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A Chinese herbal medicine preparation (PTQX) for children with moderate to severe atopic eczema: a pilot RCT

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Conflict of interest: D. Chen developed the CHM formula PTQX which has been patented. All other authors have declared no competing interests.

To the editor: Atopic eczema (AE) or atopic dermatitis is a chronic and relapsing inflammatory skin disease. The prevalence and burden of AE are increasing globally. Systemic immunomodulating medications including corticosteroids or immunosuppressive drugs are efficacious agents for difficult-to-treat or refractory moderate or severe AE, but are not used routinely due to safety concerns.¹ Some AE patients reported using complementary and alternative medicines including Chinese herbal medicine (CHM). A Cochrane systematic review of 28 studies involving 2,306 AE participants found an oral CHM formula could improve quality of life in AE children.² However, the current state of evidence is limited to support routine use of CHM for AE, further rigorous randomised controlled trials (RCTs) are needed to determine if CHM is beneficial.

A double-blind, randomised, placebo-controlled pilot trial of the nine-herb CHM preparation *Pei Tu Qing Xin* granules (PTQX) involving 30 children with moderate to severe AE was undertaken (between August 2016 and September 2017) in Guangzhou, China. PTQX was composed of Baizhu (*Atractylodes macrocephala*), Taizishen (*Pseudostellaria heterophylla*), Shanyao (*Dioscorea opposita*), Yiyiren (*Coix lachryma-jobi*), Baimiaogen (*Imperata cylindrical*), Lianqiao (*Forsythia suspense*), Gancao (*Glycyrrhiza glabra*),

Baixianpi (*Dictamnus desycarpus*) and Zhenzhufen (*Pteris martensii* (Dunker)). PTQX is currently used at the Dermatology Department of GPHCM based on expert consensus.³ An *in vivo* study reported that PTQX reduced histamine-induced itch in guinea pigs, and 4-aminopyridine- or dextrane-induced itch in mice.⁴ This pilot RCT aimed to determine protocol feasibility and compliance, to gather preliminary data and to monitor safety. Findings from this pilot RCT will inform planning of a full-scale RCT.

After obtaining written informed consent forms signed by the parents or guardians, participants were randomised to receive either oral PTQX or identical placebo twice daily for 12 weeks, with follow-up assessment conducted at 16 weeks (4 weeks after the treatment phase). The primary outcome was change in Eczema Area and Severity Index (EASI),⁵ with the secondary outcomes being change in Patient-Oriented Eczema Measure (POEM),⁶ the Children's Dermatology Life Quality Index (CDLQI),⁷ use of concomitant medications and adverse events. The trial protocol was approved by the GPHCM Ethics Committee and the RMIT University Human Research Ethics Committee. The trial was registered with the ANZCTR (ACTRN12614001172695) prior to recruiting participants. Block randomisation codes were generated by the SAS 9.2 software, and allocated to the participants with a central allocation system developed by the Department of Research Methodology of GPHCM. Neither the trial participants nor investigators knew the participant allocation to real treatment or placebo group. Data were analysed by using IBM SPSS version 22. Intention-to-treat analysis was performed using the data imputation method of last observation carried forward. All comparisons were 2-tailed with p-values <0.05 considered to be statistically significant. The full clinical trial design including inclusion and exclusion criteria, and trial medication details can be found in the published study protocol.⁸

Screened from 121 potential eligible participants, nine boys and 21 girls aged six to 16 years were recruited from the Dermatology Out-patient Department of GPHCM (n=16, PTQX group). The participants in both groups were highly compliant with the protocol in terms of taking the trial medications and completing all case record forms. The withdrawal or dropout rate was within an acceptable 10% rate (n=1 withdrawal, n=1 dropout, PTQX group; n=1 dropout, placebo group).

Characteristics of both groups were balanced at baseline. The results are summarised in Table 1. There was no between group differences in change scores for EASI, POEM and CDLQI at the end of treatment (Week 12). While not statistically significant, the mean

scores of EASI, POEM and CDLQI in the PTQX group were lower than those in the placebo group at the end of the follow-up period (Week 16) (Table 1).

During the trial, 21 children (n=10, PTQX group) used topical corticosteroid creams (TCS) as concomitant medications. While differences in the volume of use of TCS were not statistically significant between the two groups, there was a lower TCS use in the PTQX group at end of the trial (Week 16). There were three (n=1, PTQX group) mild adverse events (skin rashes or vomiting) and no severe adverse events during the trial period. No hepatic or renal function abnormalities were found for all participants during the treatment period.

Findings from this pilot RCT is limited; nevertheless, these findings can be used to calculate sample size for the full-scale RCT. The study revealed that the adverse events were mild and the protocol is implementable, hence an appropriately powered RCT is warranted.

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Table 1 Primary and Secondary Outcomes: Comparisons within Groups and between Groups

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Outcomes	Group	Baseline (Mean±SD)	End of treatment (Week 12) (Mean±SD)	End of follow- up (Week 16) (Mean±SD)	Change from baseline to end of treatment (Week 12) (within groups) Mean±SD	Change from baseline to end of follow-up (Week 16) (within groups) Mean±SD	Comparison of the mean difference between groups (95% CI)	
							End of treatment (Week 12)	End of follow-up (Week 16)
EASI	PTQX	13.66±6.96	6.71±6.32	6.23±6.35	-6.95±7.35	-7.43±5.79	0.08 (-4.81 to 4.99);	-2.95 (-9.55 to 3.67);
	Placebo	13.63±9.08	6.63±6.79	9.18±11.00	-7.01±8.16	-7.01±8.16	n=30 t = 0.04 p = 0.97	n=30 t = -0.91 p = 0.37
POEM	PTQX	20.00±5.53	12.50±7.78	13.56±8.08	-7.50±8.05	-6.44±8.24	-2.57 (-7.84 to 2.70);	-2.3 (-8.49 to 3.90);
	Placebo	18.07±4.94	15.07±6.04	15.86±8.47	-3.00±6.59	-2.21±8.39	n=30 t = -1.00 p = 0.33	n=30 t = -0.76 p = 0.45
CDLQI	PTQX	12.44±5.68	8.50±6.56	8.31±6.98	-3.94±6.29	-4.13±6.34	-1.36 (-5.83 to 3.12);	-1.90 (-6.78 to 2.97);
	Placebo	12.79±4.84	9.86±5.20	10.21±5.90	-2.93±5.99	-2.57±6.56	n=30 t = -0.62	n=30 t = -0.80

p = 0.54

p = 0.43

Abbreviations: CDLQI: Children's Dermatology Life Quality Index; CI: Confidence interval; EASI: Eczema Area and Severity Index; POEM: Patient-Oriented Eczema Measure; PTQX: Pei Tu Qing Xin granules; SD: Standard deviation.

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