



The Effectiveness and Safety of Acupuncture on Occipital Neuralgia: A Study Protocol for Systematic Review and/or Meta-Analysis

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Background: Occipital neuralgia (ON) is an established risk factor for headaches in the posterior cervical region. Several conservative treatments by nerve decompression and pain relief are available for ON, but these treatments have limitations. Acupuncture treatment, which is known to demonstrate analgesic effects, involves various stimulation methods, and several studies have reported their clinical benefit. No recent systematic review (SR) has compared each acupuncture type for ON treatment. Thus, this SR aims to investigate the clinical effectiveness of each acupuncture type for treating ON.

Methods: We will identify relevant studies using electronic databases, including EMBASE, MEDLINE, Cochrane Library, China National Knowledge Infrastructure (CNKI), Korean Studies Information Service System (KISS), Korean Medical Database, KoreaMed, and National Digital Science Library (NDSL) from the inception until August 2023. The primary outcome will include the numerical change of pain symptoms (visual analog scale and numerical rating scale) and effective rate. Safety and secondary outcomes will include adverse events and quality of life. We will compare the conservative treatment with the acupuncture treatment using network meta-analysis. The Cochrane Collaboration “risk of bias” tools will be used to assess the quality of included trials. The Grades of Recommendation, Assessment, Development, and Evaluation will be used to examine the evidence level.

Conclusion: This study will provide clinical evidence of several acupuncture types for ON and help clinicians decide on the best.

Keywords: Acupuncture; Meta-analysis; Network meta-analysis; Occipital neuralgia; Systematic review

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INTRODUCTION

Occipital neuralgia (ON) is characterized by spasmodic burning or stinging pain in the occipital region [1]. ON was first described as recurrent headaches in 1821 and was reported to be associated with the distribution of the third, greater, and lesser occipital nerves [2]. ON prevalence varies based on populations of interest, in which 3.2 out of 100,000 people in the general population reported having ON while nearly one-fourth of patients with headaches presented ON [3,4].

ON treatment generally aims to block occipital nerves and prevent compressive symptoms. Commonly used treatment options in the conventional approach include anesthetics (e.g., lidocaine or bupivacaine) plus anti-inflammatory medications (e.g., corticosteroids), or others (e.g., radiofrequency ablation and botulinum toxin) [5]. However, these approaches have reported adverse events, including dizziness, hypertension, blurring of vision (lidocaine), eyelid ptosis, muscular weakness (botulinum toxin), vomiting, and worsening headache (radiofrequency) [6-8].

An increasing number of studies have reported the analgesic effects of acupuncture [9]. The analgesic mechanisms of acupuncture involve an endogenous pain control system, cerebral plasticity, and nonspecific effects. Additionally, few serious adverse events have been reported [10]. Two previous systematic reviews (SRs) have examined the role of acupuncture on and revealed that acupuncture treatment (either acupuncture alone or in combination with other therapies compared with control therapies) was generally associated with improved pain symptoms and better effective rate (ER) [11,12].

However, gaps exist in our current understanding. First, these previous studies had several limitations. One study included (a) patients with postherpetic neuralgia and migraine as well as ON, which limit the generalizability of the findings, and (b) non-randomized trials, as well as randomized controlled trials (RCTs), which hinder causal inference [11]. Another study had an ideal methodology and impressive results, but it included most recent RCT was published in 2016 [12]. Recent studies, such as the study of Luo et al. [13] in 2021 were not included, thus updates on this topic are being requested. Moreover, an emerging body of research has reported the potential roles of various acupuncture treatment types, including manual acupuncture [14], electroacupuncture [15], acupotomy [16], and pharmacopuncture [17] in pain and related disorder management. However, to date, none of the previous research has investigated

the effect of each specific acupuncture treatment method.

This provides an important insight to understand the safety and effectiveness of treatments by acupuncture, specifically across different approaches. Therefore, this SR aims to investigate the safety and effectiveness of acupuncture by its specific treatment approach on to fill the gaps in the current knowledge.

MATERIALS AND METHODS

1. Study design

This SR and the meta-analysis will be based on the structure of the Preferred Reporting Items for Systemic Reviews and the Meta-Analyses Protocols (PRISMA-P) 2020 Statement [18].

2. Ethics

Ethical approval is waived since this study does not need to recruit subjects or collect information about subjects.

3. Study registration

The protocol was registered in PROSPERO (Registration number: CRD42023387146).

4. Eligibility criteria

1) Type of studies

This SR will include RCTs on the effectiveness of acupuncture treatment on ON. This SR will exclude studies with no randomization method or that conduct an incorrect randomization method, such as alternate allocation. Additionally, SR and case reports produced through uncontrolled clinical trials will be both excluded. The journal and the language will have no restrictions.

2) Participants

This SR will include participants diagnosed with ON. A previous study [5] indicated that a patient with unilateral or bilateral pain in the lesser, greater, and/or third occipital nerve region will be diagnosed with ON. We will include patients with occipital pain who has tenderness on palpation in the C2 region but will exclude patient complaining of pain unrelated to the upper cervical spine and occipital nerves. Participation will have no restrictions according to age and gender, but this study will exclude patients diagnosed with headaches other than ON.

3) Type of interventions

Interventions will include any acupuncture type that penetrates the skin using a needle such as electroacupuncture, manual acupuncture, pharmacopuncture, warm/fire acupuncture, auricular acupuncture, dry needling, and acupotomy. Included RCTs should compare the acupuncture group with placebo or other interventions, but we will also include add-on types. Hence, comparator treatment in the experimental group will be designed to be consistent with the control group. However, studies that describe the comparison of treatment periods and treatment points among the acupuncture treatment group will be excluded.

4) Type of comparators

The control group will have no restrictions. It will include conservative treatments, such as injections, medication, and medical procedures, for ON.

5) Outcome measures

The primary outcome measures will include ER and the change in pain intensity, including the visual analog scale (VAS) and numerical rating scale (NRS), which are frequently used scales for headache measurement [19]. Second outcome measures will include adverse events and scales on the quality of life (QoL), such as Euro-QoL-5D (EQ-5D), based on the previous study [20].

6) Language

This review will pose no restrictions on language.

5. Information sources and search strategy

We will use 3 English databases (EMBASE, MEDLINE, and Cochrane Library), 1 Chinese database (China National Knowledge Infrastructure, CNKI), and 5 Korean databases (Korean Medical Database, Korean Studies Information Service System [KISS], KoreaMed, National Digital Science Library [NDSL], and Oriental Medicine Advanced Searching Integrated System [OASIS]). Our researchers will search the baseline of the database until August 2023. We will search RCTs using terms combined with “occipital neuralgia” and intervention phase (e.g., acupuncture, electroacupuncture, pharmacopuncture, and acupotomy), as specified in Table 1. This study will search with the primary language of each database. Additionally, textbooks, theses of masters and doctors, reference lists of associated articles, and search sites, such as Google Scholar, will be searched. If necessary, the corresponding author will be contacted and a mutual check will be conducted (Table 1).

Table 1. Search strategy

No.	Search terms
1	Neuralgia
2	Headache
3	Neck pain
4	OR #1-3
5	Randomized Controlled Trials OR Random*
6	controlled clinical trial OR trial
7	Placebo
8	OR #5-7
9	Acupuncture Therapy OR Acupuncture*
10	Manual acupuncture
11	Electroacupuncture OR electric Acupuncture
12	Warm acupuncture OR Fire acupuncture
13	Pharmacopuncture OR Pharmaco-acupuncture OR Pharmaco acupuncture
14	Auricularacupuncture OR Auricular-acupuncture OR Auricular acupuncture
15	Acupotomy OR Catgut
16	Dry needling
17	Acupuncture points OR Acupoints*
18	Ashi OR Ah shi OR A shi OR A-shi OR Ah-Shi
19	OR #9-18
20	#4 AND #8 AND #20

6. Study selection

Two researchers (JHM and GP) will examine the title, abstract, and full text (if necessary) of the included studies to determine eligibility. Eligibility will be evaluated through an overall review of the full texts after excluding duplicate and inappropriate studies. Any disagreements between investigators will be resolved through a conversation between the 2 researchers and a third mediator (HRJ and WSS) if necessary (Fig. 1).

We will use Endnote X20 (Clarivate Analytics) to manage searched results.

7. Data extraction

Researchers in this study will collect bibliographic information, such as publication year, author, and title of journals. Additionally, this study will include patient characteristic information (sample size, age, gender, and disease duration), interventions of each group (type of acupuncture and comparator, acupuncture points, intervention frequency, interventions duration, and follow-up period), outcome measures extracted for the data synthesis (e.g., ER, VAS, NRS, and EQ-5D), and adverse events.

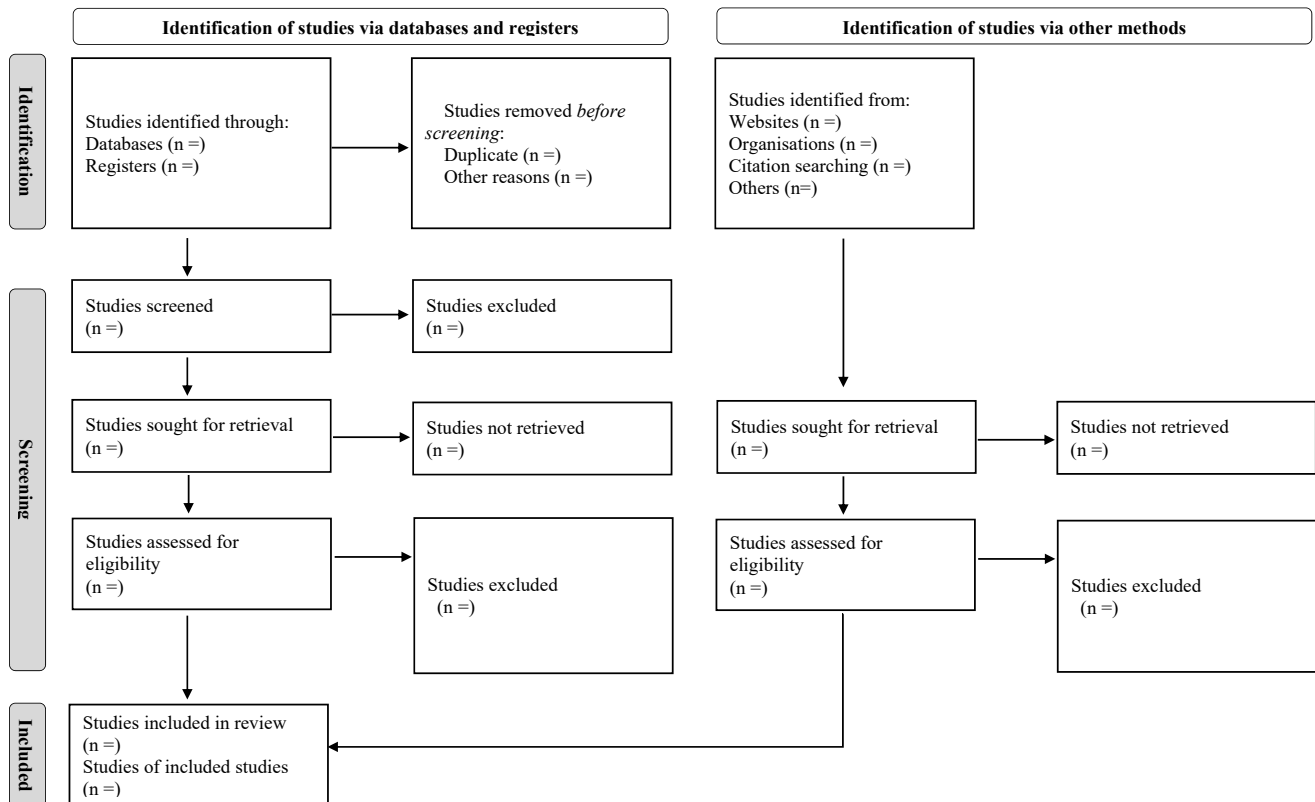


Fig. 1. Data management.

8. Addressing missing data

The corresponding author will be contacted for missing data. We will only analyze the available data and explain the potential impact of missing data in the manuscript if the corresponding author will not respond.

9. Data synthesis and analysis

The Review Manager software (Version 5.3; Copenhagen; The Nordic Cochrane Center, The Cochrane Collaboration, 2014) will be used for the SR and meta-analysis. The effective end points of this analysis will include the changes in the primary and secondary outcomes of interest before and after the treatment. The pooled mean difference and 95% confidence intervals (CIs) of continuous data will be estimated when the outcome measures are identical across studies, whereas the combined standardized mean difference (SMD) and 95% CI will be estimated when the different outcome measures are used for analysis. The risk ratio will be used for dichotomous data.

The Chi-squared and I-squared tests will determine the heterogeneity of included studies. Values of I-square will be classified into 4 sections: 0–40%, 30–60%, 50–90%,

and 75–100%, which indicate unimportant, moderate (medium), substantial, and considerable heterogeneity levels, respectively [21]. A narrative synthesis will be a substitute if quantitative synthesis is not possible. Funnel plots will be applied as an evaluation method for publication bias if a significant number of studies (> 10) are included.

10. Subgroup analysis and network meta-analysis

Subgroup analysis will be implemented to check the heterogeneity of the studies according to the main intervention of the control group if possible (e.g., medication and injection).

R software (version 4.0.3) will be used for network meta-analysis, decomposing the specific effects of each acupuncture treatment approach. The continuous variables will be changed as SMD and the odd ratios with 95% CI. The p-score by the surface under the cumulative ranking curve will be used to rank treatment [22].

11. Evidence summary

We will evaluate the quality of evidence for our findings using the Grades of Recommendation, Assessment,

Development, and Evaluation (GRADE) [23]. We will assess five domains, including the risk of bias, indirectness, effect consistency, imprecision, and publication bias, and present it with a summary.

12. Risk of bias assessment

Each of the 2 researchers (JHM and GP) will independently evaluate the risk of bias among included studies based on the Cochrane Collaboration risk-of-bias tool [24]. It consists of 7 parts, including sequence generation, allocation concealment, blinding both participants and personnel, blinding of outcome assessments, incomplete outcome data (attrition bias), selective outcome reporting (reporting bias), and other biases. Disharmony on this risk of bias assessment will be resolved or mediated through discussions or third mediators (HRJ and WSS).

DISCUSSION

Headache is a disorder that necessitates exquisite diagnostic skills [25]. Headache is caused by several factors, one of which is ON. Among the ON mechanism, nerve entrapment is the most representative and acceptable, but strong clinical evidence remains lacking [26]. ON is a debilitating chronic condition that substantially affects a personal life through sustained pain and degraded life quality, thus several treatments have been introduced. Several conventional treatments have been associated with limitations, such as insufficient effectiveness levels or unignorable adverse event levels. Acupuncture has been proposed as an alternative treatment for ON.

Acupuncture has been used as a complementary option for pain relief. Several articles have reported its analgesic effect by various acupuncture types [27-29]. However, to date, no studies have systematically examined the potential roles of acupuncture treatment across its specific approach in ON management. Additionally, clinical differences will be determined based on the type of acupuncture through multiple factors, including the needling technique [9]. Nerve entrapment is known to cause ON. Our study would be reasonable if acupuncture treatment that focuses on resolving entrapment shows superior results among various acupuncture types. Conversely, another mechanism of acupuncture treatment can be considered if unexpected stimuli show superior results.

However, there might be some limitations. First, most of the included studies in previous SR were published in a specific country. A selective bias is possible due to the

regional problem, but we will search various search engines with various languages as much as possible. Second, omission might occur while classifying ON against general headaches. We will thoroughly examine the selection criteria of ON. Despite these limitations, our study, which includes subgroup analysis, will evaluate the safety and clinical effectiveness of acupuncture for ON treatment, as well as provide critical evidence to plan for patients, clinicians, and researchers.

AUTHOR CONTRIBUTIONS

Conceptualization: WSS, EJK. Funding acquisition: EJK. Investigation: JHM, GP, SHP. Methodology: HRJ, YK, YJL. Project administration: EJK. Supervision: EJK. Writing – original draft: JHM. Writing – review & editing: WSS, JEJ, SDL, YK, EJK.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to declare.

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ETHICAL STATEMENT

This research did not involve any human or animal experiment.

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