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## Retrospective Study

# Value of Chuanjin Qinggan decoction in improving the depressive state of patients with herpes zoster combined with depression

Yi-Nan Wang, Meng-Meng Shi, Jin-Ming Zhang

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## Abstract

### BACKGROUND

Western medicine is beneficial for the recovery of neurological function in patients with depression, but some patients experience side effects such as headaches, dizziness, nausea, gastrointestinal symptoms, insomnia, and cardiac dysfunction. In recent years, integrative medicine has achieved positive results in the treatment of various diseases.

### AIM

To study Chuanjin Qinggan decoction combined with selective serotonin reuptake inhibitors (SSRIs) in patients with herpes zoster complicated by depression.

### METHODS

Patients with herpes zoster complicated by depression who were treated at the Yantai Hospital of Traditional Chinese Medicine from January 2021 to December 2022 were retrospectively selected as research participants. Among them, 43 patients with herpes zoster complicated by depression who received SSRI treatment between January and December 2021 were assigned to the Western medicine group, while those who received combined treatment of traditional Chinese and Western medicine between January and December 2022 were assigned to the combined group. Both groups were treated for eight weeks. The degree of pain, effect of herpes zoster treatment, degree of improvement in depressive symptoms, serum neurotransmitter levels, sleep quality, and occurrence of adverse reactions were compared between the two groups.

### RESULTS

We found that after eight weeks of drug treatment, the two treatment schemes achieved differing efficacy. In further comparison, we found that, compared with

patients treated with SSRIs alone, patients treated with Chuanjin Qinggan decoction combined with SSRIs showed more significant improvement in depression and a greater increase in dopamine and 5-hydroxytryptamine levels after treatment ( $P < 0.05$ ). Patients treated with Chuanjin Qinggan decoction combined with SSRIs also experienced lower pain, better treatment efficacy for herpes zoster, better sleep quality, and a lower incidence of adverse reactions compared to those treated with SSRIs alone ( $P < 0.05$ ). All minor adverse reactions occurring during treatment were resolved after symptomatic treatment.

## CONCLUSION

The treatment scheme of Chuanjin Qinggan decoction combined with SSRIs can improve the psychological state of patients with herpes zoster complicated by depression and alleviate adverse reactions.

**Key Words:** Chuanjin Qinggan decoction; Selective 5-hydroxytryptamine reuptake inhibitor; Herpes zoster; Depression; Sleep quality; Adverse reaction

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**Core Tip:** Chuanjin Qinggan decoction is an important decoction composed mainly of Ligusticum chuanxiong Hort, Curcuma, and Sedum rosea. There is a synergistic effect between the active ingredients in Chuanjin Qinggan decoction which helps to reduce neurological damage and improve the depressive state of patients by providing raw materials and energy for protein and nucleic acid synthesis in brain tissue. This study confirmed that the treatment scheme of Chuanjin Qinggan decoction combined with selective serotonin reuptake inhibitors can effectively improve the depressive state of patients with herpes zoster complicated by depression.

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## INTRODUCTION

Herpes zoster is an acute herpetic skin disease characterized by clusters of blisters on the skin and burning pain[1]. It is characterized by the sudden occurrence of these blisters arranged in a ribbon along one side of the peripheral nerve distribution area, accompanied by tingling and lymphadenopathy[2]. Herpes zoster usually occurs in spring or autumn, and older adults constitute the majority of the affected population[3]. Most patients with herpes zoster do not experience recurrence after illness, although recurrence sometimes occurs[4]. Herpes zoster can cause burning, knife-cutting, or electric shock-like pain, with erythema and blisters on the skin's surface. It affects a patient's appearance and can cause physical and mental harm. If patients with herpes zoster do not receive effective treatment for an extended period, they may experience different degrees of depressive symptoms as the pain progresses.

Recent studies suggest that secondary depression in patients with herpes zoster is related to postherpetic neuralgia (PHN)[5,6]. PHN is an intractable neuropathic pain syndrome secondary to herpes zoster that causes the irreversible destruction of nerve fibers. When PHN destroys the neural pathways regulating emotion, it leads to the dysfunction of monoamine neurotransmitters. If the lesion site involves the thalamus, basal ganglia, amygdala, frontal lobe, hippocampus, or interconnected fibers, it can damage serotonergic neurons and reduce the level of 5-hydroxytryptamine (5-HT), eventually leading to depression[7]. The World Health Organization estimates that by 2030, depression may rank first in the global burden of disease[8]. Herpes zoster combined with depression brings a great psychological burden to patients and may reduce their medication compliance and rehabilitation process.

Selective 5-hydroxytryptamine reuptake inhibitors (SSRIs) are safe and can effectively regulate the concentration of monoamine transmitters in the body and reduce depression-like symptoms. They are the first-line antidepressants recommended by various guidelines. A previous study showed that SSRIs are beneficial for the recovery of neurological function in patients with depression[9]. However, some patients experience side effects such as headaches, dizziness, nausea, gastrointestinal symptoms, insomnia, and cardiac dysfunction. SSRIs have also been shown to affect the cardiac and cerebral vessels of patients[10]. Compared to patients with depression alone, patients with herpes zoster combined with depression are more likely to have aggravated depressive symptoms due to physiological pain. Therefore, there is an urgent need to develop a treatment plan that can relieve physiological pain and improve the psychological state of patients with herpes zoster and depression.

According to traditional Chinese medicine, depressive symptoms are mainly related to the dysfunction of the five internal organs and poor emotions. The depressive symptoms of patients with herpes zoster include depression, chest and flank fullness, and irritability caused by physiological and psychological pressure. Chuanjin Qinggan decoction promotes Qi, relieves depression, maintains the liver, clears heat, and detoxifies. However, the specific efficacy of Chuanjin Qinggan decoction combined with SSRIs in treating herpes zoster complicated by depression remains unclear.

In recent years, integrative medicine has achieved positive results in the treatment of various diseases. Since 2022, our hospital has actively attempted integrated traditional Chinese and Western medicine therapy for patients with herpes zoster complicated by depression, achieving good results. This study aims to explore the effect of Chuanjin Qinggan decoction combined with SSRIs in patients with herpes zoster complicated by depression.

## MATERIALS AND METHODS

### Patients

Patients with herpes zoster complicated by depression who were treated at the Yantai Hospital of Traditional Chinese Medicine between January 2021 and December 2022 were retrospectively selected as research participants. Inclusion criteria were as follows: (1) Meeting the relevant diagnostic criteria for herpes zoster[11]; (2) Hamilton Depression Scale (HAMD) score > 8[12]; (3) age ranging from 30 to 75 years; (4) complete clinical data required for this study; and (5) no history of depression before from the onset of herpes zoster. The exclusion criteria were as follows: (1) Patients with organic mental disorders; (2) patients with significant organ dysfunction; (3) patients with congenital cognitive dysfunction; (4) patients with less than one course of treatment; and (5) patients with allergies to the drugs used in this study.

### Grouping and treatment

Eighty-six patients were finally included in the study, and all patients were treated with the same method: acyclovir tablets (specification: 0.1 g/tablet), 0.4 g each time, five times a day; acyclovir cream applied externally, once every two hours, 4-6 times a day. The treatment lasted for two weeks. According to the treatment plan for depression, the patients were divided into Western medicine and combination groups.

**Western medicine group:** Patients with herpes zoster complicated by depression who received SSRIs between January and December 2021 were included in the Western medicine group. SSRIs include fluoxetine, sertraline, paroxetine, citalopram, escitalopram, and fluvoxamine. The following SSRIs and dosages were used by the patients in this study: The starting dose of sertraline tablets (specification: 50 mg/tablet) was 50 mg/d, administered after breakfast. Clinicians can adjust the drug dose within 7-14 d according to the actual condition of the patient, and the adjustment range is 50-150 mg/d. The starting dose of the enteric-coated paroxetine tablets (20 mg/tablet) was 20 mg/d, taken after breakfast. Clinicians can adjust the drug dose within 7-14 d according to the actual condition of the patient, and the adjustment range is 20-60 mg/d. The starting dose of escitalopram tablets (20 mg/tablet) was 10 mg/d, taken after breakfast. Clinicians can adjust the drug dose within 7-14 d according to the actual condition of the patient, and the adjustment range is 10-20 mg/d. The total treatment duration was eight weeks.

**The combination group** included patients with herpes zoster complicated by depression who received combined treatment of traditional Chinese and Western medicines between January and December 2022. The Western medicine treatment method was the same as that used in the Western medicine group. The traditional Chinese medicine treatment was Chuanjin Qinggan decoction: Ligusticum chuanxiong Hort (10 g), Curcuma (10 g), Rhodiola (15 g), Bupleurum (12 g), Gardenia (10 g), Paeonia alba (12 g), Rehmannia glutinosa (20 g), Peony bark (10 g), Poria cocos (20 g), Alisma orientalis (10 g), Acanthopanax senticosus (15 g), Schisandra (15 g), Albizzia julibrissin bark (15 g), Glycyrrhiza uralensis (6 g), and Forsythia suspensa (10 g). They were added or removed according to the patient's condition and decocted in 500 mL of water. This was administered once in the morning and evening for 14 d as a course of treatment for four consecutive courses (eight weeks).

### Outcome measures

Patient depression before and after treatment was the primary outcome measure. The HAMD scale was used to evaluate the depression status of patients one week before treatment, four weeks after treatment, and eight weeks after treatment. The HAMD scale used in this study has 17 items, of which a score ≤ 7 points indicates normal; the higher the score, the more severe the participant's depression.

The secondary outcome measures were as follows. (1) Patients' pain before and after treatment: The visual analog scale (VAS)[13] was used to evaluate the degree of pain in patients one week before and at the end of treatment. The VAS scores range from 0 to 10, with 0 indicating no pain and 10 indicating severe pain; (2) The effectiveness of herpes zoster treatment: remarkable effect: more than 70% of the rash disappeared, and the pain symptoms were alleviated; effective: 30%-70% of the rash disappeared, and the pain symptoms were alleviated; ineffective: less than 30% of the rash disappeared, and the pain did not change or worsened; (3) Neurotransmitter levels: The serum levels of dopamine (DA) and 5-HT were monitored before and after treatment; (4) Sleep quality: The Pittsburgh Sleep Quality Index (PSQI)[14] was used to evaluate sleep quality. The PSQI scale was compiled by psychiatrists and scholars at the University of Pittsburgh with seven factors derived from clinical practice; each factor had a score range of 0 to 3 points. The final PSQI score was the sum of the seven factor scores. The scale's total score was 21 points; the higher the total score, the worse the sleep quality; and (5) Patients' adverse reactions during treatment were recorded, including headache, blurred vision, nausea, vomiting, and cognitive dysfunction.

### Statistical analysis

SPSS 26.0 and GraphPad 9.0 were used for statistical analysis. The statistical data were expressed by frequency and percentage, and the  $\chi^2$  test was used for comparison between groups (the rank sum test was used for the count data with hierarchical characteristics). The measurement data that conform to and do not conform to the normal distribution are

expressed by the mean (standard deviation) and median (P25, p75), respectively. The data that conformed used a *t*-test and repeated-measures analysis of variance for comparison between groups, and the data that did not conform used the Mann-Whitney *U* test. Statistical significance was set at  $P < 0.05$ .

## RESULTS

### **Clinical characteristics of study participants**

To ensure the comparability of different drug treatment results, the baseline data of the two groups of patients were compared. After comparison, the statistical analysis showed no significant differences in the baseline data of the two groups of patients receiving different drugs, such as sex, age, duration of herpes zoster, residence, and years of education ( $P > 0.05$ ) (Table 1).

### **Comparison of the degree of pain**

As shown in Table 2, after eight weeks of treatment, the overall VAS scores of the two groups decreased compared to those before treatment, and the VAS scores of patients treated with Chuanjin Qinggan decoction combined with SSRIs decreased more significantly ( $P < 0.05$ ).

### **Comparison of the therapeutic effectiveness against herpes zoster**

In the comparison of the therapeutic effects of the two treatment groups against herpes zoster, it was found that the effect observed in patients treated with Chuanjin Qinggan decoction combined with SSRIs was higher than that in patients treated with SSRIs alone, the ineffective rate was lower than that in patients treated with SSRIs alone, and there was a significant difference in the overall efficacy between the two groups ( $P < 0.05$ ) (Table 3).

### **The changing trend of patients' depression**

As shown in Figure 1, after eight weeks of treatment, the overall HAMD score of patients in both groups decreased compared to that before treatment, and the decrease in HAMD score of patients treated with Chuanjin Qinggan decoction combined with SSRIs was more significant ( $P < 0.05$ ).

### **Effects of different treatment schemes on neurotransmitter levels in patients**

Both treatment regimens improved the serum DA and 5-HT levels of patients, and patients treated with Chuanjin Qinggan decoction combined with SSRIs showed a greater increase in DA and 5-HT levels (both  $P < 0.05$ ) (Figure 2).

### **Effect of different treatment schemes on sleep quality of patients**

Both treatment regimens reduced the PSQI score of patients, and the decrease in the PSQI score of patients treated with Chuanjin Qinggan decoction combined with SSRIs was more significant ( $P < 0.05$ ) (Figure 3).

### **Occurrence of adverse reactions**

Neither treatment method had adverse effects on cognitive function. A few patients experienced minor adverse reactions such as headaches, blurred vision, nausea, and vomiting, which were alleviated after symptomatic intervention. The overall incidence of adverse reactions in patients treated with Chuanjin Qinggan decoction combined with SSRIs was lower than that in patients treated with SSRIs alone ( $P < 0.05$ ) (Table 4).

## DISCUSSION

In addition to the core symptoms of depression such as low mood, reduced willpower, and reduced interest, patients with depression also have a severe inferiority complex accompanied by varying degrees of memory loss, sluggish thinking, irritability, and refusal to eat[15]. If the psychological state of a patient with depression cannot be improved for an extended period, the development of severe depression may lead to self-mutilation or even suicide. In recent years, with the development of social psychology, people have begun to pursue comprehensive physical and mental health. Given the negative effects of depression on patients' physiology and psychology, the treatment of depressive symptoms in patients with herpes zoster combined with depression is necessary to improve their well-being. Simultaneously, the treatment of depressive symptoms in patients with herpes zoster and depression can also reduce the burden on their families and society. Therefore, society and most medical workers attach great importance to the treatment of depressive symptoms in patients with herpes zoster combined with depression.

To understand the therapeutic effects of different treatment schemes in patients with herpes zoster complicated by depression, the clinical data of 86 patients were retrospectively analyzed. The results showed that although both treatment regimens could achieve efficacy, patients treated with Chuanjin Qinggan decoction combined with SSRIs showed more significant improvement in depression and a greater increase in DA and 5-HT levels after treatment compared to those treated with SSRIs alone. SSRIs exert antidepressant effects by inhibiting the resorption of 5-HT by the presynaptic membrane, and their efficacy in treating depression has been confirmed. The depressive symptoms of patients treated with SSRIs in this study also improved, similar to the results of previous studies. Findling *et al*[16]

**Table 1 Clinical characteristics of study subjects [*n* (%)], *M* (*P*<sub>25</sub>, *P*<sub>75</sub>)**

Clinical characteristics	Western medicine ( <i>n</i> = 43)	Combination ( <i>n</i> = 43)	$\chi^2/t$	<i>P</i> value
Sex			0.427	0.514
Man	26 (60.50)	23 (53.50)		
Woman	17 (39.50)	20 (46.50)		
Age (yr)	58.53 ± 5.16	59.12 ± 5.04	-0.528	0.599
Herpes zoster disease course (d)	5.00 (4.00, 6.00)	5.00 (4.00, 6.00)	-0.317	0.751
Residence			0.187	0.665
Town	19 (44.20)	21 (48.80)		
City	24 (55.80)	22 (51.20)		
Years of education			0.466	0.792
< 9	8 (18.60)	10 (23.30)		
9-12	24 (55.80)	21 (48.80)		
> 12	11 (25.60)	12 (27.90)		

**Table 2 The pain scores between the two groups, *M* (*P*<sub>25</sub>, *P*<sub>75</sub>)**

Group	Pre-treatment	Post-treatment	<i>Z</i>	<i>P</i> value
Western medicine ( <i>n</i> = 43)	7.00 (6.00, 8.00)	4.00 (4.00, 5.00)	-6.801	< 0.001
Combination ( <i>n</i> = 43)	7.00 (6.00, 8.00)	4.00 (3.00, 4.00)	-7.960	< 0.001
<i>Z</i>	-0.448	-3.825		
<i>P</i> value	0.654	< 0.001		

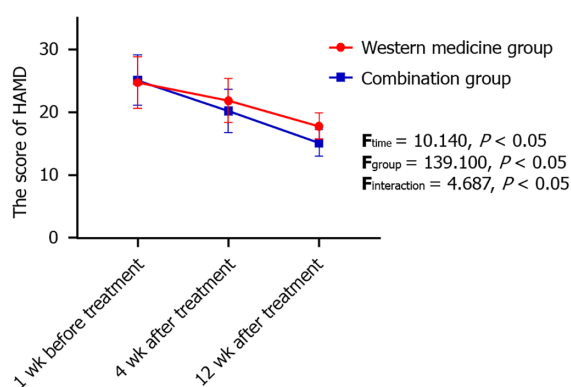
**Table 3 Effectiveness of herpes zoster treatment, *n* (%)**

Group	Remarkable effect	Effective	Ineffective
Western medicine ( <i>n</i> = 43)	11 (25.58)	22 (51.16)	10 (23.26)
Combination ( <i>n</i> = 43)	19 (44.19)	18 (41.86)	6 (13.95)
<i>Z</i>	-2.144		
<i>P</i> value	0.032		

**Table 4 Comparison of adverse reactions produced by different treatment regimens, *n* (%)**

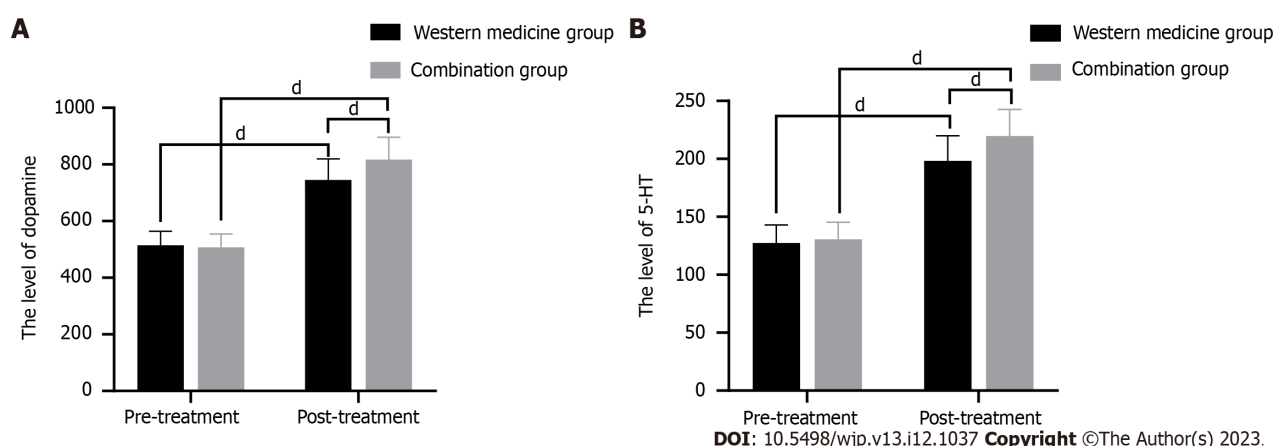
Group	Headache	Blurred vision	Nausea	Emesis	Others	Total
Western medicine ( <i>n</i> = 43)	5 (11.63)	2 (4.65)	6 (13.95)	3 (6.98)	3 (6.98)	17 (39.53)
Combination ( <i>n</i> = 43)	2 (4.65)	1 (2.33)	4 (9.30)	1 (2.33)	3 (6.98)	8 (18.60)
$\chi^2$						4.568
<i>P</i> value						0.033

reported that SSRIs can achieve good efficacy in the treatment of depression in adolescents and adults. Fagiolini *et al*[17] also reported that SSRIs could improve depressive symptoms in patients with severe depression. DA is the most abundant catecholamine neurotransmitter in the brain (accounting for approximately 80% of the total). It controls various functions, such as motor activity, cognition, emotion, food intake, and endocrine regulation. Diseases such as Parkinson's disease, schizophrenia, and addictive behavior are all related to dopaminergic system dysfunction[18,19]. Abnormal function of the serotonin system is closely related to loss of appetite, sleep disorders, decreased activity, sexual dysfunction, endocrine dysfunction, depression, and anxiety[20]. Chuanjin Qinggan decoction is mainly composed of Ligusticum chuanxiong Hort, Curcuma, Sedum rosea, and other drugs, among which Ligusticum chuanxiong Hort has

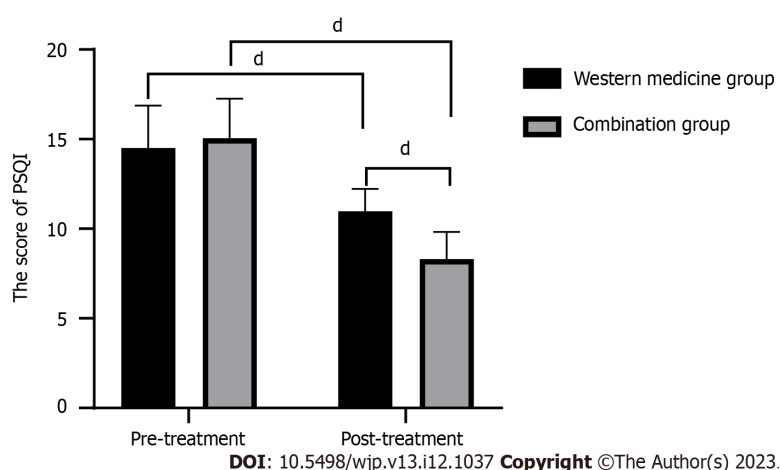


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**Figure 1** Depressive state of both groups of patients at different times. HAMD: Hamilton Depression Scale.



**Figure 2** Effects of different treatment regimens on neurotransmitter levels of patients. A: Dopamine level; B: 5-hydroxytryptamine level. <sup>d</sup> $P < 0.0001$ . 5-HT: 5-hydroxytryptamine.



**Figure 3** Effect of different treatment schemes on the sleep quality of patients. <sup>d</sup> $P < 0.0001$ . PSQI: Pittsburgh Sleep Quality Index.

antioxidant, anticoagulant, anti-tumor, anti-inflammatory, analgesic, microcirculation improvement, anti-aging, antidepressant, anti-radiation, and other effects[21]. Curcuma can regulate neurotransmitters, regulate neuroendocrine function, protect neurons, and inhibit neuroinflammation[22]. Salidroside, an effective component of *Sedum rosea*, has anti-fatigue, antidepressant, immune-enhancing, and anti-tumor properties[23]. There is a synergistic effect between the active ingredients in Chuanjin Qinggan decoction which helps to improve the depressive state of patients by reducing neurological damage and providing raw materials and energy for protein and nucleic acid synthesis in the brain tissue.

In addition, this study also found that patients treated with Chuanjin Qinggan decoction combined with SSRIs experienced less pain, better treatment efficacy for herpes zoster, better sleep quality, and a lower incidence of adverse reactions compared to those treated with SSRIs alone. These results suggest that the treatment scheme of Chuanjin Qinggan decoction combined with SSRIs can not only significantly improve the depressive state of patients but also improve the treatment of herpes zoster. Chronic pain is an adverse subjective and emotional experience with attributes in multiple dimensions, including sensory recognition, emotional motivation, and cognitive evaluation. Chronic pain increases the psychological burden on patients and causes negative emotions such as disgust, anxiety, and depression. The physical and mental suffering of patients with herpes zoster and depression is severe. Psychological state has a reverse regulatory effect on physiological state, and a good psychological state can improve the effect of treatment for physiological diseases. Shahimi *et al*[24] pointed out in their study that a good psychological state can reduce the risk of falls in older adults and the risk of cardiovascular and cerebrovascular diseases. In this study, the two groups of patients received eight weeks of drug treatment, and the symptoms of herpes zoster and depression significantly improved. However, this study has certain limitations. Specifically, the sample size of this study is small and it comes from a single research center, which may result in selection bias. Further studies with larger samples or joint studies with other centers are needed to confirm the reliability of the results.

## CONCLUSION

This study retrospectively analyzed the clinical data of patients with herpes zoster complicated by depression and found that different treatment schemes had different therapeutic outcomes. Patients treated with Chuanjin Qinggan decoction combined with SSRIs experienced less pain, better treatment efficacy for herpes zoster, more significant improvement in depression, a greater increase in DA and 5-HT levels, better sleep quality, and a lower incidence of adverse reactions compared to those treated with SSRIs alone. The overall curative effect of the Chuanjin Qinggan decoction combined with SSRIs was better than treatment with SSRIs alone.

## ARTICLE HIGHLIGHTS

### Research background

The physical and mental suffering of patients with herpes zoster combined with depression is significant. Although traditional Western medicine can alleviate the depressive symptoms in patients to a certain extent, it also causes many adverse reactions. There remains a need to identify drugs with high clinical safety that can effectively improve the depressive symptoms in patients with herpes zoster combined with depression.

### Research motivation

To search for safe drugs that can effectively improve the depressive symptoms of patients with herpes zoster combined with depression, and to provide references for the formulation and modification of the treatment plan for herpes zoster combined with depression.

### Research objectives

We analyzed the value of Chuanjin Qinggan decoction combined with a serotonin- selective reuptake inhibitor in the treatment of patients with herpes zoster complicated by depression.

### Research methods

We retrospectively analyzed depression status, treatment effect, degree of pain, neurotransmitter levels, sleep quality, and adverse reactions in patients with herpes zoster complicated by depression who received different treatment schemes.

### Research results

Compared with patients treated with selective serotonin reuptake inhibitor (SSRIs) alone, patients treated with Chuanjin Qinggan decoction combined with SSRIs showed a greater improvement in depression after treatment, and the incidence of adverse reactions was lower.

### Research conclusions

The treatment scheme of the Chuanjin Qinggan decoction combined with SSRIs can improve the depressive state of patients with herpes zoster complicated by depression, and improve the effect of treatment for herpes zoster without increasing the risk of adverse reactions.

### Research perspectives

In the future, the specific mechanism of Chuanjin Qinggan decoction in the treatment of herpes zoster complicated by depression should be clarified through cell or animal experiments, to provide references for further improving the therapeutic effect.

## FOOTNOTES

**Co-first authors:** Yi-Nan Wang and Meng-Meng Shi.

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