk of Bias Tool version 2 for parallel RCTs [28]. Two researchers (CAAR and GM) conducted the assessment independently, with a consensus reached between them in case of discrepancies. The certainty of the evidence was analyzed using GRADE, categorized as very low, low, moderate, or high,

based on factors such as bias, publication, inconsistency, indirectness, and imprecision [29]. This assessment was performed independently for each identified primary and secondary outcome.

Statistical processing and analysis

The initial analysis of the included studies was qualitative, individually describing their similarities and discrepancies. The characteristics of the populations, interventions, controls, and evaluated outcomes were detailed, summarizing the information in a table. Given the heterogeneity among the studies, a subgroup analysis was performed based on the type of intervention (single session or multiple) and control (standard of care or topiramate).

Subsequently, if sufficient information from at least two studies was available, a meta-analysis was performed comparing the intervention and control, presented in forest plots by outcome. A random-effects model was used due to the expected high heterogeneity. For dichotomous outcomes, the risk ratio with 95% confidence intervals was calculated, and for continuous outcomes, the weighted mean difference was used. Heterogeneity was assessed using the I^2 test, considering it high if ≥ 40%, and identifying its potential causes. Publication bias was not assessed due to the presence of fewer than 10 studies in total. Statistical analysis was conducted using RevMan 5.4 (Cochrane Collaboration, London, England), with a significance level set at $p < 0.05$.

Results

Study selection

A total of 1,875 records were obtained from the databases searched. After removing duplicates, 899 records were screened. The full text of 25 records was then reviewed, resulting in the inclusion of 3 studies, which consisted of two scientific articles [30, 31] and one RCT protocol with available results [32]. No observational study was found. The supplementary search in citations and bibliographic references did not identify additional studies (Fig. 1 and Supplementary Material 2).

Study characteristics

Three RCT were analyzed, including a total of 249 participants with MOH. No observational studies were found. Two studies were conducted in Turkey [31, 32] one in Iran [30], none of which reported conflicts of interest or funding. These studies included adults aged 18 and older diagnosed with MOH due to triptans [31] and/or other medications [30]. All peripheral nerve block interventions involved bilateral greater occipital nerve blocks but varied in the medication used. Two RCT assessed local anesthetic combined with corticosteroids (lidocaine with triamcinolone [30] and bupivacaine with triamcinolone

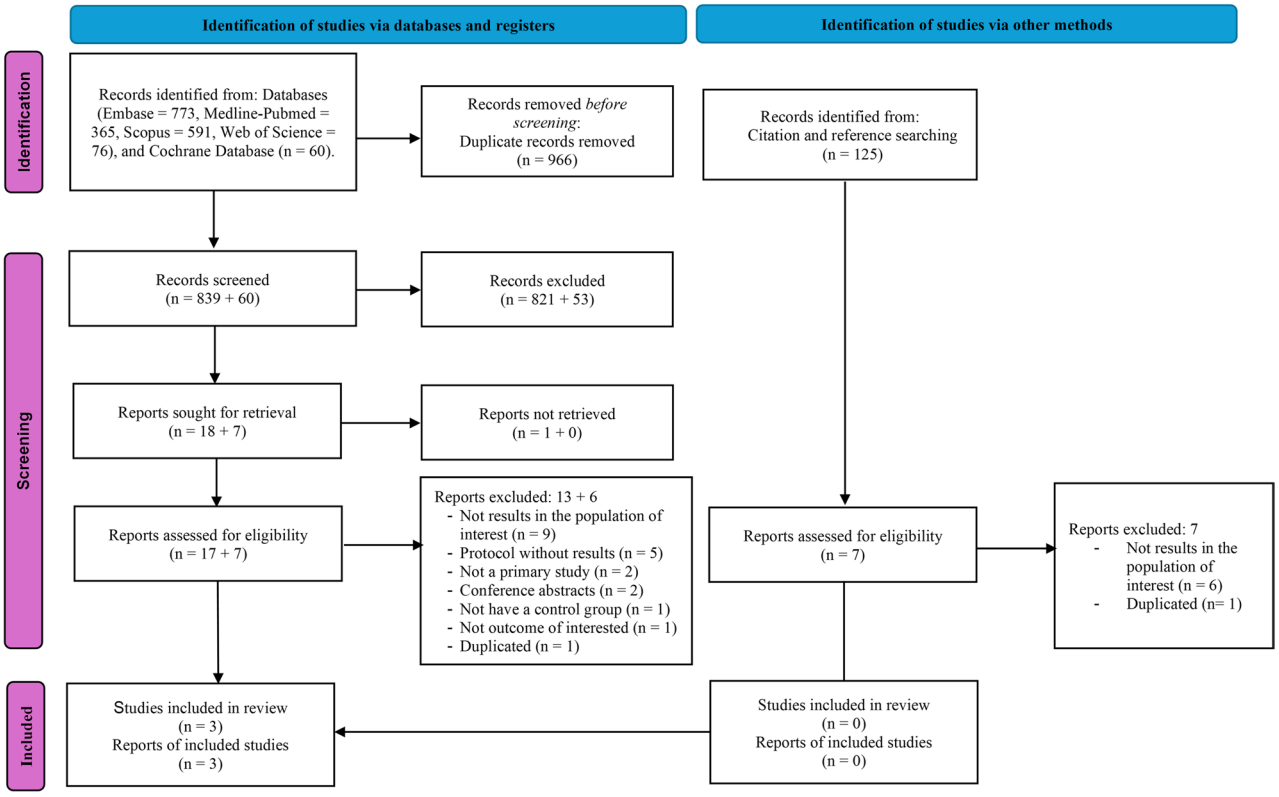

Fig. 1 Studies selection flow diagram

[32]) and the remained used lidocaine alone [31]. They also varied in frequency (a single session [30–32] or weekly sessions for three weeks [31]), or whether they had co-interventions with an additional block (supratrochlear block) [32].

All studies included usual care in both groups, which consisted of gradual or abrupt medication withdrawal, accompanied by hydration with or without the use of preventive medication. Two of the three studies used usual care without intervention as the control group [30, 31], while the other study used topiramate as the preventive medication in the control group [32]. Finally, outcomes were assessed with a follow-up period of 1 to 4 months. Monthly rescue medication use was reported as the number of doses of acute medication intake per month. While, headache intensity outcome was reported using the visual analog scale, showing a reduction in units within the scale from 0 to 10. Only one study reported that no adverse effects were identified related to the intervention [32]. The remaining studies did not assess adverse effects. No results were reported by the studies on the outcomes of headache disappearance or headache-related disability (Table 1).

Table 1 Characteristics of the studies included in the systematic review

Author and Year of Publication (Country)	Study Population	Medication Overuse	Usual Care	Intervention	Application Technique	Application Frequency	Control	Outcomes
Arab 2021 (Iran) [30]	Adults aged 18 + with MOH (ICHD-3) and primary headache (episodic migraine, chronic migraine, and/or tension headaches) ($n = 54$) Age: 38.1 vs. 38.1 years old. Female: 59.3% vs. 66.7%	Triptans with or without simple/combination analgesics	Detoxification for 3 weeks. Neurologist and nutritionist care Promethazine syrup (5 mg/5 ml) 10 mg every 8 h during the first 10 days. Preventive pharmacological therapy without changes (beta-blockers, amitriptyline, topiramate, among others).	Bilateral greater occipital nerve block ($n = 27$)	Block Site: Middle medial third between the occipital protuberance and the mastoid process Volume: 1 ml (0.5 ml of 2% lidocaine and 0.5 ml [20 mg] of triamcinolone) at each site Technique: A 2 ml syringe and a 25-gauge needle were used	Single session	No intervention ($n = 27$)	Follow-up time: 3 months • Successful detoxification • Monthly Headache Days • Headache intensity
Karadaş 2016 (Turkey) [31]	Adults aged 18 to 60 with MOH (ICHD-3) ($n = 105$) Age: 36 vs. 38 vs. 37 years old. Female: 71.4% vs. 77.2% vs. 77.2%	Triptans	Abrupt withdrawal of triptans. Hydration with 2 to 3 L daily.	Bilateral greater occipital nerve block. Intervention 1 ($n = 35$) Intervention 2 ($n = 35$)	Block Site: 2 cm lateral and 2 cm inferior to the external occipital protuberance. Volume: 1.25 ml of 1% lidocaine at each site. Technique: The periosteum was reached using a 26-gauge needle, followed by a 1 mm needle withdrawal and lidocaine injection after a three-direction aspiration.	Intervention 1: Single session Intervention 2: One weekly session for 3 weeks	No intervention ($n = 35$)	Follow-up time: 4 months • Monthly Headache Days • Headache intensity • Monthly rescue medication
Ceylan 2020 (Turkey) [32]	Women aged 18 to 65 years with MOH ($n = 90$) Age: 32.7 vs. 32.9 years old.	Not specified	No specifications	Bilateral greater occipital nerve block + Bilateral supratrochlear nerve block ($n = 45$)	Block point: Middle third between the occipital tubercle and the mastoid process (ONB) and 1 cm medial to the superior orbital fissure (SNB). Volume: 1 mL (5 mg) of bupivacaine, 0.5 mL (20 mg) of triamcinolone, and 0.5 mL of NaCl 0.9% at each point (ONB) Volume: 0.8 mL (4 mg) of bupivacaine and 0.7 mL of NaCl 0.9% at each point (SNB) Technique: Performed with a 22-gauge needle.	Single session	Topiramate 100 mg ($n = 45$)	Follow-up time: 1 month • Adverse effects • Monthly Headache Days • Headache intensity

Effect of peripheral nerve block as a single session compared to standard of care

Two studies evaluated the effect of a single session of peripheral nerve block at 3 and 4 months in comparison to usual care alone [30, 31]. In the meta-analysis, it was found that peripheral nerve block decreased the monthly headache days by −4.56 days per month (95% CI: −7.46 to −1.66), but not the headache intensity by −2.61 units of visual analog scale (95% CI: −6.00 to + 0.78) (Fig. 2). According to the study by Karadaş 2017, the intervention also decreased the monthly use of rescue medication by −2.30 (95% CI: −2.71 to −1.89) [31]. Furthermore, according to the other study [30], no effect was found on the probability of achieving successful detoxification (RR: 1.13, 95% CI: 0.95 to 1.35). Most of these results had a very low certainty of evidence (Table 2).

Effect of peripheral nerve block compared to active control

Only one study compared bilateral greater occipital nerve block with bupivacaine and corticosteroids in a single session, combined with bilateral supratrochlear block, to topiramate as an active control [32]. It was found that, after one month, the intervention resulted in 1.50 more monthly headache days (95% CI: 1.21 more to 1.79 more), with no changes in the headache intensity (−0.45 less, 95% CI: −0.90 less to 0.00 more) (Fig. 2), nor the adverse effects (RR: 0.18, 95% CI: 0.01 to 3.65). Only two cases of dizziness were reported within topiramate arm, and no case within nerve block arm. No serious adverse events were reported with the intervention nor the control. All these results had a very low certainty of evidence (Table 2).

Effect of peripheral nerve block in multiple sessions compared to standard of care

One study evaluated the effect of peripheral nerve block with at three sessions per month, in comparison to usual care alone [31]. The intervention, after four months, decreased the monthly headache days by −9.00 days (95% CI: −9.45 to −8.55), the intensity of headaches by −2.65

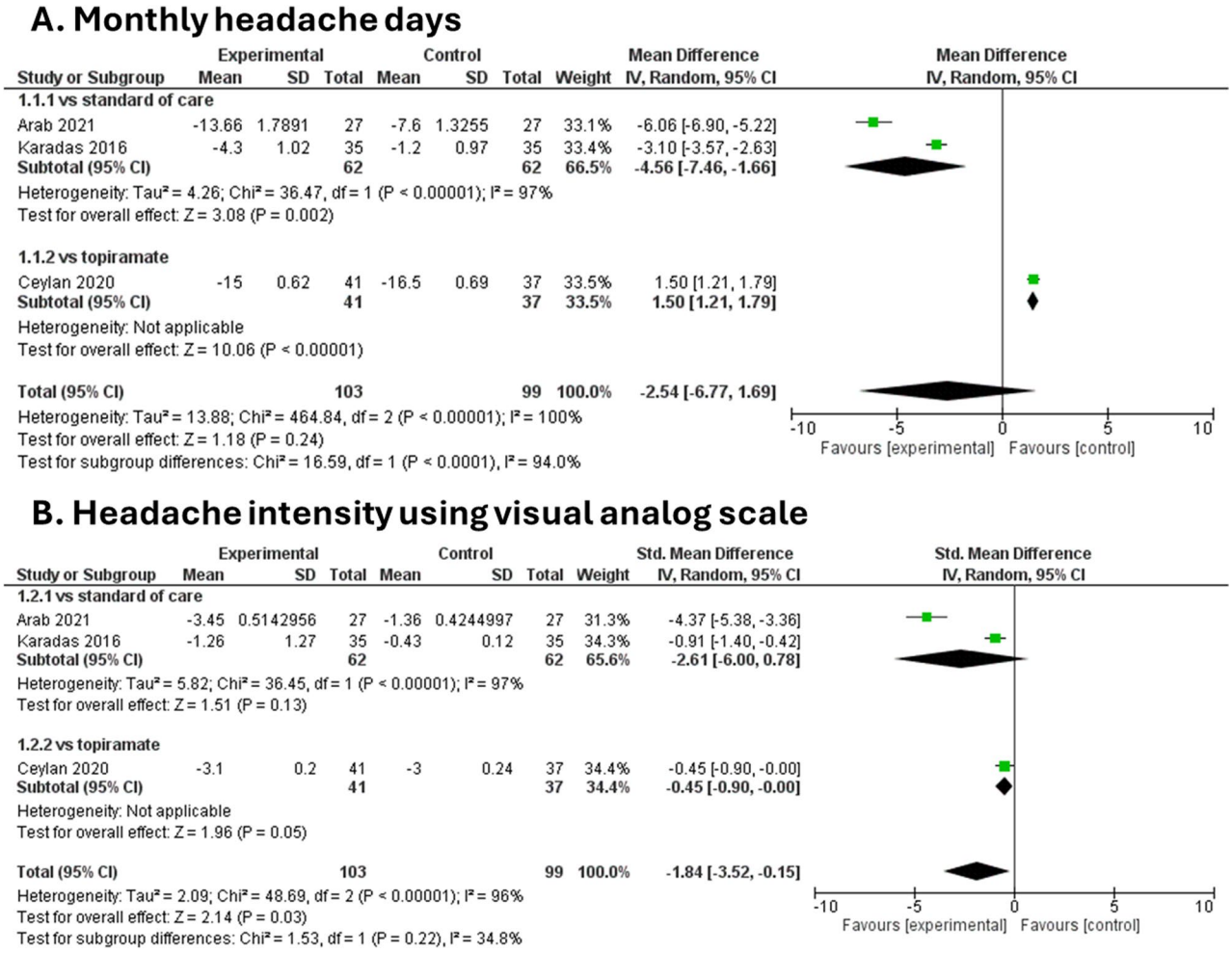

Fig. 2 Effect on (**A**) monthly headache days and (**B**) headache intensity of peripheral nerve block in patients with medication-overuse headache according to the control group

Table 2 Summary of findings

Population: Adults with medication overuse headache **Intervention: Peripheral nerve block (single session)** **Control: Standard of care**							
Outcomes and Follow-up	**Patients (Studies) *N***	**Relative Effect (95% CI)**	**Absolute Effects (95% CI)**			**Certainty**	**Interpretation**
			Standard of Care	**Peripheral Nerve Block**	**Absolute Difference**		
Monthly Headache Days Follow-up: Range 3 to 4 months	124 (2 RCTs)	-	4.40 days less	**8.96 days less**	**4.56 days less** (7.46 less to 1.66 less)	⨁◯◯◯ Very Low[a, b,c]	Peripheral nerve block (single session) may reduce monthly headache days, but the evidence is very uncertain.
Headache Intensity, Visual Analog Scale Follow-up: Range 3 to 4 months	124 (2 RCTs)	-	0.80 units less	**2.38 units less**	**2.61 units less** (6.00 less to 0.78 more)	⨁◯◯◯ Very Low[a, c,d]	Peripheral nerve block (single session) has little to no effect on headache intensity, but the evidence is very uncertain.
Monthly Use of Rescue Medication Follow-up: 4 months	(1 RCTs)	-	1.80 doses less	**4.10 doses less**	**2.30 doses less** (2.71 less to 1.89 less)	⨁⨁◯◯ Low[a]	Peripheral nerve block (single session) may reduce monthly use of rescue medication sightly.
Successful Detoxification Follow-up: 3 months	54 (1 RCT)	**RR = 1.13** (0.95 to 1.35)	852 per 1000	**963 per 1000** (809 per 1000)	**111 more events per 1000** (from 43 fewer to 298 more)	⨁◯◯◯ Very Low[a, e]	The evidence is very uncertain about the effect of peripheral nerve block (single session) on successful detoxification.
Population: Adults with medication overuse headache **Intervention: Peripheral nerve block (single session)** **Control: Topiramate**							
Monthly Headache Days Follow-up: Mean 1 month	78 (1 RCT)	-	16.50 days less	**15.00 days less**	**1.50 days more** (1.21 more to 1.79 more)	⨁◯◯◯ Very low[a, b]	The evidence is very uncertain about the effect of peripheral nerve block (single session) on monthly headache days, compared to topiramate.
Headache intensity, Visual Analog Scale Follow-up: Median 1 month	78 (1 RCT)	-	3.00 units less	**3.10 units less**	**0.45 units less** (0.90 less to 0.00 less)	⨁◯◯◯ Very low[a, d]	Peripheral nerve block (single session) has little to no effect on headache intensity, compared to topiramate, but the evidence is very uncertain.
Adverse Effects Follow-up: 1 month	78 (1 RCT)	**RR = 0.18** (0.01 to 3.65)	54 per 1000	**10 per 1000** (1 to 197)	**44 less events per 1000** (from 54 fewer to 143 more)	⨁◯◯◯ Very low[a, f]	The evidence is very uncertain about the effect of peripheral nerve block (single session) on adverse effects, compared to topiramate.
Population: Adults with medication overuse headache **Intervention: Peripheral nerve block (multiple sessions)** **Control: Standard of care**							
Monthly Headache Days Follow-up: 4 months	(1 RCTs)	**-**	1.20 days less	**10.20 days less**	**9.00 days less** (9.45 less to 8.55 less)	⨁⨁◯◯ Low[b, g]	Peripheral nerve block (multiple sessions) may reduce the monthly headache days sightly.

Table 2 (continued)

Population: Adults with medication overuse headache **Intervention: Peripheral nerve block (multiple sessions)** **Control: Standard of care**							
Headache intensity, Visual Analog Scale Follow-up: 4 months	(1 RCTs)	-	0.47 units less	**3.12 units less**	**2.65 units less** (2.77 less to 2.53 less)	⨁⨁◯◯ Low[d, g]	Peripheral nerve block (multiple sessions) may reduce headache intensity sightly.
Monthly Use of Rescue Medication Follow-up: Mean 4 months	(1 RCTs)	-	1.80 doses less	**8.50 doses less**	**6.70 doses less** (7.10 less to 6.30 less)	⨁⨁⨁◯ Moderate[g]	Peripheral nerve block (single session) probably reduce the monthly use of rescue medication sightly.

RCT Randomized clinical trial, *CI 95%* 95% Confidence Interval, *RR* Relative Risk, Bold text represents the effect on intervention group and the absolute difference.

Explanations:

[a] Decreases two levels: Very serious risk of bias due to RoB 2.0 assessment, with moderate to high risk in the included primary studies

[b] Decreases one level: Serious imprecision because, in patients with 15 or more monthly headache days, the reduction of 4.56, 1.50 or, 9.00 days less would not reach the ideal target of up to 4 days of headache per month or less

[c] Decreases two levels: Very serious inconsistency due to moderate heterogeneity (I^2: 97%)

[d] Decreases one level: Serious imprecision because the reduction of 2.61, 0.45, or 2.65 units on the Visual Analog Scale does not achieve the minimally clinically important difference between 1 to 4 units

[e] Decreases one level: Serious imprecision because the effect size of 1.13 is small

[f] Decrease two levels: Very serious imprecision because of the low sample size and width confidence intervals

[g] Decreases one level: Serious risk of bias due to RoB 2.0 assessment, with moderate risk in the included primary studies

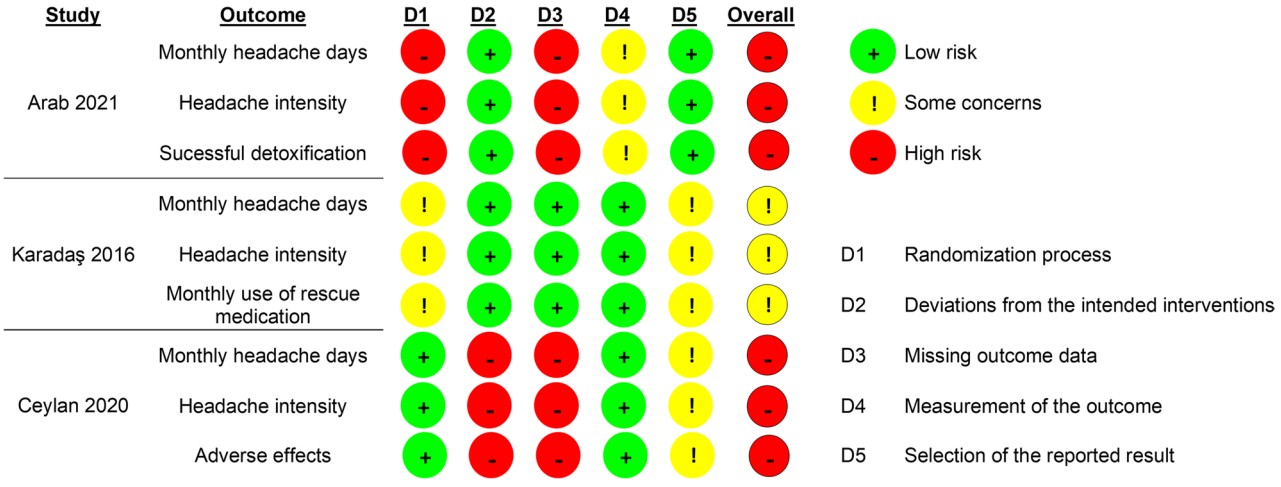

Fig. 3 Risk of bias in individual studies

units of visual analog scale (95% CI: −2.77 to −2.53), and the monthly use of rescue medication by −6.70 (95% CI: −7.10 to −6.30). All these results had a low to moderate certainty of evidence (Table 2).

Risk of bias and certainty of the evidence

The individual risk of bias in the evaluated studies was high, mainly considering the randomization process, missing outcome data, and selective reporting of results (Fig. 3). The high risk of bias in the individual studies, along with the imprecision of the overall results and the inconsistency of results, led to the certainty of the evidence being very low for most of the outcome measures analyzed in the comparison between single peripheral nerve block versus placebo or topiramate. However, the certainty of evidence was low and moderate for the outcomes in the comparison between multiple peripheral nerve block versus placebo (Table 2).

Discussion

Summary of results

Three RCT involving 249 adults with MOH were analyzed. The peripheral nerve block intervention included bilateral greater occipital nerve block, using lidocaine or bupivacaine, with or without triamcinolone, varying in method and session frequency. Despite the limited certainty of evidence due to high risk of bias, the results suggest that peripheral nerve block plus usual care, compared to only usual care (which consisted of medication withdrawal, hydration with or without the use of preventive medication), may have a positive impact on reducing the headache frequency and medication use in patients

with MOH, especially if multiple sessions are used. However, there is no information indicating that this intervention leads to a significant and lasting improvement in patients' quality of life or guarantees successful detoxification. The lack of uniformity in the technique processes, the limited number of studies, and the insufficiency of long-term assessment of adverse effects and quality of life limit the ability to suggest a recommendation for clinical practice decision-making.

Effectiveness and comparison with other preventive therapies

Peripheral nerve block might reduce by between 4 and 9 headache days per month, between 1 and 2 units in visual analog scale of pain intensity, and between 2 and 6 doses of monthly medication used for acute headache treatment. However, this reduction does not appear to be clinically relevant for reducing headaches to 4 days or less per month [33], reduce the pain intensity in their minimum clinically important difference between 1 and 4 [34], reduce to less than 15 days of rescue medication, and finally achieving successful detoxification. Other interventions like topiramate [35] or botulinum toxin [36] also show a reduction in headache days per month, compared to placebo. However, these interventions did demonstrate a reduction of at least 50% in the number of migraine days per month, as did monoclonal anti-CGRP antibodies such as eptinezumab, fremanezumab, galcanezumab, and erenumab [35, 37, 38]. This could be due to the blocking of CGRP binding to its receptors in nociceptive pathways, which inhibits peripheral and central sensitization of pain, as well as preventing its amplification and restoring its modulatory mechanisms [9].

On the other hand, when comparing peripheral nerve block with topiramate treatment, the findings show a slight inclination in favor of topiramate, although available follow up data up to one month, which means that it could have a greater effect favors topiramate. This is consistent with other analyses that compare different interventions individually, finding discrepant results, suggesting that topiramate and monoclonal anti-CGRP antibodies [22, 35] may be superior among the remaining available therapeutic options including peripheral nerve block. Despite the positive effect of peripheral nerve block in patients with MOH, compared to standard of care, these results are insufficient to consider as first-line therapy or better than other pharmacological evidence-based therapies. It is probably that a combined approach including overused medication withdrawn, preventive medication, patient education, behavioral measures offers a greater impact on quality of life in patients with MOH [39]. However, there is the need for better designed RCT comparing these multiple interventions combinations to make better decision making in clinical practice.

Heterogeneity and clinical subgroups

The variability in the frequency of peripheral nerve block sessions makes it difficult to identify which protocol optimizes the benefit. According to one RCT, administering the peripheral nerve block in multiple sessions may provide greater therapeutic benefits compared to a single application [31]. The single application of the nerve block has shown benefits for different primary headaches, including chronic migraine [40–42], especially as acute treatment. However, when compared in a retrospective study to weekly applications over four weeks, the multiple session intervention had better results in reducing acute treatment, intensity and frequency of attacks, and improving quality of life [43]. The repetitive application of peripheral nerve block is proposed as part of the preventive management of headaches [44], as with more sessions of the intervention, there is greater exposure to it, and its effect may become more sustained.

The variability in the intervention regarding the type of medication used (lidocaine vs. bupivacaine, with/without triamcinolone), the injected volume, and the method of application was also observed across studies. The available data doesn't clearly demonstrate an additional benefit of corticosteroids in peripheral nerve blocks for MOH. This observation is consistent with broader headache literature suggesting limited efficacy of corticosteroids in most headache disorders [19], except for cluster headache [45], and should be considered when designing future protocols.

Additionally, it is important to evaluate whether the response to the intervention differs between MOH induced by triptans versus opioids versus other rescue treatments. Although, none of the included RCT stratified outcomes according to the type of overused medication, this is clinically relevant, as opioid-related MOH may involve different neurobiological mechanisms and treatment response compared with triptan-related MOH or NSAIDs-related MOH [46], including differential CGRP modulation [9]. In this regard, the heterogeneity among the studies makes it difficult to formulate a recommendation for or against peripheral nerve block specifically for some specific subpopulation.

Implications for clinical practice and future research

MOH is a condition whose treatment success improves significantly when addressed in an integrated manner, combining various therapies [2]. According to the results presented in this systematic review, peripheral nerve block might be considered as a therapeutic transitional option for some patients with MOH. However, on its own, it is unlikely to be sufficiently effective to achieve therapeutic success due to its lower effect compared to topiramate. To achieve an improvement that has a significant impact on patients' quality of life and even the

disappearance of MOH, it is likely that synergy between pharmacological and non-pharmacological interventions should be sought within a multidisciplinary management framework [22]. Therefore, peripheral nerve block could be considered as a transitional or bridging strategy during the acute detoxification process, while waiting for the effect's initiation of evidence-based preventive therapies in MOH.

This review highlights the need to consider different aspects regarding the intervention type and the subpopulation group in order to assess the effectiveness of peripheral nerve block in adults with MOH. Single sessions, and more importantly multiple sessions, of peripheral nerve block appear as a potential minimally invasive alternative that provides some reduction in the frequency, intensity, and medication used in adults with MOH in cases where botulinum toxin or monoclonal antibodies are not available or cannot be used. However, to solidify its use, further studies are needed to confirm these results, compare application methods, include a homogeneous active control group, employ robust methodology in the design and execution of RCT, conduct long-term follow-up, and evaluate patient-centered outcomes: quality of life, objective detoxification rate, and detailed assessment of adverse effects.

Beyond clinical effectiveness, the feasibility of implementing peripheral nerve blocks as a repetitive or long-term strategy warrants careful consideration. Repeated interventional procedures require trained personnel, dedicated procedural time, and appropriate outpatient infrastructure, which may limit scalability in routine clinical practice. These organizational demands, along with procedural costs and patient adherence to repeated visits, may challenge the implementation of this intervention, particularly in resource-constrained settings. Consequently, while multiple peripheral nerve blocks sessions appear to provide greater short-term benefit than a single application, their use should be individualized and primarily considered as a supportive or transitional intervention rather than a chronic preventive strategy.

Limitations and strengths of the study

The main limitation is the limited number and quality of included studies, one of which possibly presented incomplete and non-peer reviewed results, and where most of our outcome's results are based in a single RCT. Also, some outcomes as successful detoxification was a poorly standardized outcome only by one RCT, thus it is not comparable to other detoxification outcomes in other trials of MOH [47]. Similarly, the heterogeneity in the protocol for peripheral nerve block application and the substantial methodological weakness of individual RCT, including poor randomization, lack of blinding, missing outcome data, and lack of peer-review significantly increase their risk of bias. These limitations decreased the precision and confidence of the pooled results, considering them as exploratory, with limitation to make a strong recommendation regarding the use of this intervention in everyday clinical practice. In addition, although an updated search through January 2025, no contemporary RCT evaluating peripheral nerve block in MOH was identified, highlighting a significant and persistent evidence gap.

Despite these limitations, strengths of this review are the prespecified protocol, comprehensive database searching, use of GRADE to transparently rate certainty, presentation of a subgroup analysis approach for the intervention, reflecting real-world options for a better understanding of the effectiveness of peripheral nerve block. In addition, this review includes the largest number of RCT that assess peripheral nerve block in adults with MOH, compared with recent previous reviews [22, 35]. Overall, although limited by quality evidence, this review provides a complex synthesis that may benefit future research.

Conclusions

This systematic review suggests that peripheral nerve block, especially in multiple sessions, may reduce the frequency and intensity of headaches and medication use in patients with MOH, with limited certainty of evidence because of the methodological weakness in their primary data. This intervention has not been completed validated in MOH population and requires more and well-designed RCT to assess their effectiveness, safety, and optimal dosing and techniques.

Abbreviations

95% CI	95% Confidence Intervals
CGRP	Calcitonin gene-related peptide
GRADE	Grading of Recommendations Assessment, Development, and Evaluation
MOH	Medication-overuse headache
PNB	Peripheral nerve block
RCT	Randomized controlled trials

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-026-04682-2.

Supplementary Material 1.

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None.

Authors' contributions

PAAT, CFCC, MESS and CAAR conceptualized the idea and designed the methodology. PAAT, CFCC and MESS conducted review and data curation. GM and CAAR conducted formal analysis. PAAT, CFCC, MESS wrote the first original draft. CAAR, GM, and MTG reviewed and edited the manuscript. All the authors approved the final version of the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
The present study adheres to the guidance listed in the latest version of the Declaration of Helsinki. The protocol for the present study was registered at Universidad Científica del Sur (Registration Code: PRE-15-2025-00046) and it was waived for approval for Institutional Review Board. Protocol was also registered at PROSPERO online platform (CRD420250617669). No patient consent was necessary because we only included primary research studies with no contact with patients.

Consent for publication
Not applicable.

Competing interests
MTG received a research grant from Pfizer (ID 89830415), received payment or honoraria from Abbvie, TEVA, and Pfizer, participated on Advisory Board from Abbvie and Pfizer, and was an IHS Co-opted trustee (2021 to 2023). The rest of the authors declare no conflicts of interest. The study was self-funded.

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