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Study on the Efficacy of Shugan Jieyu Capsules Combined with Trazodone in Patients with Post-Stroke Depression and Insomnia

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Abstract: *Objective:* To analyze the effectiveness of applying ShuGan JieYu Capsules (SGJYC) combined with trazodone in patients with post-stroke depression (PSD) with insomnia. *Methods:* 60 cases of PSD with insomnia patients admitted to the hospital from May 2022 to May 2023 were selected and randomly divided into a reference group (trazodone) and a research group (SGJYC combined with trazodone) of 30 cases each. Statistics were analyzed using the Hamilton Depression Rating Scale (HAM-D), Pittsburgh Sleep Quality Index (PSQI), and Activities of Daily Living (ADL) scale before treatment and 4, 8, and 12 weeks after treatment. *Results:* Before treatment, The results of HAM-D, PSQI, and ADL scale studies in the two groups before treatment were not statistically significant ($P > 0.05$); 4, 8, and 12 weeks after treatment, the results of HAM-D and PSQI studies in the research group were lower than that of the reference group, and the results of ADL scale studies were higher than that of the reference group. There was a significant difference between the groups ($P < 0.05$). The total adverse reaction rate of the research group was lower than that of the reference group, and there was a significant difference between the groups ($P < 0.05$). *Conclusion:* The combination of SGJYC and trazodone reduced depression in post-stroke patients, corrected insomnia, improved sleep quality, was safe, and had a low rate of adverse reactions.

Keywords: ShuGan JieYu Capsules; Trazodone; Stroke; Depression; Insomnia

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1. Introduction

Among acute cerebrovascular diseases, stroke has garnered attention as the first disease with the highest death rate in China, where the majority of complications comprised post-stroke depression (PSD) with insomnia [1] This has negatively impacted the prognosis of patients. Antidepressant drugs that have been used in the past exert strong side effects and show no effectiveness in treating insomnia. It also reduces the patient's compliance to treatment, hence it is necessary to discover more accurate and safer treatment options. ShuGan JieYu capsules (SGJYC) are made of hypericum (also known as St. John's wort) and *Acanthopanax senticosus*. SGJYC can significantly improve mild or moderate depression without serious adverse reactions. It was also found that

the use of trazodone could increase the duration of sleep, improve sleep efficiency, increase the duration of slow-wave sleep, reduce the number of awakenings, and reduce depression, with an ideal self-assessment of sleep quality [2]. SGJYC combined with trazodone demonstrated significant improvement in PSD patients with insomnia. Therefore, this paper selected 60 cases of PSD patients with insomnia admitted to the hospital from May 2022 to May 2023 to study the effectiveness of applying SGJYC combined with trazodone for the treatment of PSD and insomnia.

2. Information and methods

2.1. General information

60 PSD patients with insomnia admitted to the hospital from May 2022 to May 2023 were randomly selected and divided into a reference group and a research group of 30 cases each. The research group consisted of 17 males and 13 females with the lower/upper age limit of 53 and 71 years old respectively. The mean age was 60.92 ± 9.11 years, and the duration of the disease was 2–11 months with a mean duration of 6.69 ± 3.52 months. The reference group consisted of 18 males and 12 females with the lower/upper age limit value of 54 and 72 years respectively. The mean age was 70.00 ± 9.23 years, and the duration of the disease was 2–12 months with a mean duration of 6.73 ± 3.59 months. There were no differences in the data information ($P > 0.05$).

2.1.1. Inclusion and exclusion criteria

Inclusion criteria: (1) The enrolled subjects were diagnosed with ischemic stroke via imaging examination [3] and referred to the PSD diagnostic criteria recommended by the Chinese Expert Consensus on Clinical Practice of PSD, and conformed to the Chinese guidelines for the Diagnosis and Treatment of Insomnia in Adults (2017 edition) for the diagnosis of insomnia; (2) complete clinical information; (3) subjects were conscious, did not have cognitive dysfunctions, and could complete all questionnaires independently; (4) participants, family members voluntarily joined the experiment and consented. Exclusion criteria: (1) History of psychiatric disorders/insomnia before the onset of stroke; (2) comorbidities with other types of severe organic diseases; (3) secondary depression due to other medications/other different factors; (4) contraindications to the use of medications; (5) poor treatment compliance and inability to complete the relevant scoring requirements.

2.2. Methods

The reference group underwent the trazodone (Meishi Chemical Pharmaceutical Co., Ltd. Nantou plant; approval number: HC20160001) treatment [4] with an initial dose of 25 mg each time, once a day, for 3–4 days. According to the patient's condition, drug dosage was slowly increased but controlled at 50–100 mg per day. This treatment was carried out for 3 months. The research group was treated with trazodone combined with SGJYC (Chengdu Kanghong Pharmaceutical Group Co., Ltd; State Drug License Z20080580) [5]. Two capsules were administered each time, twice a day, for 3 months. All patients did not use other antidepressant/anxiety drugs during the treatment.

2.3. Observation indexes

The results were analyzed using the Hamilton Depression Rating Scale (HAM-D), Pittsburgh Sleep Quality Index (PSQI), and Activities of Daily Living (ADL) scales before treatment and 4, 8, and 12 weeks after treatment. PSQI was used and involved a total of 7 items [6]: sleep disorders, sleep quality (subjective), sleep efficiency, the use of sleeping medication, the time of sleep, and sleep onset. A high score of 0-21 confirms that the patient's sleep quality was poor. The HAM-D scale was used to assess depression and involved 17

items [7], with a higher total score indicating a more severe depressive mood; a score of < 7 was categorized as "no depression," a score of 8–17 was categorized as "mild depression," a score of 18–24 was categorized as "moderate depression," and a score of > 24 was categorized as "severe depression." The ADL scale was used to assess the patient's sleep quality and efficiency. It was also used to assess the ability of daily living, and a high total score confirmed a high ability of daily living. The patient was monitored for any presence of dry mouth, cardiac arrhythmia, etc. when taking the administered drugs, and any adverse outcomes were recorded.

2.4. Statistical methods

The SPSS 20.0 was used for statistical analysis and the measurement data were expressed as mean ± standard deviation and compared using the *t*-test; count data were expressed as % and analyzed using the chi-square (χ^2) test. Results were considered statistically significant at $P < 0.05$.

3. Results

3.1. Comparison of the results of HAM-D, PSQI, and ADL scales before treatment and 4, 8, and 12 weeks after treatment

Table 1, **Table 2** and **Table 3** showed that before treatment, the results of HAM-D, PSQI, and ADL scales of the two groups were not statistically significant ($P > 0.05$); after 4, 8, and 12 weeks of treatment, the results of HAM-D and PSQI of the research group were lower than those of the reference group. The results of the ADL scales of the research group were higher than those of the reference group, and there was a significant difference between the groups ($P < 0.05$).

Table 1. Comparison of HAM-D, PSQI, and ADL scale findings before treatment and 4, 8, and 12 weeks after treatment

Group	Case, *n*	HAM-D			
		Before treatment	4 weeks after treatment	8 weeks after treatment	12 weeks after treatment
Research group	30	30.28 ± 8.58	20.32 ± 9.00	17.00 ± 7.03	14.02 ± 4.59
Reference group	30	29.77 ± 9.20	24.55 ± 6.49	21.32 ± 6.50	18.20 ± 6.49
t		0.2220	2.0880	2.4713	2.8802
P		0.8251	0.0412	0.0164	0.0056

Table 2. Comparison of HAM-D, PSQI, and ADL scale findings before treatment and at 4, 8, and 12 weeks after treatment

Group	Case, *n*	PSQI			
		Before treatment	4 weeks after treatment	8 weeks after treatment	12 weeks after treatment
Research group	30	17.99 ± 2.99	14.99 ± 2.92	11.22 ± 2.58	9.08 ± 2.48
Reference group	30	17.97 ± 3.00	16.58 ± 2.99	13.98 ± 2.70	12.98 ± 2.42
t		0.0259	2.0837	4.0480	6.1646
P		0.9795	0.0416	0.0002	0.0001

Table 3. Comparison of HAM-D, PSQI, and ADL scale findings before treatment and at 4, 8, and 12 weeks after treatment

Group	Case, *n*	ADL			
		Before treatment	4 weeks after treatment	8 weeks after treatment	12 weeks after treatment
Research group	30	50.35 ± 10.32	63.33 ± 9.08	78.33 ± 10.00	89.49 ± 5.02
Reference group	30	50.42 ± 10.39	55.39 ± 9.98	65.02 ± 10.02	77.32 ± 8.32
t		0.0262	3.2232	5.1498	6.8598
P		0.9792	0.0021	0.0001	0.0001

3.2. Comparison of the results of adverse reaction rate within the group

As seen in **Table 4**, the results of the total adverse reaction rate in the research group were lower than those of the reference group, and the comparison between the groups ($p<0.05$).

Table 4. Comparison of the results of adverse reaction rate between groups

Group	Dryness of the mouth	Arrhythmia	Postural hypotension	Total adverse reaction rate
Research group ($n = 30$)	1 (3.33)	1 (3.33)	1 (3.33)	3 (10.00)
Reference group ($n = 30$)	3 (10.0)	4 (13.33)	3 (10.00)	10 (33.33)
χ^2		-		4.8118
P		-		0.0283

4. Discussion

Stroke is a common neurological disease. It occurs frequently and jeopardizes people's health and safety. In China, the morbidity and mortality rates of stroke are relatively high. PSD is usually expressed by patients after a stroke event, as well as other types of somatic symptom syndromes [8], and is a type of common complication. It is known that the incidence of depression after a stroke event can reach up to 31% within 5 years, and usually occurs during the acute, intermediate, and recovery phases of stroke. If not treated and detected promptly, it can adversely impact the neurological recovery and social reintegration of the patient, as well as exacerbate cognitive functioning in patients who may possess suicidal ideation. Insomnia may also manifest during PSD along with other symptoms such as difficulty in falling asleep, frequent awakenings, excessive sleepiness, and excessive dreaming [9]. These symptoms can contribute to the worsening of anxiety and depression, increase the risk of PSD, hinder neurological recovery, and reduce the quality of life. Hence, intervention is crucial. The current treatment options for PSD with insomnia are mostly antidepressant drugs, which tend to have unwanted adverse drug effects, do not improve insomnia promptly, and have low patient compliance. Therefore, there is a need to discover more effective and safe drugs for the treatment of PSD with insomnia [10].

There are many types of triazolopyridine derivatives, including Trazodone, which is a 5-hydroxytryptamine (5-HT2) antagonist/reuptake inhibitor. Trazodone has a sedative effect [11], does not inhibit the release of catechol, and can inhibit the activity of monoamine oxidase. Trazodone does not produce anticonvulsant effects and does not affect the normal release of prolactin, but requires long-term use during treatment, and is associated with unwanted side effects. Hence, the combination of SGJYC and trazodone is usually recommended.

SGJYC is a new Chinese patented antidepressant drug. It plays a role in liver detoxification, spleen

strengthening, and mind tranquilization, and is often used in the treatment of mild to moderate depressive disorders [12], and PSD insomnia, and has achieved remarkable results. The main components of SGJYC include hypericum and *Acanthopanax senticosus*, where the former soothes the liver and relieves depression, clears the heart, and prevents diarrhea; the latter benefits the qi and strengthens the spleen, tonifies the kidney. Both SGJYC and trazodone can be used together to balance the qi and improve the condition of the liver, spleen, and reduce depression.

Hypericum targets the non-selective cation channel transient receptor potential channel via uptake into the transient receptor potential (TRP) ion channel and significantly increases the concentration of sodium (Na^+) present in the cell while decreasing Na^+ concentration outside the cell. Hypericum acts as a better and more effective pre-synaptic membrane transmitter and facilitates an increased reuptake of neurotransmitters into the synaptic gap. This phenomenon blocks the uptake of 5-HT2, thus producing antidepressant therapeutic effects. Siberian cherry possesses the following characteristics: soluble N-ethylmaleimide-sensitive factor (NSF) adhesion proteins, receptors, and vesicles which effectively increase the release of neurotransmitters into the synaptic, and act as an antidepressant. Furthermore, the drug has a calming effect on the central nervous system. When the cerebral cortex is blocked, the effect is enhanced and sleep quality is improved.

The clinical combination of SGJYC and trazodone can treat PSD with insomnia, inhibit disease progression, and improve prognosis. Furthermore, it can improve sleep quality and efficiency, acts as an antidepressant, and can be used safely. SGJYC combined with trazodone treatment can further correct the patient's sleep disorders as the overall PSQI score of the patients after this treatment decreased significantly about 10%–30%, and patient compliance was also increased.

The experimental data confirmed that at 4, 8, and 12 weeks after treatment, the results of HAM-D and PSQI in the research group were lower than those of the reference group, and the results of the ADL scale were higher than those of the reference group. Results were significantly different between the groups ($P < 0.05$); the total adverse reaction rate in the research group was lower than those of the reference group, and results were significantly different between the groups ($P < 0.05$). It was confirmed that the combined application of SGJYC and trazodone has high therapeutic advantages. The patient's sleep quality, depression status, treatment compliance, and overall quality of life were improved.

5. Conclusion

The combination of ShuGan JieYu Capsules and Trazodone reduced depression in patients with PSD, resolved insomnia promptly, improved sleep quality, and reduced the rate of adverse effects.

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Disclosure statement

The authors declare no conflict of interest.

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