INPLASY PROTOCOL

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Review Stage at time of this submission: The review has not yet started.

Conflicts of interest: None.

Does patient's expectation benefit acupuncture treatment? A protocol for systematic review and meta-analysis

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Review question / Objective: 1. Does a higher level of patient's expectation benefit acupuncture treatment in RCTs? 2. In what kind of medical condition can a positive relationship between acupuncture expectation and outcomes be detected easily? 3. Do different expectation measurements and statistical methods affect the patients' response to acupuncture?

Condition being studied: Previous studies showed that verum acupuncture failed to show significant differences between sham acupuncture. While comparing with no treatment or usual care, verum acupuncture has better therapeutic effects. It suggests that a sizeable placebo effects may contribute to the effectiveness of acupuncture treatment. Patient's expectation has influence on outcomes in clinical practice as one part of placebo effects. Some studies reported that patients with optimistic expectation achieved better outcomes. But two systematic reviews about this relationship published in 2012 and 2015, respectively, failed to draw a confirm conclusion. In recent five years, a certain number of reports from higher-quality randomized controlled trials (RCTs) have been published. It is necessary to find out whether higher level of expectation will impact on the clinical outcomes after acupuncture treatment, and how much of this influence contributes to the effects.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 06 October 2020 and was last updated on 06 October 2020 (registration number INPLASY2020100020).

INTRODUCTION

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METHODS

Participant or population: Adult patients aged ≥ 18 years old with any medical or psychological condition will be included.

Intervention: The interventions should be acupuncture including manual acupuncture, electroacupuncture, auricular acupuncture, scalp acupuncture, intradermal needle, and TENS without moxibustion. Because combined methods, such as acupuncture with moxibustion or Chinese medicine decoction, will make the true effectiveness of acupuncture difficult to evaluate. Therefore, we will exclude studies use combined therapy.

Comparator: Comparisons include the following types will be included: (1) Placebo controls: sham acupuncture (e.g. needling at no-acupoint), placebo drugs/device (e.g. Park Sham Placebo Acupuncture Device),

sham interventions (e.g. sham laser) and so on. (2) Positive medication: participants are administrated positive medication which were recommended by guidelines. (3) No acupuncture treatment, such as waiting list: participants receive no acupuncture treatment, or receive general care or usual care (e.g. health education, exercise recommendation). We will exclude the studies which only applying Chinese medicine, or other methods that we can' not identify the effects as a control, such as cupping or tuina.

Study designs to be included: We will include randomized controlled trails (RCTs) which detect the acupuncture response to patient's expectation. For the studies applied sham controls, such as sham acupuncture, placebo acupuncture device, randomized, allocation concealment, and blinding methods should be clearly described. In order to guarantee the quality of studies, only sample size of more than 30 will be considered.

Eligibility criteria: We will include adult patients older than 18 years of age who are undergoing acupuncture treatment regardless of any physical or psychological problems.

Information sources: A systematic search will be conducted in the following databases: EMBASE, PubMed, Cochrane Central Register of Controlled Trials (CENTRAL), Chinese BioMedical Literature Database (CBM), Chinese National Knowledge Infrastructure (CNKI), and Chinese Science and Technology Periodical Database (VIP) from inception to October 1, 2020. Because of language limitation and quality assurance, only peer-reviewed publications in English or Chinses will be screened. Full articles will be included. The following search terms will be combined for systematic search, and Chinese terms will be used in Chinese databases: "acupuncture", "acupuncture therapy", "auricular acupuncture", "transcutaneous electrostimulation/TENS", "acupressure", "randomized/randomised controlled trial", "expectation", "expectancy", etc.

Main outcome(s): Because eligible RCTs in any medical condition will be included, there are no constraints on health-related outcomes. Acupuncture expectation assessment or related information collection can be any type: (1) questions such as "What do you expect from this acupuncture treatment that you will receive for this disease?", "How much improvement do you expect after acupuncture treatment?", or "How much will your symptoms alleviate after acupuncture treatment?"; (2) questionnaire such as Credibility and Expectancy Questionnaire []. Answers measured by Visual Analogue Scale (VAS)/Numerical Rating Scale (NRS) for continuous variables, or Likert scale for categorical variables will be included. The expectation should be assessed before acupuncture treatment. RCTs collected expectation information after only first or last session of acupuncture will not be included. Because both the expectation level and acupuncture outcomes will change due to variable factors, such as the doctor-patient relationship, recovery, and changes of lifestyle during the observation period.

Quality assessment / Risk of bias analysis: The methodological quality measurement of each original study will be evaluated independently by two reviewers (JHL and ZY) by using the Cochrane Collaboration's tool for assessing risk of bias (Cochrane Manual V.5.1.0). The following aspects will be assessed: randomization allocation, concealment, blinding, data integrity, selective reporting, and other bias (such as trial design, baseline similarity of groups, early cessation or treatment, etc.). The assessment results will be divided into three levels: low risk, high risk, and uncertain risk. Any discrepancy will be resolved by consensus or judged by a third reviewer (ZQH). Regarding the characteristics of acupuncture clinical trials, we will also assess the quality of acupuncture interventions according to the Standards for Reporting Interventions in Controlled Trials of Acupuncture (STRICTA) recommendation.

Strategy of data synthesis: Considering the heterogeneity in different diseases and study design, we will conduct a descriptive systematic review rather than a meta-analysis for the eligible studies. But subgroups analysis will be performed for possible meta-analysis. RevMan V.5.3 statistical software will be applied for data synthesis. Statistical analyses will be performed with RevMan V.5.3 statistical software to present direct and indirect comparisons between acupuncture treatment and controls. We will use random-effects model for data synthesis.

Subgroup analysis: We plan to perform the following subgroup analyses for explore the stable relationship between acupuncture expectation and outcomes across different studies: (1) Different medical conditions: We will classify different conditions for possible meta-analysis, such as pain diseases (e.g. musculoskeletal, visceral pain diseases, such as knee osteoarthritis or angina), functional disorders (e.g. functional dyspepsia, irritable bowel syndrome), psychological problems (e.g. depression), and other condition (e.g. hot flashes). (2) Different types of controls: Previous studies showed that verum acupuncture has no differences to sham acupuncture, but superior to no acupuncture treatment or usual care alone. This suggest that therapeutic benefits could be provided both by verum and sham acupuncture, both of which are practical intervention rather than nothing. We will classify the controls as sham acupuncture, positive medication, no acupuncture treatment/usual care, and compare with verum acupuncture. (3) Different time points: we will screen studies that collected expectation information after acupuncture treatment, to evaluate whether a better prognosis of acupuncture will impact on the expectation level. (4) Different statistical methods: we will extract the different statistical methods about the acupuncture expectations. We will separately synthesis expectation data collected in categorical and continuous ways.

Sensibility analysis: The sensitivity analysis will be based on different statistical approach, different heterogeneity quality and different sample size. Excluding the studies which were poor quality or potential contributors to heterogeneity, the meta-analysis will be reused.

Country(ies) involved: China.

Keywords: expectations, acupuncture, placebo effects, systematic review, meta-analysis.

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