


A systematic review and meta-analysis of acupuncture combined with Tuina in the treatment of insomnia

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Abstract

Background: Insomnia is a sleep disorder with insufficient sleep time or/and poor sleep quality. Relevant epidemiological studies have shown that insomnia symptoms occur in about 35% to 50% of the adult population, and it is one of the most common diseases in the elderly. Patients who often suffer from insomnia are prone to symptoms such as fatigue, weakened cognitive function, depression, and even mental illness, which bring serious physical and mental damage to individuals and a heavy economic burden to social medical care and families. Traditional Chinese medicine and modern medicine have their own advantages in the treatment of insomnia, and there is currently a lack of reports on the comparison of acupuncture combined with massage and conventional medicine.

Objective: To evaluate the clinical efficacy of acupuncture combined with Tuina in the treatment of insomnia.

Methods: Search for clinical randomized controlled trials (RCTs) of acupuncture combined with Tuina in the treatment of insomnia from PubMed, Cochrane Library, Web of Science, China National Knowledge Infrastructure, Wan Fang Database, and China Science and Technology Journal Database. The RevMan5.4 software was used for Meta-analysis after literature screening, data extraction and quality evaluation.

Results: A total of 29 studies were included with a total of 2688 cases. Compared with drugs or acupuncture alone, acupuncture combined with Tuina has advantages in the total clinical effectiveness, as well as the Pittsburgh Sleep Quality Index (PSQI) and Statistical Self-Rating Anxiety Scale score (SAS) (OR = 3.59, 95% confidence interval [CI] [2.77, 4.66], Z = 9.62 [*P* < .00001]) (MD = -2.44, 95% CI [-2.93, -1.95], Z = 9.72 [*P* < .00001]) (MD = -8.42, 95% CI [-10.23, -6.61], Z = 9.09 [*P* < .00001]). There was no statistically significant difference in Statistical Self-rating Depression Scale score (SDS) (MD = -5.26, 95% CI [-11.29, 0.78], Z = 1.71 [*P* > .05]).

Conclusion: Acupuncture combined with Tuina has obvious clinical advantages in the treatment of insomnia. This result is expected to provide a reference for the clinical treatment of insomnia, but the long-term effect of clinical efficacy still needs further study.

Abbreviations: CI = confidence interval, MD = mean difference, PSQI = Pittsburgh Sleep Quality Index, RCTs = randomized controlled trials, SAS = self-rating anxiety scale, SDS = self-rating depression scale, TCM = traditional Chinese medicine.

Keywords: acupuncture, insomnia, meta-analysis, randomized controlled trial, Tuina

1. Introduction

Insomnia is a sleep disorder with insufficient sleep time or/and poor sleep quality. International Classification of Diseases-10 defines insomnia as sleep initiation disorder and sleep maintenance disorder, so that the quality of sleep cannot meet

individual needs. It is called “BuMei” in traditional Chinese medicine. The disease can be manifested by subjective experiences such as difficulty falling asleep, light sleep and easy waking up, difficulty falling asleep again after waking up, irritability and dreaminess, and then unresponsiveness, memory loss, and impact on daytime social activities.^[1,2] Relevant epidemiological

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All data generated or analyzed during this study are included in this published article [and its supplementary information files].

This study is a systematic evaluation of the efficacy and safety of Acupuncture Combined with Tuina in the Treatment of Insomnia, meta-analysis was used to conduct a second study on the published literature, without individual data. Therefore, ethical approval is not required. The results will be reported in a peer-reviewed journal after the analysis completed.

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studies have shown that insomnia symptoms occur in about 35% to 50% of the adult population, and the prevalence in the elderly population can reach 50%, and it is one of the most common diseases in the elderly.^[3] Patients who often suffer from insomnia are prone to symptoms such as fatigue, weakened cognitive function, depression, and even mental illness, which bring serious physical and mental damage to individuals and a heavy economic burden to social medical care and families.^[4–6]

At present, the main ways of treating insomnia in modern medicine are psychotherapy, physical therapy and drug therapy. Drug therapy is the most important treatment method. Commonly used drugs are mainly tranquilizers, gamma-aminobutyric acid receptor agonist. However, long-term use of these drugs can be resistant and addictive, and it is easy to produce excessive sedative side effects such as drowsiness and fatigue.^[7] Traditional Chinese medicine (TCM) has a long history of clinical practice and diverse treatment methods in the treatment of insomnia including acupuncture, massage and traditional Chinese medicine decoction, etc. Acupuncture refers to piercing a needle into a patient's body at a certain angle under the guidance of TCM theory, and using acupuncture techniques such as twisting and lifting to stimulate specific parts of the human body to achieve the purpose of treating diseases. Tuina, also known as "massage," is based on the theory of viscera and meridians of traditional Chinese medicine, combined with the anatomy and pathological diagnosis of modern medicine, and uses manipulation to act on specific parts of the human body to adjust the physiological and pathological conditions of the body. From the perspective of modern medicine, massage mainly stimulates peripheral nerves, promotes blood, lymphatic circulation and metabolic processes between tissues, so as to coordinate the functions of various tissues and organs, and to improve the level of metabolism.

The combination of acupuncture and massage to treat diseases is a method commonly used in clinical Chinese medicine. The combination of the 2 methods can achieve the curative effects of dredging the meridians, promoting qi and blood, relieving pain, eliminating pathogens and strengthening the body, reconciling yin and yang, and prolonging life.

There are many clinical reports on the treatment of insomnia by non-drug methods such as acupuncture and massage. Some studies have reported a systematic review of acupuncture combined with massage versus acupuncture alone,^[8,9] but there is no report on acupuncture combined with massage and conventional drugs. Therefore, this study aims to use evidence-based medicine to analyze the literature of acupuncture combined with massage in the treatment of insomnia, objectively evaluate its clinical efficacy and safety, and provide a safe and reliable treatment plan for TCM clinical treatment of insomnia.

2. Methods

2.1. Literature inclusion criteria

2.1.1. Research objects. According to the diagnostic criteria of "insomnia" in traditional Chinese and Modern medicine, there are international or domestic standards with specific origins, and no restrictions on the gender, age, course of disease, region, and ethnicity of the patients included.

2.1.2. Interventions. The experimental group was limited to acupuncture combined with massage, and acupuncture was limited to body acupuncture (filigree acupuncture), The acupoint selection, manipulation, treatment frequency and course of treatment were not limited.

2.1.3. Control measures. The control group was treated with conventional Chinese, Modern medicine and use acupuncture or tuina alone.

2.1.4. Outcome indicators. The outcome indicators including the Total effective rate, The Pittsburgh Sleep Quality Index (PSQI) score, Statistical Self-rating Depression Scale (SDS) score and Statistical Self-Rating Anxiety Scale (SAS) score, all the outcome indexes were counted according to the same evaluation criteria.

2.1.5. Types of studies. The Chinese and English literatures of published randomized controlled trials (RCTs) are not limited to use of blinding and allocation concealment.

2.2. Literature exclusion criteria

Non-RCT studies, such as case reports, reviews, animal studies, etc; Mismatched interventions; Small sample research trials, limited to studies with a total sample size of <40; Incomplete data or lack of evaluation data.

2.3. Retrieval strategy

Search PubMed, Cochrane Library, Web of Science, China Science and Technology Journal Database, Wan Fang Database, and China Science and Technology Journal Database. The retrieval time limit is from the date of establishment of each database to March 31, 2022. The retrieval method is a combination of subject headings and free words, and the retrieval strategy is adjusted according to the characteristics of different databases. The search terms included "insomnia," "bumei," "acupuncture," "massage," and "random." English search terms include "Acupuncture," "Needle," "Insomnia," "Massage," "Tuina."

2.4. Literature screening and data extraction

Two researchers independently extracted data from eligible papers. According to the updated guidelines for reporting parallel group randomized trials, the content of data extraction is recommended to include publication characteristics of literature, basic characteristics of research objects and methodological characteristics. Cross check the extracted data, a third reviewer will be settled to consulting, if necessary.

2.5. Evaluation of literature quality

Quality assessment was performed according to the Cochrane Manual of Systematic Reviews. The contents of the assessment include random allocation method, allocation scheme concealment, blinding, completeness of published data, selective reporting, and other sources of bias. The quality of evidence is divided into low, high risk of bias, and unclear risk of bias. The evaluation results were displayed using the risk of bias assessment chart drawn by Review Manager 5.4.

2.6. Statistical methods

Revman 5.4 software was used for Meta-analysis, odds ratio for binary variables, mean difference (MD) for continuous variables, and 95% confidence interval (CI) for each effect size for evaluation. The heterogeneity of each combined data was tested, and the size of the heterogeneity was measured according to the I^2 value. If $I^2 > 50\%$, indicating that the heterogeneity was significant, the random effect model was used for analysis; otherwise, the fixed effect model was used for analysis. The evaluation results are displayed in a forest graph.

When there was significant heterogeneity in the results, subgroup analysis and sensitivity analysis were performed to find possible sources of heterogeneity. Finally, the effective rate was

tested for publication bias, and the results were displayed in a funnel plot.

3. Results

3.1. Literature search results and characteristics of included studies

A total of 306 literatures were retrieved. According to the inclusion and exclusion criteria, 29 literatures were finally included (Fig.1), including 28 Chinese literatures and 1 English literature. The total number of people included in the study was 2688, including 1387 in the experimental group and 1301 in the control group. Among them, 15 studies^[10-24] were acupuncture combined with massage versus acupuncture alone, and 14 studies^[25-38] are acupuncture combined with massage vs modern

medicine treatment. The baselines of all included studies were comparable. The basic characteristics of the included studies were extracted in Table 1.

3.2. Quality evaluation of included studies

All 29 included studies mentioned randomization, of which 7 studies^[10,20,21,23,25,30,36] used random number table method and were judged to be at low risk of bias, and 1 study^[31] was randomization on date of visit, judged to be at high risk of bias. The rest did not mention the specific randomization method and judged that the risk of bias was uncertain. None of the included studies mentioned allocation concealment and was judged to be at uncertain risk of bias. One study each mentioned single-blind^[15] and double-blind,^[31] and were judged to be at low risk of bias, and the rest were judged to be at uncertain risk

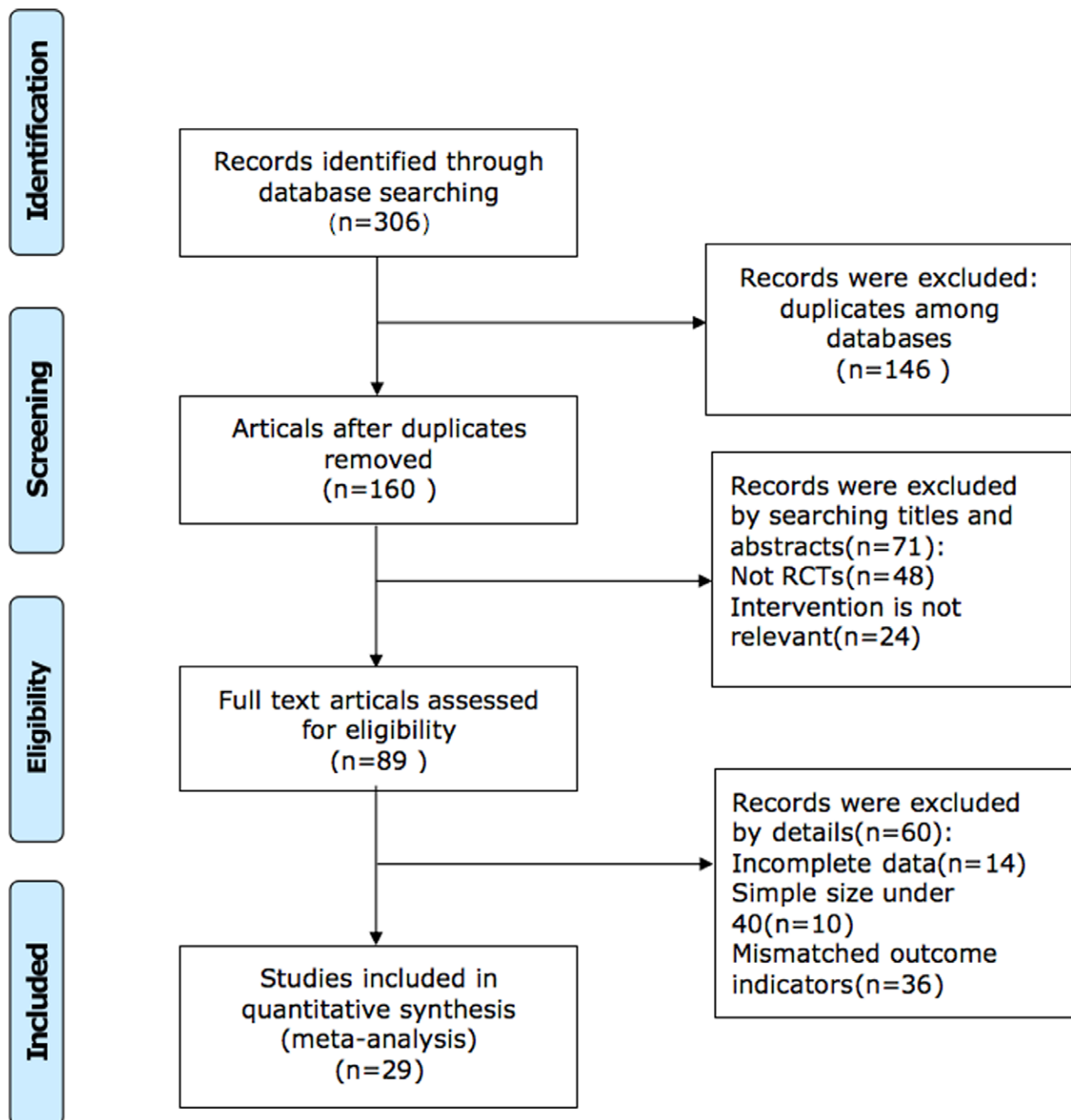


Figure 1. Flow diagram of study selection and identification.

Table 1
Characteristics of included studies.

Study ID	Test			Control			Treatment duration	Outcomes
	Intervention	Sample size	Age	Intervention	Sample size	Age		
Zhao JP 2015 ^[10]	A	46	46.0 ± 20.1	B	46	45.3 ± 20.3	30	①
He GZ 2010 ^[25]	A	35	16–75	D	35	15–71	30	①
Feng WT 2017 ^[11]	A	100	51.33 ± 7.06	B	100	52.47 ± 8.21	–	①②
Lv M 2006 ^[12]	A	49	18–65	B	43	18–65	18	①②
Zhou WJ 2014 ^[26]	A	70	45.8 ± 6.6	C	70	45.5 ± 6.2	20	①
Zhou XH 2018 ^[13]	A	50	22–57	B	50	20–60	30	①②
Pang HY 2012 ^[27]	A	65	36.1	E	60	35.6	–	①
Zhang L 2009 ^[14]	A	50	45–69	B	50	47–70	30	①
Zhang Q 2013 ^[15]	A	30	39 ± 14.3	B	30	43 ± 11.3	–	①②
Zhang SN 2016 ^[16]	A	40	12–79	B	40	12–79	30	①②
Li ZM 2012 ^[17]	A	30	35 ± 2	B	30	36 ± 3	20	①
Yang JH 2012 ^[28]	A	106	16–75	F	44	21–68	30	①
Tu XS 2009 ^[29]	A	40	40.30 ± 12.12	D	40	39.47 ± 11.99	10	①②
Wen YQ 2011 ^[30]	A	40	20–65	G	40	21–64	30	①②
Wang ZH 2019 ^[18]	A	40	51.4 ± 7.1	B	40	51.7 ± 6.9	21	①②
Shi XD 2020 ^[19]	A	52	54.3 ± 7.2	B	55	52.3 ± 5.2	70	①
Xiao YH 2021 ^[31]	A	30	46.44 ± 14.45	C	30	46.75 ± 14.37	56	①②
Dong W 2011 ^[20]	A	60	22–72	B	60	22–72	30	①
Chen C 2021 ^[32]	A	60	51.87 ± 7.71	C	60	52.32 ± 7.82	14	①②③④
Gu CC 2010 ^[33]	A	40	30–68	E	30	32–67	30	①
Ma ST 2011 ^[34]	A	42	42 ± 16	C	38	43 ± 18	15/35	①
Huang YL 2016 ^[35]	A	40	44.2 ± 19.2	C	40	44.2 ± 19.2	20	①②
Huang JJ 2008 ^[36]	A	90	42.35 ± 10.74	C	90	40.72 ± 11.28	28	①②
Wang DY 2013 ^[37]	A	20	40.55 ± 14.78	C	20	40.07 ± 15.78	20	①②
Dong QJ 2013 ^[21]	A	24	43.2 ± 13.9	B	24	42.6 ± 12.5	28	①②
Ji DS 2008 ^[22]	A	38	16–63	B	36	16–63	40	①②
Zhu LP 2019 ^[23]	A	40	51.23 ± 2.15	B	40	50.94 ± 2.01	–	①②
Zhang TY 2021 ^[38]	A	30	47.64 ± 5.78	C	30	45.19 ± 5.25	28	①②③④
Wang Y 2021 ^[24]	A	30	51.88 ± 12.38	B	30	51.81 ± 12.39	30	①②

Note: A = acupuncture combined with massage, B = ordinary acupuncture, C = estazolam, D = sulazepam, E = diazepam, F = lorazepam, G = alprazolam, ① Total effective rate ② PSQI ③ SDS ④ SAS. PSQI = Pittsburgh Sleep Quality Index, SAS = self-rating anxiety scale, SDS = self-rating depression scale.

of bias. Twenty-nine studies reported complete data and no selective reporting of results. Three studies^[10,19,34] mentioned dropouts, and reported the number of dropouts and processing methods, all of them were judged to be at low risk of bias. None of the included studies were found to be at other risk of bias, and the risk of bias was judged to be uncertain. The risk of bias assessment is shown in Figure 2 and 3.

3.3. Observation indicator results

3.3.1. Clinical effectiveness. Twenty-six studies^[10–20,22,25–38] reported the overall response rate, with a total of 2488 patients, including 1287 in the experimental group and 1201 in the control group. Subgroup analysis was performed between acupuncture combined with massage versus acupuncture alone, and acupuncture combined with massage versus conventional modern medicine for insomnia. The results showed that there was no heterogeneity among the groups, $I^2 = 0\%$, and a fixed effect model was used for statistical analysis. The combined effect size odds ratio = 3.59, 95% CI (2.77, 4.66), $Z = 9.62$ ($P < .00001$), indicating that acupuncture combined with massage in the treatment of insomnia was significantly better than acupuncture or modern medicine alone, and the difference was statistically significant ($P < .05$). The results of the meta-analysis are shown in Figure 3.

3.3.2. PSQI. Eighteen studies^[11,15,16,18,21–24,26,29–32,35–38] reported PSQI with a total of 1622 patients, including 812 in the experimental group and 810 in the control group. The results of subgroup analysis showed that $I^2 = 95\%$, combined effect size MD = -2.44, 95% CI (-2.93, -1.95), $Z = 9.72$ ($P < .00001$), indicating that acupuncture combined with

massage therapy was better than that of acupuncture or drug therapy alone, and the difference was statistically significant ($P < .05$). The results of the meta-analysis are shown in Figure 4.

3.3.3. SDS. Two studies^[32,38] reported SDS scores, with a total of 180 patients, 90 in the experimental group and 90 in the control group, and the intervention in the control group was Estazolam. Chi-square test showed $I^2 = 88\%$ ($P = .004$), and statistical analysis was performed using a random effects model. The combined effect size was MD = -5.26, 95% CI (-11.29, 0.78), $Z = 1.71$ ($P > .05$), which was not statistically significant, indicating that acupuncture combined with massage therapy for insomnia was not superior to other treatments in SDS score. The results of the meta-analysis are shown in Figure 5.

3.3.4. SAS. SAS scores were reported in 2 studies with a total of 180 patients, 90 in the experimental group and 90 in the control group, and the intervention in the control group was Estazolam. The chi-square test showed that $I^2 = 0\%$, $P = .45$, indicating low homogeneity, and statistical analysis was performed using a fixed-effects model. The combined effect size MD = -8.42, 95% CI (-10.23, -6.61), $Z = 9.09$ ($P < .00001$), indicating that acupuncture combined with massage in the treatment of insomnia is superior to other treatments in SAS, and the difference is statistically significant ($P < .05$). The results of the meta-analysis are shown in Figure 6.

3.3.5. Publication bias assessment. According to the total clinical response rate, a total of 26 studies were evaluated for publication bias. The analysis showed that the representative points of each study were concentrated and symmetrically

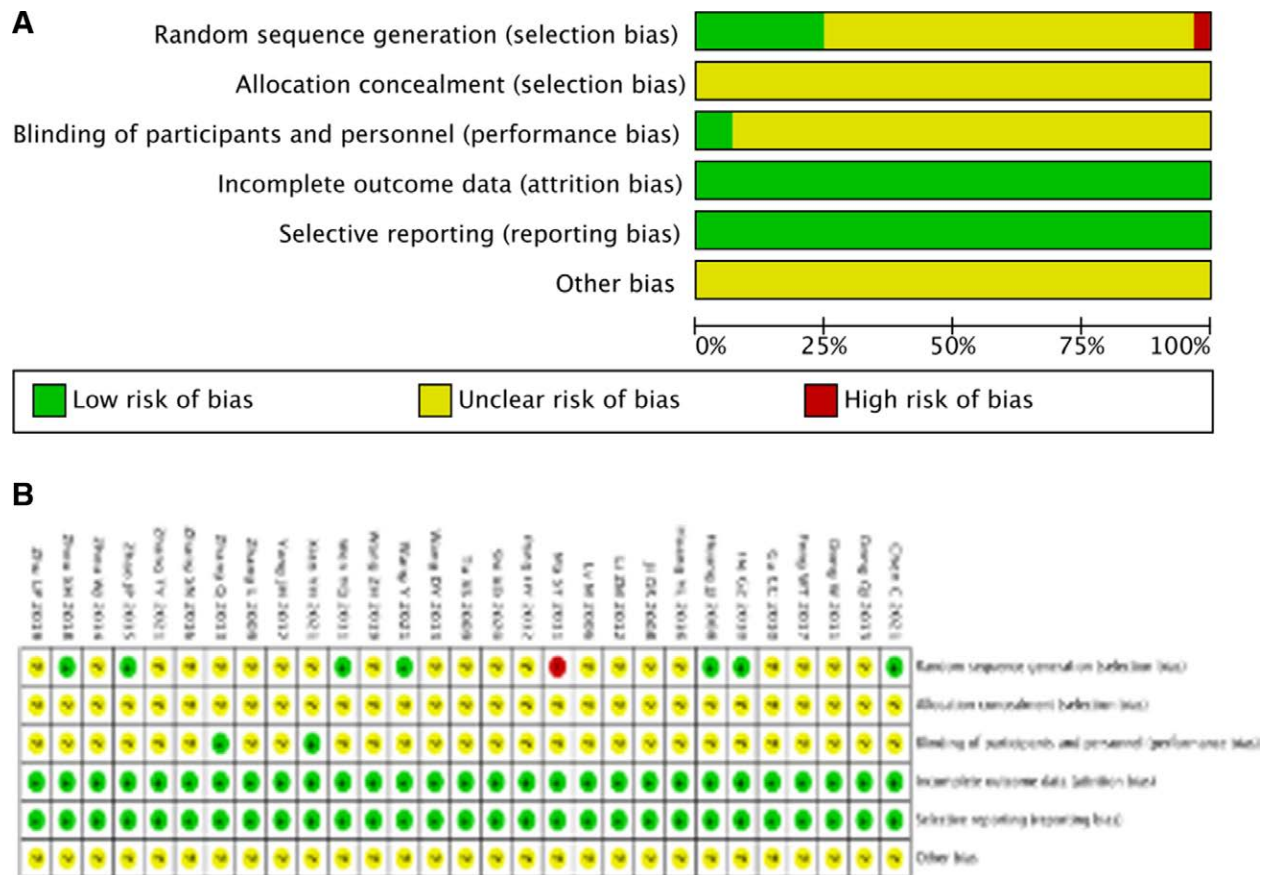


Figure 2. Assessment of risk of bias. (A) Risk of bias graph and (B) risk of bias summary.

distributed in the inverted funnel, indicating that the remaining studies may have less publication bias. The bias assessment results are shown in Figure 7.

4. Discussion

The pathogenesis of insomnia is complex and is affected by genetic susceptibility, major life events, psychological stress, and physiological or environmental factors, which in turn affect brain sleep function. A recent study reported that susceptibility to insomnia may reside in brain circuits that regulate mood, rather than circuits traditionally thought to regulate circadian rhythms.^[39] Insomnia is a chronic, recurrent disease that requires long-term drug intervention.^[40] Benzodiazepines often interfere with daytime work due to excessive sedation, the complex sleep behaviors it causes (such as sleepwalking) have been designated by the U.S. Food and Drug Administration for use with caution. And American Family Physician guidelines recommend that the drug be used for no more than 4 weeks.^[41] Non-benzodiazepines such as orexin inhibitors can lead to adverse reactions such as drowsiness and dyskinesia^[42]; antidepressants can cause male sexual dysfunction; melatonin receptor agonists are also difficult to popularize due to cost constraints. Therefore, it is of great clinical significance to find a safe and effective treatment scheme for insomnia. Considering the side effects and clinical efficacy of drugs, antihistamines, antipsychotics and melatonin are not recommended for the treatment of insomnia, and the recommendation level of evidence-based medicine is low-to very-low-quality evidence.^[43] In addition, there are studies reported that there seems to be insufficient evidence to confirm that MLT is effective for primary insomnia.^[44] Based on the method of evidence-based medicine, this study conducted a systematic

review on the total clinical efficacy rate, PSQI score, SDS score and SAS score of acupuncture combined with massage in the treatment of insomnia by collecting and sorting out literature. The results showed that acupuncture combined with massage was superior to acupuncture or modern medicine alone in improving the total clinical effective rate, PSQI score and SAS score, and the results were statistically significant. The publication bias test of the effective rate indicated that it was less likely to have publication bias.

Acupuncture treatment of insomnia has received increasing attention in the past 2 decades.^[45] Studies have found that acupuncture can regulate low-frequency fluctuations in the posterior cerebellum, temporal lobe and other regions, and regulate the functions of the parahippocampal gyrus and superior temporal gyrus of the brain, thereby improving sleep quality.^[46,47] Animal experiments have confirmed that acupuncture can regulate the content of dopamine, serotonin and norepinephrine in serum, increase the level of melatonin, and up-regulate the level of melatonin protein and its receptor mRNA in the pineal gland of the suprachiasmatic nucleus,^[48,49] and also adjust the ratio of alpha and beta waves in the cerebral cortex.^[50] As an important part of traditional Chinese medicine, massage has the advantages of simplicity, convenience, efficacy, low cost, and no adverse reactions. Massage can relieve the tension of the skin, flesh, tendons and pulses, and promote local blood circulation and metabolism, to reconcile qi and blood, balance yin and yang. Studies have reported that massage on the abdomen of insomnia rats can regulate the content of substance P, galanin, β -endorphin and collagen fibrillary acidic protein in serum and hypothalamus, and improve sleep quality.^[51] At the same time, acupuncture combined with massage to treat insomnia can reconcile the qi, blood, yin and yang of the whole body. Lin Peiqin pointed

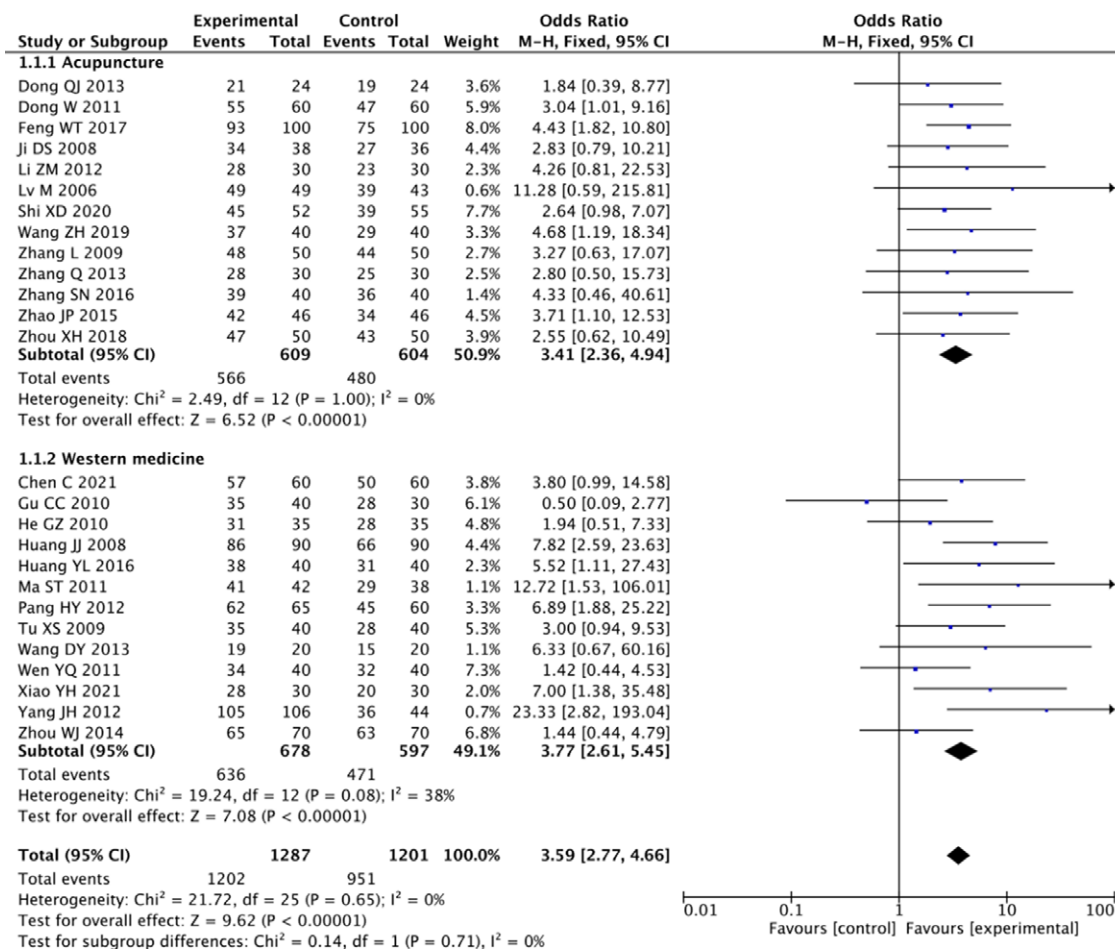


Figure 3. Forest plot of the clinical efficacy rates.

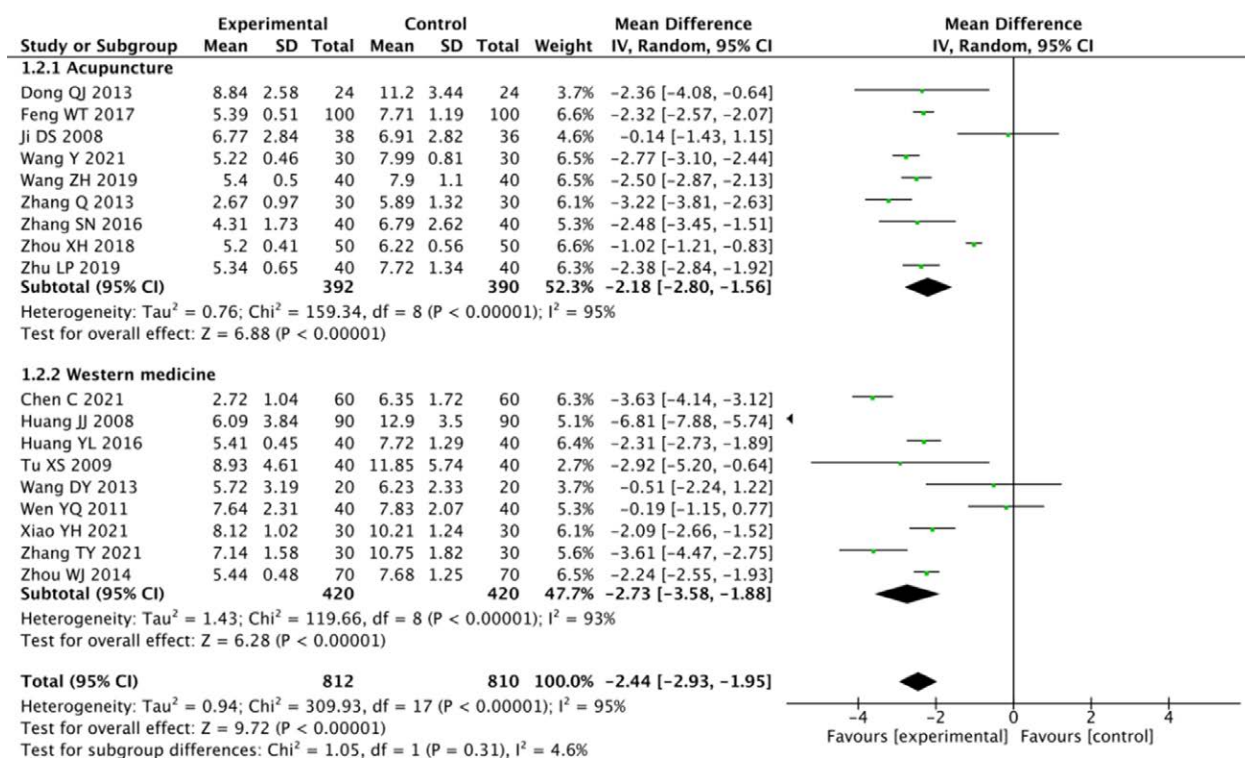


Figure 4. Forest plot of PSQI. PSQI = Pittsburgh Sleep Quality Index.

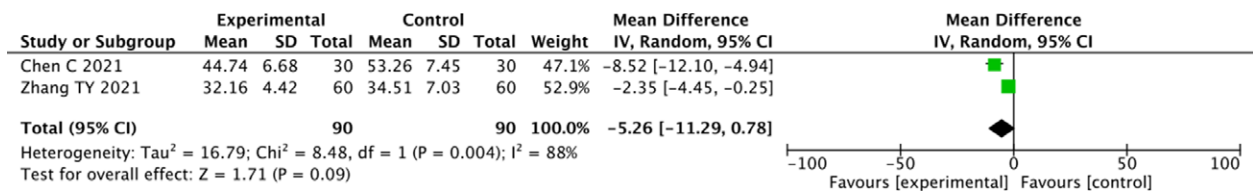


Figure 5. Forest plot of SDS. SDS = self-rating depression scale.

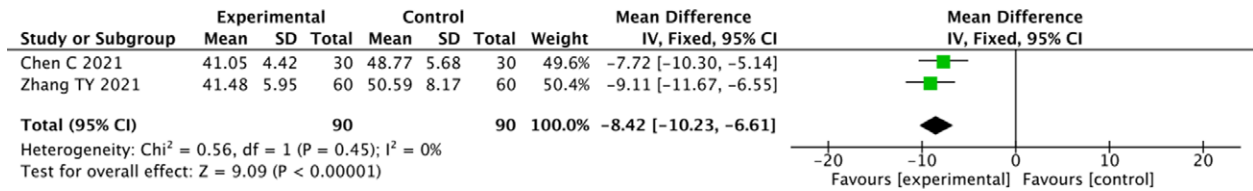


Figure 6. Forest plot of the SAS. SAS = self-rating anxiety scale.

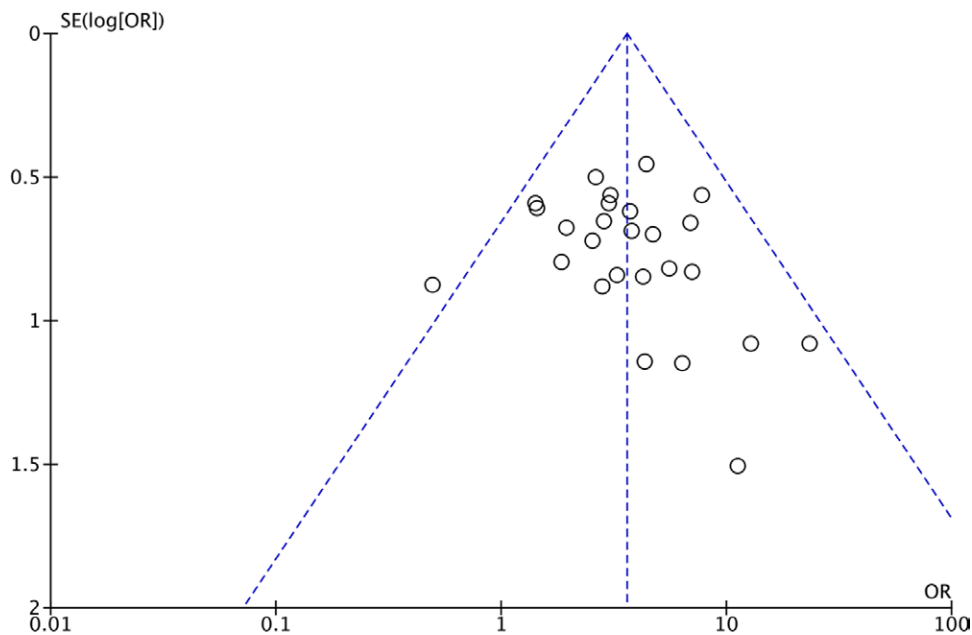


Figure 7. Funnel plot of the clinical efficacy rates.

out in “Treatment of Insomnia by Syndrome and Diagnosis” that “people who suffer from insomnia are ill and do not pay attention to yin.”^[52] Started with good results, which is the embodiment of Huangdi Neijing, “Thus, those who make good use of acupuncture should lead yang from yin, and yin from yang” and “the key to using acupuncture is to know how to adjust yin and yang.”

At present, there are many deficiencies in clinical research on acupuncture for insomnia, such as confusion of disease names, inconsistent diagnostic criteria, and lack of targeted analysis of efficacy evaluation indicators.^[53] Based on the differences in the quality of the included literature, this study has the following limitations: Part of the included literature did not use the correct randomization method, and lacked the design of blinding and allocation concealment; The included studies lacked laboratory test indicators, which led to the lack of this study. The second in-depth analysis

of laboratory test data has a certain impact on the objectivity of the results of this study. This study did not conduct a classification study on the degree of disease, nor on the selection and treatment of acupuncture and massage, which makes this study is not precise enough. It is hoped that more high-quality, large-sample RCT research data will be included in the future, and the severity of the disease, acupuncture and massage techniques, and treatment courses will be classified and discussed, and sufficient research data will be used for further evaluation.

In conclusion, compared with traditional Chinese medicine decoction, the operation is simple, which is conducive to improving patient compliance. From the results of this study, in terms of total clinical efficacy, PSQI score and SAS score, acupuncture combined with massage is superior to acupuncture or modern medicine alone. This result is expected to provide a reference for clinical treatment of insomnia.

Author contributions

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