INPLASY PROTOCOL

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None declared.

Effectiveness and Safety of Laser Acupuncture for Asthma in Children: A Protocol for Systematic Review and Meta-Analysis of Randomized Controlled Trials

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Review question / Objective: **To synthesize and assess the current available evidence regarding the effectiveness and safety of Laser acupuncture on Childhood asthma.**
Main outcome(s): **The primary outcomes of this study are been considered to be the mean change of the scores of the pulmonary function, such as the percentage of the estimated volume of forced expiratory volume in one second (FEV1), and FEV1%. Quality of life evaluation, such as Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and Asthma Quality of Life Questionnaire (AQLQ). And adverse events will also be the primary outcomes. The mean scores of the studies endpoint of these scales will be analyzed when no change data available.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 October 2021 and was last updated on 21 October 2021 (registration number INPLASY2021100081).

INTRODUCTION

Review question / Objective: **To synthesize and assess the current available evidence regarding the effectiveness and safety of Laser acupuncture on Childhood asthma.**

Rationale: **Childhood asthma (CA) is a global health challenge. Laser acupuncture is a complementary and alternative therapy of Traditional Chinese Medicine. And laser acupuncture has already been applied for treating CA clinically. However, there is a lack of robust evidence syntheses. We will carry out this systematic review and meta-analysis to synthesize and assess the current available evidence regarding the**

effectiveness and safety of laser acupuncture moxibustion on CA.

Condition being studied: Asthma is listed as one of the four persistent diseases by the World Health Organization (WHO), and the mortality of asthma in China is significantly higher than that in other countries, and 1/3 of asthma patients are children. Childhood Asthma (childhood bronchial asthma), the most common chronic respiratory disease in children, is the major cause of chronic diseases in children. It is a chronic airway inflammation involving a variety of cells and cell components, which is characterized by episodic and reversible wheezing, chest tightness, shortness of breath, and cough. Or even cannot lie flat as the main performance. Nearly 6 million of the 22 million Americans with asthma are children, and children with asthma are absent from school due to asthma each year reaching millions of times. In Europe, the total cost of asthma is approximately 25 billion dollars. Through the large-scale investigation of asthma incidence in China, it is found that the incidence of asthma in children presents a significant increasing trend, and increases by 50% every year. The prevalence rate of children under 14 years old is 3.47%, which is a main challenge for health care. So far, steroid drugs and bronchodilators commonly used in western medicine to treat asthma. Although it can relieve asthma symptoms and control acute attacks, it cannot control the development of asthma disease. In addition to this, it has many adverse reactions, severe airway damage, low lung function, and prolonged non-healing, which affects the growth and development of children. The《Global Asthma Prevention and Control Initiative》recommends long-term inhalation of low-dose hormones to control asthma attacks. However, due to parents' fear of adverse hormone reactions, which leads to poor medication compliance. Therefore, to explore the auxiliary role of nondrug therapy in children's asthma control and improve their quality of life is the primary goal of children's asthma control and management. Chinese medicine treatment of asthma has a long history, with its own characteristics. Laser acupuncture therapy (LAT) is a non-invasive, sterile and safe new method of acupuncture that uses laser microbeams to irradiate acupoints directly or in focus under the guidance of traditional Chinese medicine meridian theory, which is Easier to be accepted by children or those who are afraid of needles. Studies have shown that laser acupuncture on GV20, GV14, LI4, GB34 and LR3 can relieve the spasticity of children with spastic cerebral palsy. Currently, LA is mainly used to treat joint pain or muscle pain. Explore Laser Acupuncture's Role. Acupuncture in Modern Medicine. The mechanism of LAT in the treatment of asthma may be that laser acupoint irradiation can activate the mononuclear-macrophage system, reduce the level of eosinophils in the body and produce anti-inflammatory effects, and reduce the level of serum IgE to inhibit chronic allergic inflammation of the airways. At the same time, it regulates the responsiveness of nerve conduction, improves the sensitivity of sympathomimetic drugs, normalizes bronchial response, plays the role of anti-inflammatory, analgesic, and reduces respiratory secretions, reduces airway resistance, and quickly relieves clinical symptoms. Some studies have fully affirmed the clinical anti-asthma effect of laser, and some studies believe that the clinical effect of laser acupuncture in treating children with asthma is inaccurate or equivalent to a placebo effect. In order to further verify the effect of laser acupuncture on asthma control in children, this study collected existing data at home and abroad to conduct a meta-analysis and systematic evaluation, in order to provide a theoretical basis for achieving good control of children with asthma.

METHODS

Search strategy: The following six databases, three each Chinese and English databases, will be searched: China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), WanFang Database, the Cochrane Library,

PubMed, EMbase, will be searched from inception to December 2020 for potentially eligible RCTs. Only human researches will be included. Search terms are laser acupuncture, childhood asthma, pediatric asthma. And the equivalent search terms will be used for Chinese databases.

Participant or population: All eligible children diagnosed with asthma will be enrolled without regard to sex, race and education background. Asthma diagnoses must be based on the asthma-diagnosing standard according to the International consensus on (ICON) pediatric asthma (2012 edtion or its previous edition) or guideline of childhood asthma treatment and prevention in China (GATPC) (2008 edtion). If no specified criteria were documented in the studies, the asthma diagnosis must be based on discriminable and important characteristics of asthma symptoms as confirmed by patients' doctors or general practitioners.

Intervention: The intervention method used in the experimental group must be moxibustion. All forms of laser acupunctur will be considered. The combination therapies of laser acupuncture with other therapies will also be considered.

Comparator: Trials involving the following forms of control will be considered: (1) conventional pharmacological (regular western anti-asthmatic medications); (2) placebo; (3) blank control (no treatment).

Study designs to be included: In this study, only randomized controlled trials (RCTs) which reported in English or Chinese will be considered.

Eligibility criteria: The criteria of participants, interventions, controls and outcomes of interest should be taken into account as follows below. We will exclude the articles of non-RCTs, animal studies, clinical reports, editor comments, narrative reviews, correspondence, annual meeting abstracts and other trials that do not meet the inclusion criteria.

Information sources: The following six databases, three each Chinese and English databases, will be searched: China National Knowledge Infrastructure (CNKI), Chinese Biomedical Literature Database (CBM), WanFang Database, the Cochrane Library, PubMed, EMbase, will be searched from inception to December 2020 for potentially eligible RCTs. Only human researches will be included. Search terms are moxibustion, childhood asthma, pediatric asthma. And the equivalent search terms will be using for Chinese databases. If there are insufficient information or missing data in relation to the characteristics of the studies included in the meta-analysis, we will attempt to contact the study authors by two reviewers (HS and XL) for further information first. For missing participant data due to dropout or loss to follow-up, we will apply the following strategies to address missing data assumed to be not missing at random: 1. For the missing continuous outcome data, we will try to re-calculate MD and SD values as the first option when the medians, p values or confidence intervals are reported in the included studies. 2. If intention to-treat (ITT) analyses were performed in the included studies, we will use the ITT data instead of missing data as the first option. 3. If there are no ITT data or possible data for re-calculation, we will perform a sensitivity analysis to elucidate the influence of missing data on the effect estimates as a second option. This can be performed by a meta-regression adjusting for the amount of missing data.

Main outcome(s): The primary outcomes of this study are been considered to be the mean change of the scores of the pulmonary function, such as the percentage of the estimated volume of forced expiratory volume in one second (FEV1), and FEV1%. Quality of life evaluation, such as Pediatric Asthma Quality of Life Questionnaire (PAQLQ) and Asthma Quality of Life Questionnaire (AQLQ). And adverse events will also be the primary outcomes. The mean scores of the studies endpoint of these scales will be analyzed when no change data available.

Additional outcome(s): The secondary outcomes will include the following: (1). The frequency of asthma attacks (average number of asthma attacks per week); (2). Partial arterial oxygen pressure (PaO2); (3). anti-asthmatic medications dosage (4). Airway inflammation indicators, such as fractional exhaled nitric oxide (FeNO) and the eosinophil fraction (EOS); (5). Scores of clinical assessment tools for asthma, such as asthma control test (ACT), childhood asthma control test (C-ACT), and test for respiratory and asthma control in kids (TRACK).

Data management: Professional training will be conducted to ensure that every reviewer is familiar with the background, purpose, and process of this study. Endnote X9 will be used to manage the literatures retrieved from the databases. After removing the duplications, all titles and abstracts of the rest of the articles will be screened by two reviewers independently, then the potential full texts will be evaluated, and determined eligibility. A third review author will be invited to resolve disagreements, which cannot be resolved after discussion between the two reviewers. Two independent collaborators extracted data in duplicate according to a pre-defined data extraction form. In cases where data points were missing or ambiguously reported, the first and last author of the study were contacted by e-mail up to two times to obtain data. Each included RCTs will be read, and following data will be extracted: titles, name of the authors, publication year, country, source of publication, sample sizes, diagnostic criteria, inclusion and exclusion criteria, duration of disease, randomization methods, interventions, blinding methods, duration of follow-up, results, dropout or withdrawal rates, outcome measures, adverse events and conclusion. Any disagreement will be discussed and judged between the two authors. A third reviewer will be invited for judgement if disagreements cannot be resolved. Original authors will be contacted to request detailed information, when the data of the articles are ambiguous.

Quality assessment / Risk of bias analysis: Cochrane Handbook V.5.1.0, the risk-of-bias tool will be utilized to evaluate the risk of bias of the included RCTs. Two trained reviewers will conduct the assessment independently, and discussions will be held to resolve any differences. If necessary, a third reviewer will be invited. The risk level of each item for the studies will be ranked into 3 levers (low risk, high risk, and unclear risk of bias). We will assess the quality of evidence using the GRADE System (Grading of Recommendations Assessment, Development, and Evaluation, http://www.gradeworkinggroup.org) classify the evidence into insufficient-, low-, moderate-, or high-quality evidence. The estimated-risk and 95% CI of each outcome will be integrated into the table. The preliminary recommendations will be developed by two authors.

Strategy of data synthesis: Outcomes will be compared between the intervention and control groups. The RevMan 5.3 will be used for data analysis. The values measured at the endpoint of the treatment period will be used for data analysis. The meta-analysis will be used to combine trials with the same interventions and outcomes in similar populations to assess the effectiveness of the combined intervention. Dichotomous data will be expressed as relative risk and continuous variable as MD of 95% CI. If I2 < 50%, the fixed-effects model will be used for data synthesis. If I2 > 50%, we will use the random effects model to merge the data. When the meta-analysis is not applicable, we will be conducted describing descriptively the results.

Subgroup analysis: If the number of the included RCTs is sufficient and the heterogeneity is evaluated as significant (I2 ≥ 50%), subgroup analysis will be considered to detect possible heterogeneity of the results. We will consider investigating the effects based on the following themes: 1. treatment frequency (every day, every other day, etc.); 2. type of control group (placebo, no treatment or another active treatment or medication); 3. different categories of

asthma (extrinsic/allergic and intrinsic/non-allergic asthma). 4. Western studies vs Chinese studies. In addition, if we detect any important and significant covariates contributing to the variation of the intervention effect by meta-regression, subgroup analyses will also be conducted according to these covariates.

Sensitivity analysis: The quality and robustness of the articles will be identified by sensitivity analysis on the basis of the blind methods or randomization methods. We will carry out meta-analysis repeatedly after the trials be excluded.

Country(ies) involved: China.

Keywords: laser acupuncture, childhood asthma, systematic review, meta-analysis, protocol.

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