

Network Meta-Analysis of Non-Pharmacological Interventions for Perimenopausal Insomnia Symptoms: Postprint

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Date: 2022-10-17T00:00:00+00:00

Abstract

Background: The emergence of perimenopausal insomnia symptoms can reduce the quality of life in perimenopausal women and increase the risk of developing other diseases. Currently, numerous non-pharmacological interventions exist for improving perimenopausal insomnia symptoms, but there is still disagreement regarding which intervention is most effective. Objective: To evaluate the effectiveness of non-pharmacological interventions in improving perimenopausal insomnia symptoms using network meta-analysis. Methods: Randomized controlled trials on non-pharmacological interventions for improving perimenopausal insomnia symptoms were searched in the Cochrane Library, PubMed, EMBASE, Web of Science, CNKI, WanFang Data, VIP, and CBM databases. After two researchers independently screened the literature, extracted data, and assessed the risk of bias of the included studies, Bayesian network meta-analysis was conducted on the total effective rate, Pittsburgh Sleep Quality Index score (PSQI), Kupperman score, and estradiol (E2) using R 4.1.3 software and the GeMTC package. Results: A total of 44 RCTs were included, comprising 3386 patients and involving 12 non-pharmacological interventions (moxibustion, electroacupuncture, auricular point pressing, gua sha, fire dragon cupping, intradermal needling, tuina, warm needling, bee acupuncture, acupoint catgut embedding, music therapy, and acupuncture). Network meta-analysis results showed: in terms of total effective rate, moxibustion, electroacupuncture, and acupuncture were superior to sedative-hypnotic Western medicine ($P < 0.05$), with moxibustion ranking the highest. For PSQI scores, moxibustion, electroacupuncture, gua sha, and acupuncture were superior to sedative-hypnotic Western medicine ($P < 0.05$), and moxibustion was superior to warm needling ($P < 0.05$), with moxibustion ranking the highest. Regarding Kupperman scores, there were no statistically significant differences among the various interventions when compared with each other ($P > 0.05$), with gua sha ranking the highest. For E2 levels, there were no statistically significant

differences among the various interventions when compared with each other ($P > 0.05$), with acupuncture ranking the highest. Conclusion: Current evidence shows that moxibustion has advantages in improving the total effective rate and PSQI scores for insomnia symptoms in perimenopausal women, gua sha has advantages in improving Kupperman scores, and acupuncture has advantages in increasing E2 levels in perimenopausal women. However, more high-quality studies are needed to further validate these conclusions.

Full Text

Efficacy of Non-Drug Interventions in Improving Perimenopausal Insomnia Symptoms: A Network Meta-Analysis

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Abstract

Background: Insomnia symptoms in perimenopausal women reduce quality of life and increase the risk of developing other illnesses. Numerous non-pharmacological therapies are currently available for alleviating perimenopausal insomnia symptoms, though consensus on which intervention is most effective remains elusive. **Objective:** This study employed network meta-analysis to evaluate the effectiveness of non-drug interventions in improving perimenopausal insomnia symptoms. **Methods:** We searched the Cochrane Library, PubMed, EMBASE, Web of Science, CNKI, WanFang Data, VIP, and CBM databases for randomized controlled trials (RCTs) examining non-drug interventions for perimenopausal insomnia. Two researchers independently screened literature, extracted data, and assessed risk of bias. Bayesian network meta-analysis of total response rate, Pittsburgh Sleep Quality Index (PSQI) score, Kupperman score, and estradiol (E2) levels was conducted using R 4.1.3 software and the GeMTC package. **Results:** Forty-four RCTs comprising 3,386 patients were included, covering 12 non-drug interventions (moxibustion, electroacupuncture, auricular acupressure, scraping, fire dragon pot, intradermal needle, massage, warm acupuncture, bee acupuncture, acupoint catgut embedding, music therapy, and acupuncture). Network meta-analysis revealed that for total response rate, moxibustion, electroacupuncture, and acupuncture were superior to sedative-hypnotic Western medication ($P < 0.05$), with mox-

ibustion ranking highest. For PSQI scores, moxibustion, electroacupuncture, scraping, and acupuncture outperformed sedative-hypnotic Western medication ($P < 0.05$), and moxibustion was superior to warm acupuncture ($P < 0.05$), with moxibustion again ranking first. For Kupperman scores, no statistically significant differences were found between any interventions ($P > 0.05$), though scraping ranked highest. For E2 levels, no significant differences were observed between interventions ($P > 0.05$), with acupuncture ranking highest. **Conclusion:** Current evidence indicates that moxibustion offers advantages in improving total effective rate and PSQI scores, scraping in improving Kupperman scores, and acupuncture in elevating E2 levels among perimenopausal women. However, additional high-quality studies are needed to validate these findings.

Keywords: Non-drug intervention; Perimenopause; Insomnia; Network meta-analysis; Randomized controlled trial

Introduction

Perimenopause represents a critical transitional period in women's lives characterized by declining ovarian function and hypothalamic-pituitary axis degeneration, leading to fluctuating sex hormones that commonly trigger negative emotions such as anxiety and depression, resulting in insomnia, dizziness, and fatigue. Insomnia is a prevalent symptom among women with perimenopausal syndrome, manifesting primarily as difficulty falling asleep, short sleep duration, and frequent dreaming with easy awakening. Chronic poor sleep quality compromises physical resistance, induces low mood, and causes mental fatigue, severely impacting quality of life and significantly increasing the incidence of other diseases in perimenopausal women.

Conventional medicine typically employs hormone replacement therapy and sedative-hypnotic drugs to treat perimenopausal insomnia. However, research indicates that hormone therapy increases the risk of breast and endometrial cancers while elevating the probability of cardiovascular and cerebrovascular lesions, whereas sedative-hypnotic medications often produce adverse effects including tolerance, dependence, and rebound insomnia. Consequently, safer and more effective therapeutic approaches are urgently needed. The trend of using non-drug interventions to alleviate insomnia symptoms has grown in recent years, with studies confirming their effectiveness in improving perimenopausal insomnia. Nevertheless, the relative efficacy of various non-drug interventions remains unclear. Network meta-analysis represents a novel meta-analytic approach that enables indirect comparisons and quantitative analysis across multiple interventions, allowing for ranking of therapeutic efficacy to identify optimal treatments. This study therefore employed network meta-analysis to investigate the efficacy of non-drug interventions in improving perimenopausal insomnia symptoms, aiming to provide evidence for clinical treatment and nursing protocol

development.

Inclusion Criteria

1. **Study Population:** Perimenopausal women with insomnia, with no restrictions on disease duration or age. Western medicine diagnosis followed *Gynecology and Obstetrics* standards, while traditional Chinese medicine diagnosis followed *Gynecology of Traditional Chinese Medicine* criteria. Insomnia diagnosis was based on the *Chinese Classification and Diagnostic Criteria of Mental Disorders (CCMD-3)* or *Guidelines for Clinical Research of New Chinese Medicines*, with no restrictions on TCM syndrome types, or other internationally recognized diagnostic criteria for perimenopausal insomnia.
2. **Study Design:** Randomized controlled trials (RCTs).
3. **Interventions:** Experimental groups received non-drug interventions (specific measures determined by search results). Control groups received sedative-hypnotic Western medication (including estazolam, alprazolam, eszopiclone, oryzanol, etc.), different non-drug interventions, placebo, or blank control.
4. **Outcome Measures:** Total effective rate; Pittsburgh Sleep Quality Index (PSQI) score; Kupperman score; Estradiol (E2) level.

Exclusion Criteria

1. Studies where experimental and control groups received combined or mixed interventions making it difficult to isolate single intervention effects;
2. Reviews, animal studies, meta-analyses, or case reports;
3. Studies where full text was unavailable or represented duplicate publications;
4. Studies with duplicate or erroneous data;
5. Studies from which required data could not be extracted.

Literature Search Strategy

We searched Cochrane Library, PubMed, EMBase, Web of Science, CNKI, Wan-Fang Data, VIP, and CBM databases from inception to March 2022 for RCTs on non-drug interventions for perimenopausal insomnia, using a combination of subject headings and free-text terms. We also manually traced references from included studies. Chinese search terms included “perimenopause/menopause,” “insomnia/sleep disorder,” and “randomized/randomized control.” English search terms included “perimenopause/menopause,” “insomnia/sleep disorder,” and “randomized/randomized control.” The PubMed search strategy is shown in Box 1.

Box 1. PubMed Search Strategy

#1 Perimenopause [MeSH Terms]

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#2 Perimenopause[Title/Abstract]
#3 #1 OR #2
#4 menopause[MeSH Terms]
#5 menopause[Title/Abstract]
#6 #4 OR #5
#7 Insomnia[MeSH Terms]
#8 Insomnia[Title/Abstract]
#9 #7 OR #8
#10 sleep disorder[MeSH Terms]
#11 sleep disorder[Title/Abstract]
#12 #10 OR #11
#13 Randomized[MeSH Terms]
#14 Randomized[Title/Abstract]
#15 #13 OR #14
#16 randomized control[MeSH Terms]
#17 randomized control[Title/Abstract]
#18 #16 OR #17
#19 #3 AND #6 AND #9 AND #12 AND #15 AND #18
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Literature Screening, Data Extraction, and Risk of Bias Assessment

Two researchers independently screened literature, extracted data, and assessed risk of bias according to the Cochrane Handbook 5.1.0. Extracted data included author, publication year, country, sample size, age, disease duration, intervention measures, intervention duration, and outcome indicators. Disagreements were resolved through discussion with a third researcher.

Statistical Analysis

Continuous variables were described using mean difference (MD) and 95% confidence interval (CI), while dichotomous variables used odds ratio (OR) and 95% CI. Bayesian network meta-analysis was performed using R 4.1.3 software and the GeMTC package to generate network evidence diagrams and ranking plots. Four Markov chains were employed with initial iterations of 5,000 and subsequent iterations of 20,000. Model convergence was assessed using the Potential Scale Reduction Factor (PSRF), with values approaching 1 indicating good convergence. When closed loops existed in network diagrams, node-splitting methods were used for local inconsistency testing, with $P > 0.05$ indicating good consistency. Funnel plots were generated using Stata 15.0 to assess publication bias.

Results

Literature Screening Process and Results

Database searches yielded 3,595 Chinese and English articles, with 44 studies ultimately included after systematic screening [Figure 1: see original paper].

The screening process is detailed in Figure 1.

Basic Characteristics of Included Studies

The analysis included 41 Chinese and 3 English studies comprising 3,386 patients. Basic characteristics are presented in Table 1 .

Risk of Bias Assessment

Among the 44 included studies, 25 used random number tables or software for randomization, 2 used envelope methods, 1 used sequential allocation, and 16 merely mentioned “randomization” without specifying methods. Due to the nature of non-drug interventions, blinding was difficult to implement, with only 8 studies mentioning blinding. Allocation concealment was reported in 13 studies, and 13 studies experienced participant attrition but reported dropout groups and reasons. Risk of bias results are shown in Figure 2 [Figure 2: see original paper].

Network Meta-Analysis Results

Network Relationship Diagram The network relationship diagram included 12 non-drug interventions: moxibustion, electroacupuncture, auricular acupressure, scraping, fire dragon pot, intradermal needle, massage, warm acupuncture, bee acupuncture, acupoint catgut embedding, music therapy, and acupuncture [Figure 3: see original paper].

Consistency Testing and Convergence Assessment Node-splitting methods for local inconsistency testing yielded $P > 0.05$ for all comparisons, indicating no significant differences between direct and indirect comparisons and supporting use of consistency models. All four outcome measures showed PSRF values approaching 1, suggesting good convergence.

Total Effective Rate Thirty-three RCTs reported total effective rate. Network meta-analysis showed moxibustion, electroacupuncture, and acupuncture were superior to sedative-hypnotic Western medication ($P < 0.05$), with moxibustion also outperforming blank control ($P < 0.05$). No other significant differences were observed between interventions. Ranking probabilities indicated moxibustion as most effective: moxibustion (0.87) > fire dragon pot (0.77) > electroacupuncture (0.72) > auricular acupressure (0.63) > acupuncture (0.61) > acupoint catgut embedding (0.55) > warm acupuncture (0.53) > scraping (0.51) > intradermal needle (0.49) > massage (0.45) > music therapy (0.39) > bee acupuncture (0.39) > placebo acupuncture (0.26) > sedative-hypnotic Western medication (0.21) > blank control (0.11) [TABLE:2, FIGURE:4].

PSQI Score Thirty-five RCTs reported PSQI scores. Network meta-analysis demonstrated that moxibustion, electroacupuncture, scraping, and acupuncture

were superior to sedative-hypnotic Western medication and placebo acupuncture ($P < 0.05$). Additionally, moxibustion, electroacupuncture, auricular acupressure, scraping, intradermal needle, massage, bee acupuncture, acupoint catgut embedding, acupuncture, and sedative-hypnotic Western medication outperformed blank control ($P < 0.05$), while moxibustion was superior to warm acupuncture ($P < 0.05$). Lower PSQI scores indicate better outcomes, with ranking probabilities showing moxibustion as most effective: moxibustion (0.09) > scraping (0.26) > electroacupuncture (0.30) > bee acupuncture (0.31) > auricular acupressure (0.33) > intradermal needle (0.36) > acupuncture (0.40) > acupoint catgut embedding (0.52) > massage (0.60) > sedative-hypnotic Western medication (0.74) > placebo acupuncture (0.80) > warm acupuncture (0.80) > blank control (0.98) [TABLE:3, FIGURE:4].

Kupperman Score Eight RCTs reported Kupperman scores. No statistically significant differences were found between any interventions ($P > 0.05$). Lower scores indicate better outcomes, with ranking probabilities suggesting scraping as most effective: scraping (0.27) > acupuncture (0.34) > electroacupuncture (0.37) > warm acupuncture (0.49) > sedative-hypnotic Western medication (0.54) > blank control (0.62) > placebo acupuncture (0.87) [TABLE:4, FIGURE:4].

E2 Level Nine RCTs reported E2 levels. No significant differences were observed between interventions ($P > 0.05$). Ranking probabilities indicated acupuncture as most effective: acupuncture (0.69) > placebo acupuncture (0.67) > scraping (0.55) > sedative-hypnotic Western medication (0.33) > acupoint catgut embedding (0.25) [TABLE:5, FIGURE:4].

Safety Evaluation

Ten RCTs reported adverse events, with no serious adverse events occurring in any study .

Publication Bias Assessment

Funnel plots for total effective rate and PSQI score showed incomplete symmetry among scattered points, suggesting potential publication bias [Figure 5: see original paper].

Discussion

Perimenopause represents a significant life stage, with studies indicating that 47-65% of Chinese perimenopausal women experience insomnia. Chronic sleep deprivation adversely affects physical and mental health, severely diminishing quality of life. Modern medicine attributes perimenopausal insomnia to dysregulation of the hypothalamic-pituitary-ovarian reproductive axis during its decline,

with estrogen reduction being a key factor. Current treatments consist primarily of pharmacological and non-pharmacological interventions. Given the tolerance, dependence, and toxic side effects associated with medications, non-drug interventions have garnered increasing attention. These include acupuncture, moxibustion, scraping, electroacupuncture, auricular acupressure, massage, and music therapy. However, no previous study has evaluated which non-drug intervention is most effective. This network meta-analysis compared the relative efficacy of various interventions for improving perimenopausal insomnia symptoms.

Results demonstrated that for total effective rate, moxibustion, electroacupuncture, and acupuncture outperformed sedative-hypnotic Western medication, with moxibustion ranking highest. For PSQI scores, moxibustion, electroacupuncture, scraping, and acupuncture were superior to sedative-hypnotic Western medication, with moxibustion again ranking first. Moxibustion offers broad applicability, simple operation, and advantages of safety, efficacy, and long-term usability for treating perimenopausal insomnia. As documented in *Compendium of Materia Medica*, moxibustion penetrates meridians to treat numerous diseases by transforming harsh qi into harmony. Research indicates that appropriate moxibustion stimulation not only activates the body's self-stabilizing potential and maintains yin-yang balance but also supports healthy qi and enhances immunity. Studies have shown moxibustion can penetrate deep muscle layers, warm yang and move qi, nourish yin blood, promote metabolism, and regulate endocrine function, while also stimulating pineal gland melatonin secretion to facilitate sleep.

For Kupperman scores, no statistically significant differences emerged between non-drug interventions and sedative-hypnotic Western medication, though scraping ranked highest. Traditional Chinese medicine theory views the body as an integrated whole where organs, meridians, and skin interconnect. Scraping regulates organs, unblocks meridians, and balances yin-yang. Additionally, research demonstrates that scraping stimulates superficial skin to gradually rupture capillaries, triggering an autologous hemolytic reaction that generates new immune stimulants. This therapy not only accelerates metabolism and promotes blood and lymphatic circulation but also regulates endocrine function and enhances immunity and antioxidant capacity. However, limited research necessitates further validation.

For E2 levels, no significant differences were found between interventions, though acupuncture ranked highest. Research suggests acupuncture effectively improves neuroreflex arc function related to sleep in perimenopausal women with insomnia, thereby promoting local qi and blood circulation. Animal studies have confirmed that acupuncture regulates the hypothalamic-pituitary-ovarian and adrenal axes, improves serum E2 content in perimenopausal rats, and reconstructs partial estrogen negative feedback, thereby reducing perimenopausal symptoms.

This study has several limitations. First, some non-drug interventions had few

RCTs with small sample sizes. Second, while we examined different non-drug interventions, we did not perform subgroup analyses based on varying intervention durations. Third, all included studies were conducted in China, potentially introducing geographic bias. Fourth, although ranking results suggested scraping and acupuncture as optimal for Kupperman scores and E2 levels respectively, direct pairwise comparisons showed no statistical significance, necessitating cautious interpretation.

In conclusion, limited evidence suggests that moxibustion offers advantages in improving total effective rate and PSQI scores, scraping in improving Kupperman scores, and acupuncture in elevating E2 levels among perimenopausal women. However, additional high-quality research is required to validate these findings.

Author Contributions

HE Jingyi was responsible for conceptualization, design, and manuscript writing; WANG Fang provided overall supervision; HE Jingyi, SHUI Xiaoling, and LIANG Qian collected and organized data; HE Jingyi and LI Ling analyzed and interpreted results; HE Jingyi and WANG Fang revised the manuscript; LI Ling and LIANG Qian revised the English; WANG Fang performed quality control and final review.

Conflict of Interest

The authors declare no conflict of interest.

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