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None declared.

Network meta-analysis of curative efficacy of different acupuncture methods on obesity combined with insulin resistance

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Review question / Objective: **Population: Patients diagnosed as obesity with insulin resistance. Obesity reference: Consensus of experts on the Prevention and treatment of adult obesity in China in 2011 and Consensus of Chinese experts on medical nutrition therapy for overweight/obesity in 2016 were developed by the Obesity Group of Chinese Society of Endocrinology(CSE); BMI≥28. IR reference: According to the Expert opinions on insulin resistance evaluation published by Chinese Diabetes Society, HOMA-IR≥2.68 is regarded as the standard for the diagnosis of IR. Regardless of age, gender and course of disease. Patients diagnosed as obesity with insulin resistance. Intervention: Any kind of acupuncture, moxibustion, acupuncture+moxibustion, warm acupuncture, electropuncture, auricular point, acupoint application and acupoint catgut embedding. Comparison: Other acupuncture treatments, Drug therapy or blank control. Outcome: Primary outcomes: ①Fasting blood-glucose (FBG); ②Fasting serum insulin (FINS); ③Homeostasis model assessment-IR (HOMA-IR); ④Body Mass Index (BMI). Secondary outcomes: ①Waistline; ②Waist-hip ratio;③Triglyceride (TG); ④Total cholesterol (TC); ⑤High-density lipoprotein (HDL); ⑥Low-density lipoprotein (LDL). Study: Randomized controlled trials (RCTs) of different acupuncture methods in the treatment on obesity with insulin resistance, blind method and language are not limited. Randomized controlled trials (RCTs).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 20 August 2022 and was last updated on 20 August 2022 (registration number INPLASY202280075).

INTRODUCTION

Review question / Objective: **Population: Patients diagnosed as obesity with insulin resistance. Obesity reference: Consensus of experts on the Prevention and treatment of adult obesity in China in 2011 and Consensus of Chinese experts on medical**

nutrition therapy for overweight/obesity in 2016 were developed by the Obesity Group of Chinese Society of Endocrinology(CSE); BMI≥28. IR reference: According to the Expert opinions on insulin resistance evaluation published by Chinese Diabetes Society, HOMA-IR≥2.68 is regarded as the standard for the diagnosis of IR. Regardless of age, gender and course of disease. Patients diagnosed as obesity with insulin resistance. Intervention: Any kind of acupuncture, moxibustion, acupuncture+moxibustion, warm acupuncture, electropuncture, auricular point, acupoint application and acupoint catgut embedding. Comparison: Other acupuncture treatments, Drug therapy or blank control. Outcome: Primary outcomes: ①Fasting blood-glucose (FBG); ②Fasting serum insulin (FINS); ③Homeostasis model assessment-IR (HOMA-IR); ④Body Mass Index (BMI). Secondary outcomes: ①Waistline; ②Waist-hip ratio;③Triglyceride (TG); ④Total cholesterol (TC); ⑤High-density lipoprotein (HDL); ⑥Low-density lipoprotein (LDL). Study: Randomized controlled trials (RCTs) of different acupuncture methods in the treatment on obesity with insulin resistance, blind method and language are not limited. Randomized controlled trials (RCTs).

Rationale: Obesity, one of the leading health risk factors worldwide, whose prevalence is rapidly increasing worldwide, since 1.1 billion people are classified as overweight. Furthermore, obesity is associated with several health problems including insulin resistance, cardiovascular disease, gallbladder disease and certain malignancies. Insulin resistance (IR) is the common pathological basis of metabolic diseases such as obesity and type 2 diabetes. Obesity and overweight are closely correlated with IR and are independent risk factors for IR. The pathogenesis of IR is still unclear, but some studies suggested that it is caused by the interaction between nutritional overload, systemic fatty acid surplus, inflammatory response of adipose tissue, endoplasmic reticulum stress, oxidative stress and adipose tissue hypoxia. Acupuncture is the most rapidly growing complementary therapy which is recognised by WHO. In recent years, both experimental and clinical current data concluded that acupuncture was superior to conventional medication for obesity and insulin resistance, which can be used to improve symptoms and efficacy while reducing side effects or adverse reactions caused by western medicine therapy. Suggesting that acupuncture exerts beneficial effects on the mechanisms of obesity and insulin resistance, however, the most effective frequency of obesity combined with insulin resistance by acupuncture remains controversial. Further prospective studys are needed to establish the effectiveness of this complementary method for obesity combined with insulin resistance treatment.

Condition being studied: Obesity reference: Consensus of experts on the Prevention and treatment of adult obesity in China in 2011 and Consensus of Chinese experts on medical nutrition therapy for overweight/obesity in 2016 were developed by the Obesity Group of Chinese Society of Endocrinology(CSE); BMI≥28. IR reference: According to the Expert opinions on insulin resistance evaluation published by Chinese Diabetes Society, HOMA-IR≥2.68 is regarded as the standard for the diagnosis of IR. Regardless of age, gender and course of disease.

METHODS

Search strategy: Literature retrieval - Cross retrievaling the Chinese database (CNKI, WanFang Data, VIP and SinoMed) and the English database (PubMed, Embase, the Cochrane Library and http://www.clinicaltrial.gov) were electronically searched from database construction time to March 31, 2022. Key words or mesh terms: Acupuncture, Needle, Electro-acupuncture, Moxibustion, Fire needle, Needle warming moxibustion, Auricular point, Point application therapy, Acupoint catgut embedding, Obesity, Insulin

resistance, Controlled clinical trial, Randomized controlled trial, Drug therapy, Groups, Placebo. Considering that there may be differences in the description of outcomes in RCT, outcome indicators were not restricted in the retrieval to avoid omission.

Participant or population: Patients diagnosed as obesity with insulin resistance. Obesity reference: Consensus of experts on the Prevention and treatment of adult obesity in China in 2011 and Consensus of Chinese experts on medical nutrition therapy for overweight/obesity in 2016 were developed by the Obesity Group of Chinese Society of Endocrinology(CSE); BMI≥28. IR reference: According to the Expert opinions on insulin resistance evaluation published by Chinese Diabetes Society, HOMA-IR≥2.68 is regarded as the standard for the diagnosis of IR. Regardless of age, gender and course of disease.

Intervention: Any kind of acupuncture, moxibustion, acupuncture+moxibustion, warm acupuncture, electropuncture, auricular point, acupoint application and acupoint catgut embedding. In addition to intervention measurements, other background treating measurements were identical in both groups.

Comparator: Other acupuncture treatments, Drug therapy or blank control.

Study designs to be included: Randomized controlled trials (RCTs) of different acupuncture methods in the treatment on obesity with insulin resistance, blind method and language are not limited.

Eligibility criteria: Patients diagnosed as obesity with insulin resistance. Exclusion criteria: ①Non-RCTs research: Descriptive studies, case-control studies, cohort studies, literature review, social commentary, case reports, case series analysis, etc; ②The intervention measures take a variety of therapy combination, or study acupuncture and moxibustion different points, different techniques, the study of frequency; ③Animal studies, cellular or analytical studies, or systematic reviews, meta-analyses, and pooled analyses of multiple RCTs; ④The subjects suffered from serious diseases, such as cerebrovascular diseases and tumors; ⑤Others: Conference abstracts, comments, guidelines, letters, amendments, and other unrelated studies where full text is not available and results are incomplete.

Information sources: Electronic databases 1. The Chinese database (CNKI, WanFang Data, VIP and SinoMed) ; 2. The English database (PubMed, Embase, the Cochrane Library and http://www.clinicaltrial.gov). key words or mesh terms: Acupuncture, Needle, Electroacupuncture, Moxibustion, Fire needle, Needle warming moxibustion, Auricular point, Point application therapy, Acupoint catgut embedding, Obesity, Insulin resistance, Controlled clinical trial, Randomized controlled trial, Drug therapy, Groups, Placebo.

Main outcome(s): Primary outcomes: ①Fasting blood-glucose (FBG); ②Fasting serum insulin (FINS); ③Homeostasis model assessment-IR (HOMA-IR); ④Body Mass Index (BMI).

Additional outcome(s): Secondary outcomes: ①Waistline; ②Waist-hip ratio;③Triglyceride (TG); ④Total cholesterol (TC); ⑤High-density lipoprotein (HDL); ⑥Low-density lipoprotein (LDL).

Data management: Literature management By aggregating studies retrieved from various archives, we used EndNote 20 software to manage the retrieved literature. After excluding the literatures duplicated between different databases, two researchers independently read the title and abstract of the literatures, screened out the obvious irrelevant literatures according to the inclusion/exclusion criteria, and screened the literatures by reading the full text if necessary. Screening results are cross-checked by two

researchers, and in case of disagreement, a third expert is consulted or discussed.

Quality assessment / Risk of bias analysis: Literature quality evaluation and data extraction - We used Excel 2016 software to develop basic information extraction table and quality evaluation table. Two reviewers independently conducted quality evaluation and basic data extraction for each article that met the inclusion criteria. Detailed data were extracted by ADDIS1.16.8 software, including basic study information (author, publication year, study type, sample size, etc.), intervention measures and outcome indicators, quality evaluation, etc. Two reviewers cross-checked the results, and if there is any disagreement, it shall be decided through discussion or consultation with a third reviewer. Bias risk assessment of included studies - Two reviewers assessed the risk of bias in the included studies according to the Cochrane Manual's risk of bias assessment tool for RCTs. Projects include: randomization of assignment methods, assignment plan concealment, blinding of study subjects and protocol implementors, blinding of study outcome measures, integrity of outcome data, selective reporting of study results, and other sources of bias. Finally, the risk of literature bias was judged as "low", "high" and "uncertain". Two reviewers independently conducted, and then cross-checked, in case of disagreement, through discussion to resolve, disagreement with the third reviewer to discuss decisions, reached a consensus.

Strategy of data synthesis: Statistical Analysis - Using Stata 15.1 software and its “network”commands to draw the network diagram for comparison between intervention measures for evaluation of publication bias. Network meta-analysis was conducted for each outcome, and heterogeneity and inconsistency in mesh evidence body were tested. In this study, odds ratio (OR) and 95% confidence interval (CI) were used as expression way for The dichotomous outcome index, while the continuous outcome index was expressed as mean difference (MD) and its 95% confidence interval. The existence of publication bias was identified by drawing a corrected comparison funnel plot, and the inconsistencies of the results of the mesh meta-analysis were tested by node splitting method. If direct comparison and indirect comparison result difference of P>0.05, the inconsistency is not significant, and the consistency model is adopted. At the same time, a prediction interval graph was drawn for each outcome. If the prediction interval crossed the invalid line, inter-study heterogeneity was considered, and the random effect model was selected. Efficacy ranking was based on SUCRA(surface under the Cumulative Ranking Curve). The larger SUCRA is, the better the efficacy of the drug in this outcome. P< 0.05 was considered statistically significant.

Subgroup analysis: The existence of publication bias was identified by drawing a corrected comparison funnel plot, and the inconsistencies of the results of the mesh meta-analysis were tested by node splitting method. - If direct comparison and indirect comparison result difference of P>0.05, the inconsistency is not significant, and the consistency model is adopted. At the same time, a prediction interval graph was drawn for each outcome. If the prediction interval crossed the invalid line, inter-study heterogeneity was considered, and the random effect model was selected. Efficacy ranking was based on SUCRA(surface under the Cumulative Ranking Curve). The larger SUCRA is, the better the efficacy of the drug in this outcome. P< 0.05 was considered statistically significant.

Sensitivity analysis: The existence of publication bias was identified by drawing a corrected comparison funnel plot, and the inconsistencies of the results of the mesh meta-analysis were tested by node splitting method. If direct comparison and indirect comparison result difference of P>0.05, the inconsistency is not significant, and the consistency model is adopted. At the same time, a prediction interval graph was drawn for each outcome. If the prediction interval crossed the invalid line,

inter-study heterogeneity was considered, and the random effect model was selected. Efficacy ranking was based on SUCRA(surface under the Cumulative Ranking Curve). The larger SUCRA is, the better the efficacy of the drug in this outcome. P< 0.05 was considered statistically significant.

Language restriction: No.

Country(ies) involved: China.

Keywords: Acupuncture methods, Obesity, Insulin resistance, Systematic review, Network meta-analysis.

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