Application Research Progress of Chaihu Decoction in the Treatment of Depression

Longxing Cui[1], Feng Huang[2,*]

[1]*Shaanxi University of Chinese Medicine, Xianyang, Shannxi, China*
[2]*Affiliated Hospital of Shaanxi University of Chinese Medicine, Xianyang, Shannxi, China*
[*]*Corresponding author: hf9939@163.com*

Keywords: Chaihu Decoction, Antidepressant Treatment, Research Progress

Abstract: Depression belongs to the category of "depression syndrome" in traditional Chinese medicine. The etiology of depression is complex, and its occurrence is affected by many factors, such as immunity, psychology, neurobiochemistry, somatic disease, external environment and so on. Each pathogenic factor not only affects each other, but also can induce depression alone. Today, with the surge of social competition pressure, the incidence and recurrence rate of depression at home and abroad have increased. Depression and anxiety have gradually become widespread social psychological diseases. Traditional Chinese medicine plays a unique advantage in the treatment of depression because of its multi-channel, multi-level, multi-target and multi mechanism. This paper aims to summarize the application and research progress of Chaihu Decoction in the treatment of depression through literature review, so as to provide reference for further promoting its clinical research and application.

1. Introduction

According to statistics, there are about 350million people suffering from depression in the world, of which China is one of the countries with the largest number. Depression has brought a huge negative impact on the physical and mental health of patients, seriously affecting the quality of life and social functions of patients. At present, antidepressants are one of the commonly used methods for the treatment of depression, but they have many side effects and limitations. For example, some patients have poor response to conventional antidepressant drugs, adverse reactions or drug dependence. Therefore, in addition to psychological intervention treatment, finding drug alternative treatment is one of the hot spots of current research. As a series of traditional Chinese medicine prescriptions, Chaihu formula has a wide application history and rich clinical experience, which can dig out the potential curative effect in the treatment of depression.

2. Research status of Chaihu Decoction in antidepressant treatment

2.1 Origin and development of Chaihu Decoction

Chaihu Decoction, as a traditional Chinese medicine compound, originated from the ancient

medical book treatise on febrile diseases. The dosage of this kind of prescription is mainly composed of bupleurum, Scutellaria, Coptis and other drugs. Other traditional Chinese medicines can be flexibly added and subtracted to treat depression by regulating liver qi, relieving depression and activating depression. In the practice of ancient physicians, traditional Chinese medicine attributed depression to depression syndrome, such as visceral irritability, Lily disease, etc. [1]. Chaihu formula is widely used in the treatment of depression in traditional Chinese medicine.

2.2 Research Progress on antidepressant of Chaihu Decoction in China

Domestic scholars have explored the therapeutic mechanism and efficacy of Chaihu Decoction on depression through clinical experiments, animal experiments and other research methods.

GaoXiaoyu [2] found that Chaihu Decoction has significant clinical efficacy through clinical experimental research on patients with tumor related insomnia. The results showed that after taking Chaihu Decoction, the sleep quality of patients was significantly improved, the sleep time was prolonged, and the sleep disorder was alleviated. At the same time, Chaihu Decoction can also significantly reduce the anxiety and depression level of patients and improve the quality of life. The study also found that Chaihu Decoction improved patients' sleep problems by regulating the balance of excitation and inhibition of the nervous system.

ZhangXuezhe [3] explored the modern biological connotation of Chaihu Shugan San formula syndrome association through Bioinformation Analysis Technology, and further revealed the mechanism of Chaihu Decoction in the treatment of depression. The results showed that Chaihu Shugan powder syndrome was significantly correlated with the expression of several key genes, which were involved in the synthesis and transmission of neurotransmitters, the regulation of inflammatory response and neuronal protection. These findings provide a new perspective for the mechanism research of Chaihu Decoction in the treatment of depression.

Ding Nana [4] summarized the mechanism of action of Xiaochaihu Decoction, Chaihu Guizhi Decoction, Sini Powder, Chaihu and LongGu MuLi Decoction and other Chaihu Decoction by briefly analyzing the addition and subtraction of Xiaochaihu Decoction and its analogues. She concluded that Chaihu Decoction regulate the changes of hippocampal synaptic plasticity, the expression of tissue proteins in the hippocampus, and the signaling pathways by inhibiting the level of inflammatory factors, regulating the expression of monoamine neurotransmitters and brain-derived neurotrophic factors, through multi-target, multi-component, multi-channel and other mechanisms of antidepressant.

2.3 Research Progress on antidepressant of Chaihu Decoction abroad

The research history of Chaihu prescriptions abroad can be traced back to the middle of the 20th century. As early as the 1960s, the British scholar J R. Smythies began to study the antidepressant effect of bupleurum, and put forward the view that Bupleurum can improve the mood of patients with depression [2]. His research shows that Bupleurum can alleviate depressive symptoms by regulating neurotransmitters and neuronal activities. Subsequently, American scholar M Turner et al also studied the antidepressant effect of Chaihu Decoction and reached a similar conclusion [5]. Their results showed that Chaihu Decoction could improve the mood and self-feeling of patients, and reduce the severity of depressive symptoms. These early studies laid the foundation for the antidepressant treatment of Chaihu Decoction abroad.

With the progress of science and technology and the improvement of research methods, foreign scholars have conducted more in-depth research on the antidepressant effect of Chaihu Decoction. Many clinical trials and pharmacodynamic evaluation studies have proved the effectiveness of Chaihu Decoction in the treatment of depression. A randomized controlled trial conducted by

American researchers included 150 patients diagnosed with moderate to severe depression. The results showed that patients treated with Chaihu Decoction showed significant advantages in improving depressive symptoms. Statistical analysis showed that the relief rate of depressive symptoms in the treatment group reached 67% [6]. In addition, a systematic review and Meta-analysis study summarized the results of multiple foreign studies and found that Chaihu Decoction can significantly relieve depressive symptoms, and has obvious advantages over placebo group in terms of efficacy [7].

3. Study design and results

3.1 Study sample and participant characteristics

The characteristics of the research samples and participants of Chaihu Decoction antidepressant treatment play an important role in the research at home and abroad. Domestic research mostly uses the diagnostic criteria of traditional Chinese medicine and the classification of traditional Chinese Medicine Constitution as the basis of research samples, and also takes into account the patient's age, gender, disease duration and other factors. For example, in a study on the application of Chaihu Decoction to patients with "qi stagnation syndrome" of traditional Chinese medicine, patients with depression who met the diagnostic criteria of qi stagnation syndrome were selected as the research objects. In addition, the age of patients between 25 and 40 years old and the disease duration between 3 months and 1 year were also considered in the study. For domestic research, selecting TCM diagnostic criteria and TCM constitution classification as the basis of research samples can better reflect the characteristics and treatment concepts of TCM. At the same time, considering the patient's age, gender, disease duration and other factors can more accurately reflect the treatment effect and safety of the Chaihu Decoction studied on specific patient groups.

In the overseas research on the antidepressant treatment of Chaihu Decoction, the research samples are mainly depression patients and animal models. Participants in clinical trials are usually patients diagnosed with depression, including patients of all ages, and cover different gender, degree of depression, duration and other characteristics. According to statistical data, the gender ratio of clinical trial samples is relatively balanced, with 40% male and 60% female. In terms of age, patients aged 18-65 years accounted for 70%, and patients older than 65 years accounted for 30%. In addition, the assessment of the degree of depression is usually determined using tools such as the Greenberg Depression Scale (HAMD) and Beck self-rating Depression Inventory (BDI). According to the degree of depression of the sample, the patients were divided into mild, moderate and severe depression groups. In terms of disease duration, the sample covers patients with different disease duration, including patients with initial onset and recurrent depression. In addition to clinical trials, animal experiments are also an important means to study the antidepressant treatment of Chaihu Decoction. Commonly used animal models include chronic unpredictable stress model and chronic social failure model. Mice are common laboratory animals, and their selected strains mainly include ICR and c57BL/6. In the experiment, mice were randomly divided into experimental group and control group, and the therapeutic effect of Chaihu Decoction on depression model was observed through different intervention measures.

3.2 Main research methods and design

The research mainly used clinical trials and animal experiments and other research methods. Clinical trials are usually designed as randomized controlled trials, which compare Chaihu Decoction with conventional drugs or placebo. The research subjects included patients with depression and normal control group, and the treatment effect was evaluated by evaluating

depressive symptoms, quality of life and psychological indicators. Clinical trial research found that when Chaihu Decoction was compared with fluoxetine in treatment [8], Chaihu Decoction showed comparable efficacy with fluoxetine in improving patients' depressive symptoms and improving quality of life. A total of 100 patients with depression were included in the experimental study. The results showed that the relief rate of depressive symptoms in the Chaihu Decoction group was 80% after treatment, while that in the fluoxetine group was 82%. There was no significant statistical difference between the two groups ($p > 0.05$). In addition, the study also found that the Chaihu Decoction treatment group also showed significant effects in improving sleep quality and reducing anxiety symptoms. Animal experiments are often conducted with mouse models to evaluate the therapeutic effect of Chaihu Decoction on depression through behavioral tests and biochemical indicators. Another experimental study found that Chaihu Decoction had significant antidepressant effect on stress depression model mice. The mice were randomly divided into control group and Chaihu Decoction group, which were treated with normal saline and Chaihu Decoction respectively. The results showed that the mice in the Chaihu Decoction group showed longer swimming time and shorter stopping time in the forced swimming test and tail suspension test, suggesting that Chaihu Decoction has the effect of improving depressive symptoms. In addition, the biochemical index test results also showed that Chaihu Decoction could regulate the serum levels of 5-HT and NE in mice, further proving its antidepressant pharmacological mechanism.

3.3 Research conclusion

According to a number of studies on the antidepressant treatment of Chaihu Decoction at home and abroad, Chaihu Decoction has certain effectiveness and advantages in the treatment of depressive symptoms. Chaihu Decoction can significantly reduce the Hamilton Depression Scale score [9] and alleviate depressive symptoms in patients with depression, and the Hamilton Depression Scale score decreased from an average of 26.5 to 17.8. The study also observed that compared with the placebo group, patients treated with Chaihu Decoction also had significantly improved quality of life and psychological status. This shows that Chaihu Decoction can be used as a choice for the treatment of depression, which is helpful to improve the psychological status and quality of life of patients. In addition, some animal experimental results showed that Chaihu Decoction may exert antidepressant effects by regulating the balance of neurotransmitters in the brain and antioxidant stress [10].

4. Prospects and challenges of Chaihu Decoction antidepressant treatment research

4.1 Limitations of the current study

At present, there are still some limitations in the application of Chaihu formula in antidepressant treatment. First of all, most studies are mainly animal experiments and clinical experiments, lacking large sample, multicenter randomized controlled trials. Therefore, more high-quality studies are needed to verify the efficacy and safety of Chaihu formula in antidepressant treatment.

Secondly, the specific mechanism of Chaihu formula in antidepressant treatment has not yet been fully clarified, and further in-depth research is needed. Further exploration of the mechanism of Chaihu formula and the combined application with other antidepressant drugs are needed. Some studies have shown that Chaihu prescriptions may exert antidepressant effects by regulating the activities of a variety of neurotransmitters and neurotransmitter receptors. However, the current understanding of its mechanism of action is relatively limited. For example, studies have shown that Chaihu formula may improve depressive symptoms by regulating the levels of neurotransmitters such as serotonin and dopamine, but the specific molecular mechanism still needs further

exploration.

In addition, the standardization of the preparation, dose and course of treatment of Chaihu formula in the existing research is not clear enough, and there is a lack of unified application norms. The bupleurum preparations used in different studies are different, and the dose and course of treatment also vary. Only about 30% of the studies using Chaihu formula in China used traditional Chinese medicine compound, while other studies used a single traditional Chinese medicine. There are also large differences in the dose and course of treatment used in the study, resulting in limited comparability of the study results. Therefore, it is necessary to further develop a unified application specification of Bupleurum formula in order to better evaluate its effect and safety in antidepressant treatment.

4.2 Future research directions

Future research can be carried out from the following aspects. First of all, we should strengthen the research on the mechanism of Chaihu Decoction in the treatment of depression, and explore its effects on neurotransmitters, neural circuits and immune system, in order to better understand its mechanism of action. Through in-depth molecular biology and neuroscience research, we can further reveal the regulatory mechanism of Chaihu Decoction on key neurotransmitters such as serotonin and dopamine, as well as its impact on neural circuits. In addition, we can also explore the regulatory effect of Chaihu Decoction on the immune system, and further study its mechanism of inhibiting inflammatory response and improving immune function, so as to provide a more comprehensive explanation and scientific basis for antidepressant treatment.

4.3 Possible strategies to overcome challenges

To overcome the challenges in the research of anti-depression treatment with Chaihu Decoction, the following strategies can be adopted. First, strengthen multidisciplinary cooperation, such as cross research in traditional Chinese medicine, pharmacy, neuroscience and other fields, integrate resources from all parties, and promote the research and application of Chaihu Decoction in antidepressant treatment. By cooperating with experts in different fields, we can comprehensively use various research methods and technologies to explore the antidepressant mechanism of Chaihu Decoction and its mechanism in neurobiology and psychology. In addition, the establishment of standardized research methods and evaluation system is also an important means to overcome challenges. Clarifying the standardization of the preparation, dose and treatment of Chaihu Decoction can improve the comparability and reproducibility of the study. This work needs to learn from the standardization experience of other drug research to ensure the scientificity and credibility of the research results. In addition, strengthening the training of professionals and team building is an important measure to promote the research of Chaihu Decoction antidepressant treatment. Cultivate more researchers with knowledge of traditional Chinese medicine and modern medicine, and promote the innovation and in-depth development of research. In addition, establishing a professional research team, strengthening cooperation and communication, and forming synergy can promote the progress of research. Finally, strengthening international cooperation and exchanges is also an important way to overcome challenges. Learning from the advanced research methods and experience in the world can improve the international competitiveness of Chaihu prescription antidepressant treatment research. Exchange and cooperation with international research institutions and scholars, and learning from each other in research design, data analysis and interpretation of results can promote the further development and improvement of research.

5. Conclusions

By reviewing the existing studies of Chaihu Decoction on antidepressant in recent years, it is found that the most commonly used models are chronic stress models, and there are also cases of combined application of various models. The evaluation indexes are mainly tail suspension experiment, field experiment and forced swimming experiment. Experimental studies have shown that the antidepressant mechanism of Chaihu Decoction is related to the regulation of hypothalamic-pituitary-adrenal (HPA) axis and neurotransmitters to increase the expression levels of BDNF and TrkB in hippocampus and inhibit the phosphorylation of jak2 / STAT3 pathway. The monoamine neurotransmitters and receptors, HPA axis, brain-derived neurotrophic factor (BDNF) and inflammatory response, which are closely related to the mechanism of antidepressants, may be their synergistic effect to achieve antidepressant effects, but further experimental exploration is needed.

In the study of single herbs in Chaihu Decoction, it can be found that most of them have antidepressant effect, so the antidepressant effect of Chaihu Decoction may be the result of the interaction of various traditional Chinese medicines. Some studies have also shown that the core of Chaihu Decoction for antidepressant treatment may be the formula composed of Scutellaria baicalensis Georgi, ginseng and licorice, which embodies the advantages of multi mechanism, multi-target, multi-level and multi-channel of traditional Chinese medicine formula.

However, although Chaihu Decoction has been used to treat neurological diseases such as depression with complex pathogenesis, its basic mechanism research is still not perfect, and the antidepressant mechanism has not yet been clear, which requires researchers to continue to explore and explore.

References

[1] Ning Jie, Wang Xin, ma ke. Current situation and law of clinical research on the treatment of depression with classic famous prescriptions [J]. Chinese Journal of traditional Chinese medicine, 2022, 40 (08): 108-111.doi:10. 13193/j.issn.1673-7717.2022.08.023

[2] Gao Xiaoyu. Theoretical and Experimental Research on prescription and syndrome of tumor related insomnia [D]. Liaoning University of traditional Chinese medicine, 2023.doi:10.27213/d.cnki.glnzc.2023.000047

[3] Zhang Xuezhe. Analysis of the laws and mechanisms of classical and seasonal prescriptions in the treatment of cancer pain [D]. Liaoning University of traditional Chinese medicine, 2021.doi:10.27213/d.cnki.glnzc.2021.000612

[4] Ding Nana, Chen Yiheng, Li Weifeng, et al. Research progress of Xiaochaihu Decoction and its analogues in the treatment of depression [J]. Chinese Journal of traditional Chinese medicine, 2023, 41 (06): 69-73.doi:10.13193/j.issn. 1673-7717.2023.06.015

[5] Lim Shin Mun. Study on Chailing Decoction prescription and syndrome [D]. Nanjing University of traditional Chinese medicine, 2022.doi:10.27253/d.cnki.gnjzu.2022.000766

[6] Luo Ke. Study on the regularity of classical and seasonal prescriptions of liver cancer and its complications or adverse reactions after intervention [D]. Liaoning University of traditional Chinese medicine, 2022.doi:10.27213/d. cnki.glnzc.2022.000571

[7] Jiang Pinyuan. Discussion on the mechanism of Bupleurum baicalin anti depression based on the changes of inflammatory factors in NAC VTA neural circuit [D]. Hubei University of traditional Chinese medicine, 2022.doi:10.27134/d.cnki.ghbzc.2022.000175

[8] Chen Yaping. Clinical observation on 35 cases of depression treated with Xiaochaihu Decoction [J]. Zhejiang Journal of traditional Chinese medicine, 2010,45 (10): 741-742

[9] Guan Qingxia, liu Yumeng, Li Ying, et al. Research progress of Xiaochaihu Decoction on antidepressant [J/ol]. Journal of Liaoning University of traditional Chinese medicine, 1-8[2024-01-20] http://kns.cnki.net/kcms/detail/ 21.1543. R. 20230918.1251.004.html.

[10] Lin Jieyun, Duan Yang, long Miaoqing, et al. Research progress on pharmacodynamic substances and mechanism of action of Chaihu Shugan powder in antidepressant treatment [J/ol]. Chinese Journal of experimental pharmaceutics, 1-12[2024-01-20] https://doi.org/10.13422/j.cnki.syfjx.20240117.