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Neuromuscular electrical stimulation on hearing loss caused by skull base fracture
A protocol for systematic review of randomized controlled trial

Lin-hong Yang, MD[a], Wei-feng Wang, MM[b], Shu-hong Zhang, MB[c], Zong-xian Fan, MB[a], Jian-qi Xiao, MD[d],*

Abstract
Background: This systematic review aims to investigate the effectiveness and safety of neuromuscular electrical stimulation (NMES) on hearing loss (HL) caused by skull base fracture (SBF).

Methods: We will retrieve the following electronic databases of Cochrane Library, PUBMED, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine Database, and Chinese Biomedical Literature Database from the inception to January 1, 2019 for relevant RCTs of NMES for HL caused by SBF. Two experienced authors will independently perform the study selection, data extraction, and methodology quality assessment. A 3rd author will solve any disagreements between 2 authors through discussion.

Results: This study will provide a high-quality synthesis of latest evidence of NMES for HL caused by SBF from comprehensive assessments, including hearing loss evaluation, hearing threshold, quality of life, and any relevant adverse events.

Conclusion: The expected results of this systematic review will provide the up-to-date evidence to assess the effectiveness and safety of NEMS for patients with HL caused by SBF.

Ethics and dissemination: The results of this study will be disseminated through publication in a peer-reviewed journal or will be presented at an associated conference meeting. This study will not use individual patient data, thus, the ethical approval is not needed.

PROSPERO registration number: PROSPERO CRD42019120195.

Abbreviations: CIs = confidence intervals, HL = hearing loss, NMES = neuromuscular electrical stimulation, SBF = skull base fracture.

Keywords: effectiveness, hearing loss, neuromuscular electrical stimulation, randomized controlled trial, safety, skull base fracture, systematic review

1. Introduction

Traumatic brain injury is a leading cause of death and disability.[1–3] Skull fractures are relatively common following head trauma.[4–6] Of these, 4–20% of such fractures are occurred at the base of skull.[7,8] Many reasons that can result in skull base fracture (SBF), such as motor vehicle accidents, fall from heights, and blunt trauma.[9–12] It mainly manifests with hearing loss (HL), cranial nerve deficit, headache, behavioral changes, and hemiparesis, as well as others,[13–15] especially for the HL. If it is not treated fairly and effectively, it can greatly affect the quality of life in patients who experience such condition.[16,17]

A variety of clinical studies have reported that neuromuscular electrical stimulation (NMES) can be utilized to treat HL, and have achieved very promising outcomes.[18–24] However, up to date, no study has systematically assessed the effectiveness and safety of NMES for the treatment of HL caused by SBF. Therefore, in this systematic review, we will firstly evaluate the effectiveness and safety of NMES for patients with HL caused by SBF.

2. Methods

2.1. Inclusion criteria for study selection
2.1.1. Type of studies.
All relevant randomized controlled trials (RCTs) regarding NMES for the treatment of HL caused by SBF will be included without any language and publication status restrictions. However, non-clinical trials, non-control studies, non-RCTs and Quasi-RCTs will not be included.

2.1.2. Type of participants.
All participants who are clinically diagnosed with HL caused by SBF will be included regardless the age, sex, and race. However, they will be excluded if they had HL before the SBF, or result from other disorders or diseases, except the SBF.

[a] Department of Otorhinolaryngology, [b] Department of Neurosurgery, First Affiliated Hospital of Jiamusi University, [c] Department of Biology, Basic Medicine School of Jiamusi University, Jiamusi, [d] Department of Neurosurgery, The First Hospital of Qiqihar City, Qiqihar, China.

* Correspondence: Jian-qi Xiao, Department of Neurosurgery, The First Hospital of Qiqihar City, No. 30 of Park Road, Longsha District, Qiqihar, 161005, China (e-mail: jianqix198247@outlook.com).

2.1.3. Type of interventions. The intervention of experimental group should utilize NMES only. The combination of NMES with other therapies is not allowed in this systematic review. The interventions in the control group can be any kinds of therapies, but not any forms of NMES.

2.1.4. Type of outcomes. The primary outcome is hearing loss, as assessed according to the Brock grade, acceptable noise level test, or other related scales. The secondary outcomes are hearing threshold, as measured by pure-tone audiometry, speech audiometry or other tools; and quality of life, as measured by the 36-Item Short Form Health Survey or other scales. Any relevant adverse events are also evaluated.

2.2. Search strategy

Cochrane Library, PUBMED, EMBASE, Cumulative Index to Nursing and Allied Health Literature, Allied and Complementary Medicine Database, and Chinese Biomedical Literature Database will be searched from the inception to January 1, 2019 for relevant RCTs of NMES for HL caused by SBF. Detailed strategy for searching the Cochrane Library database is presented in Table 1. Similar strategies will be applied to the other databases.

Additionally, we will also manually search the references lists of relevant trials and reviews for any other potential eligible literatures. Besides, the websites of clinical trials registry will also be considered to search.

2.3. Data collection and analysis
2.3.1. Study selection. Two experienced authors will independently search all databases and select studies by scanning titles, abstracts, and full texts reading based on the previous eligibility criteria. Studies will be excluded with specific exclusion reasons. Any disagreements will be solved by group discussion with other authors. The whole selection process will follow the Preferred Reporting Items for Systematic Review and Meta-analysis flow diagram, and will be presented in Figure 1.

2.3.2. Data extraction and missing data management. After study selection, the same 2 authors will independently perform the data extraction by using previous designed data extraction forms. Any divided options regarding the data extraction will be resolved through discussion with a 3rd experienced author. If some important information is missing or not reported in the primary study, the original authors of the primary studies will be contacted to request this information, including the missing data. If such information can not be achieved, then we will analyze the available data.

2.3.3. Risk of bias assessment. Cochrane risk of bias tool will be adopted to assess the risk of bias for each included study. Each included study will be assessed at 7 domains, and each domain will be classified as high, unclear or low risk of bias. Two experienced authors will be independently in charge of the assessment. We will reach a consensus through discussion or consult with a 3rd experienced author involved if there are disagreements between 2 authors.

2.4. Data synthesis and analysis
2.4.1. Measurement of treatment effect. For continuous outcomes, the extracted data will be presented as mean difference with 95% confidence intervals (CIs). As for dichotomous outcomes, the extracted data will be computed as risk ratio with 95% CIs.

2.4.2. Assessment of heterogeneity. Heterogeneity is identified by I^2 index and Cochrane Q statistic test. It among included studies will be detected to assess the feasibility to pool the data, and to conduct meta-analysis. If the value of I^2 is over 50%, the substantial heterogeneity will be considered, and subgroup analysis will be performed to investigate the potential factors from clinical or methodological heterogeneity.

2.4.3. Data synthesis. RevMan 5.3 Software will be used to pool the data and conduct the meta-analysis. If the value of I^2 is less than 50%, the fixed-effect model will be used for data synthesis, and meta-analysis will be conducted. If not, random-effect model will

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Table 1

Search strategy applied in Cochrane Library database.

| Number	Search terms
1	Mesh descriptor: (skull fracture, basilar) explode all trees
2	((skull*) or (fractur*) or (basilar*) or (basilar skull fracture*) or (skull base fracture*)):ti, ab, kw
3	Or 1–2
4	MeSH descriptor: (hearing loss) explode all trees
5	MeSH descriptor: (hearing loss, sensorineural) explode all trees
6	MeSH descriptor: (hearing loss, sudden) explode all trees
7	MeSH descriptor: (sudden deafness) explode all trees
8	MeSH descriptor: (hearing impairment) explode all trees
9	((hearing*) or (loss*) or (idiopathic sudden sensorineural hearing loss*) or (sensorineural hearing loss*) or (sensorineural*) or (deafness*) or (impairment*)):ti, ab, kw
10	Or 4–9
11	MeSH descriptor: (electric stimulation) explode all trees
12	MeSH descriptor: (electric stimulation therapy) explode all trees
13	(neuromuscular electrical stimulation) explode all trees
14	((eletric stimulation*) or (electric stimulation therapy*) or (electrotherapy*) or (neuromuscular electrical stimulation *) or (NMES*) or (neuromuscular*) or (electric*) or (stimulation*)):ti, ab, kw
15	Or 11-14
16	MeSH descriptor: (randomized controlled trial) explode all trees
17	((randomized controlled trial*) or (controlled clinical trial *) or (randomly*) or (randomized*) or (trial*)):ti, ab, kw
18	Or 16-17
19	3 and 10 and 15 and 18
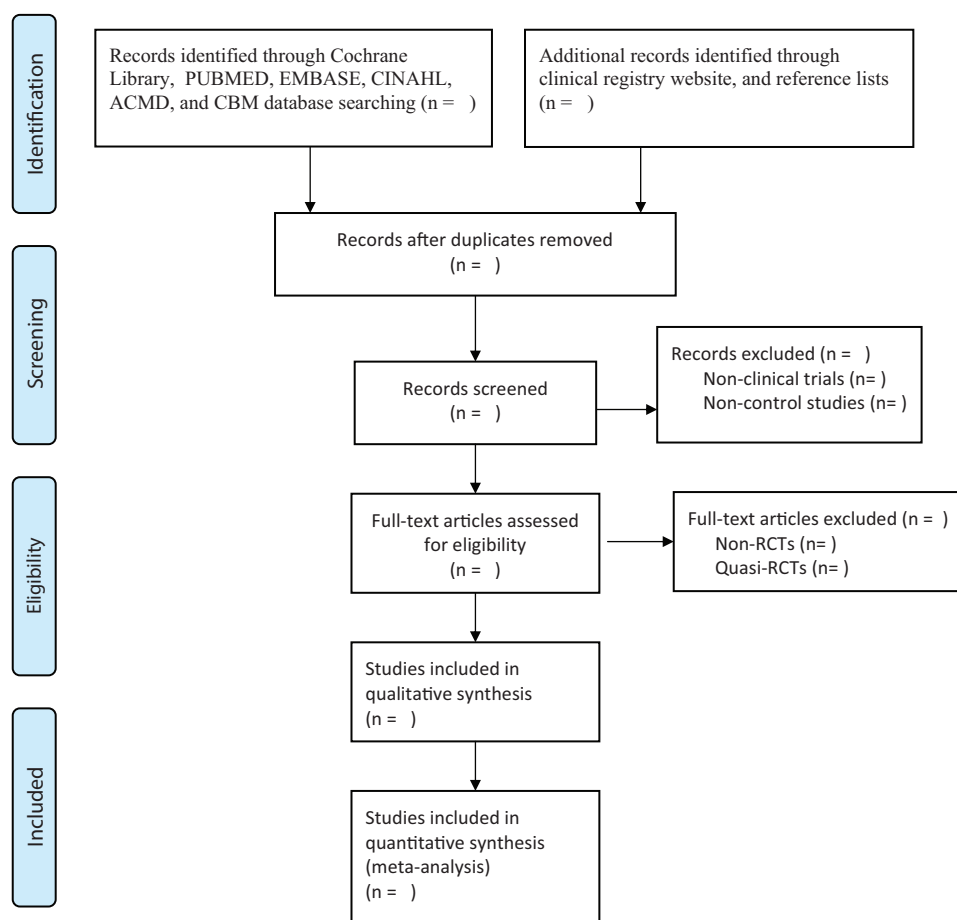
Figure 1. Flowchart of study selection process.

be employed for data synthesis. Meanwhile, subgroup analysis and sensitivity analysis will also be carried out. If it is still not available to pool the data and to perform a meta-analysis after the subgroup analysis, we will only elaborate the summary description instead.

2.4.4. Subgroup analysis. Subgroup analysis will be carried out to explore the sources of heterogeneity according to the study locations, patient characteristics, treatment dosage or duration, types of treatments, or controls, as well as different outcome measurement scales.

2.4.5. Sensitivity analysis. If the data is available to be pooled, sensitivity analysis will be adopted to assess the robustness of pooled results data, missing data, and methodological quality.

2.4.6. Assessment of reporting bias. If the number of included trials is sufficient (over 10 studies) in this review, the funnel plot and Egg's regression test will be carried out to detect the possible reporting bias.

3. Discussion

The HL, with a large population affected, is a global epidemic issue during the past decades. Lots of researches have reported that NMES is effective for the HL treatment. However, no systematic review has addressed to investigate the effectiveness and safety of NMES on HL caused by SBF. Therefore, it is very necessary to conduct the present systematic review. It will be

performed according to the Cochrane Handbook to ensure that it can provide helpful information and evidence for both clinicians and patients with HL.

Author contributions

Conceptualization: Lin-hong Yang, Wei-feng Wang, Zong-xian Fan, Jian-qi Xiao.
Data curation: Lin-hong Yang, Wei-feng Wang, Shu-hong Zhang, Zong-xian Fan, Jian-qi Xiao.
Formal analysis: Lin-hong Yang, Wei-feng Wang, Zong-xian Fan.
Funding acquisition: Jian-qi Xiao.
Investigation: Jian-qi Xiao.
Methodology: Lin-hong Yang, Wei-feng Wang, Shu-hong Zhang, Zong-xian Fan.
Project administration: Jian-qi Xiao.
Resources: Lin-hong Yang, Wei-feng Wang, Shu-hong Zhang, Zong-xian Fan.
Software: Lin-hong Yang, Wei-feng Wang, Zong-xian Fan.
Supervision: Jian-qi Xiao.
Validation: Lin-hong Yang, Wei-feng Wang, Jian-qi Xiao.
Visualization: Lin-hong Yang, Shu-hong Zhang, Zong-xian Fan, Jian-qi Xiao.
Writing – original draft: Lin-hong Yang, Wei-feng Wang, Shu-hong Zhang, Jian-qi Xiao.
Writing – review & editing: Lin-hong Yang, Shu-hong Zhang, Zong-xian Fan, Jian-qi Xiao.

References

[1] Lasry O, Liu EY, Powell GA, et al. Epidemiology of recurrent traumatic brain injury in the general population: a systematic review. Neurology 2017;89:2198–209.

[2] Zhu C, Chen J, Pan J, et al. Therapeutic effect of intensive glycemic control therapy in patients with traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials. Medicine (Baltimore) 2018;97:e11671.

[3] Iaccarino C, Carretta A, Nicolosi F, et al. Epidemiology of severe traumatic brain injury. J Neurosurg Sci 2018;62:535–41.

[4] Seule M, Brunner T, Mack A, et al. Neurosurgical and intensive care management of traumatic brain injury. Facial Plast Surg 2015;31:325–31.

[5] Chen JX, Lindeborg M, Herman SD, et al. Systematic review of hearing loss after traumatic brain injury without associated temporal bone fracture. Am J Otolaryngol 2018;39:338–44.

[6] Parikh S, Koch M, Narayan RK. Traumatic brain injury. Int Anesthesiol Clin 2007;45:119–35.

[7] Alhelali I, Stewart TC, Foster J, et al. Basal skull fractures are associated with mortality in pediatric severe traumatic brain injury. J Trauma Acute Care Surg 2015;78:1155–61.

[8] Bell RB, Chen J. Frontobasilar fractures: contemporary management. Atlas Oral Maxillofac Surg Clin North Am 2010;18:181–96.

[9] Chung CY, Chen CL, Cheng PT, et al. Critical score of Glasgow Coma Scale for pediatric traumatic brain injury. Pediatr Neurol 2006;34:379–87.

[10] Ziu M, Savage JG, Jimenez DF. Diagnosis and treatment of cerebrospinal fluid rhinorrhea following accidental traumatic anterior skull base fractures. Neurosurg Focus 2012;32:E3.

[11] Tunik MG, Powell EC, Mahajan P, et al. Clinical presentations and outcomes of children with basilar skull fractures after blunt head trauma. Ann Emerg Med 2016;68:431–40.

[12] Katzen JT, Jarrahy R, Eby JB, et al. Craniofacial and skull base trauma. J Trauma 2003;54:1026–34.

[13] Adepoju A, Adamo MA. Posttraumatic complications in pediatric skull fracture: dural sinus thrombosis, arterial dissection, and cerebrospinal fluid leakage. J Neurosurg Pediatr 2017;20:598–603.

[14] Leibu S, Rosenthal G, Shoshan Y, et al. Clinical significance of long-term follow-up of children with posttraumatic skull base fracture. World Neurosurg 2017;103:315–21.

[15] Baugnon KL, Hudgins PA. Skull base fractures and their complications. Neuroimaging Clin N Am 2014;24:439–65.

[16] Brusis T. Sensorineural hearing loss after dull head injury or concussion trauma. Laryngorhinootologie 2011;90:73–80.

[17] Salomone R, Abdu Ali Abu T, Chaves GA, et al. Sudden hearing loss caused by labyrinthine hemorrhage. Braz J Otorhinolaryngol 2008;74:776–9.

[18] Wang YH, Xue R, Yuan J, et al. Therapeutic effect of low-frequency repetitive transcranial magnetic stimulation on chronic tinnitus with different intensities. Shaanxi Med J 2018;47:1026–8.

[19] Zhu QY, Wang H. Therapeutic effect of low frequency repetitive transcranial magnetic stimulation on tinnitus. J Audiol Speech Dis 2017;25:484–7.

[20] Tang YQ, Wang YJ, Shen Q. Clinical observation of percutaneous electrical stimulation of auricular points in the treatment of sudden deafness. Chin Med Technol 2012;19:366.

[21] Ma CY, Wang JP, Bao F. Acoustic resonance deafness tinnitus treatment system electrical stimulation treatment of tinnitus. Baotou Med 2001;4:147.

[22] Shi YB, William HM, Jiang WC, et al. Deep brain stimulation for the treatment of stubborn and severe tinnitus. J Audiol Speech Dis 2000;2:113–6.

[23] Xiao HW, Pei LJ. Electrical stimulation therapy for tinnitus. Intro Jpn Med 1994;8:371.

[24] Ni BH. 20 cases of tinnitus by electric stimulation of drumsticks. J Nantong Uni (Medical Sciences) 1992;3:268.