

Liangxue Jiedu Runzhi ointment in the treatment of mild and moderate psoriasis with blood-heat syndrome

A double-blind randomized controlled trial

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Abstract

Introduction: Psoriasis is a kind of chronic inflammatory skin disease characterized by erythema, skin hyperplasia, scales and keratinocyte hyperproliferation. Psoriasis Vulgaris, the most common kind of psoriasis, severely deteriorates the life quality of patients. Traditional Chinese Medicine (TCM) is a good choice for the treatment of psoriasis, which has been proved to be safe and effective, and may reduce the recurrence rate. In clinical practice, *Liangxue Jiedu Runzhi* (LJR) ointment can effectively treat mild and moderate psoriasis with blood-heat syndrome, but there is a lack of evidence-based medical evidence. This trial aims to evaluate the efficacy and safety of LJR ointment for the treatment of mild and moderate psoriasis with blood-heat syndrome.

Methods: A multicenter, randomized, double-blind, placebo-controlled, and self-controlled clinical trial was carried out according to this paper. The symmetrical rashes of each subject were regarded as the target lesions and were randomly divided into a treatment group (LJR ointment group) and a control group (placebo group). The LJR ointment or placebo ointment were externally administered on bilateral symmetric rashes, twice a day for eight weeks. The follow-up examination was made for subjects every two weeks. The primary research finding was conveyed by Psoriasis Area and Severity Index (PASI) in 8 weeks. The secondary research finding includes adverse events.

Results: 46 subjects undergo this research project. The difference between PASI scores of the target lesions in the treatment group and control group is statistically significant were in 8 weeks ($P < .001$). The percentage of PASI 75 in treatment group and control group were 48% and 15% in week 8, respectively ($\chi^2 = 11.33$, $P < .05$). No severe adverse events were reported.

Conclusions: LJR ointment was proved to have efficacy in the treatment of mild and moderate psoriasis with the blood-heat syndrome.

Abbreviations: BSA = Body Surface Area, LJR = Liangxue Jiedu Runzhi, PASI = Psoriasis Area and Severity Index, PGA = Physician's Global Assessment, TCM = Traditional Chinese Medicine.

Keywords: blood heat syndrome of psoriasis vulgaris, *Liangxue Jiedu Runzhi* ointment, placebo, randomized, self-controlled clinical trial

1. Introduction

Psoriasis is a kind of chronic inflammatory skin disease characterized by erythema, skin hyperplasia, scales, and keratinocyte hyperproliferation. Dysfunction of the skin barrier is also one of

the characteristics of psoriasis, which is correlated with disease severity.^[1] According to an epidemiological study, there are 64.6 patients with psoriasis in every million persons.^[2] Patients with psoriasis account for about 0.12%^[3] of the total population in China. Clinically, psoriasis can fall into four types, namely,

YQ and WZ contributed equally to this work.

This work was supported by grants from the National Natural Science Foundation of China (No. 81774309) and the National Key research and development program of China (No. 2018YFC1705302).

The authors declare that they have no conflicts of interest.

Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Registration ID in Chinese Clinical Trial Registry: ChiCTR-INR-16007941.

Registration date: February 17, 2016.

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How to cite this article: Qiu Y, Zhang W, Li G, Guo X, Qu J, Lan H, Zhang C, Xu J, Sun L. Liangxue Jiedu Runzhi ointment in the treatment of mild and moderate psoriasis with blood-heat syndrome: A double-blind randomized controlled trial. *Medicine* 2022;101:45(e31784).

Received: 2 February 2022 / Received in final form: 22 October 2022 / Accepted: 24 October 2022

<http://dx.doi.org/10.1097/MD.00000000000031784>

Vulgaris Type, Erythrodermic Type, Pustular Type, and Arthritic Type. Psoriasis Vulgaris is the most common type.^[4] Disease progression takes a rapid pace at the active stage, during which new lesions constantly appear. Any acupuncture, surgery, or scratching results in psoriatic lesions in the affected area, which is called “homo-reaction.” According to the recent research findings, the total financial burden of psoriasis is estimated at USD35.2 billion, while medical costs increase by USD12.2 billion in (35%).^[5,6]

For the treatment of mild-to-moderate psoriasis, ointments are commonly used externally in Western medicine, such as corticosteroids, retinoic acid, vitamin D₃ derivatives, and calcineurin inhibitors.^[7] Oral and (or) topical use of TCM is a good choice for the treatment of psoriasis, which has been proved to be safe and effective and may reduce the recurrence rate.^[8,9] Recently, emerging evidence has suggested that natural products, like chinese herbal medicine, have many active ingredients that restore illness. For example, cucurbitacin B, isolated from *Luffa operculata*, has antiproliferative and genotoxic activities^[10]; convulxin, isolated from the venom of the snake species, stimulates platelet aggregation.^[11] Furthermore, *in Silico* studies based on natural sources also indicated that some derivatives isolated and identified from herbs with potential of anti-disease.^[12–15] Therefore, exploring the various active ingredients of TCM and combining them into different derivatives may become a popular complementary and alternative therapy.

TCM ointment is favored in the treatment of psoriasis across Asia.^[16–21] LJR ointment takes root in the basic TCM theory, with Chinese herbal medicine as the main ingredient. According to the trial design, patients were randomly assigned to the treatment group and control group under the inclusion and exclusion criteria. Patients in the treatment group were administered with LJR ointment and patients in the control group were administered with placebo ointment twice a day (morning and evening) for eight weeks, with visits every two weeks. Beijing Hospital of Traditional Chinese Medicine has taken the *Liangxue Jiedu Runzhi* (LJR) ointment topical use to treat mild and moderate psoriasis with the blood-heat syndrome, and it has good clinical efficacy. But there is a lack of evidence-based medical evidence.

This was a multicenter, randomized, double-blind, placebo-controlled, and self-controlled clinical trial designed to observe the improvement of patients' target skin lesions, and evaluate the efficacy and safety of LJR ointment in the treatment of mild-to-moderate active blood heat syndrome of psoriasis vulgaris, thereby marking a new attempt for external treatment of psoriasis vulgaris.

2. Materials and methods

2.1. Trial design and ethics

This research project was a multicenter randomized, double-blind, placebo-controlled, and self-controlled trial, which was registered at the Chinese Clinical Trial Registry (Registration ID: ChiCTR-INR-16007941) in February 17, 2016. The participants were recruited from the Dermatology Clinics of Beijing Hospital of Traditional Chinese Medicine affiliated to Capital Medical University, Dermatology Clinics of Shunyi Hospital of Traditional Chinese Medicine, and Dermatology Clinics of Beijing Gulou Traditional Chinese Medicine Hospital, from February 2016 to December 2017. Washout Period refers to a period during which no intervention was administered. A washout may be administered between different treatment periods (to “wash out” the effects of treatment before it was readministered).^[22] All patients were recruited after a two-week washout period. The written letters of informed consent were collected from all subjects. All researchers accept relevant training on the research protocol, research program, and researchers' responsibilities before the kick off of this research project, this research

project was approved by the relevant hospital ethics committee (Ethical Approval Number: 2016BL-006-03).

2.2. Patients

2.2.1. Diagnostic criteria. The Western medicine diagnostic criteria for psoriasis vulgaris^[23,24] and *Guidelines for the Diagnosis and Treatment of Psoriasis in the Chinese Medical Association Psoriasis Research Panel*^[25,26]: Typical clinical manifestations of psoriasis vulgaris include papules and macules with red lesions, which can merge into tablets. The edge of the lesions was obvious, covered with multiple layers of silvery-white scales. After scales are scraped off, bright scales are exposed. The punctate hemorrhage was found after bright scales are scraped off. The judgment for the active stage will be made based on the course of the disease.

2.2.2. Inclusion criteria. The inclusion criteria for the study were as follows:

1. meeting the above diagnostic criteria for psoriasis; patients corresponding to diagnosis standards psoriasis vulgaris with the blood-heat syndrome of Traditional Chinese Medicine; patients corresponding to the progressive stage of psoriasis vulgaris;
2. patients diagnosed with psoriasis vulgaris between 18 and 65 years old, regardless of gender and course of the disease;
3. severity of disease: mild-to-moderate skin lesions (5% < Body Surface Area (BSA) < 20%);
4. sign informed consent of Good Clinical Practice (GCP) and volunteer to participate in this research project.

2.2.3. Exclusion criteria. Participants will be excluded who meet any following conditions:

1. articular/pustular/erythrodermic psoriasis;
2. score of Self-rating Anxiety Scale (SAS) > 50 points, the score of Self-rating Depression Scale (SDS) > 53 points, or other mental disorders;
3. pregnant or lactating women, or women who have a birth plan within the next three months;
4. patients who took glucocorticoids and/or immunosuppressive drugs and retinoids acid in the past month, or took glucocorticoid preparations, retinoids acid, and vitamin D₃ derivatives for about two weeks;
5. complicating serious primary diseases in the cardiovascular and cerebrovascular system, liver, kidney, and hematopoietic system;
6. malignant tumor with concurrent infection, electrolyte imbalance, or acid-base disorder;
7. those who were allergic to drugs of this research project;
8. patients who were participating in clinical trials of other drugs;
9. patients with psoriasis, who need systemic treatment;
10. any other condition that the investigator's judge as likely to make the patient incapable to complete, comply, or unsuitable for the clinical trial.

2.2.4. Sample size calculation. The sample size was calculated through the following formula: $n = [(Z_{1-\alpha/2} + Z_{1-\beta/2})^2 \times (\sigma_1^2 + \sigma_2^2)] / \delta^2$, where “n” is the sample size, $Z_{1-\alpha/2}$ and $Z_{1-\beta/2}$ refer to the table of z values, σ_1 is the standard deviation of Treatment Group, σ_2 is the standard deviation of Control Group, and δ is the difference value between two groups with clinical significance. $\alpha = 0.05$, $\beta = 0.10$, $1 - \beta = 0.90$, bilateral $\mu\alpha = 1.96$, $\mu\beta = 1.282$. δ is the required discrimination, which is the difference between the Treatment Group and Control Group, the value was set

at 1.5 based on previous research results. The average PASI standard deviation of the treatment group compared with the control group is 2. It is required to infer that the probability of making Type I Error is controlled below 0.05 (two sides), and the probability of making Type II error is controlled below 0.1. Consequently, $n = [(1.96 + 1.28)^2 \times (2^2 + 2^2)]/1.5^2$. Considering the 15% loss to follow-up rate, the sample size was set at 50 patients.

2.2.5. Randomization and masking. Since psoriasis rash is characterized by symmetrical distribution, the clinical research was carried out through the self-matching method of bilateral symmetrical rashes on patients. Drug grouping adopts the random number table assignment method, in which the left and right rashes of the subjects were randomly assigned. Ointment A and Ointment B were respectively applied in the treatment group and control group include, which were assigned to patients with symmetrical rashes on the left and right sides under the random number table method. Statistical professionals provide a blind table of random numbers, and SAS9.3 software was used to generate fixed seed numbers. The specific grouping was determined by persons unrelated with the clinical research based on a random number table. The sealing and opaque envelopes will be used to achieve allocation concealment. At the end of the test, allocation forms were unsealed during a face-to-face meeting. If the seals were damaged, an explanation will be needed. Otherwise, the test will be considered invalid. According to the random information in the random number table, the physicians prescribe for the corresponding drug treatment in the corresponding places.

2.2.6. Blinding. The double-blind was made for both the patients and the researchers in this research project. In the process of drug formulation, Beijing Chinese Medicine Research Institute prepares the test drug and placebo. The placebo was the same as the test drug in terms of appearance, smell, and package. The blinding process was recorded on the blinding record certificate. Head of the blinding process evaluates the appearance of the consistency between drugs in the treatment group and control group to ensure that the patients were always blinded in the study.

2.3. Interventions

2.3.1. Preparation of LJR ointment and placebo ointment. LJR Ointment: each LJR ointment contains 150g Chinese angelica (*Radix Angelicae Sinensis*), 30g Arnebia root (*Radix Arnebiae*), 9g Rhubarb root and rhizome (*Radix et Rhizoma Rhei*), 9g Natural indigo (*Indigo Naturalis*), 9g Belvedere fruit (*Fructus Kochiae*), 9g Light yellow sophora root (*Radix Sophorae Flavescentis*), 9g Glabrous greenbrier rhizome (*Rhizoma Smilacis Glabrae*), 110g Sesame oil, 162.5g Vaseline, and 12.5g Beeswax (*Cera Flava*). Details of the preparation process were given as follows: Soak the above ingredients in sesame oil for two days; Fry over a gentle heat until the Chinese angelica was slightly boiled; Turn off the heat, filter the dregs, and retain the decoction; Mix vaseline and beeswax into a decoction, and stir evenly; Put into medicine boxes (20g each box), and naturally solidify. Placebo ointment: The placebo ointment, 20g per box, was prepared by vaseline and beeswax into a decoction and stirred evenly. The pigment was added into the placebo to make its physical properties similar to those of LJR ointments, such as appearance, color, dosage form, weight, and smell. But active ingredient of the drug as above was not contained.

2.3.2. Supervision and administration of LJR ointment and placebo. In this research project, patients' rashes were symmetrical on both sides, with one side of rash in the treatment

group, and the other side of rash in the control group. When distributing the ointment to the patients, the left and right sides of the ointment cover were marked, and patients were told to use the ointment according to the mark and not replace the ointment on both sides. Subjects were asked to use the ointment to the designated side of lesions twice a day for eight weeks, once each in the morning and evening. The dosage of ointment was evaluated by estimating the surface area of the target lesion in each subject. To facilitate the calculation, the fingertip unit (FTU) was used. A fingertip unit was extruded in a standard external paste tube with a nozzle diameter of 5mm to cover the ointment dosage from the distal phalanx fold of the index finger to the tip of the index finger. 1 FTU = 0.5g = 100cm² of surface area. Subjects were asked to apply the ointment to such an area that was 2mm larger than the target lesion surface, which ensures adequate coverage of the target lesion. Gently click the target lesion to form a thin layer of ointment, and then rub towards a certain direction until the ointment was fully absorbed.

2.4. Outcomes

2.4.1. Primary outcome measures. Psoriasis Area and Severity Index (PASI) of target lesions was the primary outcome indicator. PASI = (Erythema + Scale + Infiltration) × Area Score (If the target lesion area was large than 5cm², the area score before treatment will be 3 points).^[27] The severity of the patient's condition was assessed according to PASI and *Guidelines for the Diagnosis and Treatment of Psoriasis Vulgaris 2018*. PASI score < 3 indicates mild psoriasis, PASI score of 3-10 indicates moderate psoriasis, and PASI score ≥ 10 indicates severe psoriasis.

2.4.2. Secondary outcome measures. Secondary outcome indicators include the percentage of patients with a decrease by 75% in PASI score (PASI 75),^[28] the percentage of patients with a score of 0 or 1 (clear or almost clear) in Physician's Global Assessment (PGA); skin barrier function. PASI 75 = (PASI total score before treatment—PASI total score after treatment)/ PASI total score before treatment × 100%. PGA = (Erythema + Scale + Infiltration)/ 3. PGA scores range from 0 to 5, namely, Obvious (0), almost Obvious (1), Mild (2), Moderate (3), Distinct (4) and Severe (5). Indicators of skin barrier function include skin temperature, pH value, humidity, and skin lipids.^[1] Safety outcomes include skin irritation symptoms, such as erythema, desquamation, dryness, itching and rash. Laboratory tests include blood routine examination, urine routine examination, liver and kidney function and electrocardiogram.

2.5. Statistical analysis

Per-protocol set was used for data analysis through SPSS 21.0 software. Under the per-protocol principle, subjects, who were randomized and under the protocol, were included in the analysis. A per-protocol analysis was a subset of the full dataset, in which subjects were more compliant with the protocol (who take 80% to 120% of the drug dose under the protocol; primary outcome data was available; and no severe violation of the protocol). The missing value will be dealt with by carrying forward the most recent observation to the endpoint. Professionally trained dermatologists will collect all data. Members of the research team will perform the data collection and statistical analyses.

Safety analysis refers to the safety analysis set. It follows the exposure principle. In other words, for all subjects who have used the ointment at least once, adverse events will be observed and safety data will be recorded, to evaluate the correlation between any adverse events and the test drug.

Quantitative indicators were expressed as mean standard deviation. If the sample is normally distributed and the variance

is uniform, the *t*-test will be performed: the paired-sample *t*-test will be used for intra-group comparison, and the independent sample *t*-test will be used for inter-group comparison. If the variance is uneven, the approximate *t*-test will be used. If the sample is not normally distributed, the rank-sum test (nonparametric) will be applied. The Chi-square test will be used for counting data. *P* values < .05 will be considered statistically significant.

3. Results

3.1. Study population

A total of 50 participants of psoriasis vulgaris of the bloodheat syndrome were recruited for this study. The left and a right bilateral symmetric rash of 50 subjects with psoriasis vulgaris were randomly assigned to the treatment group or control group. In the research process, four subjects who did not follow the schedule were fell out. A total of 46 subjects completed this research project, with a completion rate of 92%. Figure 1 gives the flow chart of the clinical trial.

The subjects were mainly ranged 24–35 and 45–64. The male to female ratio was about 4:1. The patients without a family history of psoriasis account for about 78%. The disease duration was 1–34 years. About 63% of subjects show abnormal body mass index, 37%, a history of smoking, and 35%, a history of alcohol drinking. Baseline characteristics of subjects were as shown in Table 1.

3.2. PASI score

PASI score of the treatment group and control group at baseline was 18.20 ± 6.84 and 18.04 ± 6.75 (Mean \pm SD), and there was no statistically significant difference ($P = .89$, $P > .05$). After 8 weeks of treatment, the PASI scores of the treatment group and control group were 5.24 ± 3.03 and 9.24 ± 5.30 (mean \pm SD), in the treatment group was better than in the control group. The Rank-sum test showed that the difference between the two groups was statistically significant ($P < .001$). Inter-group significant differences start at 6 weeks ($P = .005$, $P < .01$) (Table 2).

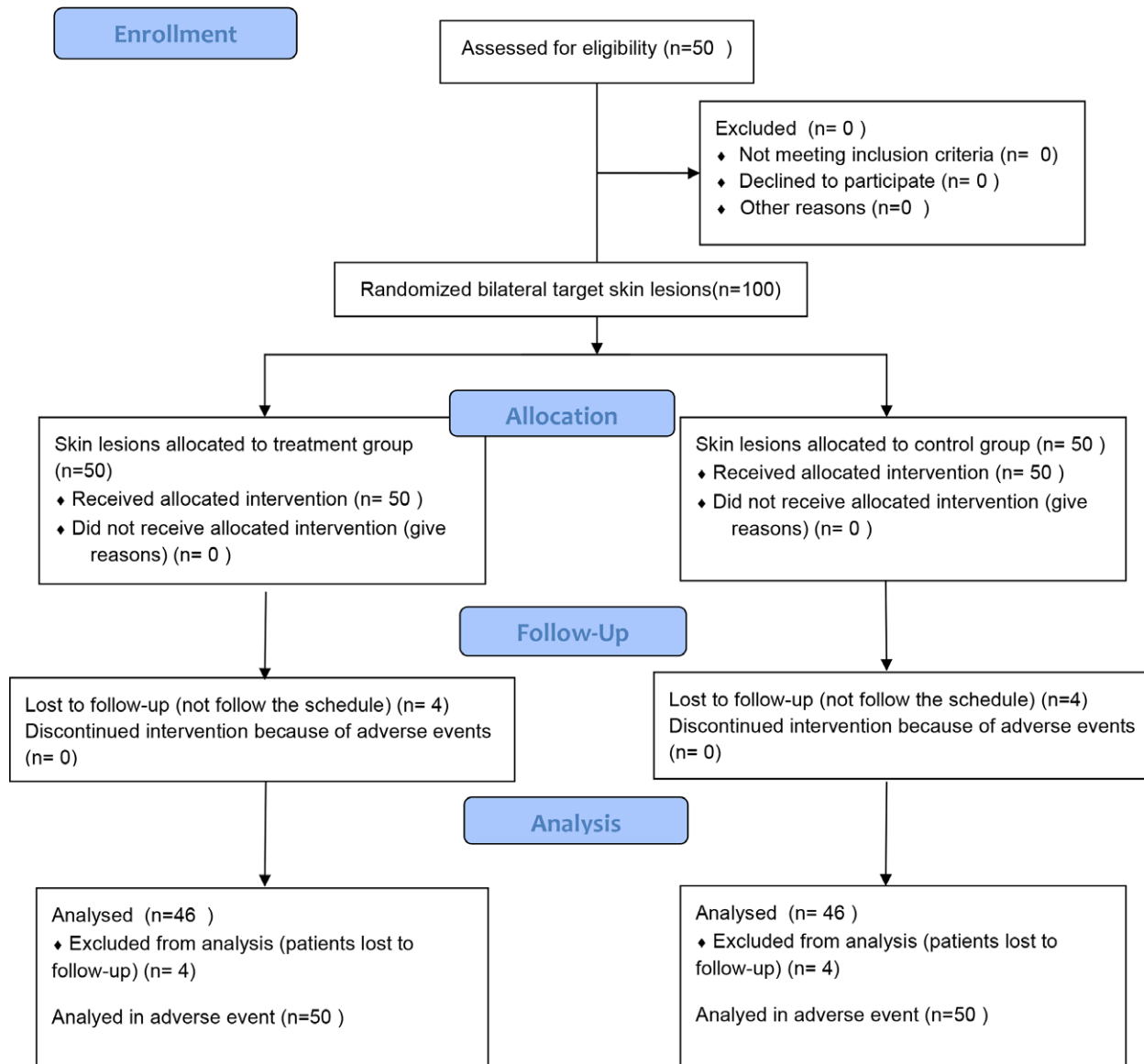


Figure 1. The flow chart of the clinical trial.

Table 1
Baseline demographic and clinical characteristics of the study population.

Characteristics		Treatment group = Control group (n = 46)
Age (yr)	Mean ± SD	34.93 ± 10.13
	Min–Max	21.00–64.00
Gender (n%)	Male	36 (78.26)
	Female	10 (21.74)
Family history of psoriasis (n%)	No	36 (78.26)
	Yes	10 (21.74)
Disease duration (years)	Mean ± SD	8.58 ± 7.829
	Min–Max	1.00–34.00
BMI before treatment (n%)	Thin	5 (10.87)
	Overweight	24 (52.17)
	Healthy	17 (36.96)
History of smoking (n%)	No	29 (63.04)
	Yes	17 (36.95)
History of alcohol drinking (n%)	No	30 (65.22)
	Yes	16 (34.78)
Heart rate (beats per minute)	Mean ± SD	72 ± 1
Systolic pressure (mm Hg)	Mean ± SD	124 ± 6
Diastolic pressure (mm Hg)	Mean ± SD	79 ± 5
Respiratory rate (breaths per minute)	Mean ± SD	17 ± 1

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared).

Table 2
PASI scores of treatment group and control group.

Follow-up examination time node (W)	Treatment group (mean ± SD)	Control group (mean ± SD)	P value
Week 0	18.20 ± 6.84	18.04 ± 6.75	.89
Week 2	15.93 ± 7.05	16.43 ± 6.99	.65
Week 4	12.87 ± 6.56	15.02 ± 7.31	.08
Week 6	8.74 ± 3.93	11.96 ± 5.80	.005**
Week 8	5.24 ± 3.03	9.24 ± 5.30	<.001**

* $P < 0.05$, ** $P < 0.01$ was statistically significant between the treatment group and the control group.
 PASI = Psoriasis Area Severity Index

3.3. PASI 75

PASI75 is a PASI score that decreases more than 75% from baseline. There was no significant difference in PASI75 between the treatment group and the control group in the first four weeks. Four weeks after, the percentage of PASI75 in the treatment group was significantly higher than that of the control group. In 8 weeks, the percentage of PASI75 in the treatment group was 48%, which was 15% in the control group. The difference between the two groups in PASI75 was statistically significant ($\chi^2 = 11.33$, $P < .05$) (Fig. 2).

3.4. PGA

In 8 weeks, Physician Global Assessment (PGA) in the treatment group and control group was 73.9% and 41.3%, respectively. The difference between the two groups in PGA was statistically significant ($\chi^2 = 10.015$, $P < .05$). PGA changes in the two groups are shown in Figure 3.

3.5. Skin barrier function

There was no statistically significant difference between the two groups at baseline in all indicators of skin barrier function ($P = .901$, $P > .05$). In 8 weeks, the differences between the two groups in skin pH value was statistically significant ($P = .011$, $P < .05$), and in humidity was statistically

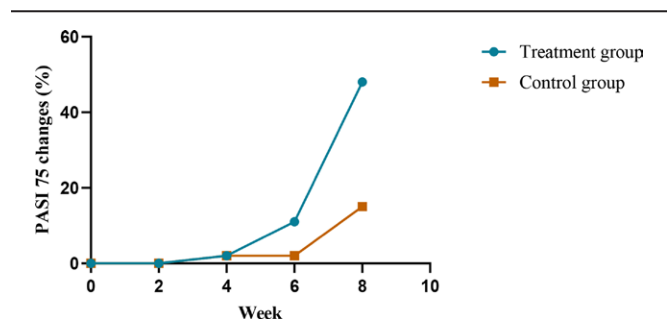


Figure 2. PASI75 changes in treatment group and control group over 8 weeks. Notes: PASI75: achievement of a 75% reduction in the PASI; * $P < 0.05$ was statistically significant between the treatment group and the control group.

significant ($P = .003$, $P < .05$). After 8 weeks, the differences between the two groups in skin temperature were not statistically significant ($P = .211$, $P > .05$), and in lipids was not statistically significant ($P = .16$, $P > .05$). Skin temperature, pH value, skin humidity, and lipids were significantly different in the treatment group before and after treatment ($P < .05$). The difference was found in these indicators in the control group before and after treatment was not statistically significant ($P > .05$) (Table 3).

3.6. Safety

A total of 12% (n = 6) of subjects experienced adverse events. The rates of adverse events in the treatment group and control group were 4% (n = 2) and 8% (n = 4), respectively. Adverse events include itching, burning sensation, desquamation, rash, and dryness. There was no statistical difference between the two groups in adverse events ($\chi^2 = 0.707, P > .05$) (Table 4).

4. Discussion

After 8 weeks of treatment, the treatment group performs better than the control group in the PASI score, the percentage of PASI 75, and PGA changes ($P < .05$). In terms of the skin barrier, the differences in the improvement of humidity and lipids between the two groups were statistically significant ($P < .05$). It

indicates that LJR Ointment may improve the PASI score, PASI 75, and PGA in patients with mild and moderate psoriasis with the blood-heat syndrome, and reconstruct the damaged skin barrier to some extent.

LJR Ointment contains Chinese angelica (*Radix Angelicae Sinensis*), Arnebia root (*Radix Arnebiae*), Rhubarb root and rhizome (*Radix et Rhizoma Rhei*), Natural indigo (*Indigo Naturalis*), Belvedere fruit (*Fructus Kochiae*), Light yellow sophora root (*Radix Sophorae Flavescens*) and Glabrous greenbrier rhizome (*Rhizoma Smilacis Glabrae*). Angelica polysaccharides can promote the apoptosis of keratinocytes of psoriasis-like lesions in guinea pig,^[29] and significantly reduce the positive expression rate of PCNA^[30] to inhibit the proliferation of psoriatic epidermal cells. In addition, Angelica polysaccharide has immunological activity and has a good curative effect on tumor treatment and radiation damage^[31] Arnebia root (*Radix Arnebiae*) inhibits the proliferative effect of IL-17A^[32] and EGF^[33] on HaCaT Cells, induces proliferation of HaCaT cells and secretes related cytokines, which can be used to treat psoriasis by inhibiting chemokine recruitment of leukocytes. In addition, the imiquimod-induced mouse model of psoriasis was restored by shikonin treatment, which ameliorated excessive keratinocyte proliferation.^[34] Rhubarb root and rhizome (*Radix et Rhizoma Rhei*), Natural indigo (*Indigo Naturalis*), Belvedere fruit (*Fructus Kochiae*), and Light yellow sophora root (*Radix Sophorae Flavescens*) inhibit the proliferation of HaCaT cells treated with serum immunoglobulin and peripheral blood mononuclear cells after treatment, in a dose-dependent manner. In particular, *Fructus Kochiae* has the strongest inhibitory effect.^[35]

The indirubin, an active component of natural indigo (*Indigo Naturalis*), can inhibit the activation of the cyclin-dependent

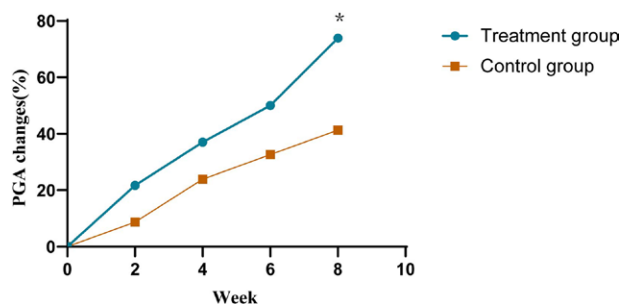


Figure 3. PGA changes in treatment group and control group over 8 weeks (%). * $P < 0.05$ was statistically significant between groups. PGA = Physician Global Assessment.

Table 3

Skin barriers function of treatment group and control group.

Skin barrier	Group	Baseline	8 weeks	Z value	P value
Temperature (°C)	Treatment group	32.78 ± 1.57	32.17 ± 1.78	-2.683	0.007**
	Control group	32.73 ± 1.66	32.72 ± 1.67	-0.014	0.99
	Z	-0.125	-1.252		
	P	0.90	0.21		
pH value	Treatment group	4.29 ± 0.30	4.42 ± 0.50	-2.079	0.038*
	Control group	4.26 ± 0.32	4.21 ± 0.34	-1.051	0.29
	Z	-0.063	-2.530		
	P	0.95	0.011*		
Humidity (%)	Treatment group	11.70 ± 18.74	22.00 ± 23.39	-3.285	0.001**
	Control group	9.63 ± 18.55	12.72 ± 19.78	-1.182	0.24
	Z	-0.809	-2.967		
	P	0.42	0.003**		
Lipids (µg/cm²)	Treatment group	9.02 ± 24.80	15.02 ± 30.55	-3.505	≤0.001**
	Control group	9.98 ± 26.33	14.85 ± 31.68	-1.567	0.12
	Z	-0.375	-1.574		
	P	0.71	0.16		

* $P < 0.05$, ** $P < 0.01$ was statistically significant between groups.

Table 4

Safety outcome of treatment group and control group after treatment.

	Treatment group	Control group	Total
Target lesions (n)	50	50	100
Pruritus (n%)	1 (2%)	2 (4%)	3 (6%)
Burning (n%)	1 (2%)	2 (4%)	3 (6%)
Scales (n%)	0 (0%)	0 (0%)	0 (0%)
Rash (n%)	0 (0%)	0 (0%)	0 (0%)
Dryness (n%)	0 (0%)	0 (0%)	0 (0%)
Adverse events (n%)	2 (4%)	4 (8%)	6 (12%)

All 50 patients report no significant abnormalities in blood routine examination, urine routine examination, liver function, renal function, and electrocardiogram before and after this research project.

kinase, signal transduction, and transcription-3 (STAT3).^[36,37] Therefore, it inhibits the excessive proliferation of keratinocytes in vitro.^[38] Glabrous greenbrier rhizome (*Rhizoma Smilacis Glabrae*) can significantly reduce serum TNF- α and IL-8 levels in patients with blood-heat-type psoriasis, inhibit chemotherapeutic effects of VEGF on inflammatory mediators and vascular endothelial cells and alleviate inflammation of the psoriasis lesions.^[39] Other studies have shown that: Topical indigo naturalis ointment is clinically proved to be an effective therapy for plaque-type psoriasis. Indirubin, as the active component of indigo naturalis, inhibits cell proliferation of epidermal keratinocytes.^[40] And indirubin ameliorated psoriasiform dermatitis by breaking CCL20/CCR6 axis-mediated inflammatory loops.^[41]

The working mechanism of LJR ointment for mild and moderate psoriasis vulgaris with the blood-heat syndrome remains unknown. Due to the functions of single Chinese herbs in LJR Ointment, it may explain the reason why LJR ointment can significantly improve skin pathological changes, inhibit related immune factors, and improve target lesions. More research is needed to explore the mechanism of such compound preparations as LJR ointment for mild and moderate psoriasis vulgaris with blood-heat syndrome. The skin barrier function refers to a “brick wall” structure composed of lipids and natural moisturizing factors between the stratum corneum cells and cells. The skin surface is covered with a sebum membrane, which retains moisture and has anti-inflammatory effects, forming a natural protective barrier for the human body.^[42,43] LJR Ointment functions in a two-pronged manner: Firstly, it prevents the loss of moisture from human skin and stops the outside water from entering the human body easily. Secondly, it prevents bacteria and fungi on the surface of the skin from invading the human body. The skin barrier function of patients with psoriasis is more vulnerable than that of healthy people. Even skin areas are not affected by lesions, while the recovery rate of barrier function sharply declines.^[44] Abnormal skin barrier function may be the underlying pathogenesis of psoriasis.

The function of the skin barrier depends on skin temperature, sebaceous gland content, pH value, and the water content of the stratum corneum. Under normal circumstances, skin pH value ranges between 4.5 and 6.5,^[45] and the normal stratum corneum water content ranges between 20% and 35%.^[46] The decrease in ceramide content of the main component of the sebaceous gland can make the keratinocytes disorderly arranged, dislocated with water loss, resulting in dryness, desquamation, and scale-like skin.^[47] Patients with psoriasis have dry skin and severe water loss and may have a pH value, high transepidermal water loss, and drop of water content in the stratum corneum.

The dermis telangiectasia accelerates blood flow, raises the skin temperature, and aggravates transepidermal water loss, complicated by chronic inflammation. As a result, the normal metabolism of the skin fails. The lipids, natural moisturizing factors, and anti-inflammatory factors reduce, resulting in dry skin and desquamation.^[48] Based on previous findings, this paper further explores the skin barrier function of patients with psoriasis. It was found that the temperature, moisture, lipid, and pH value of the skin barrier function in the treatment group were significantly improved before and after treatment, while the control group shows no significant changes. It indicates that LJR ointment can restore skin barrier function.

The reasons why no significant difference takes place in body temperature and lipids between the two groups after treatment are analyzed as follows: Firstly, participants with mild and moderate psoriasis with the blood-heat syndrome were in the active stage so that lesions may worsen in 8 weeks follow-up examination period. Secondly, the placebo ointment contains beeswax and vaseline. Vaseline has some therapeutic effects on psoriasis.^[49]

There are many limitations to the research findings of this paper. Firstly, psoriasis vulgaris is a chronic recurrent inflammatory skin disease so the long-term effect and safety of the treatment are very important for patients. This research project lasts for 8 weeks, which cannot give a long-term evaluation of the effect and safety of LJR ointment. Secondly, the sample size of this research project was relatively small, which may influence the outcomes. More clinical studies with larger sample size and longer duration and follow-up examination period are needed.

5. Conclusion

LJR Ointment can improve PASI score, PASI 75, and PGA in patients with mild and moderate psoriasis with the blood-heat syndrome. It may reconstruct the skin barrier function. LJR ointment seems safe to be used for patients with mild and moderate psoriasis with the blood-heat syndrome.

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