

## Original Article

# Combination of acupuncture improves the effect of estazolam on senile insomnia

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**Abstract:** Objective: The current study was designed to compare the effects of acupuncture, estazolam and a combination of the two on the treatment of senile insomnia. Methods: From January 2015 to December 2019, a total of 270 elderly outpatients with insomnia were recruited from the Department of Encephalopathy of Shaanxi Province Hospital of Traditional Chinese Medicine and randomly grouped into three groups (Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group, n=90). The Pittsburgh Sleep Quality Index (PSQI) and polysomnography indexes (PSG) were used to evaluate the treatment efficacy of these three methods. Results: The effective rates in Group A, Group B and Group C were 72.2%, 71.3% and 89.2%, respectively. The PSQI scores after treatment were statistically lower than those before treatment in all three groups. No significant difference existed between Group A and Group B in the total PSQI score before and after treatment. The difference in score after treatment in Group C was more significant than that in the other two groups. The sub-score analysis of the PSQI showed that a combination of acupuncture and estazolam was more effective in improving subjective sleep quality, sleep duration, habitual sleep efficiency and daytime function than acupuncture or estazolam alone. The PSG results showed that the combination group had better outcomes in terms of increasing the total sleep time and sleep efficiency, prolonging NREM sleep, decreasing the frequency of awakening, reducing the light sleep time of the S1 phase and increasing the deep sleep time of the S3 phase over Group A and Group B. Conclusion: Acupuncture has a similar effect to estazolam on senile insomnia. The combination of acupuncture and estazolam has a greater effect in improving both the quality and quantity of sleep in elderly patients suffering from insomnia over acupuncture or estazolam alone.

**Keywords:** Acupuncture, senile, estazolam, randomized controlled trial

## Introduction

China is the most populous country in the world in terms of elderly individuals. With the ageing of society, the health problems of older individuals have aroused great concern. Insomnia is one of the most common complaints among older adults, and its prevalence increases with age. It was reported that insomnia decreases the immunity of older adults and causes various kinds of diseases, including neurasthenia, cold, gastrointestinal disease and, especially, mental disease and cardiovascular disease [1, 2]. Long-term insomnia also increases the mortality of many diseases such as heart disease,

hypertension, hyperlipidaemia, depression and Alzheimer's disease [3].

Currently, benzodiazepine receptor antagonists, especially estazolam, are the first-line Western medications for insomnia. Although the short-term effect of estazolam is confirmed, there are many problems with its long-term use, such as drug tolerance and dependence. In addition, some side effects have recently been reported, including residual daytime sedation and cognitive impairment [4]. Therefore, it is urgent to find safe, alternative and effective methods for the management of senile insomnia.

Acupuncture is an important part of traditional Chinese medicine and has been used in treating many health-related problems. Studies have shown that acupuncture can relieve anxiety and depression [5, 6]. Wang XY et al developed a randomized single-blinded trial to evaluate the efficacy of short-term abdominal acupuncture for insomnia compared with estazolam. Their results showed that short-term abdominal acupuncture was more effective than medication treatment in relieving insomnia [7]. Yueng BF et al grouped insomnia patients into electroacupuncture and sham acupuncture groups, and the results showed significant improvements in sleep efficiency and sleep latency [8]. Ruan JW et al evaluated the safety and efficacy of electroacupuncture for the treatment of insomnia and found that electroacupuncture could repair sleep architecture, reconstruct sleep continuity and prolong slow wave sleep time and rapid eye movement sleep time [9]. The results from other studies were also in agreement with the above conclusions [10-14].

This research evaluated the efficacy of acupuncture in the treatment of senile insomnia and elucidated whether acupuncture could be recognized as an alternative method for the management of senile insomnia.

### Materials and methods

#### *General data*

A total of 270 outpatients recruited from the Department of Acupuncture of our hospital from January 2015 to December 2019 were randomly divided into two groups: Group A: acupuncture group; and Group B: estazolam group. Among the 90 patients in Group A, there were 48 females and 42 males, aged (72±9) years, with PSQI scores of 16.3±3.2. Among the 90 patients in Group B, there were 47 females and 43 males, aged (72±10) years, with PSQI scores of 18.2±3.5. No significant differences were detected in sex, age or PSQI score among these three groups.

#### *Randomization and masking*

This study was a single-blinded randomized controlled clinical trial. The registrar and patients had no knowledge of the group allocation. All recruited participants were allocated

according to the computer-generated random numbers. All patients signed an informed written consent form. The research was approved by the medical ethics committee of Shaanxi Province Hospital of Traditional Chinese Medicine.

#### *Diagnostic criteria*

All patients were diagnosed according to the International Classification of Sleep Disorders (ICSD-2) by the Sleep Research Society [15].

#### *Inclusion criteria*

Patients were included if they (a) were ≥60 years old, (b) conformed to the diagnostic criteria, (c) did not have substantive damages to their internal organs, (d) had not taken Western medicines or any traditional Chinese medicines or other treatments for insomnia in the past 6 months, and (e) signed an informed consent form.

#### *Exclusion criteria*

Patients were excluded if they (a) were diagnosed with serious diseases or terminal stage of diseases, (b) were diagnosed with depressive disorders, (c) did not conform to the diagnostic standards, (d) did not sign the informed consent form, or (e) had accepted other treatments in the past 6 months.

#### *Dropout or rejection criteria*

Patients who had severe side effects or used other treatments during our therapeutic period were not included. If patients failed to visit or were unwilling to continue the treatment, they were considered to have dropped out.

#### *Intervention methods*

The acupuncture points were identified with the point location method issued by the World Health Organization [16]. The needles were bought from Tianjin Huahong Medical Material Limited Company; they were 0.25 mm in diameter and 40 mm in length. For Group A and Group C, the primary acupuncture points were Baihui (GV 20), Sishencong (EX-HN-1), Anmian (EX-HN-54), Neiguan (PC 6), Shenmen (HT 7), Zusanli (ST 36), and Sanyinjiao (SP 6). The added acupuncture points were Xingjian (LR 2) and Taichong (LR 3). All acupuncture points

# Effects of acupuncture and estazolam on senile insomnia

**Table 1.** Comparison of curative effects on insomnia in patients among three groups (n)

Group	total patients	dropped-out	recovery	significant efficacy	efficacy	non-efficacy	Effective rate (%)
Group A	90	11	18	29	10	22	72.2
Group B	90	10	12	20	25	23	71.3
Group C	90	7	24	32	18	9	89.2**

\*\*means  $P < 0.01$  vs Group A and Group B.

**Table 2.** Comparison of total Pittsburgh sleep quality index score before and after treatment in three groups ( $\bar{x} \pm s$ )

Group	Total score before treatment	Total score after treatment	P value
Group A	16.3 $\pm$ 3.2	6.5 $\pm$ 1.1	<0.001
Group B	18.2 $\pm$ 3.5	7.9 $\pm$ 2.1	<0.001
Group C	16.4 $\pm$ 4.8	4.2 $\pm$ 0.9	<0.001

were punctured with sterile needles and achieved the De Qi sensation. The needles were maintained in the acupoints for 30 minutes each time. Acupuncture was performed once a day for 21 consecutive days. In the estazolam group, patients took 1 mg estazolam orally 30 minutes before sleep every day for 21 days.

## Observation index

We used the PSQI and PSG scores to evaluate the sleep quality of the patients in the three groups. The maximum score on the PSQI is 21 points. To evaluate the treatment efficacy of acupuncture and/or estazolam, the ratio of the difference in the PSQI scores before and after treatment to the scores before treatment  $\times 100\%$  was calculated. A ratio  $< 30\%$  was considered non-effective. A ratio between 30% and 70% indicated that there was efficacy, and  $\geq 70\%$  indicated significant efficacy. A ratio  $\geq 90\%$  indicated recovery [17]. Sleep structure was detected with an Embletta 13 ( $\times 100$ ) lead portable polysomnography system (Medcare, USA). PSG could record and analyse the total sleep time, waking time, and non-rapid eye movement and rapid eye movement sleep time. The PSQI and PSG were evaluated before and 7 days after treatment.

The side effects (including lethargy, dry mouth, dizziness, and headache) were observed before treatment and on the 4th, 8th and 15th days of the treatment course. The laboratory tests (including routine blood, urine and stool exami-

nations, liver and renal function examinations, blood biochemical examinations, and electrocardiogram) were given before and at the end of treatment.

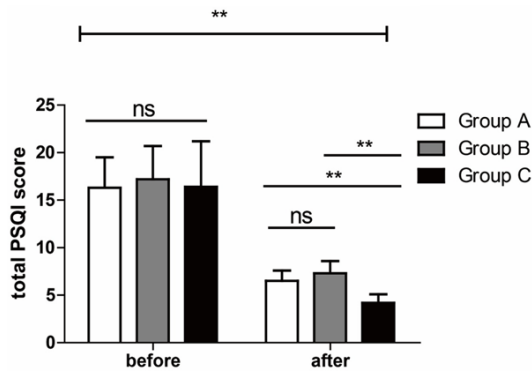
## Statistics

SPSS 16.0 software was used to analyse the data. A paired t-test was used to analyse the data before and after treatment. One-way ANOVA was used to analyse the data among the three groups. The measurement data were expressed as the mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ).  $P < 0.05$  indicated significant differences.

## Results

### Clinical efficacy in the two groups

The PSQI scores in each group were statistically comparable before treatment ( $P = 0.12$ ). There were 11, 10, and 7 patients who dropped out in Groups A, B, and C, respectively. In Group A, 18 patients recovered, 29 patients were significantly efficacious, 10 were efficacious and 22 were non-efficacious. In Group B, 12 patients recovered, 20 exhibited significant efficacy, 25 exhibited efficacy and 23 exhibited non-efficacy. In Group C, 24 patients recovered and 32 had significant efficacy, 18 had efficacy and 9 non-efficacy. According to the PSQI scores before and after treatment, we calculated the efficacy rates of different interventions (**Table 1**). The effective rates in Group A, Group B and Group C were 72.2%, 71.3% and 89.2%, respectively. The paired t-test showed that the PSQI scores after treatment were statistically lower than those before treatment in all three groups (**Table 2**). We did not detect any significant difference between Group A and Group B on the total PSQI score before and after treatment. The difference in score after treatment in Group C was more significant than that in the other two groups (**Figure 1**). This result indicates that the combination of acu-



**Figure 1.** The PSQI scores before and after treatment in each group. Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group. \*\*,  $P < 0.01$ .

puncture and estazolam is more effective in treating senile insomnia than acupuncture or estazolam alone.

#### PSQI score analysis

To further evaluate the effects of acupuncture, estazolam and combination therapy on senile insomnia, we then analysed every subscore of the PSQI score, including the scores for subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbance and daytime function (**Figure 2**). The results showed that no difference existed in any of the sub-scores among the three groups before treatment. All the sub-scores decreased significantly among the three groups after treatment. After treatment, in terms of the score for subjective sleep quality (**Figure 2A**), sleep duration (**Figure 2C**), habitual sleep efficiency (**Figure 2D**) and daytime function (**Figure 2F**), there were no differences between Group A and Group B, while Group C showed a significantly decreased score than the other two groups. Moreover, for the score of sleep latency (**Figure 2B**) and sleep disturbance (**Figure 2E**), no differences existed among the three groups after treatment. The above data demonstrate that the combination of acupuncture and estazolam is more effective in improving subjective sleep quality, sleep duration, habitual sleep efficiency and daytime function than acupuncture or estazolam alone.

#### Evaluation of PSG indexes

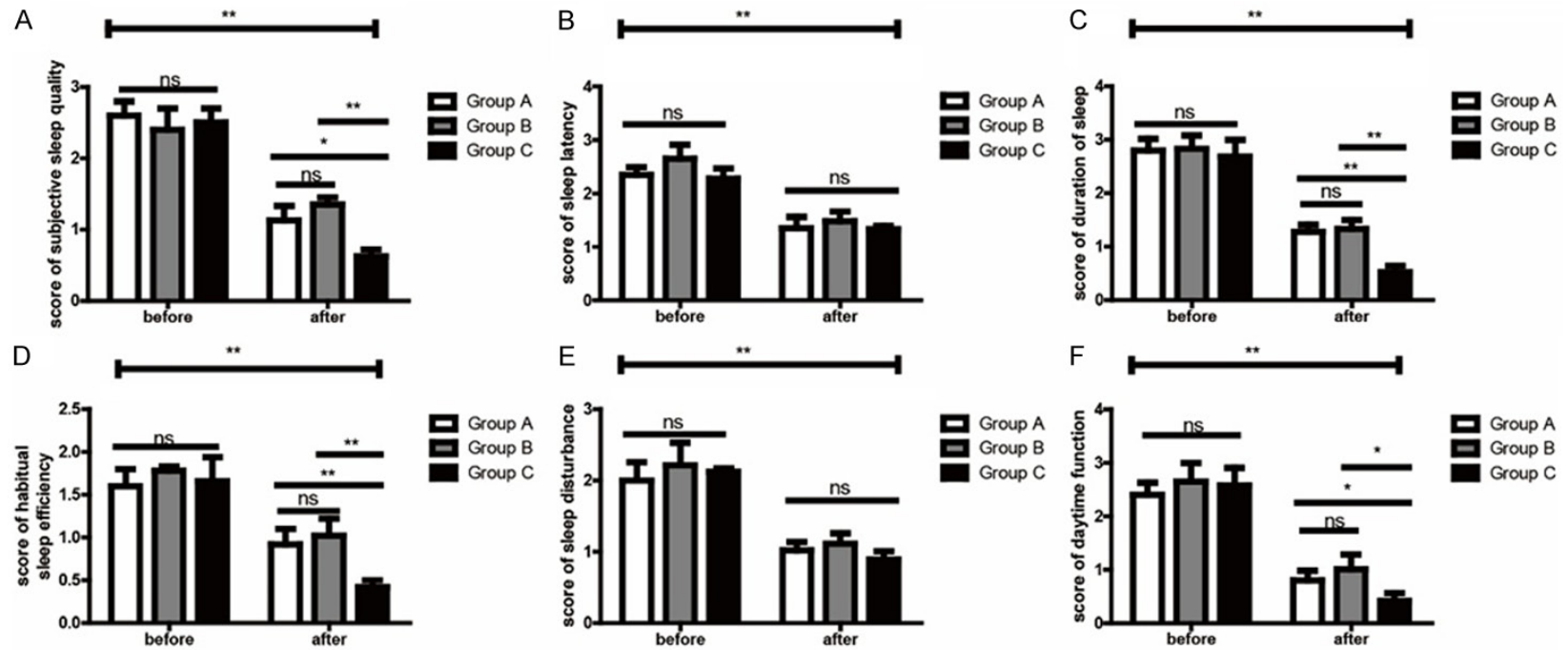
**Analysis of the sleep process:** There were significant differences in total sleep time, sleep

latency and sleep efficiency after treatment compared to before treatment in all three groups ( $P < 0.01$ ), suggesting that acupuncture, estazolam and combination therapy could all increase the total sleep time, shorten sleep latency and improve sleep efficiency. There was no significant difference among the three groups in total sleep time, sleep latency and sleep efficiency before treatment ( $P > 0.05$ ). After treatment, Group C had a greater increase in total sleep time and greater improvement in sleep efficiency than Groups A and B, while Group A and Group B had no significant difference (**Figure 3A** and **3C**). For sleep latency, the three groups had no significant differences after treatment (**Figure 3B**).

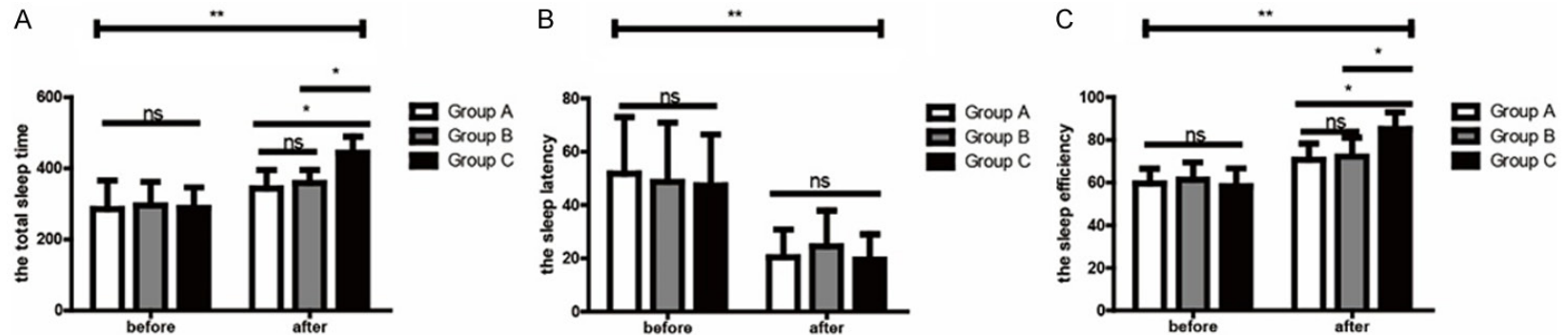
**Comparison of sleep structure:** According to the intra-group comparison of the three groups, the NREM sleep time and REM sleep time of the insomnia patients were significantly increased after treatment ( $P < 0.05$ ). There was no significant difference in the distribution of NREM time and REM sleep time among the three groups before treatment ( $P > 0.05$ ). After treatment, Group C had a greater increase in the NREM time than Groups A and B, while Group A and Group B had no significant difference (**Figure 4A**). For REM sleep time, the three groups had no significant differences after treatment (**Figure 4B**). There was no significant difference in the number of WASO (wake after sleep onset) or sleep cycles among the three groups before treatment ( $P > 0.05$ ). After treatment, Group C had a greater decrease in the numbers of WASO than Groups A and B, while Group A and Group B had no significant difference (**Figure 4C**). For the sleep cycle, the three groups had no significant differences after treatment (**Figure 4D**).

**Analysis of the percentages of NREM sleep stages:** According to the intra-group comparison of the three groups, the percentage of S1 phases significantly decreased, the percentage of S3 phases significantly increased, while the percentage of S3 phases did not change after treatment. After treatment, Group C had a greater decrease in the percentage of S1 phases and a greater increase in the percentage of S3 phases than Groups A and B, while Group A and Group B had no significant difference (**Figure 5A** and **5C**). For the percentage of S2 phases, the three groups showed no significant differences after treatment (**Figure 5B**).

## Effects of acupuncture and estazolam on senile insomnia



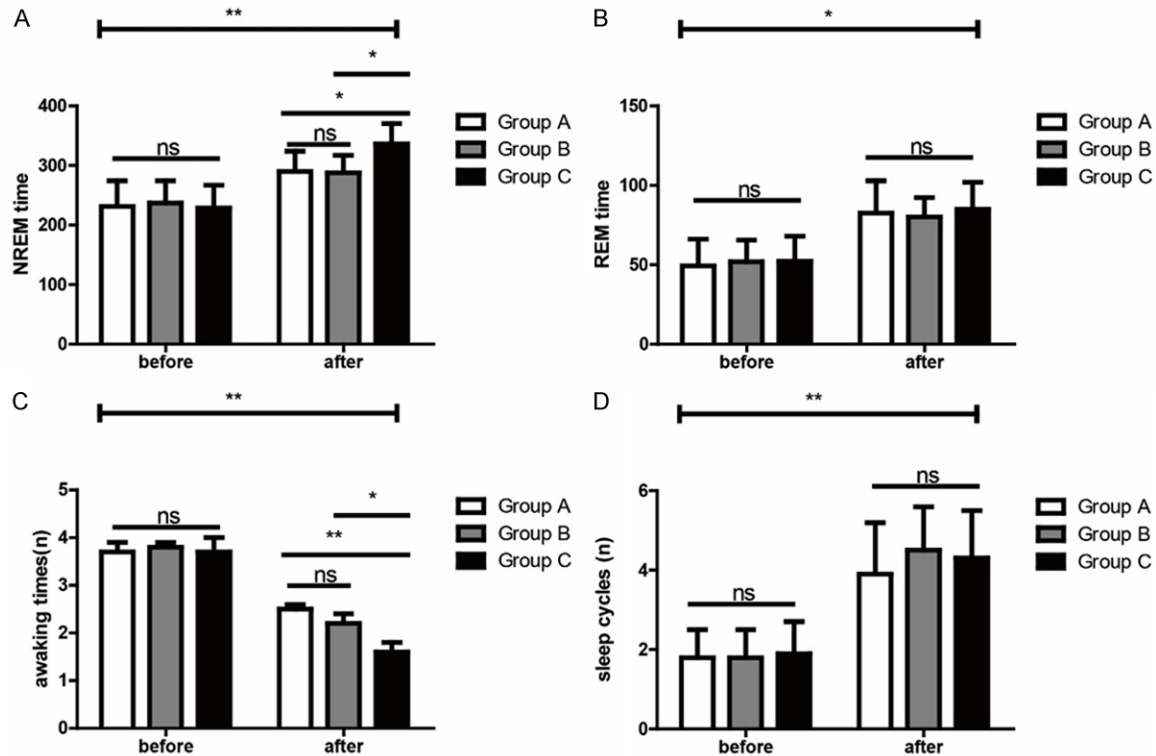
**Figure 2.** The sub-scores of the PSQI score before and after treatment in each group. Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group. A. Score of subjective sleep quality; B. Score of sleep latency; C. Score of duration of sleep; D. Score of habitual sleep efficiency; E. Score of sleep disturbance; F. Score of daytime function. Ns, no significant; \*,  $P < 0.05$ , \*\*,  $P < 0.01$ .



**Figure 3.** The PSG indexes of total sleep time, sleep latency and sleep efficiency before and after treatment in each group. Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group. Ns, no significant; \*,  $P < 0.05$ , \*\*,  $P < 0.01$ .



## Effects of acupuncture and estazolam on senile insomnia



**Figure 4.** The PSG indexes of NREM time, REM time, awaking times and sleep cycles before and after treatment in each group. Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group. Ns, no significant; \*,  $P < 0.05$ , \*\*,  $P < 0.01$ .

### Discussion

#### *Previous reports of acupuncture and insomnia*

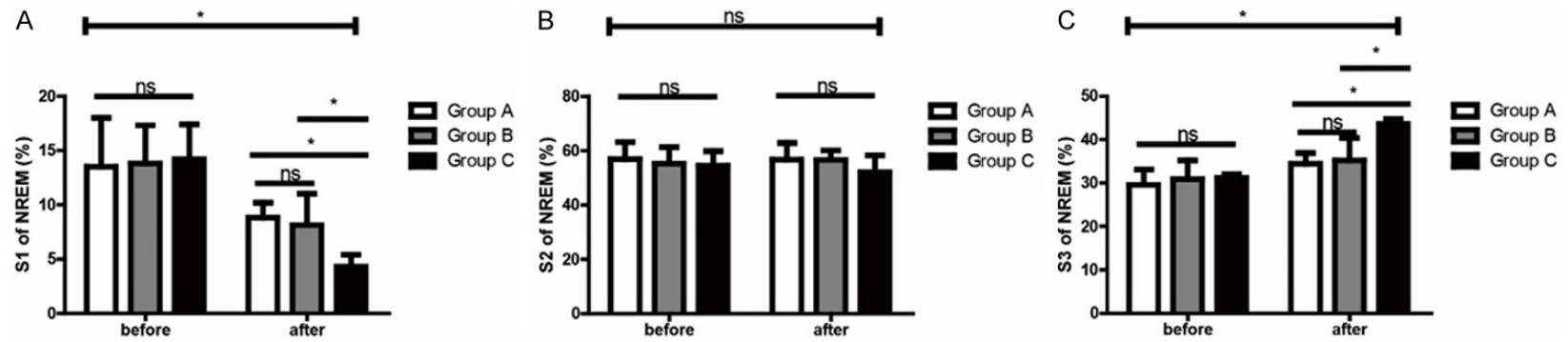
Common sleep disorders among elderly people include insomnia, sleep disordered breathing, REM sleep-behaviour disorder, restless legs syndrome and so on [18, 19]. Among these sleep disorders, insomnia, a very prevalent disorder, has influenced the quality of life of elderly individuals [20]. Insomnia was reported to occur at an annual rate of 5% [21], and more than 50% of old people were bothered by insomnia [22]. Currently, management for insomnia can be classified into three aspects: cognitive behaviour therapy, Western medications and traditional Chinese medicine, especially herbs and acupuncture. Acupuncture is based on the theories of traditional Chinese medicine and improves insomnia by balancing Yin and Yang. In recent years, increasing numbers of studies have reported that acupuncture has an effect on insomnia [23, 24]. Abad-Alegria et al reported that acupuncture at Shen Men (He-7) reduced sympathetic activity [25].

Spence et al reported that acupuncture could increase nocturnal melatonin secretion [26]. Additionally, Sok et al indicated in a review that acupuncture had a positive effect on insomnia [27].

#### *Analysis of the current results*

In this research, we aimed to evaluate the effects of acupuncture, estazolam and combination therapy on senile insomnia. The Pittsburgh Subjective Sleep Quality Index (PSQI) is a well-established sleep instrument that has been widely adopted in many sleep studies. First, we used the PSQI score to evaluate the effects of the above treatments. The results indicate that the combination of acupuncture and estazolam is more effective in treating senile insomnia than acupuncture or estazolam alone. Next, we evaluated the sub-score of the PSQI score, and the results show that the combination of acupuncture and estazolam is more effective in improving subjective sleep quality, sleep duration, habitual sleep efficiency and daytime function than acupuncture or estazolam alone.

## Effects of acupuncture and estazolam on senile insomnia



**Figure 5.** The distribution of NREM time before and after treatment in each group. Group A: acupuncture group, Group B: estazolam group, Group C: acupuncture plus estazolam group. Ns, no significant; \*,  $P < 0.05$ .

At present, the severity of a sleep disorder is mainly judged via the complaints of insomnia patients. Patients often exaggerate their illness and think that they are seriously short of sleep time and lack sleep quality, so it is often difficult to judge the severity of insomnia in patients. PSG can record EMG, EEG, blood oxygen and other signals during overnight sleep, thus obtaining a series of parameters such as sleep structure, sleep process, blood oxygen saturation, body position, waking times and so on. On the whole, PSG is an objective monitoring technique for the diagnosis of sleep disorders. In this research, the total sleep time, latency, NREM/REM time, number of awakenings and sleep cycles of insomnia patients were objectively recorded via polysomnography, providing reliable research data for the evaluation of patients' condition and post-treatment effects. PSG results show that acupuncture, estazolam or a combination of the two can effectively increase the total sleep time of insomnia patients, shorten the sleep latency, and improve sleep efficiency. However, in terms of total sleep time and sleep efficiency, the improvement of the combination therapy group was significantly better than the sole treatment groups. All three treatments can significantly increase the NREM time and REM time of insomnia patients, but prolonged NREM time in the combination treatment group was better than that in the sole treatment groups. The frequency of awakening decreased significantly after treatment in all three groups, and the combination treatment group had a greater decrease than the sole treatment groups, indicating that the occurrence of awakening events in the combination treatment group was effectively reduced. In terms of sleep cycle, there was no significant difference between the three groups after treatment, indicating that the three treatments had similar clinical effects in improving the sleep cycle. In the comparison of NREM stages, we found that the combination therapy was more effective than the other treatment groups in reducing the light sleep time of the S1 phase and increasing the deep sleep time of the S3 phase.

### *Implications of findings*

The problem of insomnia is very frequent in the elderly population and is one of middle-aged and older people's hardest problems [28]. The positive results of this study are of great impor-

tance to elderly people in that the study showed that acupuncture can improve the quality and quantity of sleep of elderly adults, similar to estazolam. The sleep efficiency of acupuncture is up to 72.2%, just as it is for estazolam, which indicates that acupuncture offers a new therapy for patients who do not want to use Western medicine or be subject to the side effects of estazolam, such as lethargy, dry mouth and so on. Moreover, for patients who want to gain more sleep efficiency with fewer doses of estazolam, the combination of acupuncture and estazolam is a good choice as combination therapy has better effect in improving both the quality and quantity of sleep in elderly patients suffering from insomnia. It is expected that the results of the current research could stimulate global interest in examining the therapeutic value of acupuncture so that more scientific evidence can be obtained to determine its clinical relevance.

### *Limitations and recommendations*

The current clinical study was only a short-term, small sample study, and long-term, multi-centre randomized controlled clinical studies need to be developed. This research focuses on the insomnia of elderly people. In the future, comparison studies with a similar approach could be applied in younger subjects.

Moreover, the final sample was formed via subject self-selection, so it may not be representative of all community-dwelling elderly individuals with insomnia. It is recommended that further evaluative work using studies adopting a similar approach should be undertaken in various institutional settings for elderly individuals.

The precise mechanisms for the relationship between acupuncture and functional changes are still unknown. Although the therapeutic effects of acupuncture were shown in this research, no efforts have been made to determine how acupuncture therapy works. Further studies from a biomedical perspective can be carried out to thoroughly explore the biological effects of acupuncture therapy on the Qi, meridians and Zang Fu organs of the body.

### **Conclusions**

In conclusion, acupuncture and estazolam have similar effects on senile insomnia, which



indicates that acupuncture offers a new therapy for patients who do not want to use Western medicine or be subject to the side effects of estazolam. The combination of acupuncture and estazolam has greater effects in improving both the quality and quantity of sleep of elderly patients suffering from insomnia over acupuncture or estazolam alone. The findings of this study could stimulate global interest in examining the therapeutic value of acupuncture and combination therapy with acupuncture and Western medicine so that more scientific evidence could be obtained to evaluate clinical applications of acupuncture.

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## Disclosure of conflict of interest

None.

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