INPLASY PROTOCOL

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None declared.

Efficacy and Safety of An External Combined Occipital and Trigeminal Neurostimulation (eCOT-NS) Device for Migraine: A Systematic Review and Meta-Analysis

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Review question / Objective: **Patient: aged over 18 years; compliant with the International Classification of Headache Disorders. Intervention: treated with eCOT-NS. Comparison: treated with an identical shape device which has a sham stimulation. Outcome: the primary outcome was the rate of pain-free patients at 2 hours post-treatment, and the secondary outcome was the rate of pain-free patients at 1 hour and 24 hours post-treatment. Study: RCT.**
Condition being studied: **Globally, more than 1 billion people are suffering from migraines. An external combined occipital and trigeminal neurostimulation (eCOT-NS) device is being developed as a treatment for migraine. Therefore, we have written this meta-analysis to clarify the effectiveness and safety of the eCOT-NS device.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 16 November 2022 and was last updated on 16 November 2022 (registration number INPLASY2022110074).

INTRODUCTION

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METHODS

Search strategy: We searched MEDLINE, Clinicaltrial.gov, EMBASE, and CENTRAL for articles related to Occipital and Trigeminal Neurostimulation and Migraine published before October 25th, 2022, and removed duplicate or ineligible records. Subsequently, we extracted data from the screened randomized controlled trials (RCTs) for migraine patients as well as for patients with moderate to severe migraine, respectively.

Participant or population: Aged over 18 years; compliant with the International Classification of Headache Disorders.

Intervention: Treated with eCOT-NS.

Comparator: Migraine patients with sham treatment.

Study designs to be included: RCTs.

Eligibility criteria: Exclusion criteria: (1)patient: treatment with neurotoxin or supraorbital or occipital nerve block in the 4 months before the study; headaches due to medication abuse; history of cerebral hemorrhage or cerebral infarction; previously treated in neurosurgery; used sedatives such as opioids 1 month before screening; foreign body implants in the head (except dental implants); history of epilepsy; skin lesions or inflammation in the area of the stimulation electrode; personality or somatoform disorders; brain or facial trauma within 3 months before screening; participated in a clinical study within the last 3 months.(2)study type: no data that can be extracted, such as review, case report, comment, letter, or non-randomized trials.(3)language: non-English article.

Information sources: Two investigators (LYT and HYT) jointly searched MEDLINE, Clinical Trials.gov, EMBASE, and CENTRAL for articles published before October 25, 2022. We have used the following keywords: ("occipital" OR "occipitally" OR "occipitals") AND ("trigeminal" OR "trigeminally") AND ("neurostimulation" OR "neurostimulations" OR "neurostimulator" OR "neurostimulators") AND ("migraine" OR "migraine disorders" OR "disorders" OR "migraines" OR "migraineurs" OR "migrainous"). We also retrieved systematic reviews and meta-analyses to ensure the integrity of the included data.

Main outcome(s): a.Pain-free subjects versus baseline, modified intent-to-treat population. b. Pain-free subjects with severe or moderate pain at baseline, modified intent-to-treat population.

Quality assessment / Risk of bias analysis: Two authors jointly used STATA software 12.0 to evaluate the risk of bias plot and also assessed the risk of bias in RCT using the Cochrane Collaboration Network uniform criteria. The risk of bias in RCT includes selection bias, performance bias, detection bias, attrition bias, reporting bias, and other potential biases. And the bias criterion was categorized as “low”, “high”, or “unclear”.

Strategy of data synthesis: First, we used I^2 statistic to estimate heterogeneity, when I^2 is less than 30% means low heterogeneity, when I^2 is less than 50% and greater than 30% means moderate heterogeneity, and when I^2 is greater than 50% means high heterogeneity. Then, we used STATA software 12.0 to evaluate the data from two randomized controlled studies and calculated 95% confidence intervals (CI) and risk ratios (RR) for the dichotomous results. Finally, we used a two-tailed test for all the analyses and defined statistically significant as a P value of less than 0.05.

Subgroup analysis: No subgroup analysis.

Sensitivity analysis: When any of these values were removed, the RR values of the remaining values remained within the 95% confidence interval, thus demonstrating the stability and reliability of our study.

Language restriction: English.

Country(ies) involved: China (First affiliated hospital of Soochow university, Suzhou, Jiangsu Province).

Keywords: Migraine, Neuromodulation, Peripheral nerve stimulation, Occipital nerve, Trigeminal nerve.

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