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Research

A Meta-Analysis of randomized Controlled trials (R.C.Ts) On The Therapeutic Effect of Electro-Acupuncture for Primary Insomnia women with perimenaupose.

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Abstract: *To explore the potential benefit of Acupuncture, a systematic review (S.R) was undertaken of published randomized controlled trials (RCTs) on the therapeutic Effect of Electro- Acupuncture for Primary Insomnia (P.I) women with perimenaupose. Women with diary-defined sleep deficiency reported more depressive symptoms (P=0.02) and perceived more depressive symptoms (p<0.01) than those who were not sleep deficient. Although there are few direct cross-cultural comparisons of insomnia, a worldwide study found that the highest prevalence rates of insomnia were in Brazil (79, 8%), followed by South Africa (45, 3%), Eastern Europe (32%), Asia (28, 3%). Methods: A comprehensive Study was conducted by four independent computerized literature databases which selected randomized clinical trials from the EBSCO Host electronic database. This database included (Pub Med, COCHRANE Central Register of Controlled Trails from database inception; and CNKI, web of science WANG FANG). Furthermore, randomized controlled trials are going to be published on 2019 without restriction to the language.*

Risk of bias was determined by the Cochrane risk of bias assessment tool. Therefore, the methodological quality of the included randomized controlled trials was assessed using de Jadad score, and the reporting of the included studies was evaluated by the Rev. Man 5.3. The key words: Primary Insomnia, Acupuncture and it is form as electro-acupuncture, Systematic review， Meta-Analysis.

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INTRODUCTION

Description of the condition

In Contrast to a narrative review, a systematic review is a form of research that provides a summary of medical reports on specific clinical questions, using explicit methods to search, critically appraise, and synthesize the world literature systematically. Moreover, the explicit methods used in systematic reviews and meta-analysis limit bias and, hopefully, will improve reliability and accuracy of conclusions. For these reasons, systematic reviews of randomized controlled trials (RCTs) are considered to be evidence of the highest level in the hierarchy of research designs evaluating effectiveness of intervention [1].

Nowadays many people around the world have a very busy, fast, stressful life often with many problems so complicated to diagnose and to cure as primary insomnia, inability to calm down and relax. Roughly we can describe this life style as too much activity, stimulation and lack of resting, quietness. Given the fact that primary insomnia is among the number one of diseases that cause morbidity and mortality in the world. Perhaps now more than ever, many patients seek options when it comes to their health. As an alternative option acupuncture is growing in popularity, but can sometimes be an afterthought due to common misconceptions, lack of education, or fear. Tradition Chinese Medicine (TCM) dates back to the early Han Dynasty, with records of doctors treating a variety of illnesses. TCM practitioners are educated from classical medical texts and apply the same techniques in clinical practice to not only manage Pain, but also treat internal diseases.

In addition, with the increasing socioeconomic stress, there are more and more middle-aged women suffering from mood disorders, such as anxiety and depression, which have been noted to be closely related to **sleep problems in perimenopausal women**. The study of women's health across the nation (SWAN) presents that the prevalence of **sleep** disturbance ascends with increasing age. Woman has to undergo the menopausal transition as an inevitable stage of life. During this period, perimenopausal females usually complain of difficulties initiating and/or maintaining **sleep** with frequent nocturnal and early morning awakenings. Recent reviews revealed that the prevalence of primary insomnia women with perimenopausal ranges from 39 to 47% [2], while it is approximately 35% in the general population. In the **perimenopausal** years–usually when a woman is in her **forties–ovarian** production of **hormones** starts to shift **[3]. Researchers** face caution in drawing conclusions because of blinding issues, and the potential bias when measuring subjective data such as Primary Insomnia. **Therefore, meta-analysis** will aim to give medical practitioners as well as patients an objective conclusion on the therapeutic effect of electro acupuncture for Primary Insomnia.

Western Medicine perspective

1.1 Definition and Etiology

*(Sleeplessness) Insomnia from **insomnis**: **In**-(not), **somnus**-(sleep)*

It may be a form of **neurosis** in western medicine. In human, our major rest period is marked by a behavior known as Sleep, defined as an easily reversible state of inactivity characterized by lack of interaction with the external environment. Most mammals and Birds show the same stages of sleep as humans, telling us that sleep is a very ancient property of vertebrate brains. Depending on how sleep is defined, it appears that could be described as sleep. Insomnia also knows as sleeplessness, it is one of the most common sleep disorders among patients. People who have insomnia have trouble falling asleep, staying asleep, or both. Almost people have insomnia problem. Getting enough sleep is an important part of a healthy lifestyle. It can affect people mentally and physically. Patients with insomnia may feel tired, depressed, irritable; tense, lazy, or have delayed reactions, always makes hard for people to concentrate or perform tasks during the days as distraction, or headache. Most adults need 7 to 8 hours of sleep each night **[4].**

Sleep is one of the unsolved mysteries in neurophysiology, and a question that may have more than one answer. Some explanations that have been proposed include conserving energy, to avoid predators, to allow the body to repair itself, and to process memories. Some of the newest research indicates that sleep is important for clearing wastes out of the cerebrospinal fluid, particularly some of the proteins that build up in degenerative neurological diseases such as **Alzheimer'**s. There is good evidence supporting the link between sleep and memory. A number of studies have demonstrated that sleep deprivation impairs our performance on tasks and tests, one reason for not pulling "all-nighters." At the same time, 20-30 minute "power naps" have also been shown to improve memory, and they can help make up a sleep deficit.

The Etiology of Insomnia

It is multifactorial, involving complex interactions among the factor background, different social and environmental factors, Such as sedentary lifestyle and unhealthy dietary habits. The etiology of Insomnia is multifactorial, involving complex interactions among the factor background, different social and environmental factors, such as sedentary lifestyle and unhealthy dietary habits.

Primary insomnia occurs in up to 10% of adults and up to 25% of elderly adults and appears slightly more common among women. The cause of primary insomnia can be different for each different for each individual but often involves a preoccupation with the inability to sleep or excessive worry about sleep, which in turns causes the individual to not sleep. Many reports that they sleep better away from home, suggesting that conditioning related to the bedroom has occurred, and resulting in bouts of sleep while watching TV, being a passenger in a car, or other area not associated with the bedroom. The pathophysiology of primary insomnia is not well understood, and essential features assist in diagnosis. The focus of management is on symptoms.

1.2 Pathophysiology

The exact pathophysiology of insomnia is unknown, resulting in countless research by medical professionals in hopes of understanding the complexity of the disease. Scientific evidence supports the notion that Insomnia pathophysiology involves inherited alteration of brain excitability, so from studies, we know that the sleeping brain consumes as much oxygen as the awake brain, **so sleep is a metabolically active state.**

Sleep is divided into **four stages;** each marked by identifiable, predictable events associated with characteristic somatic change and EEG (Electroencephalograms) patterns.
In awake states, many neurons are firing but not in a coordinated fashion. As the person falls asleep and the state of arousal lessens, the frequency of the wave's decreases. The two major sleep phases are slow-wave sleep and rapid eye movement sleep. **Slow-wave sleep (**also called deep sleep or non-REM sleep**)** is in indicated on the EEG (Electroencephalograms) by the presence of delta waves, high-amplitude, low-frequency waves of long duration that sweep across the cerebral cortex. During this phase of the sleep cycle, sleepers adjust body position without conscious commands from the brain to do so **[5].**

In contrast, rapid eye movement (REM) sleep is marked by an EEG pattern closer to that of an awake person, with low-amplitude, high-frequency waves. During REM sleep, brain activity inhibits motor neurons to skeletal muscles, paralyzing them. Exceptions to this pattern are the muscles that move the eyes and those that control breathing. The control of homeostatic Functions are depressed during REM sleep, and body temperature falls toward ambient temperature **[6].**

A typical, eight-hour sleep consists of repeating cycle. In the first hour, the person moves from wakefulness into a deep sleep. The sleeper then cycles between deep sleep and REM sleep (stage 1), with stages 2-3 occurring in between. Near the end of an eight-hour sleep period, a sleeper spends the most time in stage 2 and REM sleep, until finally awakening for the day.
If sleep is a neurologically active process, what is it that makes us sleep? The possibility of a sleep-inducing factor was first proposed in **1913**, when scientists found that cerebrospinal fluid from sleep-deprived dogs could induce sleep in normal animals.
Since then, a variety of sleep-inducing factors have been identified. Curiously, many of them are also substances that enhance the immune response, such as interleukin-1, interferon, serotonin, and tumor necrosis factor.

1.3 Epidemiology

1.3.1 Epidemiology and Incidence in the United States

According to the report of the World health Organization (WHO) as Primary Insomnia is among the most prevalent disorders of Mankind. It affects almost women than man at least 1 adult in every 7 in the world. Often is one of the most common reasons for an outpatient office visits, associated with reduced quality of life, increased risk of having a motor vehicle crash causing accidents in the world.

In the United States, Population-based studies estimate that 10% to 40% of American adults have intermittent insomnia. It is generally believed that 10-15% of the adults suffer from chronic insomnia, and an additional 25-35% has transient or occasional asleep [8]. Although there are few direct cross-cultural comparisons of insomnia, a worldwide study found that the highest prevalence rates of insomnia were in Brazil (79, 8%), followed by South Africa (45, 3%), Eastern Europe (32%), Asia (28, 3%). Furthermore Women, in particular, suffer greatly from Insomnia and depression, and are significantly more vulnerable to depression than men ($p<0.05$) with symptoms of primary. Women with diary-defined sleep deficiency reported more depressive symptoms ($P=0.02$) and perceived more depressive symptoms ($p<0.01$) than those who were not sleep deficient [9].

A cross- sectional study showed that 604 of Portuguese schoolteachers, 40.6% suffered from of symptoms of primary insomnia; the symptoms may be difficult falling asleep, sleep latency more than 30minutes, or sleep efficiency less than 85%, which usually happened more than nights a week and occurred at least 3weeks [9]..

1.4 Western Medicine Treatment

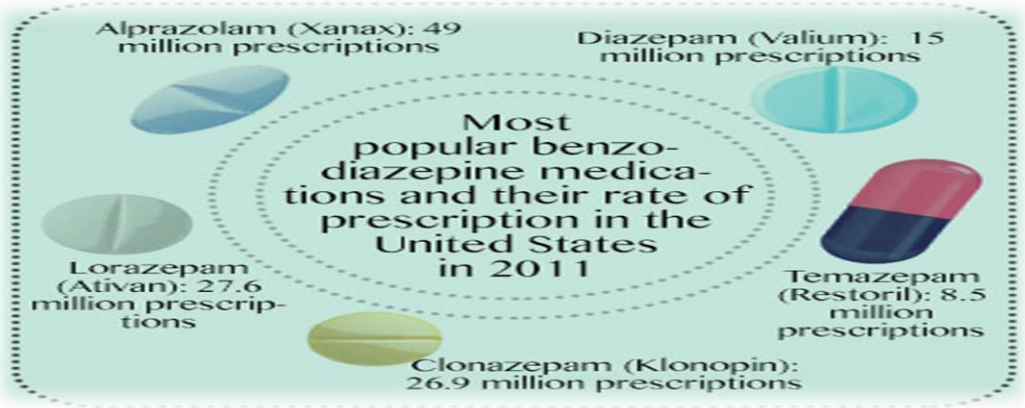
Several treatment options exist, but pharmacological therapy is the standard treatment for the Primary Insomnia. According to the World Health Organization (WHO), in response to the sharp, systematic review of numerous treatments is commonly used on these patients meaning are the class most widely preferred for Insomnia and anxiety (90% of countries). Benzodiazepines (BZDs) are one of the most used in western medicine in the world.

Widely prescribed pharmacologic agents in the United States (more than 112 million prescriptions in 2007) [12].

BZDs are used for numerous indications, including anxiety, insomnia, muscle relaxation, relief from anxiety, insomnia, relief from spasticity caused by central nervous system pathology, and epilepsy. BZDs are also used intraoperatively because of their amnesic and anxiolytic properties. However, these properties become undesired side effects in nearly all other clinical instances. The severity of BZD-induced adverse effects forces physicians to exercise caution and pay attention to side effects when prescribing this class of agents. Tolerance, dependence, age-related physiological changes, and drug-drug interactions are all important considerations.

Benzodiazepines in clinical practice general

BZDs are classified in terms of their elimination half-life. Short-acting BZDs have a median elimination half-life of 1-12 hours, intermediate-acting BZDs have an average elimination half-life of 12-40 hours, and long-acting BZDs have an average elimination half-life of 40-250 hours. As noted earlier, 5 half-lives are generally necessary for an agent to be eliminated from the body, making the number of hours that a drug is in the body considerably longer.



The table lists various BZDs and their characteristics. Another way to characterize BZDs is by relative potency. The first BZDs were low to medium potency. These include long-acting **Chlordiazepoxide**, the first BZD discovered, as well as **Oxazepam and Temazepam**. Because of their effectiveness and relatively low toxicity, they became first-line agents for conditions such as insomnia and anxiety. Later, high-potency BZDs (**Alprazolam, Lorazepam, and Clonazepam**) were discovered and are efficacious in the short-term management of insomnia. Compliance with prophylactic drugs can be low due to adverse side effects and the fact that patients dislike taking daily medication on a long-term basis **[12] .These new drug** led to new

Indications for usage: as a treatment for Insomnia, panic disorders, as adjuncts to Selective serotonin reuptake inhibitors for treatment of obsessive-compulsive disorder, and as adjuncts to antipsychotics for treatment of acute mania or agitation. The newer high-potency BZDs showed improved therapeutic effects as well as faster onset of action, making them the preferred BZDs for most applications. However, with increased potency comes an increase in the risk of undesired effects. Therefore, when prescribing drugs in this BZD group, clinicians must consider individual properties such as absorption, distribution, elimination half-life, and lipid solubility **[12].**

Dosage: One tablet is taken 30 min prior to bedtime in the day without acupuncture intervention. In the Estazolam group, six (1mg) is given 30 min prior to bedtime every day.

But there is very limited evidence of the long-term treatment efficacy of these agents. Therefore, they are constantly being debated due to their adverse side effects of residual daytime sedation, cognitive impairment, dependence, also it's could bring about many unavoidable side effects such as increase of the risk of Cardiovascular disease, gastrointestinal reaction, menstrual disorders, rhinitis, possible liver damage **[13],** lack of long-term safety assurance and the basic.

1.5 Traditional Chinese Medicine

In addition to conventional and complementary treatments for Insomnia, Acupuncture has also been sought to treat Insomnia such as primary or secondary insomnia and to relieve Insomnia symptoms. Acupuncture is one of the most commonly used therapeutic modalities in

complementary and alternative medicine [14]. In 1980, WHO recommended acupuncture as an effective alternative therapy for 43 different disorders.

In addition, the roots of Chinese Traditional Medicine (also referred to as TCM) date back more than 2000 years. Its rich history tells of the many influences on its development, including the Japanese, Europeans, and the communist revolution. Thus, the communist party of China was formed under the leadership of Chairman Mao in 1928 and took over power in 1949.

The communists realized that there were little or no medical services and actively encouraged the use of traditional Chinese remedies because they were cheap, acceptable to the Chinese, and used the skills already available in the countryside. In 1940, Yang Shao proposed to "scientificize" and «popularize" Traditional Chinese Medicine. In 1980, WHO recommended acupuncture as an effective alternative therapy for 43 different disorders.
Since then, this resurgence has opened facilities in China to provide, teach, and investigate Chinese Traditional Medicine. While both Western and medicine have been practiced in China since the late 1800s.In addition to that, in 1950s, medical staff from the Pre-Soviet Union and Eastern Europe began to learn acupuncture in China. It was also used at the same time as a technique to induce an analgesic effect instead of Anesthetics during surgical procedures [15].

The Traditional Chinese Medicine approach to medicine began to grow in popularity in the West in the 1970s, when ties to china opened. Then in 1972, the United States became interested in acupuncture after an official visit by President Richard Nixon. Since then, the Chinese government has started to invest in research funding to support the studies in the field acupuncture [WHO]. Furthermore, in 1975, entrusted by WHOM, three international training centers of acupuncture and Moxibustion were set up in the cities of Beijing, Shanghai and Nanjing respectively in china, where a great number of acupuncturists from different countries and regions have been trained. However, in 1979, WHO assured that 43 kinds of diseases are suitable indications for acupuncture and Moxibustion therapy. According to available statistics, More than 300 kinds of diseases in the specialty areas of internal medicine, surgery, gynecology, pediatrics, five sense organs and dermatology can be treated by acupuncture and Moxibustion. In addition, in November 1987, the world Federation of acupuncture-Moxibustion Societies was established and the 1st international conference on Acupuncture and Moxibustion was held in Beijing. Since then, six such conferences have been held.

Composed of 55 associations worldwide with its headquarters located in Beijing, world Federation of Acupuncture-Moxibustion Societies is the biggest acupuncture organization in the world. In 1997, it was clearly stated in the specialist's hearing of the national Institute of Health (NIH) of the United States of America that acupuncture can be effectively used for a wide range of diseases because of its significance therapeutic effects and few side effects [16].

Methods

2.1 Literature Search

Five reviews independently screened titles and abstracts followed by potentially relevant full text articles using the predefined inclusion criteria. This five independent five independently computerized literature databases which selected randomized clinical trials from the EBSCO

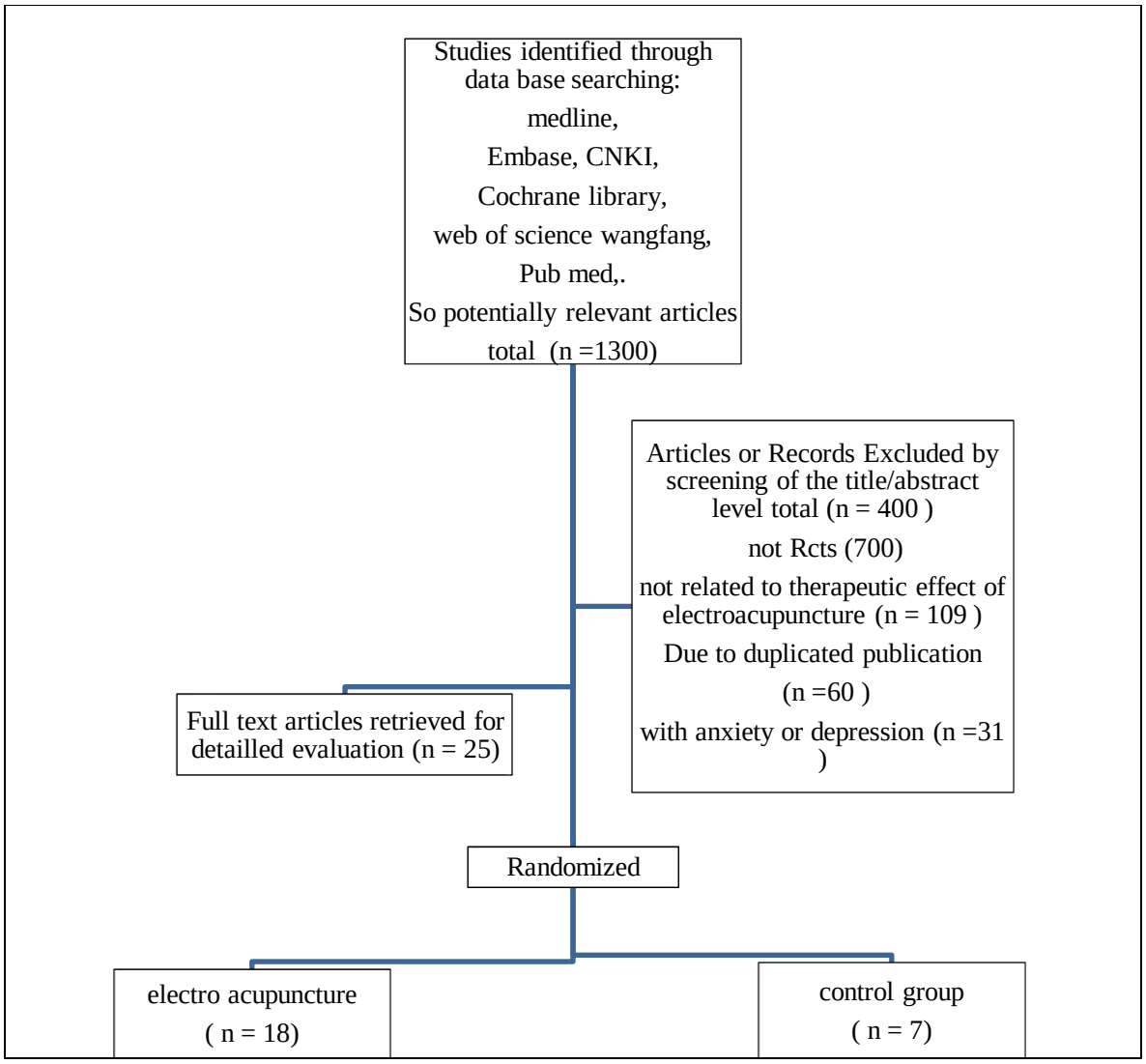
Host electronic database. An electronic database included (**MEDLINE, Pub Med, COCHRANE** Central Register of Controlled Trails from database inception; and **CNKI,** web of science **WANG FANG**) and others. The search began in March 2016 and ended in April 2019 without restriction to the language (English, Chinese, and French). Randomized clinical trials (RCTs) on Electro-Acupuncture treatment for Primary Insomnia women with Perimenopausal were assessed by their methodological quality and relevant data.

Eligible RCTs compared Elector-acupuncture with Drugs treatment, Placebo, or no-acupuncture treatment. Any disagreement regarding the eligibility of a study was resolved by discussion.

RESEARCH DESIGN METHOD

Identification of study**:**

Following the recommendations of the Cochrane protocol for the elaborations of systematic research; it was made a comprehensive search to April 2018 in the register of the Cochrane trials (Clinical Trials; CENTRAL), MEDLINE being used the strategy of Dickersin and Larson for controlled clinical trials and EMBASE, CNKI, Pub med. (Excepta Data base) until April 2018.



Risk of bias was determined by the Cochrane risk of bias assessment tool. Therefore, the methodological quality of the included randomized controlled trials was assessed using de jadad score, and the reporting of the included studies was evaluated by the **Rev.Man 5.3**.

In addition, we **Rev.Man 5.3** the methodology that used to analyze the results comparing the two groups (the electro-acupuncture group compared with control group). Doing that responsibility for assessing outcomes. **Review Manager 5.3 software** was applied to the most relevant studies to evaluate **the quality of clinical trials** of electro acupuncture [24].

2.1.1 Data Collection Method

Cochrane Protocol Version

The author extracted data in the forms suggested by Cochrane protocol version 5.0.1. There was necessary to use the statistical method to assess concordance kappa and analyzed the data.

Cochrane collaboration

- ✧ Cochrane Reviews(>4,000) registered
- ✧ Identify, appraise and synthesize research-based evidence and present it in accessible
- ✧ Format; regularly updated
- ✧ Focus on interventions
- ✧ Outstanding general resource [25].

2.1.2 Ethical Aspects

This systematic review of meta-analysis is an INVESTIGATION WITHOUT RISK, Data for this study was acquired through previously published work, no patient or hospital data was accessed, for that reason the researchers does not interferes on biological, physiological, psychological and social on any study subjects. The research was more focused on collecting more articles, selecting articles and then inclusion and exclusion were more important and useful, and again the identified outcome data were analyzed by **software Rev Man 5.3**. Significant level was set at $p<0.05$ in the following address **"Zhejiang Chinese medical university (ZCMU), International Education College (IEC), Bin wen Road 548, Binjiang District, Hangzhou, Zhejiang 310053 in China.**

2.2 TYPES OF INTERVENTIONS

2.2.1 Inclusion Criteria

After the specified assessor's evaluation, subjects who met the inclusion criteria were instructed that they would be (1) randomly assigned to electro-acupuncture group that were published from February 2011 to April 2019, with a defined period of post intervention follow up. In addition, Participants had to be diagnosed with (2) the therapeutic effect of electro-acupuncture on Primary Insomnia women with Perimenopause, over 38 and under 65 years old, and they were must be (3) randomized controlled trials (RCTs)…

2.2.2 Exclusion Criteria

The relevant clinical trials are going to be excluded if the following criteria are met (1) Study design did not allow the evaluation of therapeutic effect of electro-acupuncture on primary insomnia women with Perimenopause; (2) Not clinic trials and trials using animals were also excluded, (3) Due to duplicated publication, Herb medicine as a control, with anxiety or depression, having depression, anxiety or schizophrenia; (4) Pregnancy, breast-feeding were excluded.

2.2.3 Statistics Analysis

This study is a two-arm parallel, patient-assessor blinded, non-penetrating sham-controlled randomized clinical trial. The trial will be performed in the Zhejiang zhong Shan hospital of Zhejiang Chinese Medical University in Zhejiang province. Therefore, eligible participants were randomly allocated into two groups (the real Electro acupuncture group and Drugs treatments as control group). The outcome assessment and the statistical analysis are performed by **Rev.Man 5.3** using also Microsoft Excel (Redmond, Washington, USA and data collection forms suggested by Cochrane protocol) which entered the selected study. Anthropometric assessments were performed pre- and post-intervention. **Based on random number tables** generated in the same software, the participants were enrolled in the study after checking for the inclusion/exclusion criteria, and were arranged into pairs matched by age [25].

Random assignment or random placement is an experimental technique for assigning human participants or animal subjects to different groups in an experiment (e.g. a treatment group versus a control group) using randomization, such as by a chance procedure…Random assignment of participants helps to ensure that any differences between and within the groups are not systematical the outset of the experiment. Thus, any differences between groups recorded at end of the experimental procedures or treatment [25].

Random assignment blinding and controlling are key aspects of the design of experiments, because they help ensure that the results are not spurious or deceptive via confounding. This is why randomized controlled trials are vital in clinical research, especially ones that can be double-blinded and placebo-controlled [26].

2.3 Type of Outcomes

The Primary Outcome of this Meta-analysis was responder rate reported by researchers in RCTs [26].

Primary and Secondary Outcomes [26].

Sleep measure:

- ISI (Table 1).
- Pittsburgh Sleep Quality Index Table 2 and Figure 2, presents changes of PSQI and subscales among the two groups. Comparing with baseline, the experimental group as electro-acupuncture had better global score of PSQI and sleep quality decreased sleep-onset latency and dysomnia, longer sleep duration.

2.3.1 Randomization and allocation concealment

The central randomization was performed by the research in Zhejiang Chinese medical university. The random allocation sequence was generated with computer number. Randomization numbers were sealed in a predetermined computer-made randomization opaque envelope.

2.3.2 Blinding

This is a patient-assessor-blinded trial, which patients are not aware of their group assignments. The follow-up assessors were blinded to the patients 'group assignments as well. Although acupuncturist was not be blinded to the group assignments, they will not be involved in the outcome assessments or data analyses.

To achieve blinding, both experimental groups will use the same kind of disposable, sterile steel needles (1.5-infiliform needle, 0.32mmX40 mm); same number of needles per session (10-12 needles); same skin disinfection process with 75% alcohol; and retention for 30 min. While the control group use drugs.

2.4 Intervention Groups

The Treatment group must receive real, true, active acupuncture at least 100% which are all defined as needle insertion at an acupuncture point, according to TCM theory pertaining to Primary Insomnia.

5. Electro-Acupuncture treatment

Electro-Acupuncture was performed 3 times a week for a menstrual cycle or a month as a course of treatment. The Acupoints selection was based on our previous study on primary insomnia, literature review, and the experts' experience in treating insomnia [27].

Baihui (Du-20), Shenting (Du-24), and Sishengcong (EX-HN1), are punctured at a depth of 10 mm straightly and Shenmen (HT-7), is inserted 5mm perpendicularly. Needle manipulation, that is, lifting and thrusting, rotating or twirling, is applied to achieve "The Qi," a needle sensation of feelings of soreness, numbness, fullness, burning, heaviness, aching, and so forth, based on subjective reporting of the patients. Needles retention is 30 minutes. The acupuncture is performed every other day for six weeks [26]. In addition, with electro acupuncture, needles, 0.28-0.32 mm in diameter and 40-75 mm in length, were inserted into Acupoints with the uniform

reinforcing-reducing method. After needling sensation, needles at the bilateral Acupoints Tianshu (ST 25), Sanyinjiao (SP 6), Zhongwan (CV 12), and Qihai (CV 6). So bilateral Acupoints Pishu (BL 20), Shenshu (BL 23), Ciliao (BL 32), and Sanyinjiao (SP 6) were connected to a G6805II electric stimulator with continuous wave, 2 HZ frequency and an electrical current tolerable to patients. The needle was retained for 30 min. The rest of the Acupoints were manipulated once every 10 min [28].

Life style recommendation

- Keep mental fitness and well-controlled emotions;
- Have good sleep habits and create a peaceful and comfortable sleep environment,
- Keep away from cigarettes, alcohol, strong tea and coffee and avoid over-excitement;
- Do appropriate physical labor or exercise to strengthen the body constitution [27].

2.5 Risk of Bias Assessment

Two reviewers evaluated any risk of bias according to the Cochrane Collaboration's risk of bias assessment tool [28], and the Jadad Scale. Each study was assessed individually by the following criteria:

Cochrane Risk of Bias Tool

Selection Bias-Was the method of randomization sequence generation adequate?
Selection Bias-Was the treatment allocation adequately concealed?
Performance Bias-Was there adequate blinding during the intervention?
Detection Bias-Was the researcher blinded to the intervention?
Attrition Bias-Was the incomplete outcome data adequately addressed?
Reporting Bias-Are the reports free "yes, unclear, or no."
Yes-should be interpreted as a low of bias
Unclear-could also mean uncertain or unknown
No-should be interpreted as a high risk of bias.

2.7 Data Analysis

Rev.Man version 5.3 software was used for the statistical analysis. For Continuous and dichotomous data, risk ratios (RR) with 95% confidence intervals (CI) were calculates; for continuous data, standard mean differences (MD) with 95% CI were calculated. P-values less than 0.05 were considered statistically significant. Fixed effects or random effects were used depending on the existence of heterogeneity.

If heterogeneity was less than 50% fixed effects were used; if greater than 50% random effects were used. If substantial heterogeneity existed (>50%), then a sensitivity analysis was conducted by excluding one article each time. Funnel plots were employed to detect any publication bias.

Results

3.1 Study Selection

The search identified the Therapeutic effect of electro-acupuncture on Primary Insomnia is consistently emerging as an alternative treatment for Insomnia. So potentially relevant articles total (n =1300 participants); Records Excluded by screening of the title/abstract level total (n = 400), not RCTs= (700), due to duplicated = (60), not related to therapeutic effect of electro acupuncture (n = 109), full text articles retrieved for detailed evaluation (n = 25). In comparison, electro-acupuncture group had significantly more responders than the drug group (P<0.00001), and also proved to be superior in increases sleep duration without side effect than the drug group. Patients above 38 under 60 years of age were randomly divided into two groups: 18 patients as experimental group and 7 patients as control group.

In a systematic review, the randomized control trials were analyzed to assess the effect of electro-acupuncture on primary insomnia women with Perimenopause by comparing them with patients given a Benzodiazepine, but the results indicating that electro-acupuncture as intervention group was more effective than benzodiazepine.

Table I. Characteristics of points selected for treating Primary Insomnia

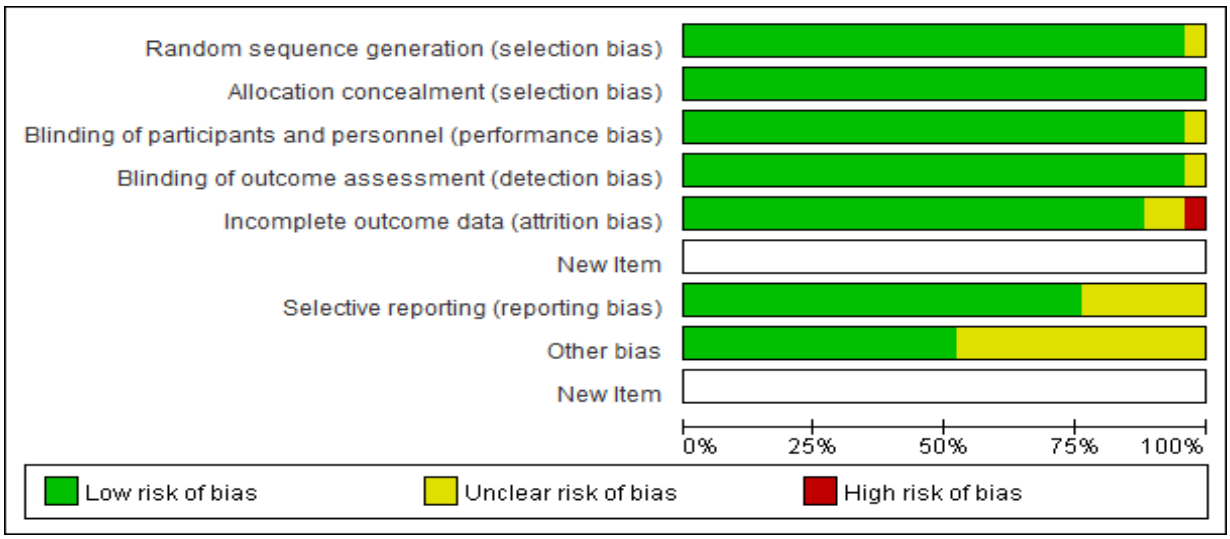
MERIDIAN	POINTS	EFFICACY
Governor meridian	**百会 Baihui (GV20), 神庭 Shenting (Du24)**	**Goes upward along the midline of the Lumbar, back, head and face, and ends at point Yinjiao (Du28). Tranquilizing mind or shen dispels interior wind.**
Extraordinary meridian	**Sishengcong 四神聪 (EX-HN1)**	**A group of 4 points, at the vertex, 1 cun posterior, anterior and lateral to cun posterior, anterior and lateral to GV20.dispels interior wind stroke, calms the Shen.**
Heart meridian	**Shenmen 神门(HT-7)**	**On the wrist, at the ulnar end of the transverse crease of the wrists in the depression on the radial side of tendon. Calms shen, tonifies and regulates the Heart Blood and Qi.**
Stomach meridian	**Tianshu 天枢(ST25)**	**On the middle of the abdomen, 2 cun lateral to the umbilicus. Regulates the spleen, the stomach, and Intestines, dispels Dampness and Damp-Heat-Heat, Regulates Qi and Blood.**
Spleen meridian	**Sanyinjiao 三阴交 (SP6)**	**On the medial aspect of the lower leg, 3 cun above the medial malleolus. Regulates menstruation, strengthens the spleen and stomach, resolves Dampness, cools and invigorates the blood.**
Urinary bladder meridian	**Pishu 脾俞(BL20), Shenshu 肾俞(BL23), Ciliao 次髎 (BL32)**	**On the back, 1.5 cun lateral to the lower border of the spinous process of the 11th thoracic vertebra. Regulates SP/ST qi as viscera function, nourishes yin blood, resolves Dampness**
Conception meridian	**Zhongwan 中腕 (CV12), Qihai (CV6)**	**On the anterior median line of the upper abdomen, 4.0 cun above the umbilicus. Strengthens and harmonizes the spleen and stomach, resolves dampness, relieves pain.**

Table .I. Shows the method of locating points including meridians. Insomnia is a potential risk factor in many diseases. Reason why proper therapeutic treatment of electro acupuncture for primary insomnia would largely reduce the occurrence or severity of other diseases at 90% and increase sleep quality [28].

3.2 Risk of bias in Studies Selected

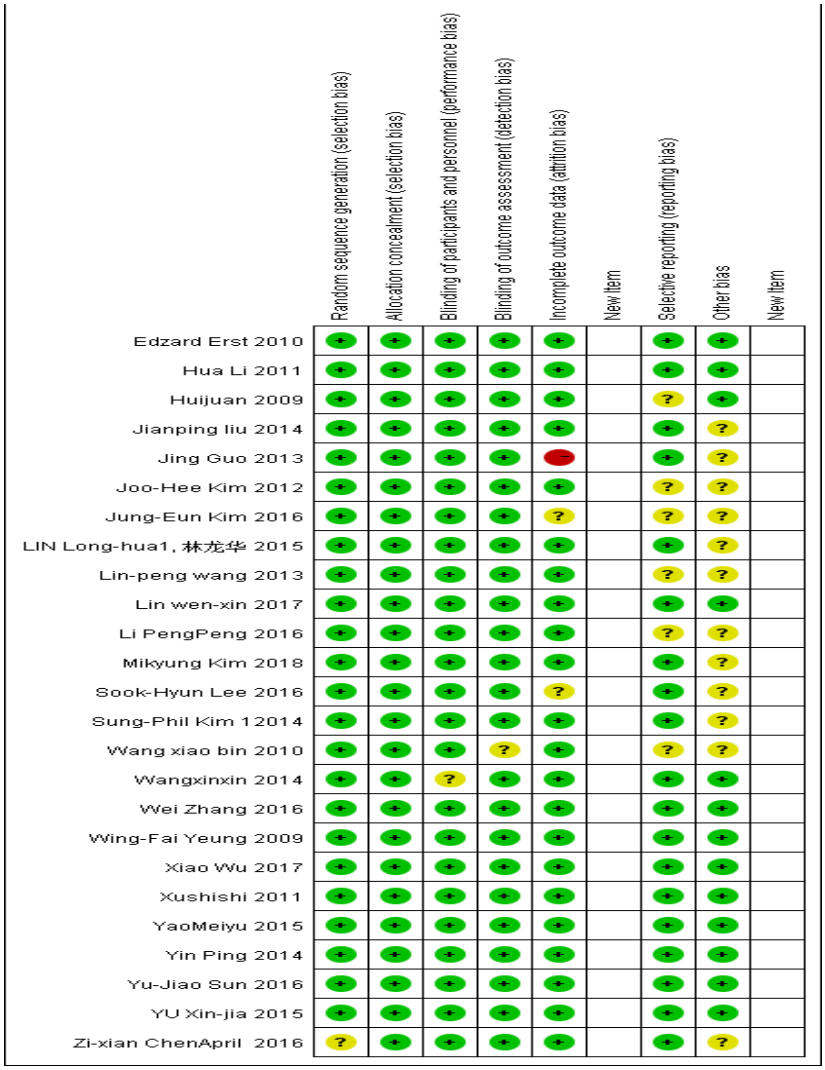
The reviewers independently assessed the methodological quality and the risk of bias of the included studies by means of **the risk of bias (ROB) tool** in the Cochrane Handbook for systematic Reviews of Interventions (Version 5.0.2). The instrument consists of **8domains**: random sequence generation; allocation concealment; blinding of patients, personnel, and outcome reporting; and other sources of bias. The tool ranks evidence from research studies as having **"high," "low," or "unclear" levels of bias**; it is also appropriate for evaluating the methodological quality of RCTs. A majority of studies used adequate sequence generation except some studies. Similarly, allocation concealment was unclear in two Studies **[31].** A low risk of bias for patient blinding was assessed in 18 studies; a high risk of bias was assessed for three studies because blinding of participants is not possible when comparing Acupuncture to Drugs**.**

Figure I. Risk of Bias graph of 25 full articles retrieved



Risk of Bias graph: review author's judgments about each risk of bias item presented as percentages across all included studies [35] [36],

Figure I. Risk of bias summary of 25 full articles retrieved [34],



Risk of bias summary: review authors' judgments about each risk of bias item for each included study.

3.3 Outcome Results

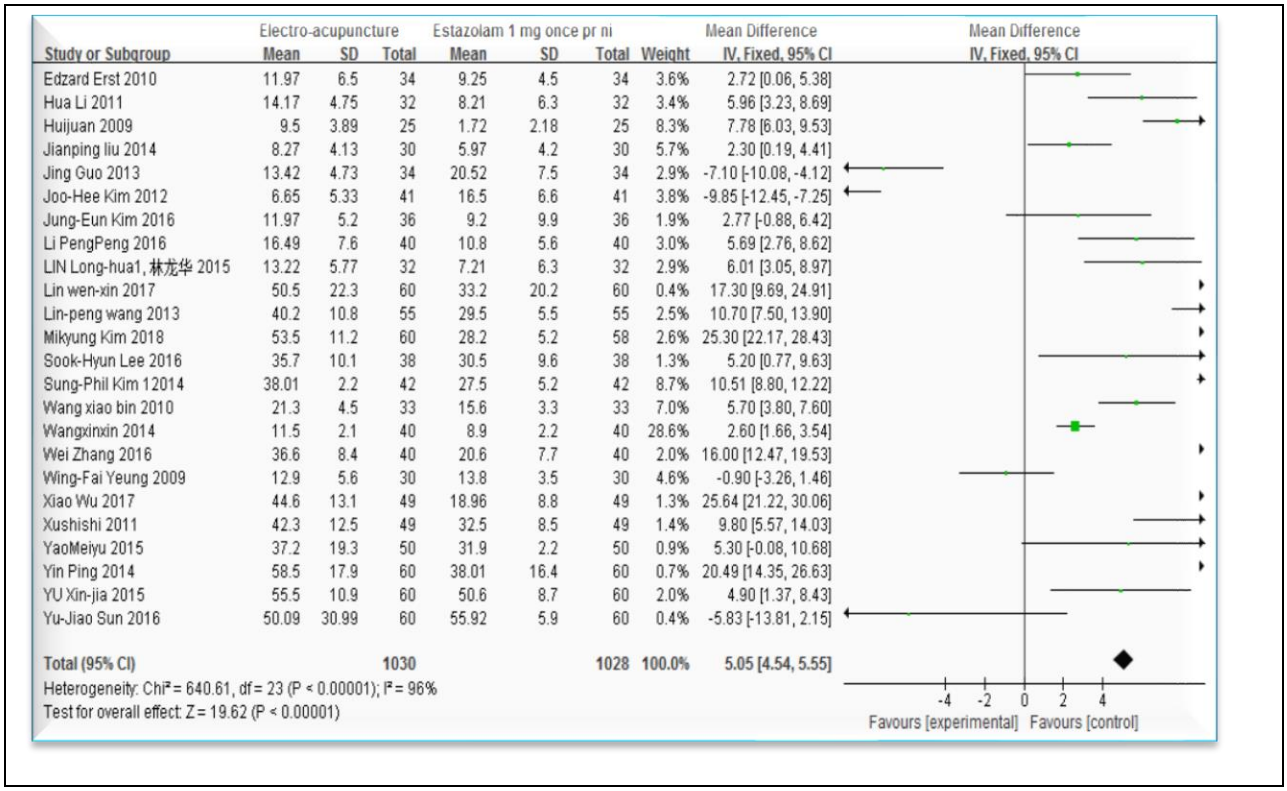
3.3.1 Comparison: Acupuncture Vs Drug treatment

1) Response Rate

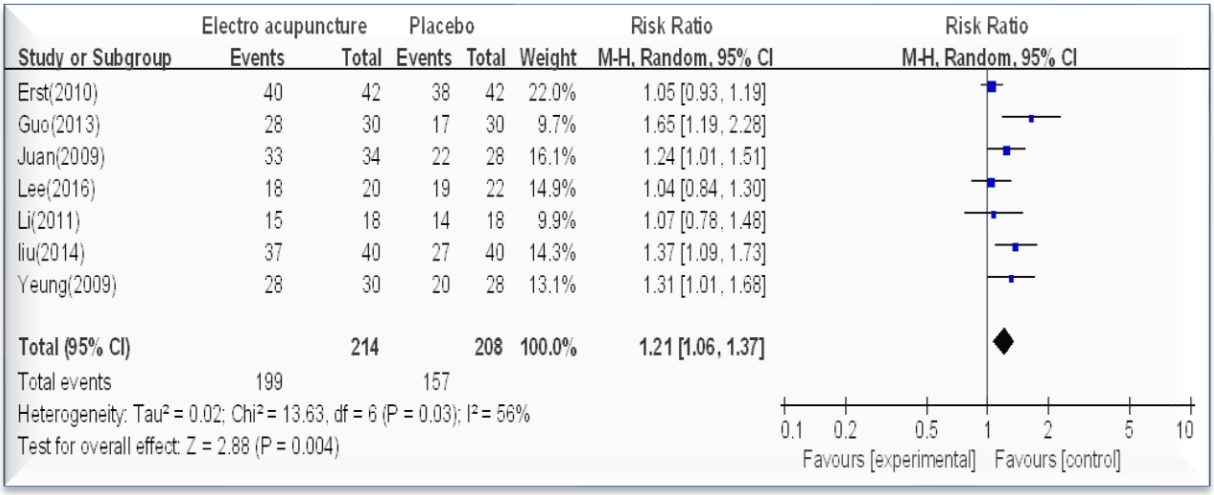
Figure I. Electro acupuncture Vs Estazolam Outcome: Response Rate.

The impact acupuncture on continuous outcomes, the mean difference was calculated with a 95% confidence Interval (CI). Therefore, twenty five [33][34]. With a total of 1300 participants tested the effect therapeutic of Electro acupuncture on response rate against Drug treatment

(Estazolam). Mean difference showed statistically significant differences between the number of responders between group [P<0.00001; I^2=96%]. The analysis revealed heterogeneity and the test for overall effect Z=1.91. (Fig I.)



Forest plot of comparison: 1 Electro-acupuncture Vs Estazolam 1 mg once per night, outcome: 1.1 PSQI total score.



Compared with noninvasive placebo acupuncture, electro acupuncture showed statistically significant improvements in subjective and objective measures of SE. The proportions of subjects achieving sleep-diary–derived WASO of 30 minutes or less and a SE of at least 85% after treatment were significantly higher in the electro acupuncture group. However, there were no between-group differences in PSQI total score, the primary outcome measure, and other secondary measures at the posttreatment visit. Therefore, Summary estimates of treatment effects were calculated using a random-effects model. The impact of electro acupuncture on dichotomous data was expressed as the risk ratio (RR)

3.4 Sensitivity Analysis

We performed sensitivity analyses in each comparison with substantial heterogeneity by excluding studies one by one after inclusion of some RCTs to determine any variability, if any, in the pooled effects. In the comparison of Electro acupuncture Vs Drugs treatments: Response Rate; the I^2 value at the value at the 24 week subgroup was 72 % and remained high despite removing studies one at a time (Fig 3). Therefore, Outcome of adverse effect with to Acupuncture was described in 10 trials; only 3 of them reported minor adverse effect in the Acupuncture group. Two trials Li (2011) [33] Yeung (2009) reported no adverse effect observed in the Acupuncture group. Another trial reported mild headache (1 case), and lassitude (1 case) in the acupuncture group compare to Placebo (n=9), whereas there was dizziness (3 cases), constipation (2 cases), dry mouth (1 case), palpitation (2 cases), and oscitation (1 case) in the Drugs group. Different Trials evaluated the scores of the adverse effect rating scale. The result showed that acupuncture was safer than Drug, placebo and Sham groups (***CI= 95%, P=0.0004, z=2.05, I^2=26%***)…

The Qi Ratio means the Ratio of ***De Qi*** points to total points in three groups. According to Sensation, In the Placebo group, ***De Qi*** sensation was obvious in 80% acupoints, while in the Sham and Estazolam groups ***De Qi*** sensation was reported in the 28% and 24% acupoints.

1. **Funnel Plot of Comparisons**

*A **Figure .I. Funnel plot of comparison: 1 Electro-acupuncture Vs Estazolam 1 mg once per night***

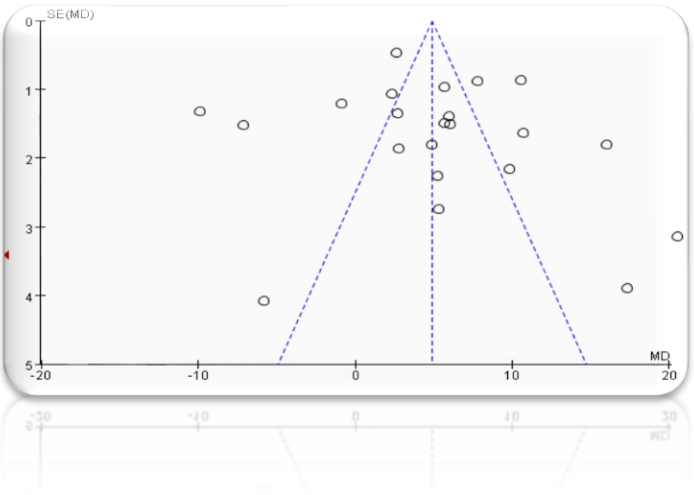
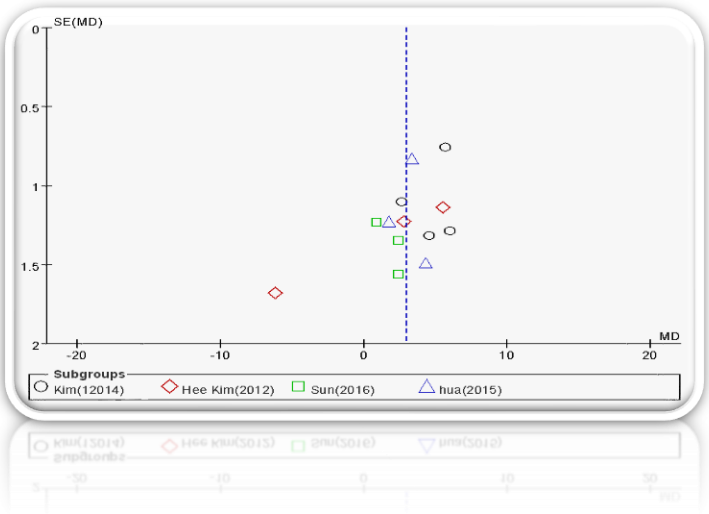


Figure .I. Funnel plot of comparison: 1 Electro-acupuncture Vs Estazolam 1 mg once per night, outcome: 1.1 PSQI total score. Funnel plot of 25 randomized controlled trials for the outcome (PSQI) of patients received electro-acupuncture which improves sleep quality and increase sleep duration

1. Funnel Plot of Comparisons

*A **Figure .II.*** **Acupuncture (type of Acupuncture) Vs Drugs**



Captions: Figure II. (Analysis 2.1)

Funnel plot of comparison: 2 Acupuncture (type of Acupuncture) Vs Drugs, outcome: 2.1 The Insomnia Severity index Vs the Anthens Insomnia Scale.

Discussion

Based on the results of Meta-Analyses, we assessed the therapeutic effect of Electro-acupuncture for Primary Insomnia women with perimenopausal. In the majority, our analysis revealed that compared to Drug treatment, Electro acupuncture might be an effective treatment for primary Insomnia women with perimenopausal, and that compared to Placebo treatment Acupuncture was superior and might have significant effects on Primary Insomnia. In addition, Compared with noninvasive placebo acupuncture, electro acupuncture showed statistically significant improvements in subjective and objective measures of SE. The proportions of subjects achieving sleep-diary–derived WASO of 30 minutes or less and a SE of at least 85% after treatment were significantly higher in the electro acupuncture group. However, there were no between-group differences in ISI total score, the primary outcome measure, and other secondary measures at the posttreatment visit.

The current review offered significant perspectives. First, we aimed to identify all studies on this topic. There were no restrictions on the review publication language, and a large number of databases were searched. We are therefore confident that our search strategy located all relevant data on the subject. Second, the outcome measures including the ISI, PSQI, the efficacy standards of Chinese medicine, the AIS and so on, were widely used in practice for the measurements of sleep quality [34]. Significant differences were found between acupuncture treatment and drugs or sham treatment in all of the included assessment tools.

4.1 Heterogeneity

Furthermore, one of the most noticeable characteristic of this meta-analysis is the high level of individual study clinical heterogeneity leading to overall statistical heterogeneity. Clinical heterogeneity existed because trials varied in their methodology, for example treatment schedule (for example number of acupuncture points treated, frequency of sessions, length of treatment period), drug control groups (**Alprazolam, Lorazepam, and Clonazepam**) or the type of Sham control used (for example superficial needling, inadequate points, non-invasive needling). Indeed, we realized that the clinical heterogeneity would be very significant due to the variations in study quality, participants, and intervention, control and outcome measures. Therefore, this analysis while informative does have significant heterogeneity at times and should be interpreted with caution.

Thus, after analysis of several researches done, we conclude that Electro-acupuncture is more effective which improves sleep quality with 25 or 99%, increases sleep duration without side effect than Estazolam, Lorazepam in treating patients with Primary insomnia women with perimenopausal.

Abbreviations

Cognitive behavioral therapy for insomnia (CBT-i)
Cohen's delta (Cohen's d)
Diagnostic and statistical manual of mental disorders, fifth edition (DSM-5)
Dysfunctional Beliefs and Attitudes about Sleep scale (DBAS-16)
Electro- acupuncture (EA)
Epworth Sleepiness scale (ESS)
Health-related quality of life (HRQoL)
Hospital Anxiety Depression scale (HAD)
Insomnia Severity Index (ISI)
Insomnia Severity Index and the Athens Insomnia Scale (ISI and AIS)

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Dedication

Not mentioned.

Conflicts of Interest

There are no conflicts to declare.