INPLASY PROTOCOL

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None declared.

Efficacy and safety of ozone autohemotherapy in the treatment of Rheumatoid Arthritis: A protocol for systematic review and meta-analysis

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Review question / Objective: **To evaluate the efficacy and safety of ozone autohemotherapy in the treatment of Rheumatoid Arthritis.**
Condition being studied: **Rheumatoid arthritis (RA) is a chronic and common autoimmune disease. It can be manifested as pain, swelling and decreased function of the affected joints. The pathogenesis of RA is complex, and there is no specific treatment at present. Ozone is a extraordinary oxidant, it can effectively enhance blood oxygen saturation, enhance tissue activity, reduce inflammatory reaction, improve immune function and alleviate local hypoxia and ischemia. Ozone has the advantage of low cost and has been widely used in lumbar disc herniation, osteoarthritis, pain and ischemic diseases. However, the efficacy and safety of ozone autohemotherapy on Rheumatoid Arthritis are not clear. Therefore, the purpose of this study is to explore the efficacy and safety of ozone autohemotherapy in patients with Rheumatoid Arthritis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 May 2022 and was last updated on 10 May 2022 (registration number INPLASY202250059).

INTRODUCTION

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METHODS

Search strategy: PubMed, Embase, The Cochrane Library, Web of Science, CNKI, CBM, Wanfang Journal database and VIP journal database were searched by computer. The search time is from inception to May 2022. Collect relevant studies on ozone autohemotherapy in the treatment of Rheumatoid Arthritis. There are no restrictions on the publication type and language of literature. The Chinese key words are: "ozone", "hyperoxia", "superoxide", "trioxide", "arthritis, rheumatoid", "rheumatoid arthritis", "rheumatoid arthritis", "randomized control", etc. The English search words are: "arthritis, rheumatoid","rheumatoid arthritis", "ozone", "ozonated", "triatomic oxygen","superxides","Autohemotherapy", "thermotherapeutics", "hemotherapy", etc. Find the repeated title information, merge the literature search results of different databases, establish the title information database and download the full text. Manually search the academic conference proceedings, and track and consult the relevant literature in the references of clinical trial reports, papers or reviews.

Participant or population: All patients with a diagnosis of Rheumatoid Arthritis will be considered for this review.

Intervention: The experimental group was treated with ozone autohemotherapy alone or combined with other therapies to treat Rheumatoid Arthritis.

Comparator: The control group was treated with conventional drugs.

Study designs to be included: Randomized controlled trials (RCTs) will be included in this review, regardless of whether the blind method and allocation concealment are used.

Eligibility criteria: 1. Types of studies Published randomized controlled trials (RCTs) were included in the present study, irrespective of the blinding methodology.2. Types of participants Patients with Rheumatoid Arthritis were enrolled in this study, regardless of their age or sex. 3. Interventions and comparators The experimental group was treated with ozone autohemotherapy alone or combined with other therapies to treat Rheumatoid Arthritis. The control group was treated with conventional drugs. 4. Exclusion criteria (1) Non-randomized controlled trials; (2) Animal experiments, mechanism studies, case and experience reports, literature review, and related literature; (3) studies with incorrect, incomplete, and unavailable data.

Information sources: In this study, we will search four Chinese databases: Chinese Academic Journal Full-text Database (CNKI), Chinese Biomedical Literature Database (CBM), Wanfang Data, and VIP, and four English databases: Embase, PubMed, Cochrane Library, and Web of Science, from inception to May 2022.

Main outcome(s): The primary outcome was clinical efficacy. The secondary outcome included pain visual analogue scale (VAS), erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) and clinical pain symptoms.

Data management: Based on the above retrieval strategy, two researchers independently extracted the data from the included studies. Any disagreement was resolved by discussion with a third reviewer . The extracted data mainly included ①basic information, including title, original research author, and

publication year; ②eligible data included in the study: original object characteristics (sample size, age, baseline data), intervention measures, outcome indicators, key conclusions, etc.; ③methodology part: design scheme, research period, literature research quality (random method, allocation concealment, blind implementation, etc.). If the data required for the study were not readily available in the published article, the corresponding author was contacted. If missing data could not be obtained, the study was excluded from analysis.

Quality assessment / Risk of bias analysis: The research methodology, which included quality and bias risk assessment, was independently assessed by two researchers using the Cochrane risk of bias (RoB) tool. If the results were different, third-party researchers were invited to discuss and analyze the source of bias. The quality of the included studies was evaluated according to the "risk of bias table" recommended in the Cochrane Handbook 5.1.0, including selection bias, implementation bias, loss of follow-up bias, measurement bias, reporting bias, and other biases. Risk assessment was divided into low-, high-, and unclear low-risk groups.

Strategy of data synthesis: Statistical analysis was conducted using RevMan 5.4.1 software (Cochrane Training sitebased in London, UK). The relative risk (RR) was used as a measure of effect size for continuous variables and the weighted mean difference (MD) for measurement data, both of which were expressed with a 95% confidence interval (CI). The decision to use a fixed- or random-effects model was determined based on the level of statistical heterogeneity assessed by the I2 index. A fixed-effects model was used in the absence of significant heterogeneity (P≥0.1, I2≤0.5). If significant heterogeneity (P0.5) was present, the source of heterogeneity was first analyzed to exclude the effects of clinical or methodological heterogeneity, and meta-analysis was performed using a random-effects model. When the meta-analysis could not analyze the data provided by the clinical trials, a descriptive analysis was performed. If high heterogeneity was present, a sensitivity or subgroup analysis was conducted. Funnel plots were used to assess the publication bias. A symmetrical funnel plot suggested an absence of publication bias, and the conclusions of this study were accurate and reliable.

Subgroup analysis: If significant heterogeneity was present among the included studies, subgroup analysis was conducted according to treatment durations, and disease severity.

Sensitivity analysis: During sensitivity analysis, one study was omitted at a time to assess the influence of any single study on the pooled estimate.

Language: No.

Country(ies) involved: China.

Keywords: ozone autohemotherapy; Rheumatoid Arthritis; Randomized controlled trial; Systematic Review

Contributions of each author:
Author 1 - chunli wu - The author drafted the manuscript.
Author 2 - Lihong Ma - The author worked out the search strategy.
Author 3 - Xiaowen Sun - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 4 - Zhe Wu - The author contributed to the development of the selection criteria, and the risk of bias assessment strategy.
Author 5 - Ying Han - The author made contributions to the manuscript of conceptualization.
Author 6 - Bo Lian - The author made contributions to the manuscript of methodology and review.
Author 7 - Kejian Li - The author read, provided feedback and approved the final manuscript.