INPLASY PROTOCOL

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None declared.

Botulinum Toxin for Drooling in Adults with Diseases of Central Nervous System: a Systematic Review and Meta-Analysis

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Review question / Objective: **P: Adult patients with diverse central nervous system diseases; I: Botulinum toxin type A injection; C: Placebo-controlled group(meta-analysis); before and after botulinum toxin type A injection comparison (systematic review); O: Drooling severity and frequency.**
Condition being studied: **Drooling has been commonly found in patients with diseases in the central nervous system such as Parkinson's disease, amyotrophic lateral sclerosis (ALS), and cerebral palsy. Numerous options have been advocated to manage drooling but none of them are universally successful. Anticholinergic medications such as glycopyrrolate and scopolamine have been used to control drooling, but they produce a few side effects such as dizziness, headache, restlessness, irritability, hyperactivity, constipation, facial flushing, thick mucoid secretions, dehydration, urinary retention, dilated pupils, slight visual impairment, and seizures. Surgeries that alter existing neural pathways for salivation may alleviate the severity of drooling, but these operations usually cause dry mouth and other complications.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 February 2023 and was last updated on 04 February 2023 (registration number INPLASY202320019).

INTRODUCTION

Review question / Objective: **P: Adult patients with diverse central nervous system diseases; I: Botulinum toxin type A injection; C: Placebo-controlled group(meta-analysis); before and after botulinum toxin type A injection comparison (systematic review); O: Drooling severity and frequency.**

Rationale: **Botulinum toxin (BoNT) injections into the salivary glands had been studied as an alternative for drooling in patients with central nervous system diseases. Injected BoNT will be**

endocytosed into the neuron and start the proteolytic cleavage of proteins necessary for synaptic transmission, thus inhibiting nerve signaling.

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METHODS

Search strategy: This systemic review and meta-analysis involved the use of the following online databases of published research: MEDLINE, Embase, and the Cochrane Library. For MEDLINE, the search syntax used is (exp *Botulinum Toxins/ or exp *Botulinum Toxins, Type A/) and exp *Sialorrhea/ and exp *Central Nervous System Diseases/. For Embase, the search syntax used is 'botulinum toxin'/exp AND 'hypersalivation'/exp AND 'central nervous system disease'/exp. For the Cochrane Database of Systematic Reviews and the Cochrane Central Register of Controlled Trials, the search syntax used is ("botulinum toxins"[MeSH Terms]) AND ("sialorrhea"[MeSH Terms]) AND ("central nervous system diseases"[MeSH Terms]).

Participant or population: The participants must have central nervous system diseases; must be older than 18 years old.

Intervention: Botulinum toxin type A injection into the salivary glands.

Comparator: Placebo-controlled group(meta-analysis); before and after botulinum toxin type A injection comparison(systematic review).

Study designs to be included: Systematic Review and Meta-Analysis.

Eligibility criteria: Meta-analysis had the following inclusion criteria: (1) the research included must use botulinum toxin type A as their treatment group(s); (2) the participants must have central nervous system diseases; (3) the included studies must be randomized placebo-controlled trials, controlled trials, or prospective studies; (4) the articles must be published in English; (5) the participants involved in the included studies must be older than 18 years old; lastly, (6) there must be sufficient quantifiable data available for meta-analysis.

Information sources: Electronic databases.

Main outcome(s): Electronic databases.

Additional outcome(s): Safety and Adverse Events of botulinum toxin injection.

Data management: Forest plot for this meta-analysis; Heterogeneity is assessed with the I2 statistic.

Quality assessment / Risk of bias analysis: Cochrane's risk of bias graph and summary table were created to assess whether different biases existed in each study included in the meta-analysis; Funnel plot of the meta-analysis to find out potential publication bias.

Strategy of data synthesis: The forest plot in this meta-analysis using Comprehensive Meta-Analysis software (Biostat Inc. NJ, USA). Since between-study variability may be present, this meta-analysis used a random effects model and standardized differences with 95% confidence intervals (CI).

Subgroup analysis: None.

Sensitivity analysis: None.

Language restriction: Inclusion criteria: the articles must be published in English.

Country(ies) involved: Taiwan.

Keywords: Botulinum toxins, drooling, central nervous system diseases, meta-analysis.

Contributions of each author:

Author 1 - Chih-Rung Chen performed data extraction for the meta-analysis and systematic review, and drafted the first version of the manuscript.
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