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ORIGINAL ARTICLE

Clinical efficacy of Xiaoyao San combined with Bazhen Decoction in the treatment of insomnia in postoperative breast cancer patients

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ABSTRACT

Objective: This study aimed to evaluate the effects of Xiaoyao San combined with Bazhen Decoction on insomnia in patients following breast cancer surgery.

Methods: A total of 86 patients experiencing insomnia after breast cancer surgery were randomly assigned to either the treatment group or the control group. The treatment group received Xiaoyao San combined with Bazhen Decoction, while the control group was treated with estazolam tablets. The treatment duration was 4 weeks. Pittsburgh Sleep Quality Index (PSQI) scores were assessed before and after treatment. The overall efficacy and incidence of adverse reactions were compared between the two groups.

Results: PSQI scores in both groups significantly decreased after treatment ($p < 0.05$). Total effective rate in the treatment group (93.02%) was higher than that in the control group (86.05%), although the difference was not statistically significant ($p > 0.05$). The incidence of adverse reactions in the treatment group (4.65%) was significantly lower than that in the control group (20.93%) ($p < 0.05$).

Conclusion: Xiaoyao San combined with Bazhen Decoction can effectively improve sleep quality in patients with insomnia following breast cancer surgery, demonstrating good clinical efficacy and fewer adverse reactions. Further studies are needed to confirm these findings and explore broader clinical applications.

KEYWORDS

Traditional Chinese Medicine, Xiaoyao San, Bazhen Decoction, breast cancer, insomnia

INTRODUCTION

Breast cancer has a high incidence and is the leading cause of malignant tumors among women in China [1]. With advancements in early screening and treatment, the survival rate of breast cancer patients has improved. However, these patients often face various psychological and physical challenges during treatment, with insomnia being one of the most prominent issues. Insomnia is common throughout the course of the disease [2], including during the diagnosis, post-surgery recovery, and after chemotherapy or radiation therapy. Postoperative patients, in particular, are highly susceptible to insomnia,

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which may be related not only to the physical burden of the disease but also to psychological stress during treatment. Conventional Western treatments for postoperative insomnia primarily rely on sedative-hypnotic medications such as benzodiazepines and non-benzodiazepine drugs. However, long-term use of these medications may lead to side effects such as drug dependence and cognitive decline, with efficacy varying among individuals. In clinical practice, it is observed that postoperative breast cancer patients often experience emotional distress and physical depletion due to surgery and chemotherapy, which is thought to contribute to insomnia caused by liver stagnation and blood deficiency. This study explored the clinical efficacy of modified Xiaoyao San combined with Bazhen Decoction in treating postoperative insomnia in breast cancer patients, comparing it with conventional Western medication. The results are presented as follows.

METHODS

Study design

A single-center, randomized, single-blind, controlled study was designed, which was approved by the Ethics Committee of the First Medical Center of the PLA General Hospital (Ethics approval number: S2023-058-01), and all patients or their families signed informed consent forms. This study employed a single-blind design, in which the outcome assessors were unaware of the patients' group allocation. Due to the obvious differences in dosage forms and administration methods between traditional Chinese medicine and Western medicine, it was not possible to implement blinding for the patients. To reduce bias, all assessment indicators were completed by independent, trained researchers who were not involved in the treatment process.

Study participants

Eighty-six female patients with postoperative insomnia from the Department of Traditional Chinese Medicine at the First Medical Center of the PLA General Hospital were included in this study between August 2023 and September 2024. All patients had breast cancer confirmed by postoperative pathology. The patients were randomly divided into two groups: the treatment group and the control group, with 43 patients in each group. The mean age of the treatment group was 41.26 ± 13.22 years, with an average disease duration of 3.53 ± 2.26 months. Among them, 38 patients underwent unilateral radical mastectomy, and 5 patients underwent breast-conserving surgery. The mean age of the control group was 42.63 ± 12.58 years, with an average disease duration of 4.16 ± 3.31 months. Among them, 39 patients underwent unilateral radical mastectomy, and 4 patients underwent breast-conserving surgery. There were no significant differences in age, disease duration, or condition between the two groups ($p > 0.05$), as shown in Table 1.

TABLE 1 Baseline characteristics of study participants.

Characteristics	Treatment group ($n = 43$)	Control group ($n = 43$)	p value
Age (years)	41.26 ± 13.22	42.63 ± 12.58	0.062
Disease duration (months)	3.53 ± 2.26	4.16 ± 3.31	0.308
PSQI baseline score	11.20 ± 2.10	10.80 ± 1.90	0.372
Insomnia duration (months)	2.75 ± 1.48	2.92 ± 1.62	0.614
Breast cancer stage, *n* (%)			0.892
I	15 (34.90)	16 (37.20)	
II	21 (48.80)	19 (44.20)	
III	7 (16.30)	8 (18.60)	
Surgery type, *n* (%)			0.725
Radical mastectomy	38 (88.40)	39 (90.70)	
Breast-conserving surgery	5 (11.60)	4 (9.30)	
Comorbidities, *n* (%)			
Hypertension	7 (16.30)	8 (18.60)	0.779
Diabetes	4 (9.30)	5 (11.60)	0.725
Thyroid disease	3 (7.00)	4 (9.30)	0.693
Other	5 (11.60)	6 (14.00)	0.748
Concomitant medications, *n* (%)			
Endocrine therapy	27 (62.80)	25 (58.10)	0.661
Targeted therapy	8 (18.60)	10 (23.30)	0.601
Analgesics	6 (14.00)	5 (11.60)	0.748
Other	12 (27.90)	14 (32.60)	0.639
Concomitant treatments, *n* (%)			
Chemotherapy	29 (67.40)	31 (72.10)	0.639
Radiotherapy	18 (41.90)	16 (37.20)	0.661
Immunotherapy	5 (11.60)	7 (16.30)	0.535

Note: Continuous variables are presented as mean ± standard deviation; categorical variables are presented as number (percentage). p values for continuous variables were calculated using independent t-tests, and for categorical variables using chi-square tests. All p values > 0.05 indicate no significant differences between groups at baseline.

Diagnostic criteria

Insomnia was diagnosed according to the "Classification and Diagnostic Criteria for Mental Disorders, 3rd edition" [3].

Inclusion criteria

Inclusion criteria for patients were as follows: (1) patients who met the diagnostic criteria for insomnia; (2) postoperative breast cancer patients without recurrence; (3) aged 18–70 years.

Exclusion criteria

Patients who met any of the following criteria were excluded from this study: (1) severe primary cardiovascular, liver, or kidney diseases; (2) organic psychiatric or neurological disorders; (3) patients with recurrent breast cancer.

Treatment methods

Control group

Patients in the control group were administered oral eszopiclone tablets (approval number: H37023047; Shandong Xinyi Pharmaceutical Co. Ltd.) at a dose of 1 mg once daily before bedtime for 4 weeks.

Treatment group

Patients in the treatment group were treated with a modified formula of Xiaoyao San combined with Bazhen Decoction. The composition of the formula included the following herbs: Chaihu (Bupleurum) 12 g, Danggui (Angelica Sinensis) 10 g, Shaoyao (Peony) 10 g, Fuling (Poria) 20 g, Chao Baizhu (Atractylodes) 15 g, Dangshen (Codonopsis) 15 g, Chuanxiong (Ligusticum) 10 g, Shudi (Rehmannia) 10 g, Yujin (Curcuma) 10 g, Chao Zao Ren (Jujube Seed) 20 g, and Sheng Gancao (Licorice) 6 g. The decoction was prepared by boiling 1 dose in water to yield 300 mL, with 150 mL taken 1 h before lunch and 1 h before bedtime, for a total of 4 weeks. The herbal materials were provided and verified by the pharmacy of the First Medical Center of the PLA General Hospital.

Observational indicators

Pittsburgh Sleep Quality Index (PSQI)

The PSQI was used to evaluate the sleep quality of the patients over the past month. The total score ranged from 0 to 21, with higher scores indicating poorer sleep quality. Both groups were assessed before treatment and 4 weeks after treatment.

Efficacy evaluation

Efficacy was evaluated based on the treatment standards for insomnia in the "Draft for the Revision of the Treatment of Mental Disorders" [4]. Significant improvement: Sleep improved significantly, with an increase in sleep duration by >3 h and better sleep depth. Effective: Sleep duration increased but by <3 h. Ineffective: No significant improvement in sleep or worsened insomnia. The total effective rate was the sum of significant improvement and effective cases.

Statistical analysis

Data were analyzed using SPSS 23.0. Continuous variables were expressed as mean ± standard deviation (SD). The chi-square test (χ^2) was used for categorical data, and independent *t*-tests were used for continuous variables. One-way ANOVA was applied for group comparisons, with $p < 0.05$ considered statistically significant. Sample size calculation was based on the results of previous similar studies and performed using SPSS 23.0 software. The expected total effective rates for the two groups were 90% and 70%, respectively, with $\alpha = 0.05$ (two-sided) and $\beta = 0.2$ (power of 80%), resulting in a calculated requirement of 38 patients per group. Considering a potential dropout rate of approximately 10%, each group was finally determined to include 43 patients.

RESULTS

Patient compliance

A total of 86 eligible patients were selected from 105 patients and randomly assigned to the treatment group and the control group. Both groups had high compliance, and no patient dropped out during the study period. The progress of the participants is shown in Figure 1.

Comparison of PSQI scores before and after treatment

As shown in Table 2, both groups demonstrated a significant decrease in PSQI scores after treatment compared to that before treatment ($p < 0.05$). However, there was no significant difference in PSQI scores between the two groups after treatment ($p > 0.05$).

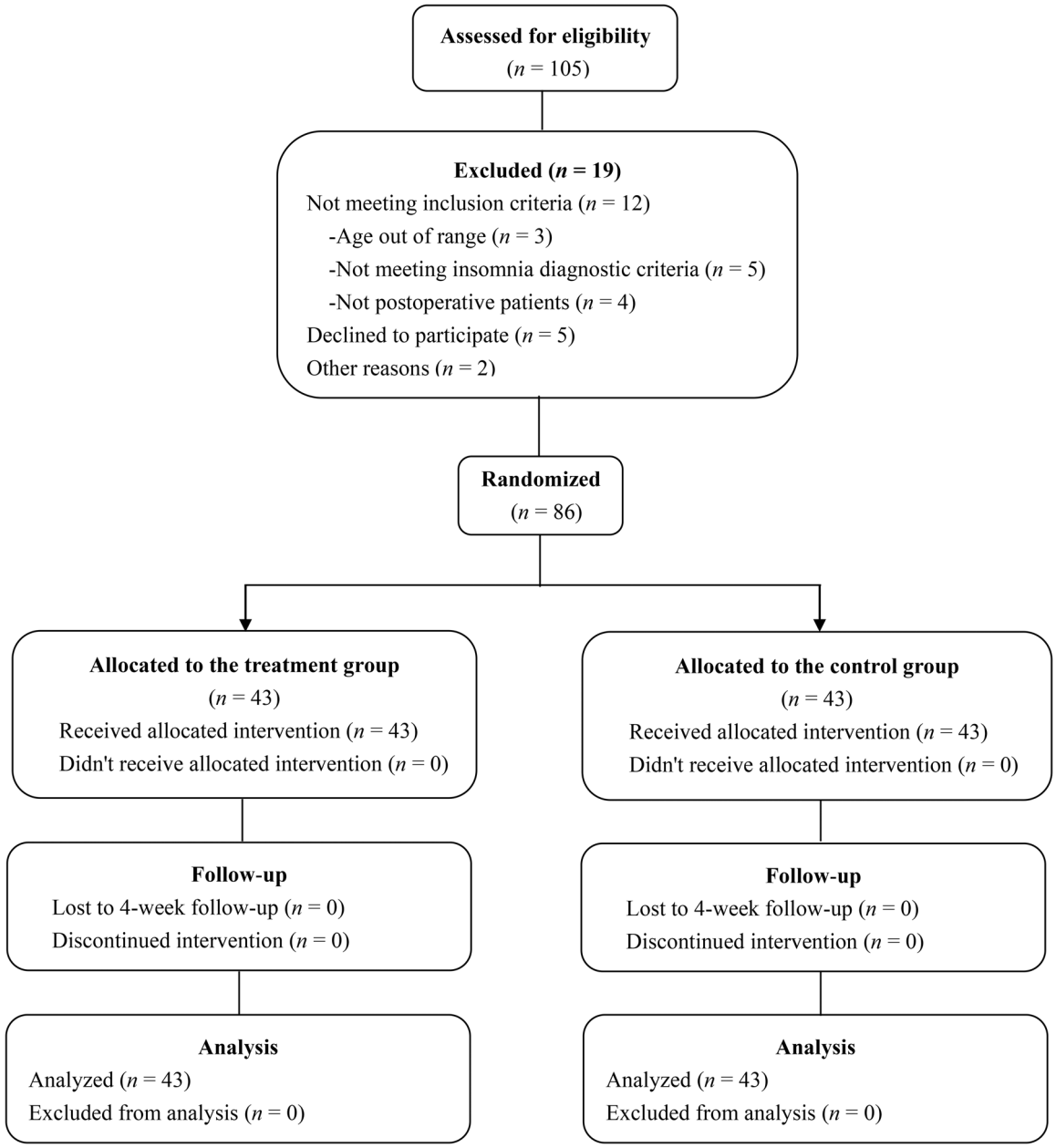

FIGURE 1 CONSORT flow diagram: Progress of postoperative breast cancer patients with insomnia.

TABLE 2 Comparison of PSQI scores before and after treatment.

Group	*n*	Before treatment	After treatment
Treatment group	43	11.2 ± 2.1	5.9 ± 1.8$^{\triangle}$
Control group	43	10.8 ± 1.9	6.1 ± 2.3$^{\triangle}$

Note: $^{\triangle}$ $p < 0.05$ compared with that before treatment within the same group.
Abbreviation: PSQI, Pittsburgh Sleep Quality Index.

Comparison of overall treatment efficacy

After 4 weeks of treatment, the total effective rate in the treatment group (93.02%) was higher than that in the control group (86.05%), but the difference between the two groups was not statistically significant ($\chi^2 = 0.496$; $p > 0.05$), as shown in Table 3.

Comparison of adverse reactions between the two groups

In the treatment group, only one patient experienced mild nausea and one patient experienced a bitter taste in the mouth, with an adverse reaction rate of 4.65%. In the control group, three patients experienced dry mouth, one patient had dizziness, two patients reported

TABLE 3 Comparison of overall treatment efficacy between the two groups.

Group	*n*	Significant improvement	Effective	Ineffective	Total effective (%)
Treatment group	43	16 (37.21%)	24 (55.81%)	3 (6.98%)	40 (93.02%)
Control group	43	18 (41.86%)	19 (44.19%)	6 (13.95%)	37 (86.05%)

Note: $\chi^2 = 0.496$, $p > 0.05$.

fatigue, and three patients had drowsiness, with an adverse reaction rate of 20.93%. The difference between the two groups was statistically significant ($\chi^2 = 5.108$; $p < 0.05$).

DISCUSSION

With changes in lifestyle and work patterns, as well as increasing pressure of daily life, the incidence of breast cancer in Chinese women continues to rise [5]. Insomnia is a common clinical issue that accompanies the entire course of breast cancer, particularly after surgery, where insomnia rates are higher [6]. Persistent insomnia not only severely disrupts daily life and work but also directly impacts the progress of postoperative adjuvant therapy, ultimately affecting the overall efficacy of breast cancer treatment. Currently, Western medicine primarily uses benzodiazepines or non-benzodiazepine sedative-hypnotic drugs [7], which are effective in the short term but come with side effects such as dry mouth, fatigue, dizziness, drowsiness, and withdrawal symptoms [8].

In our long-term clinical observations, we have found that postoperative breast cancer patients often experience emotional distress, anxiety, and frustration, leading to liver Qi stagnation and blood deficiency, which in turn disturb the spirit, resulting in insomnia. Moreover, surgery and chemotherapy deplete Qi and blood, leading to Qi and blood deficiency, which further impairs nourishment of the heart and spirit, exacerbating insomnia. Therefore, we believe that the fundamental pathogenesis of postoperative insomnia in breast cancer patients is liver Qi stagnation and Qi–blood deficiency. The treatment, combining a modified formula of Xiaoyao San and Bazhen Decoction, aims to soothe the liver, relieve Qi stagnation, nourish the blood, and calm the spirit. Xiaoyao San is a classic formula that soothes the liver, relieves depression, nourishes the blood, and strengthens the spleen, while Bazhen Decoction has the effect of benefiting Qi and nourishing blood. The combined use of these two formulas targets the pathogenesis of liver Qi stagnation and Qi–blood deficiency in postoperative breast cancer patients. It addresses the liver Qi stagnation caused by psychological stress after surgery and compensates for Qi and blood deficiency resulting from surgery and chemotherapy, aligning with the treatment principle of "seeking the root of the disease". In the formula, Chaihu and Yujin soothe the liver and relieve depression; Danggui, Baishao, Chuanxiong, and Shudi nourish and invigorate the blood; Fuling and fried Baizhu strengthen the spleen and benefit Qi; Dangshen tonifies Qi and strengthens the spleen; fried Zao Ren nourishes the heart and calms the spirit; and Sheng Gancao harmonizes the various herbs. When used together, these herbs collectively produce the effects of soothing the liver and relieving depression, tonifying Qi, nourishing blood, and calming the spirit.

CONCLUSION

The results of this study demonstrate that the modified Xiaoyao San combined with Bazhen Decoction significantly improves sleep quality in postoperative breast cancer patients, showing good clinical efficacy. Furthermore, the incidence of adverse reactions is markedly lower than that of sedative-hypnotic drugs. The therapy deserves further investigation and potential wider application.

AUTHOR CONTRIBUTIONS

Fagen Li and Feifei Lv participated in the writing and revision of the manuscript, respectively. Liang Wang and Shaodan Li participated in patient recruitment and data collection. Fagen Li and Xin Zhang analyzed the data and participated in reviewing and revising the manuscript. All authors agree with the content of this article and approve the submission of manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

Data involved in this study are available from the corresponding author upon reasonable request. Patient privacy will be respected and protected.

ETHICS STATEMENT

The study was approved by the Ethics Committee of the First Medical Center of the PLA General Hospital (Ethics approval number: S2023-058-01).

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