INPLASY PROTOCOL

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Conflicts of interest:
None.

Assessment of the efficacy of α-lipoic acid in treatment of diabetes mellitus patients with erectile dysfunction: a protocol for systematic review and meta-analysis

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Review question / Objective: **How effective is α-lipoic acid in treatment of diabetes mellitus patients with erectile dysfunction?**
Condition being studied: **α-lipoic acid. Diabetes mellitus erectile dysfunction.**
Information sources: **The English literature mainly searches Cochrane Library, PubMed, EMBASE, and Web of Science. While the Chinese literature comes from China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, the VIP information resource integration service platform (cqvip), China Biology Medicine Disc (Sino Med) with a language limitation of English and Chinese. In addition, we will also search Google scholar, Baidu Scholar to find out unpublished researches or other related literature. And above all, the Chinese Clinical Trial Registry (ChiCTR) and ClinicalTrials.gov will also be searched.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 31 July 2020 and was last updated on 31 July 2020 (registration number INPLASY202070130).

INTRODUCTION

Review question / Objective: **How effective is α-lipoic acid in treatment of diabetes mellitus patients with erectile dysfunction?**

Condition being studied: **α-lipoic acid. Diabetes mellitus erectile dysfunction.**

METHODS

Search strategy: We will retrieve each database from the built-in until July 2020. The English literature mainly searches Cochrane Library, PubMed, EMBASE, and Web of Science. While the Chinese literature comes from China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, the VIP information resource integration service platform (cqvip), China Biology Medicine Disc (Sino Med) with a language limitation of English and Chinese. In addition, we will also search Google scholar, Baidu Scholar to find out unpublished researches or other related literature. And above all, the Chinese Clinical Trial Registry (ChiCTR) and ClinicalTrials.gov will also be searched. A manual search will be conducted at the library of Chengdu University of Traditional Chinese Medicine.

Participant or population: Men with a history of diabetes who match the Diagnostic Criteria for Diabetes: Refer to the American Diabetes Association (ADA) Diabetes Care Guidelines. The diagnosis is ED after diabetes, and the International Index of Erectile Function 5 (IIEF-5) score is <21. The course of ED is ≥ 3months. The patient must be at least 18 years of age. Neuropathy caused by other causes and patients with severe heartdisease, liver and kidney dysfunction, mental illness, or a relevant drug allergic history will be not included.

Intervention: The experiment group used α-lipoic acid, with no limited of the dose and frequency of the medicine. The trial period requires more than 1 course of treatment.

Comparator: The control group of this meta-analysis applied for simple western medicine, or placebo, or no treatment. However, once the control group had accepted the therapy of α-lipoic acid, the trials will be rejected.

Study designs to be included: Take α-lipoic acid as main treatment, including randomized controlled trials of the control group (effective methods other than α-lipoic acid).

Eligibility criteria: Men with a history of diabetes who match the Diagnostic Criteria for Diabetes: Refer to the American Diabetes Association (ADA) Diabetes Care Guidelines. The diagnosis is ED after diabetes, and the International Index of Erectile Function 5 (IIEF-5) score is <21. The course of ED is ≥ 3months. The patient must be at least 18 years of age.

Information sources: The English literature mainly searches Cochrane Library, PubMed, EMBASE, and Web of Science. While the Chinese literature comes from China National Knowledge Infrastructure (CNKI) database, Wanfang Data Knowledge Service Platform, the VIP information resource integration service platform (cqvip), China Biology Medicine Disc (Sino Med) with a language limitation of English and Chinese. In addition, we will also search Google scholar, Baidu Scholar to find out unpublished researches or other related literature. And above all, the Chinese Clinical Trial Registry (ChiCTR) and ClinicalTrials.gov will also be searched.

Main outcome(s): The primary outcome measurement will be assessed using the International Index of Erectile Function 5 (IIEF-5) score. (1) Healing: IIEF-5 score ≥22 points after treatment; (2) Significant effect: IIEF-5 score <22 points after treatment, score improvement≥60%; (3) Effective: IIEF-5 score <22 points after treatment, points improved <60%, but≥30%; (4) invalid: IIEF-5 score <22 points after treatment, score improvement <30%.

Additional outcome(s): The secondary outcome measurement will be assessed according to the α-lipoic acid syndrome scoring criteria. (1) Healing: The clinical symptoms and signs of α-lipoic acid disappear or disappear, and the syndrome score is reduced by ≥90%; (2) Markedly effective: the clinical symptoms and signs of α-lipoic acid are obviously improved, the syndrome score is reduced by ≥60%; (3) Effective: α-lipoic acid clinical symptoms

Signs and signs have improved, syndrome points reduced by <60%, but ≥30%; (4) Invalid: Chinese clinical symptoms and signs have not improved, or even worse, syndrome scores reduced by <30%.Integral variation formula (Nimodipine method: [(pretreatment score - post-treatment score) ÷ pre-treatment score] × 100%.

Data management: According to the characteristics of the study, we prepare an excel form for data collection before data extraction. Outcome indicators for eligible studies were independently extracted and filled in the data extraction form by 2 reviewers. If there is any argument, it can get an agreement by discussing through 2 reviewers or seek a third party's suggestion. For each study, the following data will be extracted: title, the first authors of the article, year of publication, study countries, study design, data collection year, diagnostic criteria used for ED, interventions in experimental group, interventions in control group, time of treatment, course of disease, number of patients in each group, ages of patients, outcomes and safety data. If there is not enough data in a study, we will contact the corresponding author for more detailed data. If the methodological details are not told in papers, we will contact for more explanation.

Quality assessment / Risk of bias analysis: Two reviewers will assess the risk of bias of included articles by using the Cochrane Handbook providing the risk of bias (ROB) assessment tool. The following 7 items, such as random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias, are evaluated by 3 grades of "low bias," "high bias," and "unclear bias." Two reviewers will conduct the risk of bias assessment independently and any disagreements will be solved by a discussion of all reviewers.

Strategy of data synthesis: Review Manager software version 5.3 (The Nordic Cochrane Center, The Cochrane Collaboration, 2014, Copenhagen, Denmark) provided by the Cochrane Collaboration will be performed for data synthesis and analysis. The dichotomous data is represented by RR, continuous data is expressed by MD or SMD. If there is no heterogeneity (I2.1), the data are synthesized using a fixed effect model. Otherwise (I2≥50%, P<.1), a random effect model is used to analyze. Then subgroup analysis will be conducted basing on the different causes of heterogeneity. If a meta-analysis cannot be performed, it will be replaced by a general descriptive analysis.

Subgroup analysis: If the results of the study are heterogeneous, we will conduct a subgroup analysis for different reasons. Heterogeneity is manifested in the following several aspects, such as race, age, sex, different intervention forms, pharmaceutical dosage form, dosage, treatment course.

Sensibility analysis: Sensitivity analysis is mainly used to evaluate the robustness of the primary outcome measures. The method is that removing the low-level quality study one by one and then merge the data to assess the impact of sample size, study quality, statistical method, and missing data on results of meta-analysis.

Language: English.

Country(ies) involved: China.

Keywords: α-lipoic acid; diabetes mellitus erectile dysfunction; protocol; systematic review; meta-analysis.

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