INTRODUCTION

Review question / Objective: The aim of this meta-analysis of randomized controlled trials is to systematically evaluate the efficacy of acupuncture in the treatment of cognitive dysfunction in Alzheimer's disease (AD), in order to provide evidence-based evidence for the application of acupuncture therapy in the clinical course of AD.

Condition being studied: Meta-analysis Alzheimer's disease (AD) is a clinically common neurodegenerative disease that accounts for 80% of diagnosed cases of dementia in patients with AD, and its characteristic progressive cognitive impairment is an important cause that affects patients' activities of daily living, which in turn leads to dependence, disability and death, imposing a heavy burden on patients, families, society and medical care. The World Alzheimer's Disease 2018 Report shows that China has 6 million AD patients, the largest number of AD patients, and the number of AD patients in China is expected to exceed 40 million by 2050, but there is no strong evidence of a systematic and targeted treatment strategy to stop the development of AD cognitive impairment. The commonly used clinical acetylcholinesterase inhibitors and aspartate receptor inhibitors have only partial symptom improvement and limited efficacy. However, studies have shown that early diagnosis and treatment of Alzheimer's disease and mild cognitive impairment play a key role in improving patient prognosis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 09 March 2023 and was last updated on 09 March 2023 (registration number INPLASY202330036).
application of acupuncture therapy in the clinical course of AD.

**Rationale:** According to Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

**Condition being studied:** Meta-analysis Alzheimer's disease (AD) is a clinically common neurodegenerative, disease that accounts for 80% of diagnosed cases of dementia in patients with AD, and its characteristic progressive cognitive impairment is an important cause that affects patients' activities of daily living, which in turn leads to dependence, disability and death, imposing a heavy burden on patients, families, society and medical care. The World Alzheimer's Disease 2018 Report shows that China has 6 million AD patients, the largest number of AD patients, and the number of AD patients in China is expected to exceed 40 million by 2050, but there is no strong evidence of a systematic and targeted treatment strategy to stop the development of AD cognitive impairment, and the commonly used clinical acetylcholinesterase inhibitors and aspartate receptor inhibitors have only partial symptom improvement and limited efficacy. However, studies have shown that early diagnosis and treatment of Alzheimer's disease and mild cognitive impairment play a key role in improving patient prognosis.

**METHODS**

**Search strategy:** Chinese and English databases such as Pubmed, Embase, Cochrane Library Database, CBM, CNKI, VIP, Wanfang were searched by computer, and randomized controlled clinical trials related to acupuncture in the treatment of Alzheimer's disease were searched. The time limit of retrieval is from the establishment of the database to July 31, 2021, and the retrieval method is a combination of subject words and free words. English search terms: acupuncture, Alzheimer's disease, randomized controlled trial; Chinese keywords included acupuncture, Alzheimer's disease, randomized controlled trials.

**Participant or population:** Patients who were diagnosed with cognitive dysfunction in Alzheimer's disease, and there's no limitation on nationality, race, gender, age, disease duration.

**Intervention:** The subjects in the intervention group were given acupuncture alone or combined with other treatments the same as the control group; The control group received conventional western medicine treatment; Treatment course ≥ 4 weeks.

**Comparator:** Usual care and medications such as Dementia drug, Statins Antihypertensive drugs and so on.

**Study designs to be included:** Only RCTs

**Eligibility criteria:** ① Review, review, discussion and other non-clinical studies; ② Animal experiments or cell tissue studies; ③ Clinical studies of cases without randomized controlled trials or control groups; ④ Comparative study of disease group and non-disease group; ⑤ The treatment group combined with other TCM therapies, such as TCM therapy, massage therapy, acupoint application, foot bath therapy, etc.; Self-cross-control study; ⑦ Clinical studies that cannot be traced back to original data or whose existing data are incomplete; ⑧ Clinical studies without access to original texts.

**Information sources:** (1) Participants: Patients who were diagnosed with cognitive dysfunction in Alzheimer's disease, and there's no limitation on nationality, race, gender, age, disease duration. (2) Interventions and comparisons: The subjects in the intervention group were given acupuncture alone or combined with other treatments the same as the control group; The control group received conventional western medicine treatment; Treatment course ≥ 4 weeks. (3) Outcomes: The main outcome indicators of this study were cognitive
function evaluation, including: ① Simple Mental State Examination Scale (MMSE); ② Daily Living Ability Assessment Scale (ADL); ③ Alzheimer's Disease Cognitive Function Assessment Scale (ADAS-Cog); ④ TCM syndrome score (SDSD); ⑤ Montreal Cognitive Test (MoCA). The secondary outcome indicators were: ⑥ adverse reactions. In this network meta-analysis, RCT which included one of the primary outcomes was sufficient. (4) Study design only RCTs were taken into our consideration.

Main outcome(s): The main outcome indicators of this study were cognitive function evaluation, including: ① Simple Mental State Examination Scale (MMSE); ② Daily Living Ability Assessment Scale (ADL); ③ Alzheimer's Disease Cognitive Function Assessment Scale (ADAS-Cog); ④ TCM syndrome score (SDSD); ⑤ Montreal Cognitive Test (MoCA).

Additional outcome(s): The secondary outcome indicators were: ⑥ adverse reactions.

Data management: NoteExpress was used to manage retrieved literatures stata 16.0 was used to perform network meta analysis and make graphs.

Quality assessment / Risk of bias analysis: Cochrane risk of bias tool and GRADE assessment.

Strategy of data synthesis: It followed the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA).

Subgroup analysis: First: age=60; Second: stable angina pectoris of Simple Mental State Examination Scale (MMSE).

Sensitivity analysis: The total of patients in trials with case numbers \( \geq 100 \) trials.

Language restriction: No language limitation.

Country(ies) involved: China.

Keywords: Alzheimer's disease; cognitive dysfunction; acupuncture; efficacy.

Contributions of each author:

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