

Study on the Synergistic Effect of Chaihu Shugan San and Liuzijue in Treating Depression: Traditional Chinese Medicine Formula

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Zeng *et al.*: Effect of Chaihu Shugan San and Liuzijue in Treating Depression

To explore the synergistic effect of traditional Chinese medicine formula Chaihu Shugan and the liuzijue of health preservation on the treatment of depression patients. 75 patients with depression were randomly assigned to the ordinary group, control group, and treatment group through Excel, with 25 people in each group randomly assigned ordinary group selected theoretical knowledge related to depression for dissemination and treatment. Control group used the liuzijue practice of health preservation to treat depression patients, requiring 60 min of exercise every afternoon, three times a week. The treatment group used traditional Chinese medicine Chaihu Shugan San combined with the liuzijue practice to treat depression patients. The liuzijue practice for health preservation requires 40 min of exercise in the morning and 40 min in the afternoon every day, a total of 80 min, seven times a week. Chinese medicine Chaihu Shugan San requires taking 2 doses daily, once in the morning and once in the evening. Three groups were quantitatively evaluated using the Hamilton 17 item depression scale to analyze and compare the statistical differences and clinical efficacy among the ordinary group, control group, and treatment group after intervention. The traditional Chinese medicine formula Chaihu Shugan San combined with the liuzijue practice for health preservation in the treatment of depression is significantly superior to the ordinary group and control group ($p < 0.01$), and the control group was significantly superior to the ordinary group ($p < 0.05$). The traditional Chinese medicine formula Chaihu Shugan San combined with the liuzijue practice of health preservation has a good therapeutic effect on depression.

Key words: Traditional Chinese medicine formula, Chaihu Shugan San, Liuzijue, depression, fatigue, cognitive behavior

Patients with long-term physical illnesses have a risk of depression that is 3-4 times higher than ordinary citizens, accounting for 63.2 % globally, leading to a gradual increase in medical costs^[1]. The World Health Organization estimates that as of March 31, 2023, 5 % of adults worldwide suffer from depression, and more women than men are affected by depression. In severe cases, depression can lead to suicide^[2]. Some scholars pointed out that persisting in taking antidepressants is the main factor in the treatment of depression^[3]. For example, statins can protect the nervous system and reduce the risk of depression^[4]. However, some studies have also shown that antidepressants are

highly dependent and have large side effects, such as sertraline. After taking the drug, the sequelae are very obvious (headache, vomiting and fatigue). Scholars have also used non pharmacological methods such as cognitive behavior, control training, mindfulness based cognition, and physical exercise (such as Tai Chi, fitness qigong, aerobic exercise, yoga, etc.) to treat depression patients. Although there is a therapeutic effect, the treatment effect is slow. Without scientific guidance on physical exercise, it can easily cause physical harm. Some scholars pointed out that from the perspective of toxicology, there are many drugs to treat depression in modern medicine, such

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as hypnotic, fluoxetine, sertraline, paroxetine, etc., but these drugs are not only difficult to cure, most of them have certain side effects and use taboos, and long-term use will lead to drug resistance and cause some harm to the physical and mental health of patients, this is consistent with the studies of Anderson *et al.*^[5] and Readdean *et al.*^[6] Recent studies have shown that during and after COVID-19, citizens experience higher levels of anxiety, depression, and stress^[7-13]. A large amount of research has been conducted on the treatment of depression with drugs and non-drugs, but through sorting out, it has been found that drug treatment has a high risk of sequelae, while non-drug treatment, although effective, does not have ideal treatment effects. The difference between this study and previous studies is that it uses traditional Chinese medicine prescriptions. Some scholars have shown from a clinical medical perspective that traditional Chinese medicine has good therapeutic effects, with relatively safe medication, flexible treatment, and relatively low medical costs^[14]. Moreover, the drugs used in traditional Chinese medicine are mostly derived from related plants in nature, and have no harm or side effects on the human body. Therefore, in response to the current situation of high incidence of depression, this study used Chaihu Shugan powder combined with the Liuzijue practice of health preservation to treat depression patients. On the basis of previous research, this study abandons the side effects and injuries caused by drug and non-drug treatment, and from the perspective of traditional Chinese medicine, select the combination of traditional Chinese medicine formulas and health exercise interventions to treat depression patients. This has important practical significance and value for the treatment of depression. This study achieved good clinical results during the exploration process.

MATERIALS AND METHODS

Diagnostic criteria:

This study recruited a total of 75 patients with depression from January 3rd to January 8th, 2023. The experiment started from January 10th to March 10th, 2023, and lasted for a total of 8.6 w and 60 d. 75 patients with depression were randomly assigned to the Ordinary Group (OG), Control Group (CG), and Treatment Group (TG) through EXCEL, with 25 people in each group. The diagnostic criteria must all comply with the latest

version of the American Psychiatric Association (APA) classification and Diagnostic and Statistical Manual of Mental Disorders (DSM) released in May 2013, as well as the diagnostic criteria for depression in patients that fully comply with the Chinese Classification of Mental Disorders Version 3 (CCMD-3)^[15]. The research was approved by the academic integrity committee of Shenyang Sport University, and 75 participants signed the electronic informed consent form.

Treatment methods:

The OG uses theoretical knowledge related to the treatment of depression to spread and treat depression patients (sending relevant depression knowledge through WeChat groups). The CG used the liuzijue practice of health preservation to treat depression patients, requiring 60 min of exercise every afternoon, three times a week. The TG used traditional Chinese medicine Chaihu Shugan San combined with the liuzijue practice to treat depression patients. The liuzijue practice for health preservation requires 40 min of exercise in the morning and 40 min in the afternoon every day, a total of 80 min, seven times a week. Traditional Chinese medicine formula, Chaihu Shugan San-the root of Chinese *Thorowax* 15 g, dried tangerine peel 15 g, jujube 15 g, *Citrus aurantium* L 15 g, *Paeonia lactiflora* Pall 12 g, radix *Liquiritiae* 10 g, *Cyperus rotundus* 10 g, *Ligusticum wallichii* 10 g, immature wheat 30 g, for those with liver Qi stagnation, add 15 g of dried tangerine peel and 10 g of radix *Curcumae*. Qi Stagnation and phlegm stagnation, plus 10 g each of *Pinellia ternata* and *Magnolia officinalis* and add 6 g of Huang Lian and 15 g of bile grass to those with Qi depression and fire transformation. Add 20 g of *Codonopsis pilosula* to those with deficiency of both heart and spleen. For those with Yin deficiency and excessive fire, add 12 g of golden *Cypress*, 15 g of fructus corni, 30 g of prepared rhizome of *Rehmannia*, 15 g of Tuckahoe with pine, *Angelicae sinensis* radix, and *Polygala tenuifolia* Willd. Traditional Chinese medicine prescription requires taking 2 doses daily, once in the morning and once in the evening.

Exclusion and inclusion criteria:

Complies with DSM-5 and CCMD-3 standards; no physical illness; no drug allergy; exclude individuals who have taken psychiatric medication before treatment; exclude individuals with serious suicidal tendencies and exclude individuals with

organ and system diseases.

Scoring criteria and observation indicators for depression:

The Hamilton 17 Item Depression Scale (HAMD) was used for quantitative evaluation, with a score of 0-4 for each indicator (0 for no depression, and so on, with 4 for very severe depression). A total score of <7 is considered normal, a total score of 7-17 may indicate depression, and a total score of 17-24 is definitely indicative of depression total score >24 points for severe depression. Total score is an indicator that can better reflect the severity of the condition, that is, the milder the condition, the lower the total score, and the more severe the condition, the higher the total score. At the same time, the reduction rate is used as an observation indicator for the effectiveness of treating depression.

Score reduction rate=(Total score before treatment-total score after treatment)/total score before treatment)×100

Among them, if the score is reduced to below 7 points and the score reduction rate is 80 %, it is considered a cure. Most of the symptoms disappear, with a score reduction of more than 10 points, and a score reduction rate of 50 %-80 % is considered effective. If there is no change in symptoms and the score reduction rate is less than 25 %, it is considered invalid. After randomization, the OG, CG, and TG were subjected to anterolateral measurements, and after 8.6 w, the three groups were measured again to evaluate the changes in the level of depression among the respondents.

Total effective rate of treatment=(Cured+significantly effective) cases/total cases)×100 %

Statistical analysis:

The Statistical Package for the Social Sciences (SPSS) 24.0 version of statistical software was

used for data processing, with measurement data represented by mean±standard deviation and t-test performed on the measurement data. $p < 0.05$ shows statistically significant differences.

RESULTS AND DISCUSSION

The results in Table 1 show that the mean±standard deviation of age for males and females in OG were 31.58 ± 3.23 and 28.69 ± 2.84 , respectively, and the course of disease was 3.67 ± 1.49 and 3.31 ± 0.94 , respectively. The mean±standard deviation of CG age was 29.25 ± 3.10 and 31.15 ± 3.33 , respectively, and the Disease Course (DC) was 3.17 ± 1.85 and 4.46 ± 0.96 , respectively. The age mean±standard deviation of TG were 30.21 ± 3.98 and 29.00 ± 3.84 , respectively, and the DC was 4.50 ± 1.65 and 4.55 ± 1.36 , respectively. The results showed that among the three groups of DCs, the TG group had the highest average (4.50-4.55, females higher than males), followed by CG (3.17-4.46, males lower than females), and finally OG (3.31-3.67, males higher than females). There was no statistically significant difference in baseline data between OG, CG, and TG ($p > 0.05$), and the three groups were comparable.

By comparing the total effective rates of OG, CG, and TG (Table 2), in the OG group, there were 0 cured cases, 1 significantly improved case, 2 effective cases, and 22 ineffective cases, with a total effective rate of 4 %. In the CG group, there were 0 cured cases, 3 significantly improved cases, 11 effective cases, and 11 ineffective cases, with a total effective rate of 12 %. There were 0 cured cases, 22 significantly improved cases, 3 effective cases, and 0 ineffective cases of TG, with a total effective rate of 88 %. The above analysis of results indicates that the synergistic effect of traditional Chinese medicine Chaihu Shugan San and liuzijue practice in the treatment of depression patients shows that the total effective rate of TG is significantly higher than that of OG and CG.

TABLE 1: COMPARISON OF BASELINE DATA BETWEEN THREE GROUPS ($\bar{x} \pm s$)

Index		OG (n=25)	CG (n=25)	TG (n=25)	p
Age	Male (12)	31.58 ± 3.23	29.25 ± 3.10	30.21 ± 3.98	0.695
	Female (13)	28.69 ± 2.84	31.15 ± 3.33	29.00 ± 3.84	-
DC (year)	Male (12)	3.67 ± 1.49	3.17 ± 1.85	4.50 ± 1.65	0.5
	Female (13)	3.31 ± 0.94	4.46 ± 0.96	4.55 ± 1.36	-

TABLE 2: COMPARISON OF TOTAL HAMD SCORES AMONG THREE GROUPS OF PATIENTS BEFORE AND AFTER TREATMENT ($\bar{x}\pm s$)

Group (n=25)	Before treatment	After treatment	t	p
OG	21.20±3.53	20.64±4.76	0.545	0.21
CG	21.44±4.05	15.04±2.74	5.475	0.021
TG	20.56±4.06	7.96±1.62	18.99	0.001

By comparing the total effective rates of OG, CG, and TG (Table 3), in the OG group, there were 0 cured cases, 1 significantly improved case, 2 effective cases, and 22 ineffective cases, with a total effective rate of 4 %. In the CG group, there were 0 cured cases, 3 significantly improved cases, 11 effective cases, and 11 ineffective cases, with a total effective rate of 12 %. There were 0 cured cases, 22 significantly improved cases, 3 effective cases, and 0 ineffective cases of TG, with a total effective rate of 88 %. The above analysis of results indicates that the synergistic effect of traditional Chinese medicine Chaihu Shugan San and Liuzijue practice in the treatment of depression patients shows that the total effective rate of TG is significantly higher than that of OG and CG.

Depression is a psychological disorder, also known as emotional disorder. At present, most of the causes of its onset are believed to be related to various social pressures, personal psychological trauma, bad personality, and genetic factors. Symptoms mainly include depression, mental retardation, decline in willpower activities, suicidal ideas and behaviors, somatic symptoms, and hypochondriasis^[16-19]. At this stage, the treatment of depression is mainly a drug, such as paroxetine hydrochloride tablets, amitriptyline hydrochloride tablets, imipramine hydrochloride tablets, fluvoxamine maleate tablets and trazodone. From the perspective of drug toxicology, many antidepressant drugs have large side effects and long drug treatment course, which lead to patients being unable to adhere to taking drugs for a long time, seriously affecting the physical and mental health of patients^[16-20]. From the perspective of traditional Chinese

medicine's syndrome differentiation and treatment, depression belongs to the category of "depression syndrome". In severe cases, it can be manifested as "hysteria syndrome" or "madness syndrome". Its common diseases are caused by the deficiency of both the heart and spleen, and the stagnation of liver qi. If left untreated this stage, the condition will further develop and deficiency syndrome may occur. Therefore, the treatment of depression should be fundamentally started, so it is necessary to nourish the heart, replenish the spleen, and relieve liver depression. Chaihu Shugan San is selected from the Chinese "Neijing" and "Mu Yu Da Zhi" is aimed at treating the method of soothing the liver and regulating qi. In traditional Chinese medicine formulas, Chaihu has the effects of soothing the liver, relieving depression, and elevating yang qi. Its main active ingredients, saponins and triterpenoids, have good effects in anti-depression, anti-liver injury, antipyretic, and analgesic effects. Xiangfu regulates qi and soothes the liver to relieve pain, Chuanxiong promotes blood circulation and qi circulation to relieve pain, and the combination of the two drugs can help Chaihu relieve the stagnation of the liver meridian, serving as an auxiliary medicine. Dried tangerine peel and *Citrus aurantium* L regulate qi circulation stagnation. *Paeonia lactiflora* Pall and *Liquiritia Glycyrrhiza* the blood and soften the liver, relieve pain slowly, and are all adjuvants. The function of licorice is to harmonize various herbs. The combination of various herbs plays the role of soothing the liver, promoting qi circulation, promoting blood circulation, and relieving pain, and regulate depression.

TABLE 3: COMPARISON OF TOTAL EFFECTIVE RATES OF TREATMENT AMONG THREE GROUPS OF PATIENTS (n=25, %)

Group (n=25)	Cure (case)	Significant effect (case)	Effective (case)	Invalid (case)	Total effective rate (%)
OG	0	1	2	22	1 (4)
CG	0	3	11	11	3 (12)
TG	0	22	3	0	22 (88)

The liuzijue of health preserving skill is a health preserving method with breathing as the main means. Its main function is to smooth the movement of the qi of the internal organs of the human body, and the ascending and descending of the qi between the internal organs are in a coordinated unity of opposites, thus ensuring that the human body continuously absorbs the substances needed for life activities from the nature, and through the gasification process, it can raise the purity and reduce the turbidity, absorb the essence, and excrete waste, Maintain the dynamic equilibrium of material metabolism and energy conversion, complete the metabolism of the whole body together, and promote the normal progress of life activities. The pronunciation of "Xu" in the liuzijue is mainly to dredge the liver meridian, release the turbid qi of the liver, and regulate liver function. The pronunciation of the word "He" is mainly to clear the heart meridian, release the turbid qi of the heart, and regulate heart function. The pronunciation of the word "Hu" is mainly to dredge the spleen meridian, release spleen and stomach qi, and regulate the function of the spleen and stomach. The pronunciation of the word "Si" is mainly to clear the lung meridians, release turbid qi from the lungs, and regulate lung function. The pronunciation of the word "Chui" is mainly to clear the kidney meridian, release turbid qi from the kidneys, and regulate kidney function. The pronunciation of the word "Xi" is mainly to unblock the Shaoyang meridians, regulate the upper, middle, and lower jiao, and regulate the overall qi flow^[21,22]. The synergistic effect of the traditional Chinese medicine Chaihu Shugan San and the liuzijue is precisely complementary, with internal regulation and external guidance to eliminate stagnant qi from the body and maintain a balance between the internal and external environment. The combination of the two can better treat patients with depression. The synergistic effect of traditional Chinese medicine Chaihu Shugan San and liuzijue is significantly more beneficial for treating depression patients than CG and OG. The synergistic effect of traditional Chinese medicine Chaihu Shugan San and the liuzijue, as well as the combination of internal and external treatment, is more conducive to the treatment of depression patients.

Research has found that the synergistic effect of traditional Chinese medicine formula Chaihu

Shugan San and liuzijue in treating depression patients is better than CG and OG, and CG has a significant effect than OG. By further comparing the total effective rates of the three groups, the total effective rate of TG reached 88 %, with 22 cases showing significant improvement, which is 19 cases higher than CG and 21 cases higher than OG. Therefore, the synergistic effect of traditional Chinese medicine Chaihu Shugan San and liuzijue can effectively improve the liver depression and qi stagnation in patients with depression, regulate their physical and mental health, and have no adverse reactions or side effects on patients with depression. It has certain promotion and application value in the treatment of depression. The main limitations of the study are the small sample size, insufficient representativeness, and difficulty in achieving blind observation. It is hoped that in future research, the sample size can be expanded to further explore traditional Chinese medicine ingredients and exercise interventions for treating depression, anxiety, or other mental disorders. This will provide effective clinical treatment plans for patients with related diseases worldwide and improve their physical and mental health.

Conflict of interests:

The authors declared no conflict of interests.

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