

Efficacy of Modified Baihe Dihuang Decoction Combined with Escitalopram in Treating Depression and Its Impact on Serum Levels of 5-HT and ACTH

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Abstract: *Objective:* To evaluate the therapeutic effects of Modified Baihe Dihuang Decoction combined with Escitalopram (ESC) in treating depression. *Methods:* A total of 200 patients with depression admitted to the hospital from May 2023 to May 2025 were selected and randomly divided into two groups using a random number table. The experimental group received combined treatment with Modified Baihe Dihuang Decoction and ESC, while the control group received ESC monotherapy. The therapeutic effects of the two groups were compared. *Results:* The total effective rate of the Hamilton Depression Rating Scale (HAMD) and the total effective rate of traditional Chinese medicine (TCM) syndromes in the experimental group were higher than those in the control group ($p < 0.05$). After 6 weeks of treatment, the cortisol (Cor) level in the experimental group was lower than that in the control group. The HAMD scores after 2, 4, and 6 weeks of treatment were lower in the experimental group than in the control group. The levels of 5-hydroxytryptamine (5-HT), adrenocorticotrophic hormone (ACTH), and corticotropin-releasing hormone (CRH) were better in the experimental group than in the control group, and the Treatment Emergent Symptom Scale (TESS) score was lower in the experimental group than in the control group ($p < 0.05$). *Conclusion:* Combined treatment with Modified Baihe Dihuang Decoction and ESC for patients with depression can improve clinical efficacy, alleviate TCM syndromes, reduce depressive symptoms, regulate neurotransmitter and hormone secretion, and exhibit high medication safety.

Keywords: Modified Baihe Dihuang Decoction; Escitalopram; Depression; Serum 5-HT; ACTH

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1. Introduction

Depression is a mental illness characterized by low mood and pessimism, which can have a long-term impact

on patients' physical and mental health and even lead to self-harm or suicidal tendencies. The primary treatment method for this disease is oral administration of Western medications, which can alleviate disease symptoms and reduce the incidence of adverse events^[1]. ESC is a first-line antidepressant drug that can regulate neurotransmitter levels, increase 5-HT secretion, and thereby correct depressive states. However, monotherapy with this drug can only achieve relatively good short-term efficacy, with numerous adverse reactions during long-term use and a tendency to develop drug dependence, presenting certain treatment limitations. Traditional Chinese medicine believes that the pathogenesis of depression is related to the nourishment deficiency of the heart and mind as well as heart and lung deficiency. The treatment principles include nourishing the lungs and heart, clearing heat and calming the mind, among others. Modified Baihe Dihuang Decoction can be selected for treatment. Based on this, this study selected 200 patients with depression to evaluate the efficacy of combined treatment with Modified Baihe Dihuang Decoction and ESC.

2. Materials and methods

2.1. General information

A total of 200 patients with depression admitted to the hospital between May 2023 and May 2025 were selected and divided by the random number table method. The experimental group consisted of 100 cases, including 45 males and 55 females, aged 12 to 75 years, with a mean age of (45.68 ± 5.17) years. The TCM syndromes were as follows: 44 cases of liver Qi stagnation, 19 cases of Qi stagnation transforming into fire, 10 cases of Yin deficiency and fire excess, 10 cases of deficiency of both the heart and spleen, 12 cases of internal disturbance of phlegm-heat, and 5 cases of liver depression transforming into fire. The marital status was as follows: 59 married cases, 30 unmarried cases, 5 divorced cases, and 6 widowed cases. The educational levels were as follows: 14 illiterate cases, 14 primary school cases, 26 junior high school cases, 12 senior high school cases, 19 junior college cases, and 15 undergraduate cases. In the control group, there were 36 males and 64 females, aged 15–85 years, with a mean age of (46.84 ± 5.20) years. The TCM syndromes were as follows: 45 cases of liver Qi stagnation, 19 cases of Qi stagnation transforming into fire, 9 cases of Yin deficiency and fire excess, 8 cases of deficiency of both the heart and spleen, 14 cases of internal disturbance of phlegm-heat, and 5 cases of liver depression transforming into fire. The marital status was as follows: 69 married cases, 27 unmarried cases, 2 divorced cases, and 2 widowed cases. The educational levels were as follows: 14 illiterate cases, 11 primary school cases, 22 junior high school cases, 11 senior high school cases, 22 junior college cases, and 20 undergraduate cases. The basic data of the two groups were compared, with $p > 0.05$.

2.1.1. Inclusion criteria

Diagnosed with depression according to the “Expert Consensus on Integrated Traditional Chinese and Western Medicine Diagnosis and Treatment of Depression (2020)”^[2]; HAMD score between 20 and 35 points; complete basic data; highly informed about the study.

2.1.2. Exclusion criteria

Presence of eating disorders and other diseases in the past six months; concurrent schizophrenia; suicidal tendencies in the past month; electroconvulsive therapy in the past six months; allergy to the study drugs; presence of cardiovascular or cerebrovascular diseases or metabolic diseases; pregnancy or lactation.

2.2. Methods

The control group received ESC monotherapy: The initial dosage was 5 mg once daily; after one week of medication, the dosage was increased to 10 mg twice daily, and treatment was continued for 4 weeks.

The ESC treatment method in the experimental group was the same as above, combined with Modified Baihe Dihuang Decoction treatment: Granules were selected, and the drug composition was as follows: Baihe (20 g), Yujin (10 g), Shengdihuang (20 g), Chenpi (10 g), Jiangbanxia (5 g), Fushen (10 g), Chaihu (10 g), and Xiangfu (5 g). The granules were dissolved and taken after breakfast and dinner 30 minutes later, with one dose each time, and treatment was continued for 4 weeks.

2.3. Observation indicators

(1) HAMD score

The HAMD includes five categories of factors such as weight loss, cognitive impairment, and anxiety somatization, with a total of 17 items. Each item is scored from 0 to 4 points. A score below 7 indicates no depression, and the degree of depression is positively correlated with the score.

(2) Neurotransmitter and hormone levels

Before and after treatment, 2 mL of fasting venous blood was collected, centrifuged for 10 minutes at a speed of 2500 r/min and a centrifugal radius of 8 r, and the levels of 5-HT, ACTH, Cor, and CRH were evaluated using an automatic biochemical analyzer.

(3) TESS score

Before and after treatment, the TESS scale was used, which includes 33 items such as excitement and agitation, nausea and vomiting, and constipation. Each item is scored from 0 to 4 points, with a total of 132 points. If a single item score is > 2 points, it is judged as having the corresponding adverse reaction. The severity of adverse reactions is positively correlated with the score.

2.4. Efficacy evaluation criteria

HAMD efficacy: Reduction rate = $(\text{HAMD score before treatment} - \text{HAMD score after treatment}) / \text{HAMD score before treatment} \times 100\%$. Recovery is defined as a reduction rate of HAMD exceeding 75%; marked improvement as a reduction rate between 50% and 75%; improvement as a reduction rate between 25% and 49%; and no improvement as a reduction rate below 25%.

According to the TCM Syndrome Score Scale, TCM syndrome efficacy is evaluated as follows: Reduction rate = $(\text{TCM syndrome score before treatment} - \text{TCM syndrome score after treatment}) / \text{TCM syndrome score before treatment} \times 100\%$. Recovery is defined as a reduction rate of TCM syndrome score exceeding 80%; marked improvement as a reduction rate between 50% and 80%; improvement as a reduction rate between 30% and 49%; and no improvement as a reduction rate below 30%.

2.5. Statistical analysis

The data were processed using SPSS 28.0 software. Measurement data were compared using *t*-tests, and count data were compared using chi-square tests. Statistical significance was defined as $p < 0.05$.

3. Results

3.1. Comparison of HAMD scores between the two groups

At different time points after treatment, the HAMD scores in the experimental group were lower than those in the control group ($p < 0.05$). See **Table 1**.

Table 1. Comparison of HAMD scores between the two groups [$\bar{x} \pm s$, points]

Group	Number of cases	Before treatment	After 2 weeks of treatment	After 4 weeks of treatment	After 6 weeks of treatment
Experimental group	100	29.67 \pm 3.22	14.88 \pm 2.61	11.06 \pm 1.64	10.33 \pm 1.26
Reference group	100	29.94 \pm 3.15	19.93 \pm 2.57	15.87 \pm 2.31	12.79 \pm 2.05
<i>t</i>		0.599	13.787	16.979	10.223
<i>p</i>		0.550	0.000	0.000	0.000

3.2. Comparison of neurotransmitter and hormone levels between the two groups

After 6 weeks of treatment, the Cor level in the experimental group was lower than that in the control group. At different time points after treatment, the levels of other neurotransmitters and hormones in the experimental group were superior to those in the control group ($p < 0.05$). See **Table 2** and **3**.

Table 2. Comparison of neurotransmitter and hormone levels between the two groups (5-HT and ACTH) [$\bar{x} \pm s$]

Group	Number of cases	5-HT (ng/mL)				ACTH (pmol/L)			
		Before treatment	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment	Before treatment	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment
Experimental group	100	86.54 \pm 6.14	89.02 \pm 3.34	91.46 \pm 3.41	95.12 \pm 5.11	8.58 \pm 3.86	7.10 \pm 1.51	10.56 \pm 0.44	10.68 \pm 1.32
Reference group	100	86.51 \pm 6.10	87.15 \pm 3.45	89.41 \pm 3.50	91.15 \pm 5.06	7.59 \pm 3.73	9.68 \pm 1.26	10.04 \pm 0.51	8.46 \pm 1.27
<i>t</i>		0.035	3.894	4.195	5.521	1.844	13.119	7.720	0.035
<i>p</i>		0.972	< 0.001	< 0.001	< 0.001	0.067	< 0.001	< 0.001	0.972

Table 3. Comparison of neurotransmitter and hormone levels between the two groups (Cor and CRH) [$\bar{x} \pm s$]

Group	Number of Cases	Cor (nmol/L)				CRH (pmol/L)			
		Before treatment	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment	Before treatment	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment
Experimental group	100	153.92 \pm 15.95	134.48 \pm 5.11	121.60 \pm 5.36	131.46 \pm 4.17	11.07 \pm 2.42	9.98 \pm 1.58	9.36 \pm 1.04	6.65 \pm 1.43
Reference group	100	157.37 \pm 15.18	133.73 \pm 5.40	122.73 \pm 5.30	149.12 \pm 2.36	10.57 \pm 2.55	11.44 \pm 1.66	10.92 \pm 1.10	10.03 \pm 1.68
<i>t</i>		1.567	1.009	1.499	36.857	1.422	6.371	10.305	15.320
<i>p</i>		0.119	0.314	0.135	< 0.001	0.157	< 0.001	< 0.001	< 0.001

3.3. Comparison of TESS scores between the two groups

At different time points after treatment, the TESS scores in the experimental group were all lower than those in the control group ($p < 0.05$). See **Table 4**.

Table 4. Comparison of TESS scores between the two groups [$\bar{x} \pm s$, points]

Group	Number of cases	2 weeks after treatment	4 weeks after treatment	6 weeks after treatment
Experimental group	100	13.65 \pm 2.74	14.53 \pm 2.85	16.12 \pm 2.91
Control group	100	19.22 \pm 3.45	20.56 \pm 3.74	22.04 \pm 3.42
<i>t</i>		12.643	12.824	13.183
<i>p</i>		0.000	0.000	0.000

3.4. Comparison of HAMD therapeutic efficacy between the two groups

The total effective rate of HAMD in the experimental group was higher than that in the control group ($p < 0.05$). See **Table 5**.

Table 5. Comparison of HAMD therapeutic efficacy between the two groups [n/%]

Group	Number of cases	Recovery	Markedly effective	Effective	Ineffective	Total effective
Test group	100	46	34	16	4	96.00% (96/100)
Reference group	100	42	30	16	12	88.00% (88/100)
χ^2						4.348
<i>p</i>						0.037

3.5. Comparison of therapeutic efficacy for TCM syndromes between the two groups

The total effective rate for TCM syndromes in the experimental group was higher than that in the control group ($p < 0.05$). See **Table 6**.

Table 6. Comparison of therapeutic efficacy for TCM syndromes between the two groups [n/%]

Group	Number of cases	Cure	Markedly effective	Effective	Ineffective	Total effective
Experimental group	100	45	38	14	3	97.00 (97/100)
Reference group	100	41	36	13	10	90.00 (90/100)
χ^2						4.031
<i>p</i>						0.045

4. Discussion

The main symptoms of depression include decreased energy, low mood, etc. The continuous progression of the condition can lead to severe symptoms such as delusions and hallucinations, thereby reducing the patient's quality of life^[3]. The pathogenesis of this disease is relatively complex, involving disorders such as hypothalamic-pituitary-adrenal axis dysfunction, gut microbiota imbalance, and neuroinflammatory

responses. The primary treatment approach involves oral administration of Western medications, with ESC being a commonly used drug. Derived from cyclic hydroptalide, ESC is an isomer of citalopram. It exerts a long-lasting blocking effect on the reuptake of 5-HT within central neurons and has low sensitivity to neurotransmitters such as dopamine, making it less likely to cause severe side effects after administration ^[4]. However, the long-term efficacy of ESC monotherapy is suboptimal, necessitating combination with traditional Chinese medicine (TCM) treatments.

According to TCM, depression is located in the liver and is a relatively common disease affecting the mind and orifices. Its causes include insufficient kidney Yang, brain dysfunction, and emotional stimuli, while its pathogenesis involves nourishment deficiency of the mind's residence and stagnation of phlegm, blood stasis, and Qi. Symptomatic treatments such as clearing heat and reducing fire, opening the orifices and resolving phlegm, and calming the mind and nourishing the heart are required ^[5]. Lily Bulb and *Rehmannia* Decoction (modified) is a classic formula for this disease, with lily bulb and fresh *rehmannia* root as the sovereign herbs. Lily bulb has the effects of clearing the heart and calming the mind, moistening the lungs and nourishing Yin, etc.; fresh *rehmannia* root has the effects of nourishing Yin and promoting saliva production, nourishing the lungs and supplementing Qi, and clearing heat and cooling the blood, etc. ^[6]. The ministerial herbs are turmeric tuber, *poria* with hostwood, *bupleurum* root, and *cyperus rhizome*. Turmeric tuber can relieve depression and move Qi, open the orifices and clear the heart; *poria* with hostwood can calm the mind and soothe the nerves; *bupleurum* root and *cyperus rhizome* can open the orifices, soothe the liver and relieve depression. The assistant herbs are dried tangerine peel and *pinellia* tuber prepared with ginger. The former has the effects of drying dampness and resolving phlegm, strengthening the spleen and regulating Qi, etc.; the latter has the effect of resolving phlegm and stopping vomiting. The combined use of these herbs can exert therapeutic mechanisms such as calming the mind, relieving depression, and nourishing Yin ^[7].

The results showed that at different time points after treatment, the HAMD scores of the experimental group were lower than those of the reference group; after 6 weeks of treatment, the Cor levels of the experimental group were lower than those of the reference group, and the levels of other neurotransmitters and hormones in the experimental group were superior to those of the reference group at different time points after treatment ($p < 0.05$). The analysis suggests that lily bulb is rich in alkaloids and lily bulb polysaccharides, which can exert antidepressant, neuroprotective, and sedative effects; fresh *rehmannia* root contains catalpol and other components, which have a long-lasting antidepressant effect; *bupleurum* root can act on multiple signaling pathways and regulate the secretion of various hormones such as Cor and CRH; turmeric tuber can act on multiple signaling pathways such as calcium ions and cyclic adenosine monophosphate, thereby regulating the secretion level of 5-HT; *cyperus rhizome* can act on the depressive metabolic pathway and has a strong regulatory mechanism on the release process of neurotransmitters ^[8]. Combined with ESC, it can enhance the antidepressant effect, allowing normal secretion of neurotransmitters and various hormones in patients ^[9]. At different time points after treatment, the TESS scores of the experimental group were lower than those of the reference group ($p < 0.05$). The analysis suggests that integrated traditional Chinese and Western medicine treatment can reduce the dosage of ESC, prevent the accumulation of drug components, and thereby alleviate adverse reactions after medication. In addition, Lily Bulb and *Rehmannia* Decoction is a pure TCM preparation with low drug toxicity. It can eliminate the pathogenesis in a relatively short time, thereby shortening the course of treatment and reducing treatment side effects ^[10]. The HAMD efficacy and TCM syndrome efficacy of the experimental group were higher than those of the reference group ($p < 0.05$). The analysis suggests that Lily

Bulb and *Rehmannia* Decoction (modified) have a long-lasting antidepressant effect, can accelerate the speed of nerve regeneration, protect brain neurons, regulate the secretion level of neurotransmitters, prevent the massive apoptosis of dopaminergic neurons, improve the patient's neurological function, and thereby promote the improvement of the condition^[11]. Combined with Western medications, it can exert a synergistic mechanism and act on brain neurons through multiple targets, thereby enhancing the efficacy and significantly improving the overall treatment response rate of patients.

5. Conclusion

In conclusion, the combined treatment of Lily Bulb and *Rehmannia* Decoction (modified) and ESC for patients with depression has a good effect. It can improve the secretion status of 5-HT and ACTH, effectively exert an antidepressant effect, and have few side effects after treatment. It can be used as a common treatment plan for patients with this disease.

Disclosure statement

The authors declare no conflict of interest.

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