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Comparison of efficacy and safety of complementary and alternative therapies for constipation caused by antipsychotic drugs A Bayesian network meta-analysis protocol

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ADMINISTRATIVE INFORMATION

Support - 1. Shandong Traditional Chinese Medicine Science and Technology Project (Q-2023185) 2. Shandong Traditional Chinese Medicine Science and Technology Project (M-2022198).

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

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 8 September 2025 and was last updated on 8 September 2025.

INTRODUCTION

Review question / Objective 1. Participants: (1) No constipation before taking antipsychotic medication. (2) Patients who took antipsychotic drugs steadily and regularly and developed constipation (according to scores derived from any validated clinical rating scales, such as the Rome criteria, Constipation Assessment Scale, the Weekly Defecation Frequency, Completely Spontaneous Defecation Frequency, Gastrointestinal(GI) Symptom Rating Scale [GSRS], Bristol Stool Form Scale, and so on), which was considered a side effect of the antipsychotic drugs. 2. Interventions: The observation group accepted complementary and alternative therapies except for basic treatment. That therapies mainly contain traditional Chinese medicine, acupuncture, massage, qigong, yoga, biofeedback therapy, acupoint catgut embedding therapy, the acupoint application of chinese herb, traditional Chinese medicine enema, traditional Chinese Medicine suppository, enterobacteria transplantation, sacral nerve stimulation, transcutaneous electrical acupoint stimulation, Chinese herbal medicines, traditional Chinese medicine targeted drug penetration and so on.) 3. Comparison: The control group was medicated with antipsychotic drugs, at the same time, with or without laxatives. 4. Outcomes: The primary outcome is the score change of authenticated scales, which can estimate the degree of constipation. The key secondary outcomes mainly include the total efficacy rate, adverse effects, and traditional Chinese medicine symptoms score. 5. Study type: Study type is all RCTs related to supplementary and replacement therapies for constipation caused by antipsychotic drugs. There are no language restrictions.

Condition being studied Among patients taking antipsychotic drugs, constipation is one of the common adverse reactions, and western medicine

treatment is prone to dependence. Complementary and alternative therapies can improve effective in the treatment of constipation as well as the quality of life for patients, and they are also benefit to reduce side effects.

METHODS

Participant or population 1. Inclusion criteria: (1) No constipation before taking antipsychotic medication. (2) Patients who took antipsychotic drugs steadily and regularly and developed constipation (according to scores derived from any validated clinical rating scales, such as the Rome criteria, Constipation Assessment Scale, the Weekly Defecation Frequency, Completely Spontaneous Defecation Frequency, Gastrointestinal(GI) Symptom Rating Scale [GSRS], Bristol Stool Form Scale, and so on), which was considered a side effect of the antipsychotic drugs. 2. Exclusion criteria: (1) The type of study is incomplete RCTs; (2) Patients without constipation; (3) Research with defective analysis blueprint and poor quality; (4) Studies with deficient data and obscur outcome effects; (5) Repeated report study.

Intervention The observation group accepted complementary and alternative therapies except for basic treatment. That therapies mainly contain traditional Chinese medicine, acupuncture, massage, qigong, yoga, biofeedback therapy, acupoint catgut embedding therapy, the acupoint application of chinese herb, traditional Chinese medicine enema, traditional Chinese Medicine suppository, enterobacteria transplantation, sacral nerve stimulation, transcutaneous electrical acupoint stimulation, Chinese herbal medicines, traditional Chinese medicine targeted drug penetration and so on.) .

Comparator The control group was medicated with antipsychotic drugs, at the same time, with or without laxatives.

Study designs to be included Study type is all RCTs related to supplementary and replacement therapies for constipation caused by antipsychotic drugs. There are no language restrictions.

Eligibility criteria 1. Study type: Study type is all RCTs related to supplementary and replacement therapies for constipation caused by antipsychotic drugs. There are no language restrictions. 2. Participants: (1) No constipation before taking antipsychotic medication. (2) Patients who took antipsychotic drugs steadily and regularly and developed constipation (according to scores derived from any validated clinical rating scales, such as the Rome criteria, Constipation Assessment Scale, the Weekly Defecation Frequency, Completely Spontaneous Defecation Frequency, Gastrointestinal(GI) Symptom Rating Scale [GSRS], Bristol Stool Form Scale, and so on), which was considered a side effect of the antipsychotic drugs. 3. Interventions: The control group was medicated with antipsychotic drugs, at the same time, with or without laxatives. The observation group accepted complementary and alternative therapies except for basic treatment. That therapies mainly contain traditional Chinese medicine, acupuncture, massage, qigong, yoga, biofeedback therapy, acupoint catgut embedding therapy, the acupoint application of chinese herb, traditional Chinese medicine enema, traditional Chinese Medicine suppository, enterobacteria transplantation, sacral nerve stimulation, transcutaneous electrical acupoint stimulation, Chinese herbal medicines, traditional Chinese medicine targeted drug penetration and so on.) 4. Outcomes: The primary outcome is the score change of authenticated scales, which can estimate the degree of constipation. The key secondary outcomes mainly include the total efficacy rate, adverse effects, and traditional Chinese medicine symptoms score.

Information sources From the establishment of the database until August 2025, we will explore the following databases: PubMed, EMBASE, OVID, Allied and Alternative Medieine (AMED), The Cochrane Library, China Biology Medicine disc (CBMdisc), Wanfang database, China National Knowledge Infrastructure database(CNKI), VIP database, Japan Science and Technology Information Aggregator Electronic(J-STAGE) and so on. Two independent researchers will dig these databases. RCTs, associated with complementary and alternative therapies of constipation caused by antipsychotic drugs, will be collected after conducting a computer search.

Main outcome(s) The primary outcome is the score change of authenticated scales, which can estimate the degree of constipation.

Additional outcome(s) The key secondary outcomes mainly include the total efficacy rate, adverse effects, and traditional Chinese medicine symptoms score.

Quality assessment / Risk of bias analysis The worth of collected studies shall be graded through the Jadad scale. The studies of Jadad score at least 3 should be included. And the disagreement will be treated through the third party.We will assess publication bias via mapping funnel plots. If

there is no publication bias, each study will be evenly distributed on both sides of the research line, showing a symmetrical distribution. If the funnel is asymmetric, it will be confirmed through visual inspection. Potential publication bias using Egger's tests.Based on consistency, accuracy, directness, deviation risk and publication deviation, we will incorporate the method of Grading of Recommendation Assessment, Development and Evaluation to analyze the quality of the relevant evidence. The evaluation standard for the quality of evidence points to four categories: high, medium, low, and very low.

Strategy of data synthesis 1. Assessment of heterogeneity: To comprehensively evaluate the heterogeneity of the studies, we will use x2 test and I2 statistics. By x2 test, if $P \leq 0.05$, it indicates significant. The I2 statistics will be used to test the degree of heterogeneity. If $I2 > 50\%$, it suggests significant heterogeneity. Therefore, if $P \leq 0.05$ or $I2 > 50\%$, it is considered to have heterogeneity.
2. Data Synthesis: We will conduct a meta-analysis using the RevMan 5.3 software (version 5.3; International Cochrane Collaboration Network to produce and preserve the Cochrane system evaluation special software). We will Use a fixed-effect model ($P > 0.05$ or $I2 \leq 50\%$). Conversely, with high diversity, a random-effects model will be used. Markov chain Monte Carlo in WinBUGS 1.4.3 will be used for NMA and the Brooks-Gelman-Rubin will be used to appraise the convergence of the model.

Subgroup analysis If statistical heterogeneity is found, subgroup will be performed to clarify the source of it. This research will perform the subgroup analysis based on different design scheme, quality of literature, printing year, and so on.

Sensitivity analysis The value of the study will be judged according to the Cochrane manual, and the low quality studies (such as those with missing or poor quality data) will be removed. Then, we will conduct merger analysis, and the merger analysis will be used to determine whether it will be significantly affected by the excluded studies. If there is no notable alteration in the merger effect previous and later exclusion, it is considered that stability and reliability of the NMA results are high; otherwise, they are poor.

Language restriction There are no language restrictions.

Country(ies) involved China.

Keywords constipation, antipsychotic drugs, complementary and alternative therapies, network meta-analysis.

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