



Review

Efficacy of a Chinese herbal medicine for the treatment of atopic dermatitis: A randomised controlled study



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ABSTRACT

Background: More randomised control trials are required to assess the efficacy of traditional Chinese medicine. This multi-centre, randomised, assessor-blind, controlled study assessed the efficacy of the Chinese herbal formula Pei Tu Qing Xin Tang (PTQXT) for treating patients with atopic dermatitis (AD).

Methods: Patients aged 5–25 years with moderate-to-severe AD were randomised to receive a 12-week treatment involving either oral administration of PTQXT; oral administration of PTQXT combined with an external application of Chinese herbs; or oral administration of antihistamine and a placebo of PTQXT pills added to topical 1% mometasone furoate. The primary end-point measure was the change in the Scoring Atopic Dermatitis Index (SCORAD) at the end of the observation period, and secondary end-points included quality of life (QOL). The outcomes were evaluated at baseline, then every 4 weeks from week 4 to week 12 and every 8 weeks from week 12 to week 36.

Results: Two hundred and seventy-five patients were recruited. During the 12-week treatment period, up to the primary end-point, the mean SCORAD decreased gradually in all three groups. At week 28 and week 36, there was a significantly greater decrease in the mean SCORAD for the Chinese herbal medicine-treated groups than for the control group (at week 28, $P=0.002$ and $P=0.036$, respectively; at week 36, $P<0.001$ and $P=0.002$, respectively). At week 36, the difference in QOL scores showed a significantly greater improvement in both Chinese herbal medicine-treated groups than in the control group ($P<0.001$ and $P<0.001$, respectively).

Conclusions: PTQXT is effective in decreasing the severity of the disease and improving the QOL in patients with moderate-to-severe AD.

Trial registration: Chinese Clinical Trial Registry: ChiCTR-TRC-08000156.

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1. Introduction

Atopic dermatitis (AD) is a chronic, relapsing, inflammatory skin disease that affects 8.3% of children aged 3–6 years in urban areas of China.¹ AD has serious negative effects on patients' quality of life (QOL) due to pruritus, sleep disturbance and affected daily activities. The management of AD includes the use of topical emollients–topical corticosteroids that are the mainstay for the treatment of flares and are the standard with which other treatments are compared. Topical calcineurin inhibitors are popular among AD patients because of the lack of side effects of corticosteroids. However, despite this range of treatments, some patients remain unresponsive. In an effort to avoid the potential adverse effects and to attain better clinical outcomes, various dietary therapies including Chinese medicine have been adopted, especially in Asia,² although its beneficial effects in patients with AD have not been consistently demonstrated.^{2,3} The few trials of Chinese medicine have not produced convincing results to date, thus highlighting the need for further large-scale trials.⁴

For centuries, Chinese herbal medicine has been routinely used for the treatment of AD in China,⁵ and an expert consensus recently recommended it for this purpose.⁶ The formula of Pei Tu Qing Xin Tang (PTQXT) is one of the recommended prescriptions. According to the fundamental principles of traditional Chinese medicine, the treatment should be tailored to the individual clinical presentation of each patient, even though they all have the same medical diagnosis, and should be modified at different stages of the illness. The formula of PTQXT has been derived from long-term clinical experience, and its therapeutic effects on AD have been demonstrated in a preliminary study.⁷ The purpose of this study was to evaluate the efficacy of modified PTQXT in the treatment of AD. We compared individualised therapy with western medicines for the treatment of AD using a multi-centre, randomised, assessor-blind, controlled study design.

2. Methods

2.1. Study design

This study was designed as a multi-centre, randomised, controlled, parallel-group, prospective, assessor-blind trial and was conducted nationally at six sites in China. The 36-week study comprised a 12-week treatment period followed by 24 weeks of follow-up. The Ethics Committee of our hospital approved the protocol and sent a copy of the approval to each site. The trial was registered in the Chinese Clinical Trial Registry with the registration of ChiCTR-TRC-08000156.

2.2. Participants

The participants were male and female patients aged between 5 and 25 years, with a diagnosis of AD (based on the criteria of Han-ifu and Rajka⁸), defined as moderate-to-severe (according to the scoring system of Rajka and Langeland⁹), a course of disease ≥ 1 year and a remission period < 3 months within a year. The patients were recruited between February 2009 and February 2011 from the dermatological outpatient clinics of the six participating hospitals, and were required to have normal routine blood, urine and stool examinations, and liver and renal function tests at baseline. The criteria for inclusion were no serious bacterial infections and no use of systemic antihistamines, corticosteroids, immunosuppressants, ultraviolet light treatments or other preparations of traditional Chinese herbal medicine (TCHM) during the 2 weeks before enrolment. The parents or guardians of the children were told that they had an equal probability of being assigned to any of the groups in the informed consent process. Written informed consent was obtained from each adult patient or from the parents or guardians of children under 18 years of age (not inclusive).

2.3. Randomisation and blinding

Eligible patients were randomly allocated at a ratio of 1:1:1 to receive three different treatments in chronological order by an independent controller of the investigators. Randomisation was performed using a computer-generated random number code in our university. This code and the drugs used by the patients were concealed from the assessors, to whom all patients were requested not to reveal their allocated treatment. To examine whether the blinding had been successful, after assessment the assessors were asked to guess which group the patients had been assigned to.

2.4. Treatment

2.4.1. Oral administration of PTQXT (group A)

The basic prescription of PTQXT is composed of nine herbs (the composition and action of each herb are summarised in Table 1^{10,11}), and was modified according to traditional Chinese medicine (TCM) differentiation: to counter the relative predominance of heart-fire, 10 g of Cornu Bubali (Shuiniujiao) was added; and to counter the relative predominance of spleen deficiency, 10 g of Poria (Fuling) and 10 g of Rhizoma Atractylodis Macrocephalae (Baizhu) were added. The medicinal plants were manufactured, packaged and labelled by Kangmei Pharmaceutical Co., Ltd. (Guangzhou, China) and met the Good Manufacturing Practice standards. The clinicians who chose the appropriate treatment had been practicing medicine for at least 10 years, and had attended continuing medical education lectures on evidence-based herbal medicine interventions.

Table 1
Composition and action of PTQXT.

Medicinal plants	Weights	Action
Radix Pseudostellariae	10.0 g	TCM: replenishing qi, strengthening the spleen, promoting the production of body fluid and nourishing the lung Pharmaceutical study: anti-ageing effect, reinforcing the immune function and regulation of the digestive function
<i>Forsythia suspensa</i>	10.0 g	TCM: clearing heart-fire, relieving the toxicity of sores and dissipating externally contracted wind-heat Pharmaceutical study: antimicrobial, anti-inflammatory and hepato-protective effects
Ramulus Uncariae cum Uncis	10.0 g	TCM: extinguishing wind, alleviating tetany, clearing heart-fire and pacifying the liver Pharmaceutical study: sedative, anticonvulsant and hypotensive effects
Medulla Junci	3 bundles	TCM: clearing heart-fire and promoting urination Pharmaceutical study: anti-oxidative and antimicrobial effects
Herba Lophatheri	10.0 g	TCM: clearing heat, draining fire, relieving restlessness, quenching thirst, promoting urination and freeing Lin syndrome Pharmaceutical study: antipyretic and diuretic effects, and reinforcing immune function
Semen Coicis	10.0 g	TCM: clearing damp, promoting diuresis and invigorating the spleen to stop diarrhoea Pharmaceutical study: antipyretic, analgesic, hypoglycaemic and antineoplastic effects
Rhizoma Dioscoreae	10.0 g	TCM: supplementing qi, nourishing yin, nourishing the spleen, lung and kidney and treating spontaneous emission and leukorrhagia. Pharmaceutical study: reducing blood sugar, regulating immune function and anti-oxidative effect
Concha Ostreae	10.0 g	TCM: settling fright, quieting the spirit, subduing Yang, supplementing yin and resolving hard lumps Pharmaceutical study: calming effect, reinforcing immune function and anti-ulcerative effect
Radix Glycyrrhizae	3.0 g	TCM: invigorating the spleen, replenishing qi, clearing heat, relieving toxicity and moderating the properties of herbs Pharmaceutical study: hormone-like, anti-inflammatory and antineoplastic effects

Children who weighed less than 40 kg were told to take one dose per decoction, whereas those who weighed 40 kg and above took two doses per decoction. A dose of herbs was decocted in water twice. The dose was boiled, simmered for between 20 and 30 min, then reduced to approximately 150 mL and then given orally 30 min after a meal at a dose of 150 mL twice a day. Non-medicated topical emollients were permitted throughout the study for all patients.

2.4.2. Combination of TCM therapy (group B)

The oral decoction was the same as that for group A. The external wash formula was composed of four dispensing granules containing Flos Lonicerae (2.0 g), Rhizoma Polygonati (4.0 g), Herba Menthae (2.0 g) and Radix Glycyrrhizae (2.0 g), which were manufactured by Jiangyin Tianjiang Pharmaceutical Co., Ltd. (Jiangyin, China) and fulfilled the Good Manufacturing Practice standards.

A dose of external wash dispensing granules was added to 2000 mL of boiling water and was used as an external wash for 20 min twice daily after the water temperature dropped to below 20°.

2.4.3. Positive control group (group C)

Mometasone furoate (0.1%) was applied once a day to the affected skin. For pruritus, loratadine or cyproheptadine hydrochloride was applied according to instructions. The placebo water pills were black, composed of starch (which tasted slightly bitter), manufactured by our hospital and taken by the patients twice a day. Children who weighed less than 40 kg took 3 g in a single dose, whereas those who weighed 40 kg or above took 6 g. Patients in group C received a 12-week treatment period followed by 24 weeks of follow-up.

2.5. Outcome measures

The primary end-point measure was the change in the Scoring Atopic Dermatitis Index (SCORAD) from baseline to the end

of the observation period. The SCORAD measures the extent and intensity of the patient's eczema and subjective symptoms. The maximum score was 103, with higher scores indicating more severe symptoms.¹² Participants were seen at regular intervals: at baseline, week 4, week 8, week 12, week 20, week 28 and week 36. The severity of AD was assessed by a specially trained assessor who was blinded to the treatment assignment.

The secondary study end-points comprised a QOL index and the patients' self-assessment. The QOL index was assessed using the certified Chinese translations of the questionnaires published on www.dermatology.org.uk/index.html: the Children's Dermatology Life Quality Index (CDLQI) for children aged between 5 and 16 years¹³ and the Dermatology Life Quality Index (DLQI) for patients over the age of 16 years.¹⁴ The QOL was calculated by summing the score of each question, resulting in a maximum of 30 and a minimum of 0. A higher score denoted a greater impairment of QOL.

The patients' self-assessment was recorded on a visual analogue scale (VAS) on each visit. Independently of the investigator, the patients rated the severity of their condition on a VAS from 0 to 10 (10 = no complaints, 0 = maximum severity). The patients' self-assessment and the CDLQI were completed by the parents of the children who were too young to comprehend.

Safety evaluation included general physical examinations, routine blood, urine and stool examinations, hepatic and renal function examinations and an electrocardiogram test both before treatment and at the end of the 12-week course. An adverse event was defined as any untoward occurrence in a patient, regardless of whether it was related to the study treatment. Additionally, any adverse events were reported at each clinic visit and recorded.

The patients' compliance with the allocated treatments was closely monitored by a compliance chart diary. Any leftover medication was requested to be returned and the physicians asked questions on the medication taken at each monthly visit.

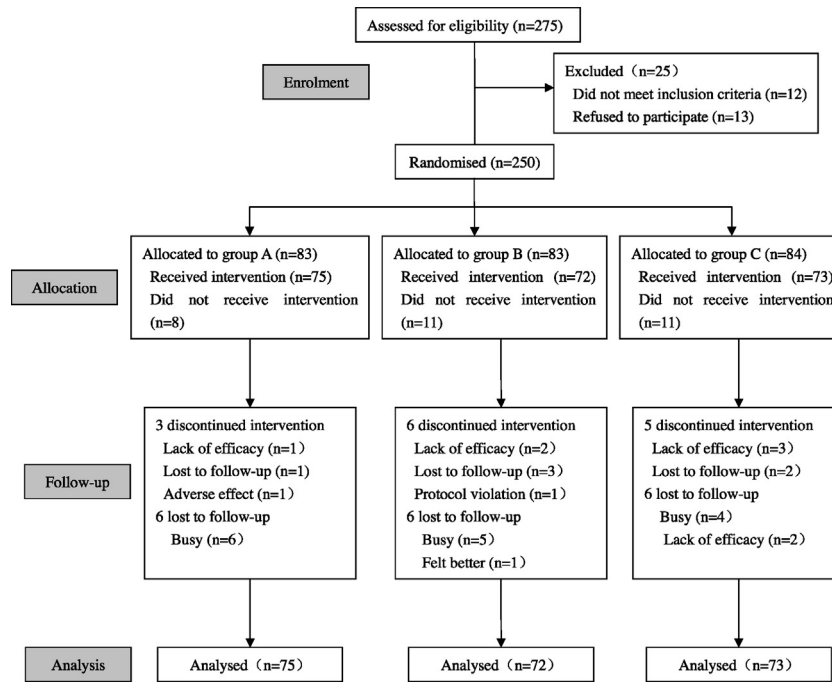


Fig. 1. Enrolment, randomisation and treatment flowchart.

3. Statistical methodology

The sample size was determined based on the comparison of multiple sample means. In our pilot study,⁷ the total mean (standard deviation) SCORAD score in our AD patients was 55 (± 15). Therefore, 72 patients were required in each group to achieve 90% power ($\beta = 0.10$) and an α error of 0.05 (two-tailed). With an estimated drop-out rate of 15%, the final optional sample size was determined to be 83 in each group, with 249 participants in total.

This analysis was based on the intention-to-treat (ITT) for the patients. Three groups were compared using one-way analysis of variance and differences between two groups were compared with LSD-*t* test. Comparisons of continuous variables of a plurality of observation points between the three groups were performed using repeated measure analysis of variance. Comparisons of categorical variables were made by the chi-square test. *P* values <0.05 were considered to be statistically significant. The results are presented as between-group differences with 95% confidence intervals (CI). The analyses were carried out using the Statistical Package for the Social Sciences (PASW Statistics 18.0) software package.

4. Results

4.1. Baseline characteristics

A diagram showing the disposition of the patients and the flow of participants through each stage of the study is shown in Fig. 1. Initially, 83, 83 and 84 patients were randomly divided into groups A, B and C, respectively. All of them were Chinese Hans. Of these, 30 patients, i.e., 8 in group A, 11 in group B and 11 in group C, refused to participate immediately after randomisation. Thus, a total of 220 patients were included in the ITT population, of whom 206 (93.64%) completed the treatment and 188 (85.45%) completed the entire study.

The baseline characteristics for the ITT population are shown in Table 2. A significant difference in sex was found between the three groups ($P = 0.03$). No statistical difference was observed with regard to other baseline characteristics.

4.2. Efficacy outcomes

Fig. 2 and Table 3 show the changes from baseline to 36 weeks in the three groups for all outcomes. During the 12-week treatment

Table 2
Demographic and baseline characteristics for the intention-to-treat population.

Variable	Group A n = 75	Group B n = 72	Group C n = 73	<i>P</i> value
Age, years	13.59 $\pm$ 6.08	13.90 $\pm$ 6.14	13.44 $\pm$ 5.74	0.95
Sex				
Male	46	31	30	0.03 [*]
Female	29	41	43	
Height, cm	148.08 $\pm$ 20.11	146.99 $\pm$ 19.30	149.26 $\pm$ 20.97	0.75
Weight, kg	42.26 $\pm$ 17.19	40.50 $\pm$ 14.63	45.52 $\pm$ 20.94	0.58
Duration of illness, years	8.26 $\pm$ 5.55	9.44 $\pm$ 5.77	8.38 $\pm$ 5.02	0.39
SCORAD	50.28 $\pm$ 16.78	47.45 $\pm$ 14.60	44.99 $\pm$ 15.29	0.12
Patients' self-assessment	3.62 $\pm$ 2.50	4.40 $\pm$ 2.30	4.25 $\pm$ 2.64	0.13
QOL	12.44 $\pm$ 5.72	11.49 $\pm$ 6.00	11.73 $\pm$ 7.03	0.51

For each variable except sex, values are expressed as the mean $\pm$ standard deviation.

^{*} $P < 0.05$.

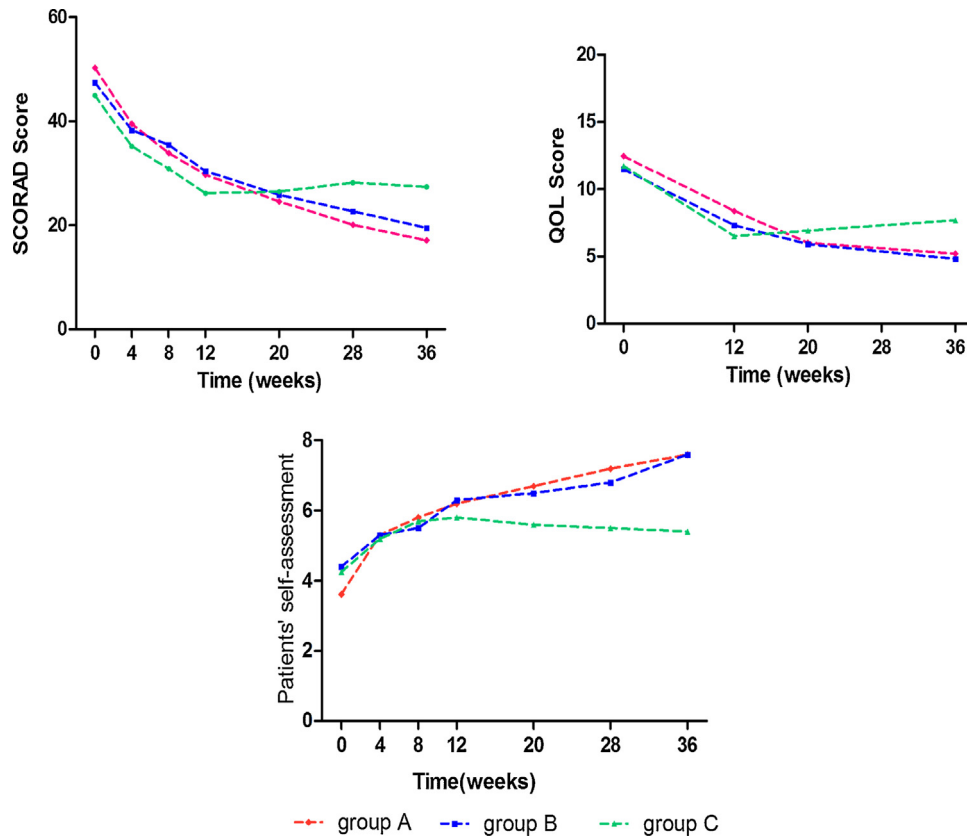


Fig. 2. Mean score of SCORAD and QOL and the patients' self-assessment.

period, the mean SCORAD scores decreased gradually in all three groups. No statistically significant differences in the average change were found between any of the three groups. During the follow-up period, the mean SCORAD scores decreased in both TCM groups but increased in the control group. The difference in the average change in SCORAD scores between groups A and C was -0.89 (95% CI, -13.18 to -3.00 ; $P=0.002$) at week 28 and -5.52 (95% CI, -10.67 to -0.38 ; $P=0.036$) at week 36. The difference between groups B and C was significant, with a difference of -5.52 (95% CI, -10.67 to -0.38 ; $P=0.036$) at week 28 and -7.86 (95% CI, -12.87 to -2.85 ;

$P=0.002$) at week 36. No statistically significant differences were found between the two TCM groups during the follow-up period.

The difference in the average change in QOL between groups A and C was significant: 1.85 (95% CI, -0.25 to 3.45 ; $P=0.023$) at week 12 and -2.58 (95% CI, -4.09 to -1.07 ; $P<0.001$) at week 36. The difference between groups B and C was also significant: -2.89 (95% CI, -4.42 to -1.37 ; $P=0.036$, $P<0.001$) at week 36.

At week 20, the average change in the patients' self-assessment scores in both TCM groups increased significantly compared with the control group. The mean difference was 1.11 (95% CI, 0.33 – 1.89 ;

Table 3
The changes in primary and secondary outcomes.

Variable	Between-group difference (95% CI)					
	Group A versus group B	P value	Group A versus group C	P value	Group B versus group C	P value
SCORAD						
Week 4	1.08 (–3.98 to 6.14)	0.674	4.24 (–0.80 to 9.28)	0.099	3.16 (–1.94 to 8.25)	0.223
Week 8	–1.60 (–6.89 to 3.68)	0.551	3.01 (–2.25 to 8.28)	0.261	4.61 (–0.71 to 9.93)	0.089
Week 12	–0.73 (–6.16 to 0.70)	0.791	3.46 (–1.95 to 8.87)	0.209	4.19 (–1.28 to 9.65)	0.132
Week 20	–1.32 (–6.54 to 3.90)	0.619	–1.90 (–7.10 to 3.30)	0.473	–0.58 (–5.83 to 4.68)	0.828
Week 28	–2.57 (–7.68 to 2.55)	0.324	–8.09 (–13.18 to –3.00)	0.002 [*]	–5.52 (–10.67 to –0.38)	0.036 [*]
Week 36	–2.41 (–7.39 to 2.57)	0.341	–10.28 (–15.24 to –5.32)	0.000 [*]	–7.86 (–12.87 to –2.85)	0.002 [*]
QOL score						
Week 12	1.04 (–0.57 to 2.65)	0.203	1.85 (–0.25 to 3.45)	0.023 [*]	0.81 (–0.80 to 2.43)	0.323
Week 20	0.14 (–1.32 to 1.60)	0.852	–0.90 (–2.36 to 0.55)	0.221	–1.04 (–2.51 to 0.42)	0.163
Week 36	0.31 (–1.20 to 1.83)	0.685	–2.58 (–4.09 to –1.07)	0.000 [*]	–2.89 (–4.42 to –1.37)	0.000 [*]
Patients' self-assessment score						
Week 4	–0.03 (–0.72 to 0.66)	0.936	0.08 (–0.61 to 0.77)	0.815	0.11 (–0.59 to 0.81)	0.756
Week 8	0.35 (–0.35 to 1.04)	0.328	0.15 (–0.55 to 0.84)	0.682	–0.20 (–0.90 to 0.50)	0.572
Week 12	–0.01 (–0.76 to 0.75)	0.980	0.42 (–0.33 to 1.17)	0.272	0.43 (–0.33 to 1.19)	0.266
Week 20	0.13 (–0.65 to 0.91)	0.744	1.11 (0.33–1.89)	0.005 [*]	0.98 (0.19–1.77)	0.015 [*]
Week 28	0.41 (–0.38 to 1.20)	0.304	1.74 (0.95–2.52)	0.000 [*]	1.33 (0.54–2.12)	0.001 [*]
Week 36	0.32 (–0.45 to 1.09)	0.407	2.49 (1.73–3.26)	0.000 [*]	2.17 (1.39–2.94)	0.000 [*]

All values are means, with 95% confidence intervals. *P* values were calculated with analysis of variance.

^{*} $P<0.05$.

Table 4
Adverse events.

Variable	Group A n = 75	Group B n = 72	Group C n = 73
Cold, n (%)	9 (12.00)	9 (12.50)	6 (8.22)
Diarrhoea, loose stools, n (%)	3 (4.00)	2 (2.78)	2 (2.74)
Sleepiness, n (%)	–	–	2 (2.74)
Folliculitis, n (%)	–	–	1 (1.37)

Table 5
The results of the test for blinding.

Group	True	False or not know	Total
Group A, n (%)	32 (42.67)	43 (57.33)	75 (100%)
Group B, n (%)	30 (41.67)	42 (58.33)	72 (100%)
Group C, n (%)	35 (47.95)	38 (52.05)	73 (100%)

Chi-squared test, *P*-value: 0.715. PTQXT is effective in decreasing the severity of atopic dermatitis (AD). PTQXT can improve the quality of life of patients with AD. Long-term use of topical antistaphylococcal treatments for AD is not beneficial.

P=0.005) between groups A and C and 0.98 (95% CI, 0.19–1.77; *P*=0.015) between groups B and C. This significant difference lasted through to the end of the follow-up.

4.3. Safety outcomes

A patient in group A complained of slight diarrhoea, which disappeared when the patient stopped taking the medication. Diarrhoea reappeared when she took the medicine again and it was defined as an adverse effect (Table 4). No severe adverse events occurred during the trial. All patients had normal blood, urine, stools, liver function, renal function and electrocardiogram readings following treatment.

4.4. Medications in the follow-up period

Twelve patients in group A, 14 in group B and 33 in group C received treatment due to relapses. The decision on the type of intervention that would be applied was dependent on the patient's previous allocation. If the patient had been allocated to a certain group, e.g., group A, he or she received the same type of intervention as that used during the treatment period. Except for 20 patients in group C who used topical corticosteroids, the remaining 13 refused to use their former treatment when they relapsed.

4.5. Blinding

The actual allocation and the allocation guessed by the blind assessor are summarised in Table 5, which indicates that the blinding of the assessors was satisfactory (*P*=0.715).

4.6. Participant adherence

During the treatment period, the adherence rate was 96% and 95.83% with the use of study medications in groups A and B, respectively, and 93.15% in group C. No statistically significant differences were found between the three groups.

5. Discussion

This randomised, controlled trial showed that PTQXT is a useful therapy for patients with AD. The effect was evident in SCORAD, a well-validated, multidimensional instrument for the assessment of AD, and in patient-reported outcomes, including the QOL and the patients' self-assessment. The patients with AD in both of the TCM

groups and the control group had lesser disease severity as well as improved QOL and patients' self-assessment during the treatment period. The SCORAD in both TCM groups was significantly lower than that in the control group at week 28 and week 36 during the follow up period. The QOL in both TCM groups was better than that in the control group at week 36, and the patients' self-assessment was also better than that of the control group throughout the follow-up period. No significant difference was observed between the two TCM groups.

Our results were consistent with those of a previous placebo-controlled trial, which found that the Xiao-Feng-San formula significantly lessened the severity of the disease in AD patients and that the therapeutic effect persisted for 4 weeks after the cessation of treatment,¹⁵ and with the findings of another clinical trial that showed that the Pentaherbs formulation improved the QOL of AD patients.¹⁶ The external wash formula was composed of four dispensing granules containing *Flos Lonicerae*, *Rhizoma Polygonati*, *Herba Menthae* and *Radix Glycyrrhizae*, which have good antibacterial activity, especially against *Staphylococcus aureus*. Our previous study showed that the external wash formula can reduce the colonisation of *S. aureus* and improve clinical scores after 14 days of treatment¹⁷; the clinical improvement in acute lesions was more significant than that in chronic lesions.¹⁸ However, in this study, at week 4, week 8 and at the end of the treatment period, no significant difference in the clinical scores was found between the two treatment groups. Similar results were reported in some randomised controlled trials when oral or topical antibiotic treatment was compared with placebo.^{19–21}

Liver damage and kidney failure have been reported to be associated with Chinese herbal medicine treatment.²² However, the PTQXT used in this study was found to be safe. Adverse effects were relatively uncommon and were mild and self-limiting when the affected patient stopped taking the medicine. All patients had normal renal and liver function following the Chinese herbal medicine treatment. Moreover, unlike many bitter-tasting TCM remedies, the children in this study found the decoction easy to take.

Patients with AD have skin barrier and immune abnormalities and a unique propensity to be colonised or infected by microbes, especially *S. aureus*, which can be cultured from 90% of skin lesions and importantly can colonise normal appearing skin in AD.²³ Various studies have also indicated a positive correlation between the clinical severity and the colonisation by superantigen-producing strains of *S. aureus* in AD.²⁴ *S. aureus* can exacerbate or contribute to persistent skin inflammation and pruritus in AD by secreting toxins with superantigenic properties, resulting in the marked activation of T cells and other immune cells.^{25,26} In addition, colonisation is a risk factor for infection. The role of *S. aureus* in exacerbating AD contributes to a plausible rationale for the use of antibiotics in its treatment even in the absence of signs of clinically infected lesions. Although antibiotic treatment usually reduces or totally eliminates *S. aureus* colonisation, the clinical improvement is temporary and not consistent or sustained, and recolonisation usually accrues within 4–8 weeks.^{27,28} An updated Cochrane review failed to find any evidence that commonly used antistaphylococcal treatments are clinically helpful in people with AD that is not clinically infected.²⁹ As a result, when overt signs of bacterial superinfection are present on skin lesions, the short-term use of oral or topical antibiotics is justified, but the long-term use of topical antibiotics for AD is not beneficial.

With regard to TCM, the formulae are based on the individual physiological and pathological characteristics of the patient, whereas the studies mentioned above used specific herbal preparations to treat patients with AD. According to the TCM theory, the interaction of over-active heart-fire and a deficiency of the spleen is the main pathogenesis of AD.³⁰ As decoction is the most widely used form of medication in the clinical practice of TCM,³¹

a decoction of PTQXT was therefore used and modified according to the predominance of heart-fire and/or spleen deficiency for each patient, a modification that contributed to its clinical effects. PTQXT has an integrated efficacy to invigorate the spleen and reduce dampness, clear heart-fire and relieve itching. AD is a chronic inflammatory skin disease, in which an immunological balance between Th1 and Th2 forms part of the pathogenesis. Some experimental studies have proved the effectiveness of some herbs in an AD model; *Poria cocos* protein, which is the main ingredient of *Poria cocos*, can activate the Th1 immune response and inhibit the production of Th2 cytokine and immunoglobulin (Ig) E,³² and *Uncaria rhynchophylla* may suppress the development of AD-like dermatitis in 2,4-dinitrofluorobenzene-treated NC/Nga mice by regulating the Th1 immune response.³³ Hao et al.³⁴ reported that extracts of *Forsythia suspensa* significantly suppressed β -conglycinin-induced T lymphocyte proliferation and interleukin-4 (Th2 cytokine) synthesis. Therefore, the efficacy of PTQXT may be due to the modulation of the immunological balance between Th1 and Th2, but further studies are needed to elucidate the exact mechanisms of action of the Chinese herbal formula.

The lack of a double-blinded arm was a limitation to this study. Because traditional Chinese medicine is prescribed individually, it is difficult to make a placebo that matches the decoction in form, colour and taste. It is also contradictory to use topical creams and lotions at the same time. The non-uniform form of the interventions in the three groups may therefore have resulted in outcome bias. In addition, as chronic skin disease is characterized by periods of remission and relapse, it was not medically advisable or ethical to prevent patients with AD from using medications during the follow-up period when they experienced relapses. We recorded the number of patients who experienced at least one relapse during the follow-up period in each group. Although the medications we used to control their relapses were coordinated with their previous treatments, 13 patients in group C refused the therapy. The reasons provided by some of the patients for preferring not to use the topical corticosteroids included the fear of side effects of the drug or a lack of confidence in their effectiveness.

In conclusion, this clinical trial demonstrated that PTQXT was efficacious in relieving the symptoms of the disease and improving the QOL and self-assessment in patients with moderate-to-severe AD.

Authors' contributions

D.C.C., J.F.L., X.M.M. and D.R.W. designed the study, and drafted and revised the manuscript. X.M.M., J.F.L., H.Y.L., C.L. and W.Z. were in charge of the recruitment of the interviewers and the acquisition of data, and revised the manuscript. A.H.O., Z.H.W. and S.Q.X. dealt with data management and the data analysis, and revised the manuscript. All authors read and approved the final version of the manuscript.

Conflicts of interest

The authors declare that they have no competing interests.

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