Psoriasis: Targets and Therapy

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CLINICAL TRIAL REPORT

A Randomized Controlled Trial for the Optimal Implementation of Psoriasis Treatment by Integrating Chinese and Western Medicine

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Background: Psoriasis is a refractory inflammatory disease affecting people worldwide. Currently, the prevalent guideline-recommended regimen is based on psoriasis severity; however, no corresponding studies have been conducted on the hierarchical selection of integrated Chinese and Western medicine treatments.

Objective: To explore the optimal implementation of psoriasis treatment by integrating Chinese and Western medicine.

Methods: We conducted a 16-week multicenter single-blind randomized controlled trial in China between December 2019 and July 2022. Patients with mild-to-moderate psoriasis (n=107) were randomized to receive oral Jueyin granules (JYG) or moving cupping treatment for 4 weeks, and then transferred to combine the internal or external TCM treatment for another 4 weeks base on the Psoriasis Area and Severity Index (PASI) score. Patients with severe psoriasis (n=193) were randomized to receive treatment with JYG and moving cupping (Group C), narrow-band ultraviolet B (Group D), or JYG, moving cupping and narrow-band ultraviolet B (Group E). Corresponding placebo therapies are applied to ensure single blind implementation. The primary outcome was the effective rate at week 8 and the incidence of relapse at week 16.

Results: The mild-to-moderate psoriasis group showed no differences in the efficacy or relapse resulting from the sequence of internal or external TCM treatment. However, both groups showed significant improvements in PASI score at week 8 compared to baseline ($P < 0.001$). The severe psoriasis group showed no significant difference in effective rates. While, more participants of Group E achieved PASI 75 (26.79%, P=0.02) at week 8, and Group D had a higher relapse rate at week 16 (21.57%, P=0.03).

Conclusion: Patients with mild-to-moderate psoriasis whether start with internal or external TCM treatment would be viable alternative. Integrated Chinese and Western medicine treatment favors patients with severe psoriasis in the improvement of skin lesions and reduction of recurrence.

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Keywords: plaque psoriasis, integrated Chinese and Western medicine, hierarchical therapy, Jueyin granules, moving cupping therapy, NB-UVB

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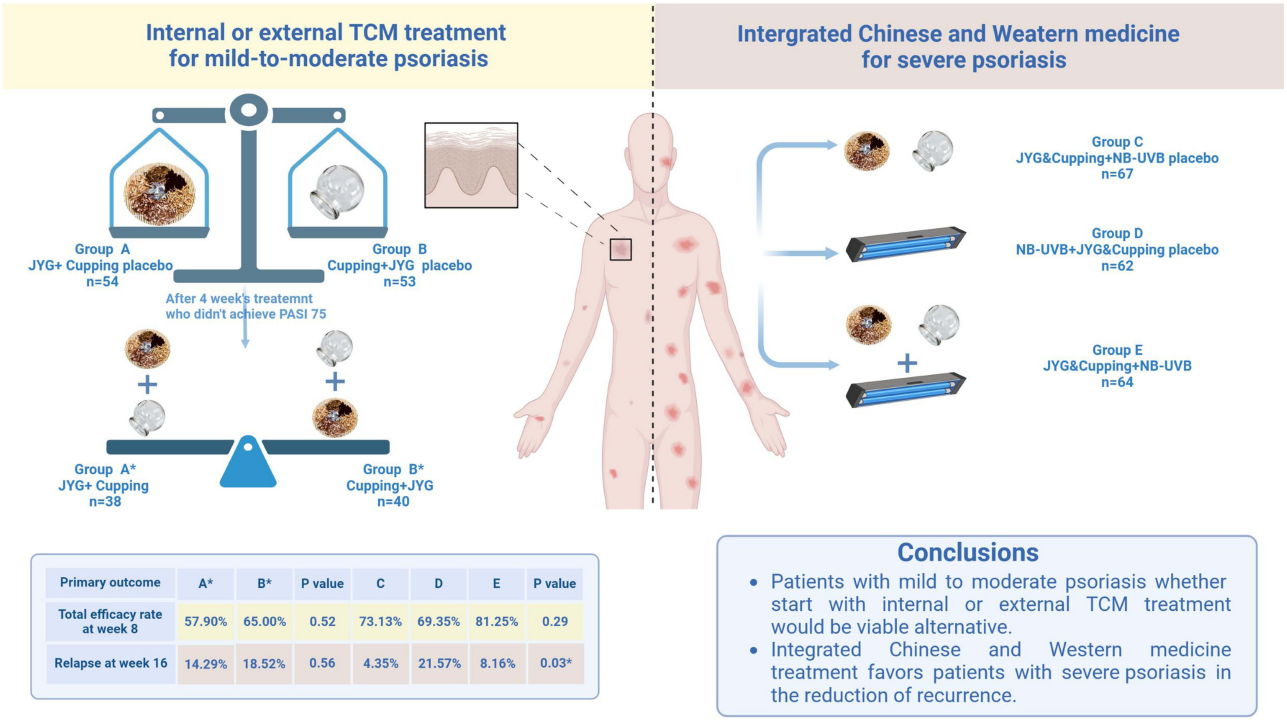
Graphical Abstract



Introduction

Psoriasis, a common chronic inflammatory disease, is characterized by an excessive proliferation of keratinocytes and inflammatory infiltration. It affects 2–4% of the world's population,[1] and plaque psoriasis is the most common variant, accounting for approximately 80% to 90% of clinical cases.[2] Typical lesions present with scattered erythema, scaling, and pitting hemorrhages.

The treatment of psoriasis is challenging because of its high recurrence rate and economic burden. Topical therapies, such as corticosteroids and vitamin D analogs, which target mild disease, are limited by treatment cycles and skin irritation. Systemic drugs, such as calcineurin inhibitors, acitretin, cyclosporine A, immunosuppressants, and biological agents, can rapidly suppress inflammation. However, drug–drug interactions and cumulative organ toxicities limit their long-term clinical application.[2] Thus, a regimen with few side effects and long-term efficacy is urgently needed.

In the traditional Chinese medicine (TCM) theory of treating psoriasis, the blood-heat syndrome primarily manifests as scarlet red lesions, increased scales, intense itching and continually expanding new rash accompanied by irritability, dry stool, and reddish-coloured tongue, which is most commonly seen in the progressive stage of psoriasis vulgaris, and accounts for 53.9% of psoriasis vulgaris cases.[3] Jueyin granules (JYG) is an effective formula developed by our research team for treating psoriasis with blood-heat syndrome.[4] We have demonstrated that the therapeutic effect of JYG lies in the upregulation of the vitamin D receptor, downregulation of phosphorylation signaling, and correlation with activator factor 3 transcription.[5] We also processed a network pharmacology analysis verified that Rutin, the main monomer of JYG, mitigates inflammation by downregulating AGE-RAGE signaling pathway in psoriasis.[6] Besides, we conducted another proteomics analysis proved that JYG may induce autophagy by up-regulating ApoA1 and inhibit the infiltration of CD4+ T cells and macrophages.[7] Acute and chronic toxicology tests demonstrated promising safety properties.[8]

Cupping is a popular complementary and alternative medicine (CAM) therapy in dermatology for conditions such as psoriasis and urticaria.[9,10] It is suitable for treating guttate and plaque psoriasis in the quiescent and degenerative phases

by promoting blood circulation, removing blood stasis, facilitating qi, and clearing collaterals. Although no definitive mechanism has yet been identified, it has been proven that cupping can improve skin barrier function and lipid metabolism to alleviate psoriasis.[11,12] A clinical study reported that cupping combined with herbal plaster was preferred over calcipotriol in terms of clinical efficacy and modification of serum vascular endothelial growth factor levels.[13]

The American Academy of Dermatology–National Psoriasis Foundation guidelines recommend phototherapy for treating moderate-to-severe psoriasis.[14] Narrow-band ultraviolet B radiation (NB-UVB) is a more common and effective method than the broadband form for the treatment of plaque psoriasis, with an optimal wavelength of 313 nm.[15] NB-UVB works through keratinocyte apoptosis and immune suppression.[16]

The current principles for treating psoriasis include standard, safe, and personalized medicine. The predominant strategy is sequential therapy, which effectively and rapidly controls disease progression and then switches to safer methods to maintain therapeutic benefit. The Psoriasis Professional Committee of the Chinese Society of Dermatology and Venereology and the American Medical Association (AMA) suggest hierarchical treatment for different psoriasis severities.[2] Topical ointments and targeted phototherapy are suitable for mild psoriasis in Western medicine (WM), while different TCM treatments can be applied externally or internally for different stages of progression. Phototherapy and systemic medications such as oral agents, and biologics are prescribed for patients with moderate-to-severe psoriasis. However, a hierarchical selection of integrated Chinese and Western medicine treatments for psoriasis of different severities is lacking. Therefore, our study aimed to optimize internal and external TCM treatments and establish treatment norms for integrating Chinese and Western medicine for mild-to-moderate and severe psoriasis.

Methods

This multicenter, single-blind, randomized controlled trial evaluated the hierarchical selection of treatment combinations according to the severity of skin lesions. The trial protocol has been previously registered (ClinicalTrials.gov, NCT03941431) and published,[17] also the study was approved by six centers' ethics committees respectively. This study was conducted according to the Consolidated Standards of Reporting Trials (CONSORT) statements. This study strictly adhered to the Declaration of Helsinki, and all participants provided written informed consent (Supplementary file). The inclusion and exclusion criteria were described amply in the previously published protocol, and we collected patients strictly according to the criteria. All participants were informed of the trial details and signed an informed consent form.

Randomization and Masking

According to the latest Chinese guidelines, psoriasis was classified as mild-to-moderate (BSA < 10%, Physician Global Assessment (PGA) ≤ 3) or severe (BSA ≥ 10%, PGA > 3).[18] In this study, the severe psoriasis group included only those patients with skin lesions involving 10–15% of the BSA. Patients with mild-to-moderate psoriasis were randomly assigned in a 1:1 ratio to Groups A or B for their second visit, whereas those with severe psoriasis were randomly assigned in a 1:1:1 ratio to Groups C, D, or E. The central layering and block randomization approach of SAS software (version 9.4) was used to randomize the data using a computer-generated random assignment sequence.

Interventions

Jueyin Prescription

The Jueyin prescription is a Chinese herbal preparation containing seven constituents (abalone shell, honeysuckle, tree peony bark, dried Rehmannia root, Hedyotis diffusa folium, and turmeric root tuber). JYG was administered twice daily after meals for eight weeks.

Moving Cupping Therapy

The patients were asked to assume the proper position and expose their localized skin while wearing a blindfold. Each group of concentrated points was generally targeted for approximately 5–10 seconds and five times before replacing the can. Force was evenly applied when pushing the can until the local skin appeared light red, red, deep red, or slightly purple colored. The standard operating procedure for moving the cup was performed in accordance with Part 5 of the People's Republic of China Cupping Standard G/B21709.5–2008. Moving cupping therapy was conducted three times weekly for eight weeks.

NB-UVB Phototherapy

NB-UVB therapy was performed using an initial dose of 0.5 J/cm^2, with incremental increases of 20% according to the patient's skin lesion response. Irradiation was performed three times weekly for eight weeks. In order to consolidate therapy till the completion of the following phase, patients need progressively taper down to weekly or biweekly exposure after the treatment period.

As for the placebo therapy, we implemented it in accordance with the registered scheme.

Outcome Measures

Primary Outcome

The primary outcome was the total efficacy rate at week 8 and the incidence of relapse at week 16. Efficacy Index = [(Pre-treatment PASI Credits - Post-Treatment PASI Credits)/ Pre-Treatment PASI Credits]×100%. Efficacy Index <30% referred to ineffective. The total efficacy rate is calculated as 100% minus the rate of ineffective improvement. Elapse is defined as when the maximum improvement from the baseline is attained but is reduced by 50%.[19] A more subjective definition can refer to calls for restarting therapy.[20]

Secondary Outcome Measures

Improvement in PASI, BSA, PGA, visual analog scale (VAS) scores for pruritus, TCM symptom score, Dermatology Life Quality Index (DLQI), patient-reported quality of life (PRQoL) at week 8 and the incidence of serious adverse events (SAEs) were estimated as secondary outcome measures. PASI, BSA, PGA, and VAS scores were assessed at week 0, 2, 4, 6, 8, 12 and 16. The TCM symptom scores for blood-heat syndrome, DLQI, and PRQoL were evaluated at week 0, 2, 4, 6, 8 and 16. AEs and SAEs were recorded throughout the treatment and follow-up period. Laboratory tests including the blood routine and blood biochemical parameters were performed at week 0 and week 8.

Trial Procedures

The trial procedure is illustrated in the flowchart (Figure 1). Group A received a combination of Jueyin prescription and moving cup placebo therapy, whereas Group B received a combination of moving cup therapy and JYG placebo for the first four weeks. And the group of patients with mild-to-moderate was categorized into internal treatment, external treatment or conversion groups based on whether they had achieved a PASI score of 75 in week four. More specifically, the internal and external groups which achieved PASI 75 continued the JYG or moving cupping treatments, respectively. Patients in the conversion groups (A* and B*) continued to receive combined treatment in the following four weeks. Group C received a combination of JYG prescription, moving cup therapy, and NB-UVB placebo. Group D received a combination of JYG placebo, moving cupping placebo, and NB-UVB phototherapy. Group E received JYG prescription, moving cupping therapy, and NB-UVB phototherapy. At the end of the eight weeks of treatment, the follow-up phase was initiated, with assessments every four weeks. All participants were provided with a free-of-charge emollient (YuZe Skin Barrier Recovery Body Lotion®; produced by Shanghai Jahwa United Co., Ltd) as basic skin care during the treatment period.

Statistical Analysis

All analyses were performed using IBM SPSS Statistics for Windows, version 21.0 (IBM Corp., Armonk, NY, USA) and a data network platform designed by the Data Management Center of Jiangsu Famous Medical Technology. Efficacy was evaluated using the full analysis set (FAS) supplemented by per-protocol analysis (PPS). Safety evaluation was analyzed in the safety set population.

Numerical variables with a normal distribution and uniform variance are expressed as means ± standard deviation (SD); the statistical inference was expressed using F and S-N-*K* tests; and repeated-measures analysis of variance was used for comparisons among the groups at multiple time points. Numerical variables with skewed distributions were assessed using rank-sum and Nemenyi tests, and the generalized estimation equation was used for comparison among groups at multiple time points. Categorical variables are expressed as frequencies, constituent ratios, and rates and analyzed using chi-square and nonparametric tests. A generalized estimation equation was used to compare the groups at

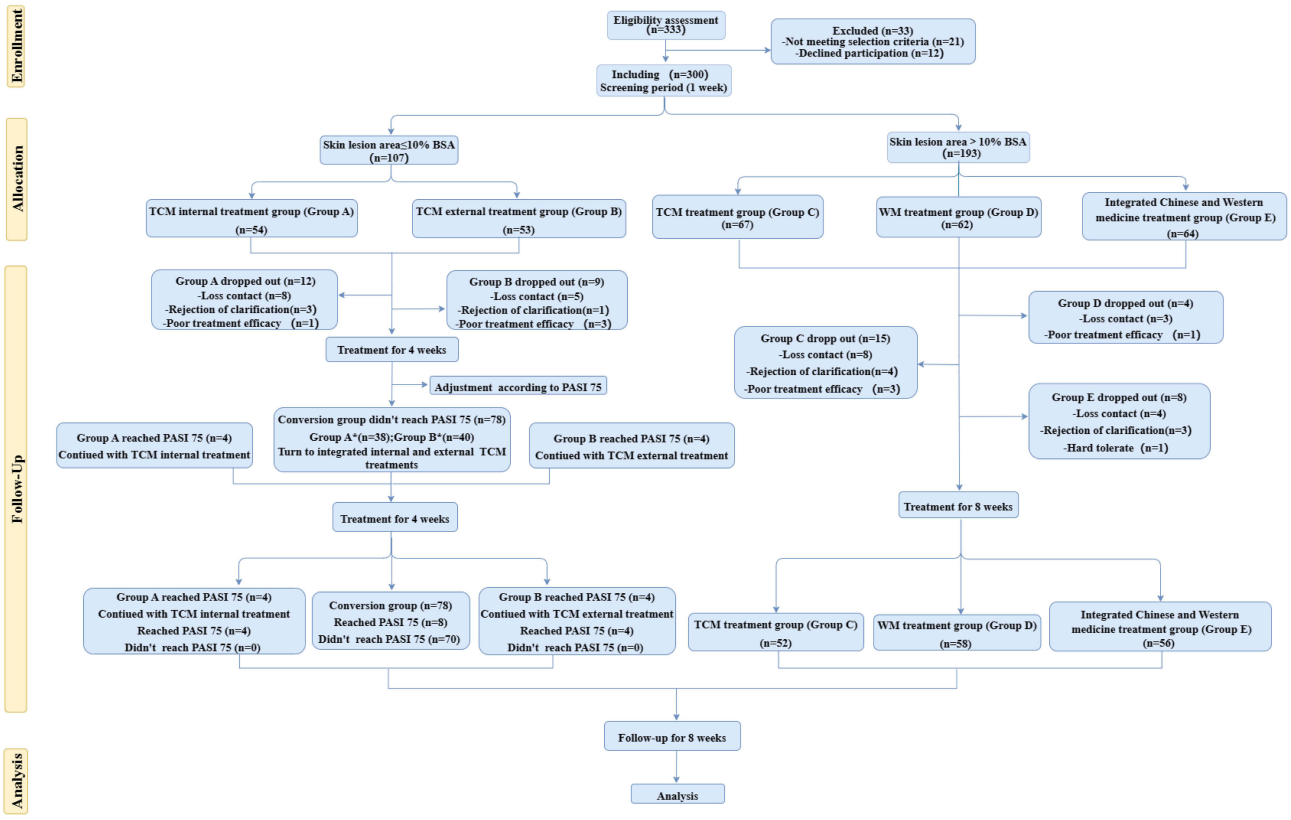


Figure 1 Flow diagram of trial procedure.

multiple time points. Hypothesis testing was performed using two-sided tests with 95% confidence intervals. Differences were considered statistically significant at $P < 0.05$.

Results

Trial Recruitment and Compliance

Among 333 individuals screened for inclusion, 33 were excluded for not meeting the selection criteria (n=21) and declining to participate (n=12). Finally, among the remaining 300 patients, 107 with mild-to-moderate plaque psoriasis were randomly assigned to Group A (n=54); and Group B (n=53). A total of 193 patients with severe plaque psoriasis were treated with Group C (n=67), Group D (n=62), or Group E (n=64). During the treatment phase, there were 12 dropouts in Group A, 9 in Group B, 15 in Group C, 4 in Group D, and 8 in Group E, mainly due to loss of contact.

Baseline Characteristics

The baseline characteristics did not differ significantly both the mild-to-moderate and severe groups. General information, including sex, age, body mass index (BMI), and symptom measures such as PASI score, BSA, and PGA, were comparable at baseline (Table 1).

Clinical Outcomes

After four weeks of treatment, Groups A and B both had four patients who achieved PASI 75 and continued their protocols. The remaining participants (n=78) were assigned to the conversion group, which received combined internal and external therapy. We redefined the group that received internal TCM treatment followed by internal and external combination TCM treatment as Group A* (n=38), while Group B* (n=40) underwent external TCM treatment first and then continued to combination with internal TCM treatment to explore the influence of the treatment sequence on TCM treatment efficacy (Figure 1).

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Table 1 Baseline Participant Characteristics of Mild-to-Moderate and Severe Plaque Psoriasis Groups

Characteristic and Clinical Outcomes	Mild-to-Moderate Plaque Psoriasis Group		Severe Plaque Psoriasis Group		
	Group A (n =54) Mean (SD) or Numbers	Group B (n = 53) Mean (SD) or Numbers	Group C (n = 67) Mean (SD) or Numbers	Group D (n = 62) Mean (SD) or Numbers	Group E (n = 64) Mean (SD) or Numbers
Sex (M/F)	33/21	34/19	54/13	44/18	50/14
Age (years)	40.04±12.70	44.70±12.51	43.67±12.84	43.11±14.29	45.53±13.50
BMI (kg/m^2)	23.40±3.49	23.67±2.62	24.18±3.05	25.06±4.10	24.59±4.64
Psoriasis duration (months)	99.00±77.99	126.94±125.56	118.13±91.18	144.65±132.65	129.20±91.95
Family history of psoriasis (n, %)	20 (37.04)	14 (26.42)	13 (19.40)	15 (24.19)	17 (26.56)
PASI	5.04±3.46	4.76±2.72	9.36±3.83	9.81±4.35	9.61±4.53
BSA	4.94±2.46	5.08±2.87	12.34±1.90	12.41±2.78	12.67±2.00
PGA	2.06±0.76	1.91±0.74	2.64±0.79	2.77±0.76	2.78±0.86
DLQI	8.63±5.39	7.70±5.27	13.64±6.10	13.00±5.75	14.03±5.53
PRQOL	8.96±5.53	9.43±6.24	14.46±6.79	12.84±6.78	14.19±6.33
VAS	32.91±24.19	32.89±25.45	54.51±23.71	48.97±26.55	56.58±23.89
TCM symptom score	3.20±1.71	3.62±1.51	4.16±1.71	3.82±1.59	4.13±1.82

Note: Group A, traditional Chinese medicine (TCM) internal treatment group; Group B, TCM external treatment group; Group C, TCM treatment group; Group D, Western medicine (WM) treatment group; Group E, integrated TCM and WM treatment group.

Abbreviations: PASI, Psoriasis Area and Severity Index; BSA, body surface area; PGA, improvement in physician's global assessment; DLQI, dermatology life quality index; PRQoL, patient-reported quality of life; VAS, visual analog scale; SD, standard deviation.

Compared with baseline, Groups A* and B* showed improved PASI scores in the mild-to-moderate group at weeks 8 and 16 (P<0.001). At the endpoint of the follow-up period, the PASI scores of Groups A* and B* had decreased by averages of 1.54 and 1.57, respectively (Figure 2A, Mean ±SEM). The total effective ratios in Groups A* and B* reached 57.89% and 65.00%, respectively. However, the efficacy ratios at week 8 and the relapse rate at weeks 12 and 16 based on PASI scores did not differ significantly between groups A* and B* (Table 2).

The group of patients with severe psoriasis showed no significant difference in efficacy rates (P=0.29). However, Group D, which received NB-UVB phototherapy, had a higher relapse rate at week 16 (Group C: 4.35%, Group D: 21.57%, Group E: 8.16%, P=0.03). The proportion of patients with a PASI 75 response at week 8 was greater in Group E (n=15, 26.79%) than in the other groups (Group C: n=5, 9.26%; Group D: n=13, 22.41%; P=0.02). While Group E showed a greater reduction in BSA, PGA, VAS, and DLQI scores, the difference was not significant. Group C had a lower TCM symptom score for blood-heat syndrome after JYG treatment (P < 0.01). However, the VAS scores were better in Group D versus Group C at week 8 (42.45±21.52 vs 32.97±25.29, P=0.03). During the follow-up period, the efficacy of Groups C and E was more stable than that of Group D, and efficacy-related indicators improved continuously. After the end of the treatment, Group D demonstrated a trend toward deterioration of the efficacy evaluation index.

Safety

Among patients with mild-to-moderate psoriasis, JYG and cupping therapy were safe and well tolerated. No serious adverse events were observed. During the treatment phase, mild nausea (n=1) and diarrhea (n=2) were reported in patients receiving JYG therapy, which accounted for 60% of the AEs. Pruritus (mild, n=2; moderate, n=2) comprised most of the AEs in patients receiving cupping therapy (57.14%). The gastrointestinal reactions and itching resolved without intervention.

Among patients with severe psoriasis, six in Group C, three in Group D, and eight in Group E reported AEs at least once during the treatment phase (P=0.72). The AEs in Group C occurred only in the treatment phase and included mild pruritus (n=3) and diarrhea (n=3). In Group D, 60% of AEs were pruritus (n=3) during the entire study period. In Group E, one patient reported three occurrences of moderate lower extremity edema, which was reduced to mild edema after medical intervention (Table 3).

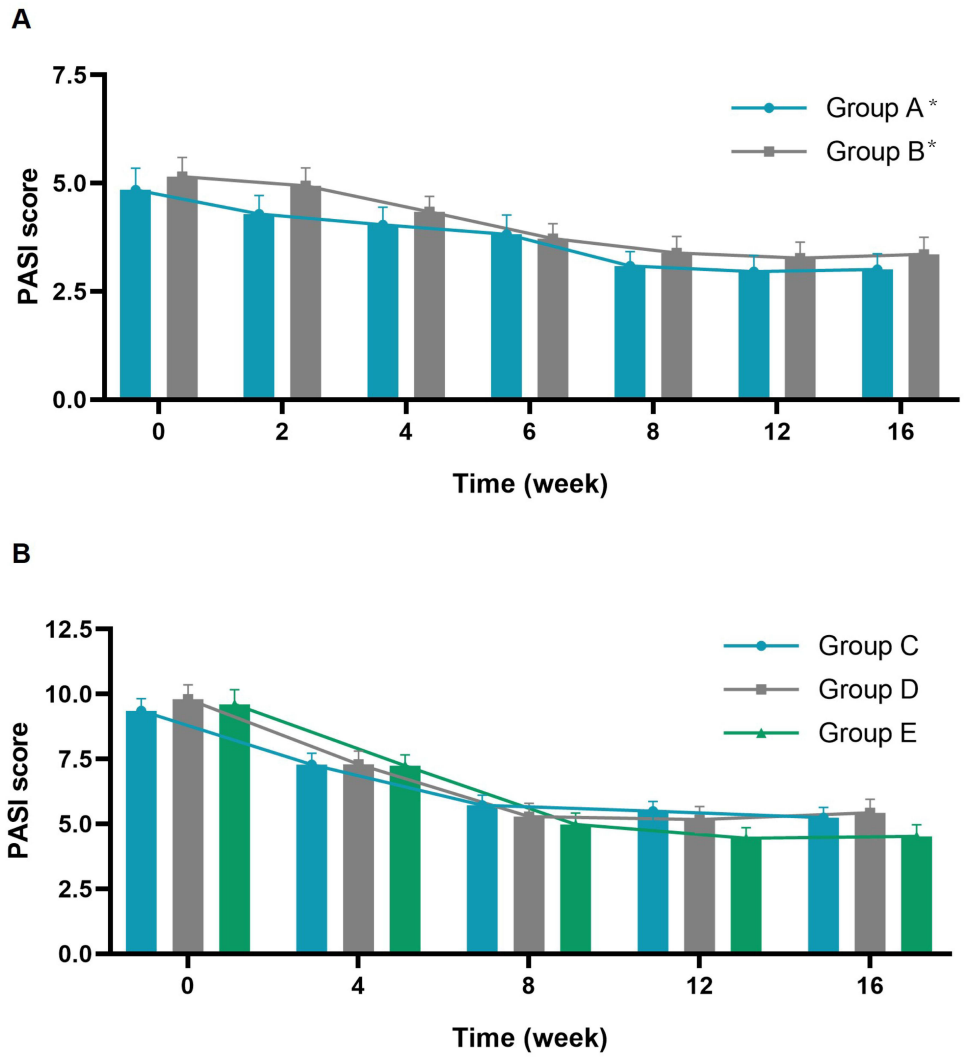

Figure 2 PASI score of mild-to-moderate group (**A**) and severe group (**B**) (Mean ±SEM).

Discussion

The sequential therapy investigated whether the order of JYG or cupping therapy affected subsequent combination therapy for mild-to-moderate psoriasis. Although it turned out that there was no significant difference, early oral TCM treatment controlled systemic inflammation, followed by topical treatment, including external TCM or WM treatment to

Table 2 Primary and Secondary Outcomes (Full Analysis Set)

Outcome Measurements		Mild-to-Moderate Plaque Psoriasis Group			Severe Plaque Psoriasis Group			
		Group A* (n=38) Number (rate)	Group B* (n=40) Number (rate)	P-value	Group C (n=67) Number (rate)	Group D (n=62) Number (rate)	Group E (n=64) Number (rate)	P-value
Primary outcomes	Total efficacy rates (week 8)	22(57.90)	26(65.00)	0.52	49(73.13)	43(69.35)	52(81.25)	0.29
	Relapse rate (week 12) yes/no	3/32	4/33	0.62	4/49	7/52	8/52	0.59
	Relapse rate (week 16) yes/no	4/28	5/27	0.56	2/46	11/51	4/49	0.03§

(*Continued*)

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Table 2 (Continued).

Outcome Measurements		Mild-to-Moderate Plaque Psoriasis Group			Severe Plaque Psoriasis Group			
		Group A* (n=38) Number (rate)	Group B* (n=40) Number (rate)	P-value	Group C (n=67) Number (rate)	Group D (n=62) Number (rate)	Group E (n=64) Number (rate)	P-value
Secondary outcomes	PASI 50 (week 8)	16 (42.11)	15 (37.50)	0.65	17 (31.48)	30 (51.72)	28 (50.00)	0.03§
	PASI 75 (week 8)	3 (7.89)	5 (12.50)	0.51	5 (9.26)	13 (22.41)	15 (26.79)	0.02§
	PASI 90 (week 8)	2 (5.26)	1 (2.50)	0.53	1 (1.85)	5 (8.62)	4 (7.14)	0.34
	BSA #	−0.94±1.62	−0.88±2.84	0.72	−2.36±3.34	−3.56±4.70	−3.72±5.54	0.27
	PGA #	−0.71±0.84	−0.43±0.71	0.09	−0.77±0.86	−0.98±0.83	−1.00±0.98	0.31
	VAS #	−11.50±19.82	−7.70±28.03	0.66	−14.31±24.81	−17.40±23.28	−19.51±22.80	0.40
	TCM symptom score^	−1.44±2.12	−1.71±2.41	0.53	−2.61±1.89	−1.72±2.07	−2.35±1.93	0.13
	DLQI #	−2.82±4.40	−1.33±6.05	0.19	−6.30±5.90	−5.25±4.44	−6.65±6.79	0.53
	PRQoL #	−0.97±4.38	−1.05±5.62	0.88	−3.27±5.64	−3.85±5.25	−2.56±4.84	0.29

Note: Group A*, conversion group with initial traditional Chinese medicine (TCM) treatment followed by combination of internal and external TCM treatments; Group B*, conversion group with initial external TCM treatment followed by the combination of external and internal TCM treatments; Group C, TCM treatment group; Group D, Western medicine (WM) treatment group; Group E, integrated TCM and WM treatment group; Relapse, when the maximum improvement from the baseline is attained but is reduced by 50%; PASI, Psoriasis Area and Severity Index; BSA, body surface area; PGA, improvement in physician global assessment; VAS, visual analog scale; SD, standard deviation; DLQI, dermatology life quality index; PROoL, patient-reported quality of life. The mild-to-moderate group was analyzed using per-protocol analysis. The severe group was analyzed using the full analysis set. # Change in scores from Week 0 to Week 8. ^ Change in scores from Week 0 to Week 16. § P<0.05.

target refractory areas such as the calf or back, can ensure efficacy and increase patients' compliance by reducing the frequency of visits. This regimen concept was tested and verified in a precedent study.[21] The efficacy of the combination of internal and external therapy in the second part is also consistent with the results of some studies. For example, there is a study showed that calcipotriol achieves better clinical efficacy when combined with JYG (Efficacy rate: 80.77%, P<0.05).[22] A randomized controlled study conducted by Parker in 2021 also found that oral Chinese medicine combined with calcipotriene had a better therapeutic trend, but there is no significant difference.[23]

Among patients with severe psoriasis, compared with monotherapy (Group C: 9.80%, Group D: 22.41%, P=0.02), the combined treatment had a synergistic effect on reducing the relapse rate (3.13%) and increasing effectiveness (Group E achieved PASI 75 up to 26.79% at week 8). Furthermore, Group E showed continuous improvement in efficacy during the follow-up period (Figure 2B, Mean ± SEM). The result supported by a meta-analysis which demonstrated the enhanced efficiency of the oral administration of Chinese medicine in combination with NB-UVB for treating psoriasis vulgaris, and the combination therapy resulted in a 24% increase in the rate of PASI60 and a decrease in the rate of adverse events.[24] And according to a retrospective study, recurrence rates in NB-UVB treatments was up to 42.9% at 3 months,[25] the use of TCM can just make up for this shortcoming. Meanwhile, problems with patient compliance were observed in the TCM group during the early stages of treatment. The proportion of patients lost to follow-up in the TCM group was higher than that in the other treatment groups, which may indicate poor efficacy. WM can help improve the VAS scores of patients receiving TCM treatment, which may help patient compliance and ensure continuous TCM treatment. Overall, the combination of the TCM and WM regimens was comprehensive for the entire course of therapy. Compared to the other protocols, Group E achieved the desired effect and lower recurrence.

In terms of primary outcomes, although the combination group achieved good success in controlling the recurrence rate. It was not satisfactory on efficacy indicators, for the PASI 75 response rate appeared to be somewhat low in both the UVB and UVB combined TCM groups. As a meta-analysis showed that the patients accepted UVB regimen achieving PASI 75 reduction was 61% (95% CI50–71%).[26] However, as a stratified design study, we only performed phototherapy and comprehensive treatment on patients with BSA ≥10% or PGA>3, which would affect the final improvement result, since the baseline level of PASI is high. Furthermore, we retrieve a review of phototherapy protocols for psoriasis treatment published in the Journal of American Dermatology. It suggests the typical regimens for NB-UVB involve dosing 3 times every week for at least 3 months.[27] So, we consider the low PASI 75 of NB-UVB may also cause by shorter treatment cycle. Through our study, we can see that the advantage of combining TCM is mainly focusing on the

Table 3 Adverse Events

(1) Mild-to-Moderate Plaque Psoriasis Group				
Adverse events	**Treatment phase (weeks 0–8)**		**Follow-up phase (weeks 8–16)**	
	Group A* (n=38)	**Group B* (n=40)**	**Group A* (n=38)**	**Group B* (n=40)**
Pruritus	0	2-mild 2-moderate	0	2-mild
Nausea	1-mild	1-moderate	0	0
Diarrhea	2-mild	0	0	0
Dizziness	0	1-mild	0	0
Common cold	1-mild	1-mild	0	0
Hepatic function abnormalities	0	0	1-moderate	1-mild 1-moderate
Sore throat	1-mid	0	0	0
All adverse events reported	5	7	1	4
Number of participants who reported adverse events (%)	4 (10.53%)	6 (15.00%)	1 (2.63%)	4 (10.00%)
χ2 (P-value)	0.063 (0.80)		0.749 (0.39)	

(2) Severe plaque psoriasis group						
Adverse events	**Treatment phase (weeks 0–8)**			**Follow-up phase (weeks 8–16)**		
	Group C (n=67)	**Group D (n=62)**	**Group E (n=64)**	**Group C (n=67)**	**Group D (n=62)**	**Group E (n=64)**
Pruritus	3-mild	2-mild	1-mild	0	1-moderate	1-moderate
Urticaria	0	0	0	0	1-mild	0
Dermatitis	0	0	1-moderate	0	0	0
Lesion aggravation	1-moderate	0	0	0	0	0
Stomach ache	0	0	1-mild	0	0	0
Hepatic function abnormalities	0	0	0	0	0	1-moderate
Diarrhea	3-mild	0	1-mild	0	0	0
Lower extremity edema	0	0	1-mild 3-moderate	0	0	0
Xerophthalmus	1-mild	0	0	0	0	0
Dizziness	1-mild	0	0	0	0	0
Nosebleed	0	1-mild	0	0	0	0
All adverse events reported	9	3	8	0	2	2
Number of participants reported adverse events (%)	6 (8.96%)	3 (4.84%)	4 (6.25%)	0 (0%)	2 (9.68%)	2 (3.13%)
χ2 (P-value)	0.888 (0.72)			2.266 (0.40)		

Note: Group A*, conversion group with initial internal treatment with traditional Chinese medicine (TCM) followed by the combination of internal and external TCM treatments; Group B*, conversion group with initial external treatment with TCM followed by the combination of external and internal TCM treatments; Group C, TCM treatment group; Group D, Western medicine (WM) treatment; Group E, integrated TCM and WM treatments. Week 0, baseline; week 8, end of the treatment phase; week 16, end of the follow-up phase.

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reduced recurrence rate during the follow-up period in Table 2, so the comprehensive protocol had similar results with NB-UVB with efficacy rate. On all accounts, we will optimize the frequency of NB-UVB in future and clinical trials.

This study had several limitations. Firstly, the treatment and follow-up duration in the present study was only eight weeks, which was not long enough to reflect the long-term advantages of TCM in chronic disease management or the average time to relapse in each group. Secondly, because of the specificity of moving cupping, even after unified training, investigators have individual differences in operational force, distance, and speed. Additionally, participants should be allowed to add or subtract two to three types of Chinese herbal medicine on the basis of JYG to address some important accompanying symptoms, such as gastrointestinal reactions and sleeping problems for fully utilize the benefits of syndrome differentiation and treatment.

Conclusion

The order of internal and external treatments exerts insignificant impact, but given the clinical implementability, we recommend the patient with mild-to-moderate psoriasis take JYG first to control condition. As for severe psoriasis, integrated treatment with JYG and moving cupping with NB-UVB is a safe and effective method for reducing the relapse rate. Our pilot study provides a practical and sound integrate Chinese and Western medicine treatment program to enhance treatment effects for psoriasis patients. However, more rigorous study and uniform evaluation standards are required to determine the best course of therapy.

Key Points

- Why was the study undertaken?

Currently, there is a vacant in the hierarchical selection of integrated Chinese and Western medicine therapies for different severities of psoriasis.

- What does this study add?

We propose integrative medicine treatment options for different severity of psoriasis including internal and external TCM treatment and phototherapy therapeutic regimen.

- What are the implications of this study for disease understanding and/or clinical care?

A regimen with few side effects and long-term efficacy is brought up by our study, which is promising to improve patients' quality of life and reducing the financial burden.

Abbreviations

TCM, Traditional Chinese medicine; WM, Western medicine; NB-UVB, Narrow-band ultraviolet B; PASI, Psoriasis Area and Severity Index; JYG, Jueyin granules; CAM, Alternative medicine; AMA, American Medical Association; BSA, Body surface area; PGA, Physician Global Assessment; VAS, Visual analog scale; DLQI, Dermatology Life Quality Index; PRQoL, Patient-reported quality of life; SAEs, Adverse events; FAS, Full analysis set; PPS, Per-protocol analysis; SD, Standard deviation; SEM, Standard error of mean; BMI, Body mass index; TNF-α, Tumor necrosis factor-alpha; IL-17, Interleukin-17.

Ethical Approval

The trial protocol has been previously registered (ClinicalTrials.gov, NCT03941431) and published. The study was approved by the Institutional Ethics Committees of six centers in China separately, including Ethics Committee of Yueyang Hospital of Integrated Traditional Chinese and Western Medicine affiliated to Shanghai University of Traditional Chinese Medicine (2019-031), Wuhan No. 1 hospital Medical Ethics Committee (2019-09), Ethics Committee of the Traditional Chinese Medicine Hospital of southwest medical university (KY2019087/FS-01), Ethics Committee of the Second Affiliated Hospital of Fujian Traditional Chinese Medical University (SPHFJP-K2019034-02), Ethics Committee of Jiangsu Provincial Hospital

of Traditional Chinese Medicine affiliated to Nanjing University of Traditional Chinese Medicine (2019NL-119-02), and The Ethics Committee Dermatology Hospital of Shanghai (2019-29). This study strictly adhered to the Declaration of Helsinki.

Data Sharing Statement

The data for this study are available upon request from the corresponding author. The request should state the title and aim of the research for which the data are requested.

Ethical Statement

The patients in this manuscript have given written informed consent to the publication of their case details.

Consent for Publication

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that there are no conflicts of interest in this work.

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