INPLASY PROTOCOL

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None declared.

Efficacy of Intranasal Insulin in Improving Cognition in Mild Cognitive Impairment or Dementia: A Systematic Review and Meta-analysis

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Review question / Objective: **How does the efficacy of Intranasal Insulin in improving Cognition in Mild Cognitive Impairment or Dementia.**
Condition being studied: **Insulin regulates many aspects of brain function related to mild cognitive impairment (MCI) or dementia, which can be delivered to the brain center via intranasal (IN) devices. Some small, single-site studies indicated that intranasal insulin can enhance memory in patients with MCI or dementia. The pathophysiology of Alzheimer disease (AD) and diabetes mellitus (DM) overlap, making insulin an attractive therapy for people suffering from MCI or dementia. The goal of the study is to evaluate the effectiveness of IN insulin on cognition in patients with MCI or dementia.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 August 2022 and was last updated on 15 August 2022 (registration number INPLASY202280054).

INTRODUCTION

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IN insulin on cognition in patients with MCI or dementia.

METHODS

Participant or population: Inclusion: patients diagnosed with dementia or mild cognitive impairmentExclusion: adults diagnosed with diabetes mellitus, psychiatric disorders, alcoholism, severe head trauma, neurologic disease other than dementia or mild cognitive impairment, renal or hepatic disease, COPD, CHF, arrhythmias, other major pathologies.

Intervention: The intervention is intranasal insulin in 10 or 20 or 40 or 60 international units (IU).

Comparator: Patients with mild cognitive impairment or dementia in each study taking intranasal insulin will be compared with patients taking placebo or other conventional treatments.

Study designs to be included: We will include randomized controlled trials to assess the beneficial effects of the treatments.

Eligibility criteria: Qualification criteria for inclusion in the study were as below: Types of studies: Only RCTs were included. Participants: Studies of human participants with MCI or dementia eligible for inclusion, all of these people were excluded from diabetes mellitus. Interventions: Studies that include receiving any dose of intranasal insulin at any time. Comparator: Any study containing a control group receiving placebo treatment is eligible for inclusion. Outcomes: Studies investigating the efficacy or progression of cognitive disorders or performance (the study reported specific cognitive scores at baseline and endpoints) and dementia (including subtypes of dementia, such as AD or VD) were eligible for inclusion.

Information sources: We will search the following electronic bibliographic databases: PubMed, EMBASE, The Cochrane Library (Cochrane Database of Systematic Reviews, Cochrane Central Register of Controlled Trials (CENTRAL), Cochrane Methodology Register), Web of Science (Science and Social Science Citation Index), CNKI、Wanfang database and Clinical Trials. There were no restrictions based on language or publication period.

Main outcome(s): The main outcome measure of this study is to evaluate if intranasal insulin has beneficial effects on cognition in humans. Domains of cognition including, but are not limited to, executive function, problem-solving, decision making, attention, verbal memory, visuospatial memory, working memory, declarative memory, visual memory, and visual learning were assessed.

Additional outcome(s): Biochemical measures (glucose, insulin, glucocorticoids, plasma AB, APOE genotype) and side-effects of intranasal insulin.

Quality assessment / Risk of bias analysis: The risk of bias will be assessed by two reviewers independently using The Cochrane Collaboration's tool for assessing the risk of bias（ROB).

Strategy of data synthesis: The combined cognitive performance score change was calculated by the inverse variance method (random effect model) as the standardized mean difference (SMD).χ^2 test was used for statistical heterogeneity. The Review Manager (Revman, version 5.3) will be used for data analysis.

Subgroup analysis: Subgroup analyses will be conducted separately based on types of patient populations and types of dementia and combined disease type.

Sensitivity analysis: When the heterogeneity is high (I^2 >50%), the random effect model is recommended, while the fixed effect model is the opposite. Each included study was eliminated one by one and then the effect size was merged. The inclusion and exclusion criteria were

changed or a certain type of literature was eliminated.

Country(ies) involved: China.

Keywords: Mild Cognitive Impairment (MCI); Dementia; Cognitive Impairment; Intranasal insulin; Systematic review; Meta-analysis.

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