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Protective Effect of Shengdi-Cogongrass Decoction on Patients with Blood Heat Psoriasis

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DY and YT conducted the experiments in this study. BS and YT contributed to the design and interpretation of the current study and wrote the article. All authors read, revised, and approved the final manuscript.

Key words
Shengdi-cogongrass decoction, Blood heat psoriasis, Clinical efficacy, Interleukin-6, Tumor necrosis factor-α, Conventional western medicine

ABSTRACT

Shengdi-cogongrass decoction (SCD) is a traditional Chinese medicine formula, mainly composed of raw *Rehmannia glutinosa* (RG) and lalang grass rhizome (LGR). However, little is known about the molecular pharmacological activity of Shengdi-cogongrass on blood heat psoriasis (BHP). This study aims to explore the clinical and protective efficacy of SCD on interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) levels in serum of patients with BHP. One hundred patients with blood fever psoriasis who were treated in our hospital from May 2020 to May 2023 randomly were selected as study subjects and included into an observation group (group SCD, n=50) and a control group (group CWM, n=50). The group CWM were treated with conventional western medicine, while the group SCD were treated with SCD. After one month, the clinical efficacy, IL-6 and TNF-α levels of the groups were compared. The results showed that the total effective rate was significantly higher in the group SCD than the group CWM ($P<0.05$). Moreover, the psoriasis area and severity index (PASI), four item itching questionnaire (FIIQ) scores, and the IL-6/TNF-α levels at 1 and 3 weeks of treatment were lower in the group SCD than the group CWM ($P<0.05$). The findings of this study support the protective effect of SCD in serum of patients with BHP through alleviating disease symptoms and reducing the expression level of inflammatory factors.

INTRODUCTION

Blood heat psoriasis (BHP), also known as acute simple psoriasis or acute erythematous scaling disease (Ogawa and Okada, 2020). According to relevant research surveys, globally, the prevalence of psoriasis is about 0.1%~3%, and the specific incidence rate of BHP lacks complete and consistent data (Singh and Easwari, 2021). For patients with this type of disease, oral medication, biological agents, and ultraviolet therapy are commonly used in clinical practice to regulate immune system function and improve disease symptoms (Wu *et al*., 2022).

In recent years, with the increasing proportion of BHP patients, research on the clinical treatment of patients with this disease has continued to deepen. Multiple studies have shown a close correlation between the development of this disease and the expression levels of interleukin-6 (IL-6) and tumor necrosis factor-α (TNF-α) (Lin *et al*., 2022). Patients with BHP may experience elevated levels of serum IL-6/TNF-α during the onset of the disease (Lian *et al*., 2020). IL-6 and TNF-α, as key inflammatory mediators in the immune system, play important roles in immune cell interactions and inflammatory response regulation. When there are abnormalities in the immune system of BHP patients, it can lead to excessive release of such inflammatory factors (Xie *et al*., 2022). Regulatory T cells (Treg) can be over-activated, leading to imbalances in the immune system (Moludi *et al*., 2022). Moreover, the inhibitory effect of Treg is weakened, making the immune response more stimulated (Kamata and Tada, 2020). Simultaneously IL-6 and TNF-α can trigger multiple signaling pathways, including Janus Kinase-Signal Transducer and Activator of Transcription (JAK-STAT) and Nuclear Factor-Kappa B (NF-κB), (Marrakchi and Puig, 2022). The activation of these pathways may lead to an enhanced inflammatory response, which in turn promotes an increase in the levels of inflammatory factors in BHP patients (Boehncke, 2018). At the same time, the skin lesions of BHP may also release IL-6 and TNF-α, forming a local inflammatory environment and

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triggering systemic inflammatory reactions (Shen *et al*., 2022). Therefore, effective treatment can be achieved by regulating the serum IL-6/TNF-α in BHP patients, in order to promote their rapid recovery.

With the rapid growth of modern society, the medical technology in China has been increasing year by year, and the treatment options for BHP patients have become increasingly diverse. However, conventional Western medicine treatment methods have gradually shown some limitations, such as long-term use of glucocorticoids and immunosuppressants, which can lead to a certain tolerance in the patient's body and a decrease in treatment effectiveness (Prinz *et al*., 2023). Moreover, patients are prone to adverse effects such as immune suppression and endocrine disorders (Hawkes *et al*., 2016), and when discontinuing medication, there may be recurrent episodes of the condition (Kashani *et al*., 2021). For widely distributed skin lesions, conventional topical drugs may not be able to cover all lesion areas, severely limiting clinical efficacy (Croitoru *et al*., 2023). This provides a broader space for the development of traditional Chinese medicine treatment, which has a certain effect on improving symptoms and alleviating discomfort. It can adopt an individualized approach, comprehensively considering the patient's constitution, condition, symptoms, etc., starting from the overall adjustment and balance of the body, emphasizing the concepts of treating diseases before they occur and adjusting the balance of yin and yang (Lu *et al*., 2014).

Compared with conventional western medicine (CWM) treatment methods, traditional Chinese medicine (TCM) has relatively fewer side effects and rich treatment methods, highlighting its potential value (Su *et al*., 2021). SCD is a TCM formula, mainly composed of raw *Rehmannia glutinosa* (RG) and lalang grass rhizome (LGR). It has dual effects of clearing heat, cooling blood, and dispersing swelling and nodules (Guo *et al*., 2020). However, there are currently few studies indicating a clear mechanism of the effect of this formula on the serum IL-6/TNF-α in the BHP patients. The present study aims to evaluate the protective effects of SCD on IL-6 and TNF-α levels in serum of patients with BHP.

MATERIALS AND METHODS

Subjects

Among patients with BHP who were treated in the Renmin Hospital from May 2020 to May 2023, a total of one hundred patients were enrolled and randomly put into an observation group (group SCD, n=50) and a control group (group CWM, n=50). Inclusion criteria: (a) In accordance with the diagnostic criteria for psoriasis provided in the 2019 AAD/NPF guidelines: (Application of Biological Agents for the Treatment of Psoriasis Menter *et al*. (2019); (b) Comply with the BHP syndrome differentiation standards provided in the "Expert Consensus on Traditional Chinese Medicine Treatment of Psoriasis of the Dermatology Branch (2017 Edition) (Dermatology Branch of Chinese Association of Traditional Chinese Medicine, 2018); (c) Age ≥ 18 years old; (d) Those who have not received other medication treatment within one week before treatment; (e) First time sick; (f) Volunteer participants in this study. Patients with incorporation of other organ dysfunction, allergic to the medication used in this study and cognitive dysfunction were excluded from the study.

Study design

The CWM group received 2.5 mg Oral methotrexate tablets (Shanghai Shangyao Xinyi Pharmaceutical Co., Ltd. SFDA approval number: H31020644. Specification: 2.5mg/tablet), per day, supplemented by external application of beclomethasone propionate ointment (Guangdong Huarun Shunfeng Pharmaceutical Co., Ltd. SFDA approval number: H44021269. Specification: 10g: 2.5mg), applied externally to the affected area 2-3 times a day, and if necessary, sealed for 3 weeks of continuous treatment.

The SCD group was treated with Shengdi-cogongrass decoction with Rehmannia glutinosa (RG) and lalang grass rhizome (LGR) of 15g each. The decoction was prepared by simmering the cut pieces of RG and LGR with water over low heat for 30 min. The extract was filtered used for 2 oral doses of 50ml per day and topical application not in combination with conventional western medicine soft caps once a day for 3 weeks.

The clinical efficacy of both groups was evaluated after 3 weeks of treatment (Amatore *et al*., 2019). with the following outcomes (i) Positive response (PR) showing decrease in the area of skin lesions and improvement of symptoms such as itching and redness. (ii) Preliminary improvement (PI): with reduced skin lesion area and symptoms, have not completely disappeared. (iii) No improvement (NI). Overall effective rate was calculated as (OER)=(PR+PI)/total number of cases * 100%.

For assessing improvement of disease symptoms before treatment, 1 week, and 3 weeks after treatment, the psoriasis area and severity index (PASI) (Mattei *et al*., 2014) and four item itch questionnaire (FIIQ) (Ju and Xie, 2018) were used. PASI scale measures redness, thick scales, and severity of lesions on the scalp, trunk, limbs, and nails. The total score is 0-74 points, and higher scores mean more serious disease symptoms. The Cronbach's α coefficient of this scoring scale is 0.747-0.830. The

FIIQ score includes questions on itching, severity of itching scraping or rubing to reduce itching? Comfortable level duct itching. The answer options for each question are divided into 0, 1, 2, and 3 points, with a maximum score of 0-12 points. The Cronbach's α coefficient of this questionnaire is 0.6924~0.903.

Expression level of inflammatory markers IL-6/ TNF-α levels were measured by ELISA in pre-treatment, 1 week, and 3 weeks after treatment in both groups.

Statistical analysis

The data in the study was entered in an Excel spreadsheet and processed using statistical software SPSS 26.0. Mean ± standard deviation was used to describe econometric data that conforms to a normal distribution, and perform independent sample *t*-value tests and repeated variance *F*-value tests between groups. Describe the counting data with [n (%)], conduct a 2-test between groups, and indicate statistical significance with a difference $P<0.05$. Describe the counting data with [n (%)], conduct χ^2-test between groups, and indicate statistical significance with a difference $P<0.05$.

RESULTS

For the 100 enrolled people, the gender distribution was 46 female and 54 male patients aged between 30 and 68 years, with a M (SD) age of 40.35±5.98 years. Table I shows demographic and clinical-related variables of the patients with BHP who were enrolled in the study. As the table shows, there are no significant differences between the group CWM and the group SCD ($P>0.05$).

The results of descriptive data for the total effective rate among the two groups in Table II shows that the total effective rate of the group SCD was significantly higher than those of the group CWM. While the PR and NI ratios of the group CWM are lower, the PI and OER ratios are higher.

Table I. Comparison of basic data between the two groups of patients.

Item	Group CWM (n=50)	Group SCD (n=50)	P value
Sex (male/female)	26/24	28/22	0.012
Age (years)	40.26±5.95	40.53±6.01	0.019
BMI (kg/m^2)	25.35±1.03	25.35±1.10	0.046
COD (days)	3.35±1.43	3.37±1.40	0.004
Education (below/above)	29/21	31/19	0.033

BMI, body mass index; COD, course of disease. CWM, conventional westren mediciens; SCD, shengdi-congongrass.

Table II. Comparative results of TER among patients [n(%)].

Indicator	Group CWM (n=50)	Group SCD (n=50)	X^2	P-value
PR	14(28.00)	25(50.00)		
PI	28(56.00)	23(46.00)		
NI	8(16.00)	2(4.00)		
OER	42(84.00)	48(96.00)	4.000	0.046

PR, positive response; PI, preliminary improvement; NI, no improvement; OER, overall effective rate. For other abbreviations see, Table I.

The comparison results of improvement of disease symptoms and expression levels of inflammatory markers are shows in Table III. In pre-treatment, there was no statistically significant difference in PASI score and FIIQ score of patients (P>0.05). At 1 week and 3 weeks of treatment, the PASI score and FIIQ score of the group SCD were lower than those of the group CWM (P<0.05).

Table III. Comparison of improvement of disease symptoms and expression levels of inflammatory markers between two groups.

Indicator	Group CWM (n=50)			Group SCD (n=50)			t	P
	Time 0	Time 1	Time 3	Time 0	Time 1	Time 3		
PASI score	50.21±2.35	37.20±6.82	20.96±7.17	50.33±2.48	12.11±2.43	8.75±3.39	10.886	<0.001
FIIQ score	9.82±0.43	7.22±0.46	5.59±1.02	9.79±0.51	3.33±0.28	1.07±0.13	31.083	<0.001
IL-6 (ng/L)	19.46±4.45	17.38±3.74	9.25±3.28	19.39±4.01	6.69±1.08	5.28±1.29	7.965	<0.001
TNF-α (ng/L)	86.91±7.34	80.84±8.98	75.40±6.06	87.02±7.29	42.01±6.20	34.11±7.01	31.508	<0.001

PASI, psoriasis area and severity index; FIIQ, four item itch questionnaire; IL-6, interleukin-6; TNF-α, tumor necrosis factor-α; Time 0, pre-treatment; Time 1, treatment for 1 week; Time 3, treatment for 3 weeks. FMA Scale Rating: $F_{inter\text{-}group}/F_{time}/F_{interaction}$=14.409/74.522/2.257, $P_{inter\text{-}group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.022; FIIQ score: $F_{inter\text{-}group}/F_{time}/F_{interaction}$=18.632/70.198/2.322, $P_{inter\text{-}group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.018. IL-6 level: $F_{inter\text{-}group}/F_{time}/F_{interaction}$=12.584/61.878/2.198, $P_{inter\text{-}group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.025. TNF-α level: $F_{inter\text{-}group}/F_{time}/F_{interaction}$=15.826/52.966/1.993, $P_{inter\text{-}group}/P_{time}/P_{interaction}$=<0.001/<0.001/0.044.

As shown in Table III, there was no significant difference in IL-6 and TNF-α levels between the two groups before treatment (P>0.05). At 1 and 3 weeks of treatment, the IL-6 and TNF-α levels in the group SCD were lower than those in the group CWM (P<0.05).

DISCUSSION

Traditional Chinese medicine (TCM) believes that BHP is classified as a heat toxic disease in the theory of TCM syndrome differentiation, often combined with differentiation of dampness heat, stasis heat, and other syndromes (Li *et al*., 2022). The main characteristics of BHP are skin redness, scales, itching, etc., similar to the dampness and heat syndrome in TCM theory (Dai *et al*., 2022). At this point, TCM believes that dampness and heat accumulate in the body, and heat toxins accumulate in the skin, leading to skin lesions (Xing *et al*., 2022). The focus of treatment is to clear heat and detoxify, dispel dampness and phlegm, unblock meridians, in order to eliminate dampness and heat pathogens, and improve skin symptoms (Tan *et al*., 2011). SCD can regulate heat toxicity in the body, promote blood circulation, clear heat and detoxify, and improve skin symptoms through its pharmacological effects of clearing heat and cooling blood (Zhang *et al*., 2020). In addition, BHP patients may have symptoms such as itching and dryness, which is consistent with the TCM syndrome of Qi deficiency and blood heat (Zhong *et al*., 2022). TCM believes that qi deficiency is weak and unable to produce blood, leading to blood disharmony and skin lesions. Therefore, the focus of treatment should be on supplementing qi and nourishing blood, clearing heat and detoxifying, improving the state of qi and blood deficiency, and alleviating skin symptoms (Sun *et al*., 2023). SCD can stimulate the secretion of bodily fluids, such as saliva and sweat, which contributes to the moisturizing effect in the body. At the same time, it can regulate the skin barrier function, improve symptoms such as dryness and itching, and accelerate the recovery progress of patients. The results of this study: The PASI score and FIIQ score of the group SCD at 1 and 3 weeks of treatment were lower, which can effectively confirm the accuracy of this viewpoint, and this result is consistent with research by foreign scholars (Chen *et al*., 2020).

In addition, this study shows that SCD has a significant effect on reducing serum IL-6/TNF-α levels in BHP patients. Analyzing the reasons, the TCM RG in SCD contains various active ingredients, such as phenolic compounds [such as Salicylic acid (SA), Cinnamic acid (CA), etc.], flavonoids [Rehmannioside (RH), rhamnanthin (RT), etc.], and polysaccharides (PS) (Ning, 2009). These ingredients have various effects such as antioxidant, anti-inflammatory, and immune system regulation (Cui *et al*., 2016). Phenolic acids and flavonoids can inhibit the release of inflammatory factors IL-6 and TNF-α, alleviate oxidative stress, and reduce the production of inflammatory factors (Benteldjoune *et al*., 2021). Polysaccharides may affect the immune response in the body by regulating the activity of immune cells and the secretion of immune regulatory factors, thereby affecting the expression of IL-6 and TNF-α (Zeng *et al*., 2019). In addition to polysaccharides and flavonoids, LGR also contains a specific bioactive natural compound, namely tannins (Wang *et al*., 2022), which has a significant astringent effect and can contract tissues, reduce exudation and secretion. In the theory of TCM, convergence can be used to treat skin inflammation, eczema, burns and other diseases, helping to alleviate symptoms such as skin redness, itching, and thereby reducing inflammatory reactions. At the same time, these substances have anti-inflammatory effects, can alleviate inflammatory reactions, inhibit the release of inflammatory mediators (Ajebli and Eddouks, 2019), and have certain antioxidant activity. It can help alleviate cellular oxidative stress, protect cells from oxidative damage, and regulate immune system activity by affecting the function of immune cells (Wu *et al*., 2018), comprehensively reducing the expression level of inflammatory factors.

CONCLUSION

In general, the findings of this study support the protective effect of SCD in serum of patients with BHP through alleviating disease symptoms and reducing the expression level of inflammatory factors. However, this study still has some limitations, such as relatively small sample size and lack of diversity, which may limit the external effectiveness of the study. Future research requires a larger sample size to comprehensively evaluate treatment effectiveness. In addition, different studies use different doses or times of medication, which makes the comparison and comprehensive analysis of results complex. Therefore, future related research can quantify the standardization of treatment parameters to ensure the repeatability of results. At the same time, the author suggests that more clinical trials can be conducted in the future to validate the clinical efficacy of SCD in treating BHP patients, and to conduct in-depth research on potential biomarkers.

DECLARATIONS

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IRB approval

This study was approved by the Advanced Studies Research Board of Renmin Hospital, Hubei University of Medicine, China.

Ethical approval

The study was carried out in compliance with guidelines issued by ethical review board committee of Renmin Hospital, Hubei University of Medicine, China. The official letter would be available on fair request to corresponding author.

Statement of conflict of interest

The authors have declared no conflict of interest.

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