INPLASY PROTOCOL

Corresponding author:
Zhen Wang

1163294461@qq.com

Author Affiliation:
Shandong University of Traditional Chinese Medicine.

Review Stage at time of this submission: Preliminary searches.

Conflicts of interest: None declared.

Effectiveness and Safety of Kidney-tonifying Chinese Patent Medicine for Oligoasthenozoospermia: A Systematic Review and Network Meta-analysis

Wang, Z[1]; Zhou, ZY[2]; Zhang, LJ[3]; Li, XJ[4]; Li, MX[5]; Pan, YK[6]; Jiao, TY[7]; Shi, XY[8]; Liu, Q[9]; Wang, CA[10]; Wang, YQ[11].

Review question / Objective: Although several traditional meta-analyses have proved that [9-11] Chinese patent medicines for tonifying kidney do have advantages in the treatment of OAT, they are mostly comparisons between single drugs and cannot be compared among multiple drugs. The advantages and disadvantages between different kidney-tonifying Chinese patent medicines are not clear Therefore, this study used network meta-analysis method to compare the efficacy and safety of commonly used kidney tonic Chinese patent drugs in the treatment of OAT, and to study the advantages of various drugs in each outcome index, so as to provide some ideas and evidence-based medical support for the clinical treatment of OAT.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 26 August 2022 and was last updated on 26 August 2022 (registration number INPLASY202280101).

INTRODUCTION

Review question / Objective: Although several traditional meta-analyses have proved that [9-11] Chinese patent medicines for tonifying kidney do have advantages in the treatment of OAT, they are mostly comparisons between single drugs and cannot be compared among multiple drugs. The advantages and disadvantages between different kidney-tonifying Chinese patent medicines are not clear Therefore, this study used network meta-analysis method to compare the efficacy and safety of commonly used kidney tonic Chinese patent drugs in the

treatment of OAT, and to study the advantages of various drugs in each outcome index, so as to provide some ideas and evidence-based medical support for the clinical treatment of OAT.

Condition being studied: Oligoasthenospermia (OAT) is a general term for oligospermia and asthenospermia, which is an important cause of male infertility and is clinically characterized by decreased sperm concentration and sperm motility. In recent years, under the influence of many harmful factors such as environmental pollution, mental pressure and unhealthy lifestyle, the prevalence of OAT is increasing year by year. Western medicine is commonly used in clinical treatment, mainly including L-carnitine, antioxidants, estrogen receptor antagonists and androgens. The efficacy of these drugs is acceptable, but they are easy to reach the treatment bottleneck, and there are many adverse reactions, which are often difficult for patients to tolerate. Therefore, it is necessary to seek effective, stable and safe treatment methods.

METHODS

Participant or population: All patients in this study were diagnosed with oligoasthenozoospermiadepression according to Chinese or international authoritative criteria regardless of age or race

Intervention: Kidney-tonifying Chinese patent medicine was used in the experimental group.

Comparator: The control group was treated with conventional western medicine or above-mentioned Chinese patent medicine.

Study designs to be included: Published randomized controlled trial (RCT), the language is limited to Chinese and English

Eligibility criteria: (1) Study types as following: reviews, meta-analysis,cluster RCTs, animal experiments, expert experience, or case-control studies; (2) Diagnostic assessment criteria was not

mentioned; (3) Duplicate publications; (4) Literature with obvious statistical errors.

Information sources: A computerized search of published relevant studies on kidney-tonifying Chinese patent medicine in the treatment of OAT was performed. PubMed, Cochrane Library, Web of Science, Embase, China National Knowledge Infrastructure(CNKI), Chinese Biomedical Literature Database(CBM), Chinese Scientific Journals Database(VIP) and Wanfang database were searched.

Main outcome(s): Effectiveness indicator: (1)Total effective rate, with reference to the curative effect standards formulated by the State Administration of Traditional Chinese Medicine and WHO[13,14], total effective rate=[(cure + markedly effective + effective) number of cases÷total number of cases] ×100%; (2) Sperm concentration; (3) Sperm motility grade a; (4) Sperm motility grade a+b; (5) Sperm viability. Safety indicator: (1) Incidence of adverse reactions.

Quality assessment / Risk of bias analysis: The assessment of risk of bias literatures was evaluated by 2 investigators according to the risk of bias assessment tool in Cochrane Reviewers Handbook 6.1.0, mainly including the following 7 aspects: random sequence generation; allocation concealment; implementation of blind method for patients and trial personnel; implementation of blind method for outcome assessors; incomplete result data; selective reporting; and other biases (such as potential bias related to special study design in studies, false statement, etc.). Eventually, it is necessary to make a judgment on "low risk", "high risk" and "unclear risk" in the literatures. Disagreement will be settled by team discussion. Review manager V.5.4 will be used to make the risk of bias diagram.

Strategy of data synthesis: The data analysis of all outcome indicators used random or fixed effect models according to heterogeneity, the odds ratio (OR) was used as the effect size for dichotomous variables, and the standardized mean difference (SMD) was used as the effect

size for continuous variables and calculate the 95% confidence interval (CI).According to the Bayesian model, Stata16.0 software is used for network meta analysis, the data is preprocessed by using the network group command, and the evidence network diagram of each indicator is drawn. The curative effect of the indicators was sorted to obtain the area under the curve (SUCRA), and the probability sorting was drawn as a graph. The dots in the evidence network diagram represent an intervention, and the larger the area, the more the number of patients with the intervention. The line connecting the two dots indicates a direct comparison between the two interventions, and the thickness of the line represents the number of included studies. The SUCRA is expressed as a percentage. The larger the percentage, the more effective the intervention is, and the value of 0 indicates that the intervention is completely ineffective. When there is a closed loop, the node splitting method is used to check the inconsistency. When the number of studies on the outcome indicator was >10, a "comparison-adjusted" funnel plot was drawn to determine whether there was a possibility of a small sample effect.

Subgroup analysis: To explore the sources of heterogeneity and improve the persuasiveness of the evidence, we conducted a subgroup analysis based on the study characteristics(types of CWM).

Sensitivity analysis: To further confirm the stability of the results of the meta-analysis, sensitivity analysis was conducted by excluding the studies from the analysis one by one.The results showed there were not significantly different from those described above, suggesting our meta-analysis results are robust and reliable.

Country(ies) involved: China.

Keywords: Oligoasthenospermia; Chinese patent medicine; Kidney-tonifying; Systematic review; Network Meta-analysis

Contributions of each author:
Author 1 - Zhen Wang.
Email: 1163294641@qq.com
Author 2 - Ziyang Zhou.
Email: 769980192@qq.com
Author 3 - Lijuan Zhang.
Email: 1050096075@qq.com
Author 4 - Xujie Li.
Email: 1091723118@qq.com
Author 5 - Miaoxiu Li.
Email: wby362089@163.com
Author 6 - Yankun Pan.
Email: a1ster@qq.com
Author 7 - Tiyong Jiao.
Email: 1142827980@qq.com
Author 8 - Xiaoyun Shi.
Email: 1263318634@qq.com
Author 9 - Qing Liu.
Email: 1017162038@qq.com
Author 10 - Congan Wang.
Email: 2544861615@qq.com
Author 11 - Yongquan Wang
Email: 3053451770@qq.com