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Therapeutic effect and safety of a traditional Chinese medicine for atopic dermatitis in children: a randomised, double-blind, placebo-controlled study

Key Message

The traditional Chinese medicine concoction using five herbs was palatable and well tolerated and was efficacious in reducing topical corticosteroid usage in children with moderate-to-severe atopic dermatitis.

Introduction

Atopic dermatitis (AD) is a common chronic relapsing skin disease affecting about 15% of children aged less than 15 years. As there is no definitive cure for the condition, the use of traditional Chinese herbal medicine (TCHM) is a potential adjunctive therapy. In an open-label study, a concoction of five herbal extracts twice daily has been found to be beneficial.[1] The five herbs included *Flos lonicerae* (*Jinyinhua*), *Herba menthae* (*Bohe*), *Cortex moutan* (*Danpi*), *Rhizoma atractylodis* (*Cangzhu*) and *Cortex phellodendri* (*Huangbai*). The formulation was based on a widely used traditional concoction, with no corticosteroid or related compound.[2] This study aimed to determine the therapeutic efficacy, tolerability, and safety of this concoction in children with AD.

Methods

This was a randomised, placebo-controlled, double-blind study conducted from November 2004 to November 2005. The sample size calculation was based on our pilot data.[1] In each arm (TCHM and placebo) of the study, it was estimated that 40 subjects would be required to achieve an 80% power (b=0.20) and an α error of 0.05 (2-tailed) for detecting a 25% difference (13-point changes) in mean total SCORAD between the two groups. The SCORAD is a validated scoring system that assesses objective parameters (area [A] and intensity [B] signs) and subjective symptoms (pruritus and sleep loss [C]). As the dropout rate was estimated to be 5%, 84 children were needed to be recruited.

The diagnosis of AD was based on criteria defined by Hanifin and Rajka.[3] Patients aged 5 to 21 years with moderate-to-severe AD (defined as a SCORAD of >15)[4] and attended the paediatric dermatology outpatient clinic of our university hospital were invited to participate. Patients were excluded if they had any other inflammatory dermatitis (eg psoriasis, seborrhoeic dermatitis, ichthyosis) or experienced overt asthmatic symptoms (eg cough, wheeze, shortness of breath or exercise-induced bronchospasm) in the preceding 4 weeks. Patients were not recruited if they had had systemic corticosteroids, immunomodulating drugs or other TCHMs in the preceding 4 weeks. The Clinical Research Ethics Committee of the Chinese University of Hong Kong approved the study. Written informed consent was obtained from each patient.

Patients were randomised to receive either TCHM or placebo. Both were matched, manufactured, packaged, and labelled by the Chinese Medicine Industry Development Centre, of the Hong Kong Institute of Vocational Education, which fulfilled Good Manufacturing Practice standards. The formula consisted of *Flos lonicerae* (*Jinyinhua*) 2 g, *Herba menthae* (*Bohe*) 1 g, *Cortex moutan* (*Danpi*) 2 g, *Rhizoma atractylodis* (*Cangzhu*) 2 g, and *Cortex phellodendri* (*Huangbai*) 2 g. The dosage was based on the standard prescription for this concoction for children (aged ≥7 years) and teenagers.[1] It was formulated into standard-weight capsules according to established procedures under the supervision of the Clinical Trials Section. The medications were distributed monthly, and three capsules were to be taken twice daily for 12 weeks.[2] As all patients had moderate-to-severe disease, it

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was not advisable to discontinue other routine medications during the trial, which included emollients, bath oils, soap substitutes, topical corticosteroids, and oral or systemic antihistamines. Patients were asked to record the frequency of both the trial and routine medications used. The amount of topical corticosteroids used was also recorded.

Participants were followed up at regular intervals at baseline (before treatment), and 4, 8, 12, and 16 weeks later. The severity of AD was assessed using the SCORAD.[4,5] Symptoms of coexisting allergic rhinitis (sneezing, watery rhinorrhoea, nasal congestion, itching nose, itching eyes, and eye watering) were quantified by the Allergic Rhinitis Score. All severe adverse events were investigated to determine whether they were directly related to the drugs or underlying condition. Hospitalisation was considered a severe adverse event. Blood samples for complete blood counts, eosinophil counts; total IgE levels as well as liver and renal function were assessed before treatment, and at the end of the 12-week treatment course. Unused trial and routine medications were quantified. Statistical analysis of the clinical and laboratory data was performed independently by a statistician not involved in the clinical trial.

Results

A total of 85 patients (42 taking TCHM and 43 on placebo) participated in the trial. The characteristics of the two groups were similar; there was no significant difference in pre-treatment SCORAD, Allergic Rhinitis Scores, IgE values, and eosinophil counts. Patients were treated with a combination of emollients, moderately potent topical corticosteroids (93% were on 0.1% mometasone furoate and 7% received no regular corticosteroids) or oral antihistamines (86% were taking chlorpheniramine and 14% received no regular antihistamine). Of 85 patients, 71 had co-existing allergic rhinitis.

In the TCHM and placebo groups, 93% and 92% of the prescribed capsules were taken, respectively. The respective mean SCORADs decreased from 58.3 to 49.7 and from 56.9 to 46.9 (Fig), but there was no significant difference between the groups at the end of treatment, nor in their component SCORAD scores. In contrast, there was a >30% improvement in the Children's Dermatology Life Quality Index in the TCHM group at the end of treatment (P=0.008) but no improvement for the placebo-treated patients (Fig).

Corticosteroid usage in the TCHM group was significantly reduced by a mean of 4 days per month compared to baseline usage, whereas in the placebo group it was reduced by one day. Of 79 patients using 1% mometasone furoate as the topical corticosteroid, the amount used was also significantly reduced in the TCHM group, but antihistamine usage was not significantly different between the groups. Addition of a more potent topical corticosteroid and antihistamine occurred during follow-up in two and seven patients on TCHM, and 3 and 5 patients on placebo, respectively. Anti-staphylococcal antibiotics, including cloxacillin and erythromycin were prescribed for 16 and 17 patients in the TCHM and placebo groups, respectively.

In the respective TCHM and placebo groups, 35 and 36 patients had symptoms of allergic rhinitis, but the total allergic rhinitis scores and most corresponding symptoms were not significantly different. Only sneezing score improved significantly in the TCHM group from 1.5±0.9 to 1.1±1.1.

The TCHM was well tolerated. There was no significant difference in the frequency of adverse events. Analysis of biochemical data also revealed no significant change in IgE levels, or haematological (complete blood counts, eosinophil counts) and biochemical (electrolytes, renal and liver function) parameters monitored. All patients had normal renal and liver functions following TCHM treatment. No patient complained that the capsule was unpalatable.

Discussion

In both the TCHM and placebo groups, the SCORADs, the extent of disease, the intensity of lesions and subjective symptoms decreased during the study period, but no significant difference was observed between the two groups. However, compared to baseline, the duration and quantity of corticosteroid (mometasone furoate) usage in the TCHM group was significantly reduced but not so in the placebo group. This suggests that TCHM may possess corticosteroid-sparing effects and that the improvement in the placebo group was at the expense of a greater use of topical corticosteroids. Using thin-layer chromatography,

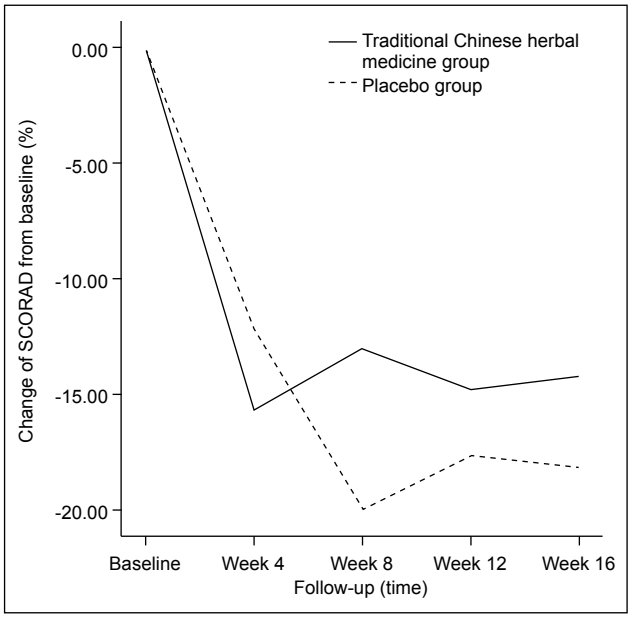

Fig. Percentage improvement of SCORAD from baseline

infrared spectrophotometry and liquid chromatography–mass spectrometry, we have previously reported that there were no corticosteroid or related precursors in this TCHM formulation.[2]

Adverse effects from this TCHM were uncommon, mild and self-limiting. There was no significant difference in haematological and biochemical parameters at baseline or following use of trial medications, and no derangement of liver and renal function during the 3 months of assessment. Unlike many bitter-tasting TCHM soups, children found the capsule easy to swallow and palatable.

This TCHM concoction was efficacious in reducing topical corticosteroid usage in children with moderate-to-severe AD. The formulation was palatable and well tolerated, and there was no derangement in haematological or biochemical parameters after treatment. This formulation can probably be used as an adjunctive treatment for children with refractory AD.

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