

## Original Article

# The efficiency and safety of the Chinese herbal medicine liang xue huo xue decoction (LXHXD) in patients with psoriasis vulgaris of blood heat syndrome

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**Abstract:** Background: Published research evidence evaluating the use of topical and oral formulae in psoriasis is lacking. The purpose of this study was to evaluate the efficiency and safety of liang xue huo xue decoction (LXHXD) in treating psoriasis vulgaris (PV) of blood heat syndrome. Material and methods: A total of 50 eligible patients with PV were randomized 3:2 into two groups (A and B). The patients in group A received LXHXD while those in group B received a placebo for 6 weeks. PASI was recorded at baseline, and after 2, 4, and 6 weeks of treatment, and 6 weeks after treatment. Serum IL-17a and IL-1 $\beta$  levels were determined before and after treatment. Conclusions: LXHXD is effective and safe in the treatment of psoriasis vulgaris. LXHXD can significantly reduce the symptoms of skin lesions in patients with psoriasis, effectively reduces the PASI score and peripheral blood IL-17a concentration and has only mild side effects. It can be used as a treatment for psoriasis.

**Keywords:** LXHXD, psoriasis vulgaris, blood heat syndrome, randomized controlled trial

## Introduction

Psoriasis is characterized by keratinocyte hyperplasia, inflammatory cell infiltration into the dermis, and neo-vascularization [1]. This disease is estimated to affect 2-3% of the general population worldwide [2]. Psoriasis vulgaris (PV), or plaque-type psoriasis, is the most common type of psoriasis, representing 90% of the psoriatic cases [2]. PV is causing increased concern due to its highly prevalent, harmful, and therapy-resistant characteristics in China and other countries [3]. From the perspective of the Chinese traditional medicine (TCM), the lesions of psoriasis are mainly caused by an excess heat in the blood which can manifest as blood-heat syndrome (53.8%), blood-dryness syndrome (27.4%), and blood-stasis syndrome (18.1%) [4]. Recently published research evidence evaluating the use of topical and oral formulae in psoriasis is lacking [5, 6].

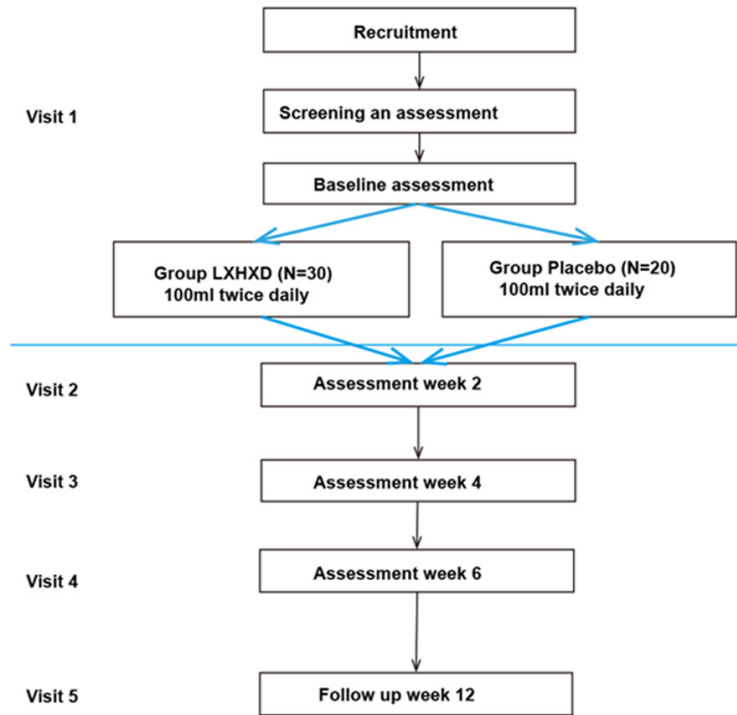
The Chinese herbal medicine liang xue huo xue is used for treating PV of the blood-heat syn-

drome. The LXHX decoction (LXHXD) therapy is based on TCM theory and clinical observations. Developed by Professor Zhao Bingnan of the Beijing Chinese Medicine Hospital, the LXHXD formula is the most commonly used proprietary Chinese medicine for treating the blood heat syndrome of PV. This classic formula has been registered with the Beijing Food and Drug Administration for more than 50 years. Nevertheless, its effectiveness has not been tested in rigorously designed clinical trials. Hence, the present study aimed to test the efficiency and safety of LXHXD for PV of blood heat syndrome in a multicenter, double-blind, randomized controlled trial.

## Materials and methods

This was a multi-center, randomized, double-blind, placebo-controlled clinical trial. We enrolled patients with PV blood heat syndrome. The participants were recruited from three centers: Beijing Hospital of TCM, Beijing Dong Zhi Men Hospital, and Beijing Shun Yi Chinese

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**Figure 1.** Trial procedure flowchart. LXHXD: Liang xue huo xue decoction.

**Table 1.** Study visits

	Visit 1 Baseline	Visit 2 Week 2	Visit 3 Week 4	Visit 4 Week 6
Inclusion/Exclusion criteria	x			
Informed consent	x			
History/Demographics	x			
PASI	x	x	x	x
Safety assessment	x			x
Cytokine (IL-17a)	x			x
Cytokine (IL-1 $\beta$ )	x			x

PASI, psoriasis area and severity index.

Medicine Hospital. The trial protocol was approved by the ethical committee of each participating center.

The potential participants were invited to an initial screening assessment during which the patients were screened using the inclusion and exclusion criteria listed below. If eligible, the participants were asked to sign an informed consent form before undergoing the PASI assessment [7]. Four visits were scheduled for each patient: baseline, week 2, week 4, and week 6.

The patients were randomized using a ratio of 3:2 to receive either an oral dose of 100 ml of

the Chinese herbal medicine LXHXD twice daily or a dose of 100 ml of placebo twice daily (Figure 1). Out of humanitarian considerations for the patients, the proportion of patients between the treatment and control groups was set to 3:2 (Figure 1).

### Ethical issues

This trial was approved by the Research Ethics Committee of the Beijing Hospital of Traditional Chinese Medicine Affiliated with Capital Medical University (2013BL-099-01). The patients willing to participate signed a consent form prior to participation.

### Setting and patients

The study was conducted in the outpatient departments of three dermatological hospitals in China. Patients with psoriasis were consecutively invited to participate in the study after a medical decision was made to start Chinese herbal medicine with LXHXD. Patients eligible for the study were the ones diagnosed with moderate to severe PV. Recruitment was held at three centers: Beijing Hospital of TCM, Beijing Dong Zhi Men Hospital, and Beijing Shun Yi Chinese Medicine Hospital.

### Inclusion criteria

(1) Aged between 18 and 65 years; (2) A history of symptoms of psoriasis vulgaris for at least 6 months, diagnosed by a dermatologist; (3) Meeting the standards of TCM syndrome blood heat syndrome psoriasis; (4) Voluntarily signed the informed consent form.

### Exclusion criteria

(1) Pregnant; (2) Breastfeeding; (3) Systemic drugs or phototherapy for psoriasis within 4 weeks prior to screening; (4) Taking topical drug treatment for psoriasis within 2 weeks prior to screening; (5) Complications of serious diseases.

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**Table 2.** Comparability analysis between the two groups

	LXHXD group (30 cases)	Control group (20 cases)	Statistics
Age (years)	28.13±9.71	31.50±10.03	$t=0.39, P=0.43$
Gender (% male)	61%	65%	$F=0.18, P=0.62$
Family history (%)	26%	20%	$F=0.97, P=0.26$
History of allergies (%)	68%	60%	$F=0.86, P=0.39$
Body mass index	28.5±2.6	29.0±3.1	$t=0.54, P=0.59$
Course of disease (month)	32.7±9.3	36.5±8.7	$t=1.43, P=0.16$

es of the heart, liver and kidney, immune, or hematopoietic systems; (6) Diagnosed with depression, mental disease, or cognitive impairment; (7) Allergic to a Chinese herbal compound.

### Diagnostic criteria for psoriasis vulgaris

The diagnostic criteria for PV were developed according to the standards of the *Chinese Medical Association clinical diagnosis and treatment guidelines: Division of Dermatology and Venereology* (People's Medical Publishing, January, 2006) and *Clinical Dermatology* (Third edition) (Jiangsu Science and Technology Press, April, 2001): red infiltrating papules and macules, fused into integrated film with a clear boundary, covered by layers of silver white scales; after removing the scales, a shiny film can be observed; and spotting can be observed after removing the film (named film phenomenon and spotting phenomenon).

### Diagnostic criteria of psoriasis vulgaris with blood heat syndrome

The diagnostic criteria for PV with blood heat syndrome were developed based on the experiences of the Chinese medicine syndrome differentiation and treatment of psoriasis and reference *TCM differential diagnosis system summary* (People's Medical Publishing, September 2002 edition) and *Traditional Chinese medicine new medicine clinical research guidelines* (China Medicine Science and Technology Press, May, 2002).

The main symptoms are: 1) the number of new rashes continues to increase, expanding rapidly; and 2) skin flushing. The secondary symptoms are: 1) red tongue with thin white coating; 2) slippery pulse string slide; and 3) dark urine. The syndrome was diagnosed in the presence

of the two main symptoms and at least one secondary symptom.

### Sample size

The sample size determination was based on one of our previous studies [8]. The study was planned to detect a one-unit difference in changes between the intervention

and control groups. This was a pilot study of 50 participants enrolled at the Beijing Hospital of TCM for testing the feasibility of the trial protocol and to determine the sample size for a full-scale trial.

### Randomization and blinding

Fifty eligible patients were randomized into the intervention group LXHXD and the placebo group in a 3:2 ratio. Patients were randomized through a statistical analysis system. Group allocation was double-blind; both the participants and researchers were blinded.

### Intervention

Patients who met the inclusion criteria received a randomly generated number. The pharmacy then prepared the LXHXD or a placebo. The drug and placebo were matched as closely as possible in terms of appearance, weight, odor, and taste so that they could not be distinguished in order to ensure the double-blind nature of the trial. The intervention period lasted 6 weeks.

LXHXD originated from Zhao Bingnan's *Clinical Experience Collection* and was made of Radix Rehmanniae 30 g, sophora flower 30 g, *Salvia miltiorrhiza* 15 g, *Rhizoma imperatae* 30 g, Puccoon 15 g, Red peony 15 g, and *Caulis Spatholobi* 30 g. As a treatment medicine, 175 g of the these seven herbs were added to a solution of about 400 mL of drinkable water, then boiled for 30 minutes in a traditional Chinese medicine decocting machine; the decoction was poured out and volumized to 400 mL by adding water, and bottles of 200 mL of medicine were prepared. The patients were instructed to orally take the 200 mL twice per day, within 30 minutes after finishing breakfast and dinner.

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**Table 3.** Comparison of the PASI scores between the two groups

Grouping	Week 0	Week 2	Week 4	Week 6	Statistics
30 cases in the LXHXD group	11.1±4.9*	9.2±3.7	8.1±3.2	5.9±2.7*,#	$t=4.26, P<0.001$
20 cases in the control group	10.7±4.6	10.1±4.1	9.1±4.3	7.9±3.0#	$t=1.97, P=0.059$
Statistics	$t=0.19, P=0.85$	$t=0.69, P=0.49$	$t=0.76, P=0.45$	$t=2.18, P=0.036$	

Note: \*There was a significant difference between the 0th week and the 6th week of the study group; #The 6th week of the study group was significantly different from the control group.

**Table 4.** Comparison of serum IL17a and IL-1 $\beta$

Grouping		IL-17a	IL-1 $\beta$
30 cases in the LXHXD group	Before treatment	248.6±68.4	21.6±11.6
	After treatment	202.7±49.8	18.6±10.8
	Statistics	$t=2.72, P=0.016^*$	$t=1.4, P=0.18$
20 cases in the control group	Before treatment	252.4±71.3	20.4±7.3
	After treatment	237.2±56.1	19.4±6.9
	Statistics	$t=4.12, P=0.51$	$t=2.14, P=0.36$

Note: \*There was a significant difference between the 0th week and the 6th week of the study group.

The placebo was made by boiling water with tea and edible pigments. The decocting method was the same as the one used in traditional Chinese medicine, with a similar color and taste, but with no medicine ingredients. It was also put into 200 mL bottles, without any distinguishable difference in appearance. The patients received the exact same instructions for administration.

### Results

#### Outcome assessment

The primary outcome in the trial was the change in PASI after treatment, which is the internationally accepted evaluation criterion for psoriasis [9]. This change is considered the gold standard and is a well-recognized indicator to evaluate the efficiency of a psoriasis treatment. The PASI [10] includes four elements: psoriasis area, scaling, infiltration, and erythema. Each element in the four parts of the body-head, face, upper limbs, trunk, and lower limbs-can efficiently evaluate the situation. The PASI was assessed every 2 weeks throughout the treatment period.

The secondary outcomes included time to relapse and time to onset. Any adverse events were recorded by the participants and assessed by blinded assessors at each visit. Routine blood, feces, urine, kidney and liver function tests were completed before and after therapy (Table 1). Samples of serum were collected and

stored in order to investigate the changes to the concentration of key cytokines (IL-17a and IL-1 $\beta$ ).

The statistical analyses were performed using the Statistical Package for Social Science statistics (SPSS 18.0, IBM, Armonk, NY, USA). Two-tailed  $P$ -values  $<0.05$  were considered to be statistically significant. Continuous variables were expressed as the means  $\pm$  standard deviation or medians and range, as appropriate. Comparisons between the two groups were conducted using Student's  $t$  test.

### Discussion

#### Comparability analysis

There were no significant differences in age, gender, weight, family history, or medical history between the two groups (Table 2).

#### Comparison of clinical PASI scores

In the study group (30 cases), the erythema gradually became pale, the scales gradually became scarce, the skin gradually became smooth, and the thickening phenomenon gradually decreased. After 6 weeks of treatment, the symptoms of the skin lesions were significantly improved ( $t=4.26, P<0.001$ ). Compared with the control group (20 patients), the PASI score was lower than the control group's PASI score after 6 weeks of treatment ( $t=2.18, P=0.036$ ) (Table 3).

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**Table 5.** Comparison of adverse reaction records

Grouping		Abnormal blood routine	Abnormal urine function	Abnormal liver and kidney function	Total
30 cases in the LXHXD group	Before treatment	2	3	2	7
	After treatment	3	4	4	11
	Statistics	$\chi^2=0.22, P=0.64$	$\chi^2=0.16, P=0.69$	$\chi^2=0.16, P=0.39$	$\chi^2=1.25, P=0.26$
20 cases in the control group	Before treatment	1	4	3	8
	After treatment	2	3	4	9
	Statistics	$\chi^2=0.36, P=0.55$	$\chi^2=0.17, P=0.68$	$\chi^2=0.17, P=0.68$	$\chi^2=0.10, P=0.75$

### Comparison of serum IL17a and IL-1 $\beta$

The levels of IL-17a and IL-1 $\beta$  in the peripheral blood of patients in the LXHXD and control groups at 0 and 6 weeks were measured by ELISA. The results showed that IL-17a in the study group was decreased significantly before and after treatment ( $t=2.72, P=0.016$ ). There was no significant difference in the expression of IL-1 $\beta$  before and after treatment (**Table 4**).

### Adverse reaction

A total of 50 subjects (30 in the study group and 20 in the control group) were studied. None of the 50 patients had abnormal vital signs before or after treatment. There was no significant difference in adverse reactions between the two groups (**Table 5**).

### Conclusions

LXHXD is effective and safe in the treatment of psoriasis vulgaris. LXHXD can significantly reduce the symptoms of skin lesions in patients with psoriasis, effectively reduce the PASI score and peripheral blood IL-17a concentration. LXHXD had mild side effects and can be used as a treatment for psoriasis. The use of Chinese herbal medicine for the treatment of diseases in China has a long history [11]. However, traditional Chinese medicine decoctions are composed of a complex composition and their mechanisms of action is not clear, hindering research on herbal mixtures. At present, treatment with Western medicine has severe side effects, but no other effective treatment is available [12]. Chinese herbal medicine (LXHXD) has been used at the Beijing Chinese Medicine Hospital for the treatment of psoriasis for at least 50 years. Its efficacy is well-recognized but lacks scientific evidence to support it. We hope that this study can be used as an effective basis for LXHXD treatment of PV blood heat syndrome, paving the way for larger studies in the future.

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### Disclosure of conflict of interest

None.

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