INPLASY PROTOCOL

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None declared.

Efficacy and safety of Prunella vulgaris preparation in the treatment of Graves disease: A protocol for systematic review and meta-analysis

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Review question / Objective: **P: Graves disease; I: Prunella vulgaris preparation; C: Prunella vulgaris preparation combined with Western Medicine; O: Effective rate; S: randomized controlled.**
Condition being studied: **Graves disease is an autoimmune disease. Its typical characteristics are goiter and hyperthyroidism, which is the main cause of hyperthyroidism. The clinical manifestations mainly include irritability, insomnia, sweating, weight loss, etc., which can be accompanied by hyperthyroid cardiomyopathy, hyperthyroid liver injury, periodic paralysis, etc. Serious person can accompany send myasthenia gravis. At present, the treatment of Graves disease mainly depends on these three methods: antithyroid drug therapy, 131I radiotherapy and thyroidectomy. However, antithyroid drugs have side effects such as rash, leucopenia, toxic liver injury and vasculitis. 131I radiotherapy will cause lifelong irreversible hypothyroidism. Whether to choose them or not needs to weigh the interests of hyperthyroidism and hypothyroidism. Complications of surgical treatment also include permanent hypothyroidism, hypoparathyroidism, and injury of recurrent laryngeal nerve. Thyroid toxicity can be effectively controlled, but long-term prognosis is affected. In recent years, with the deepening of the study of thyroid diseases in Traditional Chinese medicine, the advantages of Traditional Chinese medicine in the treatment of Graves disease have been constantly revealed. Prunella vulgaris was first published in Shennong Bencao Jing. It can clear away heat and fire, brighten eyes, disperse nodules and reduce swelling. It is widely used in goiter and thyroid diseases, but its efficacy and safety need to be verified clinically. Therefore, the purpose of this study is to explore the efficacy and safety of Prunella vulgaris preparation in the treatment of Grave disease.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 08 February 2022 and was last updated on 08 February 2022 (registration number INPLASY202220017).

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 database establishment to December 2021. There are no restrictions on the publication type and language of literature. The Chinese key words are: Graves disease; Exophthalmos goiter; Graves disease; Diffuse goiter; Toxic diffuse goiter; Prunella vulgaris ointment; Prunella vulgaris tablets; Prunella vulgaris capsule; Prunella vulgaris granules; Prunella vulgaris oral liquid; Randomized control, etc. The English search term is Graves disease; Prunella; Randomized controlled trial, 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 Graves disease will be considered for this review.

Intervention: The experimental group was treated with oral Prunella vulgaris preparation combined with western treatment. The dosage form of Prunella vulgaris preparation is unlimited, and the administration method is oral.

Comparator: In the control group, the intervention means may include medicine (western medicine), routine symptomatic treatment, etc.

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 inclusion criteria 1.1 study type: randomized controlled trial (RCT).1.2 research object: Patients with Graves disease, regardless of age and gender. The diagnostic criteria of hyperthyroidism and Graves disease are formulated according to the Chinese guidelines for the diagnosis and treatment of thyroid diseases.1.3 intervention measures: the experimental group was treated with oral Prunella vulgaris preparation combined with western medicine; The control group was treated with western medicine. The dosage form of Prunella vulgaris preparation is unlimited,

and the administration method is oral.1.4 expected main outcome indicators:The main outcome measures included the total effective rate of clinical treatment, the improvement of thyroid function and autoantibodies, the improvement of goiter, the reduction of thyroid gland size, the incidence of adverse reactions and so on. Outcome indicators include at least one of the above indicators.2 exclusion criteria ① Non randomized controlled trials or literature with wrong random methods; ② Animal experiments, mechanism studies, case and experience reports, literature review and related literature; ③ Incorrect, incomplete and inaccessible data and repeatedly published literature; ④ Intervention measures: those who use other traditional Chinese medicine or proprietary Chinese medicine other than Prunella vulgaris preparation; ⑥ The number of cases in the experimental group and the control group was less than 30.

Information sources: PubMed, Embase, The Cochrane Library, Web of Science, CNKI, CBM, Wanfang Journal database and VIP journal database will be searched by computer. The search time is from database establishment to December 2021.

Main outcome(s): The main outcome indicators included total clinical response rate, thyroid function and autoantibody improvement, and incidence of adverse reactions. Outcome indicators should include at least one of the above indicators.

Additional outcome(s): Improvement of goiter, reduction of thyroid gland size.

Data management: Two evaluators independently read the title and abstract of the literature, read the full text if necessary, and screen the literature according to the predetermined inclusion criteria and exclusion criteria. The extracted data mainly include ① basic information: including title, original research author and publication year; ② Eligible data included in the study: original object characteristics (sample size, age, baseline data), intervention measures, outcome indicators, key conclusions, etc; ③ Methodology: design scheme, research period, literature research quality (random method, allocation concealment, blind implementation, etc.). If the article has no specific description or relevant materials are missing, contact the author for further information.

Quality assessment / Risk of bias analysis: The assessment was done independently by two study members, using the Cochrane Risk Assessment Tool to assess the risk of bias using the following seven criteria: Random sequence generation, allocation hiding, blind of participants and personnel, blind of outcome evaluators, incomplete result data, selective reporting and other biases, and assessment of low bias risk, unclear bias risk and high bias risk is given item by item.In the event of a disagreement between two study members, the third study member will determine the final assessment.

Strategy of data synthesis: Using the statistical software revman5 provided by the international evidence-based medicine collaboration network 4.1 make statistics on the collected data. Relative risk (RR) was used for counting data, and mean difference (MD) was used for measurement data, both of which were expressed by 95% confidence intervals (CI). The heterogeneity of each test result is tested. When the result shows that I2 ≤ 50%, the fixed effect model is used; When the results show that I2 > 50%, it indicates that there is heterogeneity among various studies. First, explore the source of heterogeneity. If the clinical heterogeneity cannot be used to explain, the random effect model is selected for the combination of index effect quantities. The potential publication bias was analyzed by inverted funnel diagram; The stability of statistical results is estimated by sensitivity analysis and failure safety number. Convert the random effect model and fixed effect model, or exclude the included literature one by one for sensitivity analysis.

Subgroup analysis: In the case of high heterogeneity, subgroup analysis will be done to identify the sources of heterogeneity. Subgroup analysis will be carried out from the following aspects: the different dosage forms and treatment duration of Prunella vulgaris preparation, etc., to explain the heterogeneity between the studies.

Sensitivity analysis: We will use the leaveone-out method for sensitivity analysis to judge the stability of outcome indicators.

Language: No.

Country(ies) involved: China.

Keywords: Prunella vulgaris preparation; Graves disease; Randomized controlled trial; Systematic Review.

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