Influence of greater occipital nerve block on pain severity in migraine patients: A systematic review and meta-analysis

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A B S T R A C T

Aims: Greater occipital nerve (GON) block may be a promising approach to treat migraine. However, the results remained controversial. We conducted a systematic review and meta-analysis to explore the efficacy of GON block in migraine patients.

Methods: PubMed, EMBase, Web of science, EBSCO, and Cochrane library databases were systematically searched. Randomized controlled trials (RCTs) assessing the efficacy of GON block versus placebo in migraine patients were included. Two investigators independently searched articles, extracted data, and assessed the quality of included studies. Meta-analysis was performed using the random-effect model.

Results: Six RCTs were included in the meta-analysis. Overall, compared with control intervention in migraine patients, GON block intervention was found to significantly reduce pain score (Std. mean difference = −0.51; 95% CI = −0.81 to −0.21; P = 0.0008), number of headache days (Std. mean difference = −0.68; 95% CI = −1.02 to −0.35; P < 0.0001), and medication consumption (Std. mean difference = −0.35; 95% CI = −0.67 to −0.02; P = 0.04), but demonstrated no influence on duration of headache per four weeks (Std. mean difference = −0.07; 95% CI = −0.41 to 0.27; P = 0.70).

Conclusions: Compared to control intervention, GON block intervention can significantly alleviate pain, reduce the number of headache days and medication consumption, but have no significant influence on the duration of headache per four weeks for migraine patients.

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1. Introduction

Migraine is one common form of headache which is one of the leading causes of emergency department presentations. Significant economic and social burdens are caused by migraine in patients who often seek emergency care [1]. Migraine can result in substantial disability of patients [2-4]. The incidence of migraine is almost equal in men and women during childhood, but the prevalence of migraine increases more rapidly in girls after puberty [5,6]. The prevalence of migraine was reported to be 17.6% of women and 5.7% of men in European countries and United States [7]. Migraine headaches are quite severe, painful and incapacitating. The management of migraine is challenging based on current treatments [8-11].

After migraine becomes refractory to pharmacologic management, some minimally invasive techniques are feasible to treat migraine. Peripheral nerve blocks and radiofrequency treatment is a safe and effective approach for headache disorders [12-16]. Greater occipital nerve (GON) block is reported to have important potential in the diagnosis and treatment of primary headaches [17-20]. The GON carries sensory fibres originating predominantly at C2 and have a cutaneous distribution in the posterior part of head. GON blocks local anesthetics and/or corticosteroids have been employed for decades in the treatment of migraine and other headache disorders possibly through reducing neuronal hyperexcitability at the second-order neuron level [21,22]. Some studies revealed that GON block could significantly reduce pain severity and the number of headache days in patients with migraine [23,24]. In contrast to this promising finding, some relevant RCTs showed that GON block had no influence on the pain control, the number of headache days, duration of headache per four weeks, and medication consumption for migraine patients [25-28]. Considering these inconsistent effects, we therefore conducted a systematic review and meta-analysis of RCTs to investigate the influence of GON block on pain severity in migraine patients.

2. Materials and methods

This systematic review and meta-analysis were conducted according to the guidance of the Preferred Reporting Items for Systematic Reviews and Meta-analysis statement [29] and the Cochrane Handbook for Systematic Reviews of Interventions [30].

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2.1. Literature search and selection criteria

PubMed, EMBase, Web of science, EBSCO, and the Cochrane library were systematically searched from inception to April 2017, with the following keywords: GON block, and migraine or headache. To include additional eligible studies, the reference lists of retrieved studies and relevant reviews were also hand-searched and the process above was performed repeatedly until no further article was identified.

The inclusion criteria were as follows: (1) patients were diagnosed as migraine; (2) the intervention treatments were GON block versus GON injection; (3) and the study design was RCT.

2.2. Data extraction and outcome measures

The following information was extracted from the included RCTs: first author, publication year, sample size, baseline characteristics of patients, GON block intervention, control, pain score, number of headache days, duration of headache per four weeks (hour), and medication consumption (day). The author would be contacted to acquire the data when necessary.

The primary outcome were the pain score, and number of headache days. Secondary outcomes included duration of headache per four weeks (hour), and medication consumption (day).

2.3. Quality assessment in individual studies

The Jadad Scale was used to evaluate the methodological quality of each RCT included in this meta-analysis [31]. This scale consisted of three evaluation elements: randomization (0–2 points), blinding (0–2 points), dropouts and withdrawals (0–1 points). One point would be allocated to each element if they have been mentioned in article, and another one point would be given if the methods of randomization and/or blinding had been detailedly and appropriately described. If methods of randomization and/or blinding were inappropriate, or dropouts and withdrawals had not been recorded, then one point was deducted. The score of Jadad Scale varied from 0 to 5 points. An article with Jadad score ≥ 2 was considered to be of low quality, if the Jadad score ≥ 3, the study was thought to be of high quality [32].

2.4. Statistical analysis

Standard mean differences (Std. MDs) with 95% confidence intervals (CIs) for continuous outcomes (pain score, number of headache days, duration of headache per four weeks, and medication consumption) were used to estimate the pooled effects. All meta-analyses were performed using random-effects models with DerSimonian and Laird weights. Heterogeneity was tested using the Cochran Q statistic (P < 0.1) and quantified with the I² statistic, which described the variation of effect size that was attributable to heterogeneity across studies. An I² value > 50% indicated significant heterogeneity. Sensitivity analysis was performed to detect the influence of a single study on the overall estimate via omitting one study in turn when necessary. Owing to the limited number (<10) of included studies, publication bias was not assessed. P < 0.05 in two-tailed tests was considered statistically significant. All statistical analyses were performed with Review Manager Version 5.3 (The Cochrane Collaboration, Software Update, Oxford, UK).

3. Results

3.1. Literature search, study characteristics and quality assessment

The flow chart for the selection process and detailed identification was presented in Fig. 1. 598 publications were identified through the initial search of databases. Ultimately, six RCTs were included in the meta-analysis [23-28]. The baseline characteristics of the six eligible RCTs in the meta-analysis were summarized in Table 1. The four studies were published between 2008 and 2016, and sample sizes ranged from 23 to 72. Patients in GON block group and control group demonstrated similar basic characteristics. Three included studies reported GON block with bupivacaine versus saline [24,26,27]. Three included studies reported GON block with corticosteroids, bupivacaine or (and) lidocaine versus bupivacaine or (and) lidocaine [23,25,28].

Among the six RCTs, four studies reported the pain score [23-26], three studies reported the number of headache days [23,24,27], two studies reported the duration of headache per four weeks [26,28], and three studies reported the medication consumption [25,27,28]. Jadad scores of the six included studies varied from 3 to 5, and all six studies were considered to be high-quality ones according to quality assessment.

3.2. Primary outcome: pain score and number of headache days

These two outcome data were analyzed with a random-effect model, and the pooled estimate of the four included RCTs suggested that compared to control group in migraine patients, GON block intervention was associated with a significantly decreased pain score (Std. mean difference = −0.51; 95% CI = −0.81 to −0.21; P = 0.0008), with no heterogeneity among the studies (I² = 0%, heterogeneity P = 0.54) (Fig. 2). GON block intervention was also found to significantly reduce the number of headache days (Std. mean difference = −0.68; 95% CI = −1.02 to −0.35; P < 0.0001) compared to control intervention, with no heterogeneity among the studies (I² = 0%, heterogeneity P = 0.72) (Fig. 3).

3.3. Sensitivity analysis

No heterogeneity was observed among the included studies for the pain score and number of headache days. Thus, we did not perform sensitivity analysis by omitting one study in each turn to detect the source of heterogeneity.

3.4. Secondary outcomes

Compared with control intervention in migraine patients, GON block intervention showed no influence on the duration of headache per four weeks (Std. mean difference = −0.07; 95% CI = −0.41 to 0.27; P = 0.70; Fig. 4), but resulted in significantly decreased medication consumption (Std. mean difference = −0.35; 95% CI = −0.67 to −0.02; P = 0.04; Fig. 5).

4. Discussion

Migraine headache is a common and potentially exhausting disorder in emergency department. Patients with migraine suffer from an average of 1–8 attacks per month, but the frequency and severity of episodes varies individually [33]. It can result in a major public health problem, particularly among reproductive aged women [34]. When conventional pharmacologic management becomes ineffective to migraine, minimally invasive techniques such as peripheral nerve blocks serve as an important alternative for pain relief, and the decrease in the frequency of the attacks. Previous studies demonstrated that peripheral nerve blocks were safe and effective to treat headache disorders and they not only provided adequate analgesia but also decreased systemic side effects of pharmacologic therapy [35-37]. GON block has emerged as an important approach for pain relief of migraine. Our meta-analysis clearly suggested that compared to control intervention, GON block intervention was associated with a significantly reduced pain severity, the number of headache days and medication consumption, but showed no significant impact on duration of headache per four weeks in patients with migraine.
GON block has an important ability for pain relief for migraine through the modulation of the nociceptive afferences reaching the trigeminal nucleus caudalis. The trigeminal spinal nucleus neurons are located in the upper cervical spine and are functionally and anatomically associated with the sensory neurons that innervate the occipital region [28,38]. Trigeminal and occipital afferents were reported to converge on the trigeminal-cervical complex, and result in the sensory GON feed-forward effect. Trigeminal and occipital afferents were reported to converge on the trigeminal-cervical complex, and result in the sensory GON feed-forward effect. GON: greater occipital nerve.

There were very few adverse reactions after GON block or injection and no serious adverse events were reported in the included RCTs [23-28]. GON block was performed in conjunction with corticosteroids, and corticosteroids were combined with bupivacaine or (and) lidocaine in three included RCTs [23,25,28]. The pain relief of headache may be prolonged with corticosteroid [40]. GON block with triamcinolone and lidocaine also did not result in substantially reduced pain severity compared to only lidocaine [25]. In another RCT, triamcinolone was added to lidocaine 2% and bupivacaine 0.5% for GON block in patients with migraine, and the results concluded that triamcinolone supplementation was not associated with a significantly reduced pain severity, but could significantly decrease the number of headache days [23]. These revealed that corticosteroids supplementation is not able to decrease pain severity, but to prolong the duration of pain relief. And more RCTs are needed to investigate this issue.

Several limitations should be taken into account. Firstly, our analysis is based on only six RCTs but all of them have a relatively small sample size (n < 100). Overestimation of the treatment effect is more likely in smaller trials compared with larger samples. The type and dosages of local anesthetic in the included studies are different and they may have an influence on the pooling results. Next, the optimal dose and local anesthetic for migraine remains unknown and requires more clinical studies. Finally, some unpublished and missing data may lead bias to the pooled effect.

5. Conclusion

GON block intervention has an important ability to reduce pain severity, the number of headache days and medication consumption for migraine patients. GON block intervention is recommended to be administered in migraine patients.

Table 1

<table>
<thead>
<tr>
<th>No.</th>
<th>Author</th>
<th>GON block group</th>
<th>Control group</th>
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<tr>
<td></td>
<td></td>
<td>Number</td>
<td>Age (years)</td>
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<td>35.7 ± 8.6</td>
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<tr>
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<td>39.00 ± 9.67</td>
</tr>
<tr>
<td>3</td>
<td>Inan</td>
<td>39</td>
<td>37.3 ± 8.8</td>
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<tr>
<td>4</td>
<td>Dilli</td>
<td>33</td>
<td>44 ± 11</td>
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<tr>
<td>5</td>
<td>Kashipazha</td>
<td>24</td>
<td>37.00 ± 4.41</td>
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<tr>
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<td>Ashkenazi</td>
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GON: greater occipital nerve.
Compliance with ethical standards

Disclosure of potential conflicts of interest

The authors declare no conflict of interest.

Research involving human participants and/or animals

Not applicable.

References


