

Randomized, Double-Blind, Placebo-Controlled Trial of Herbal Therapy for Children with Asthma

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Abstract

Objectives: The purpose of this trial was to evaluate whether the herbal formula of CUF2 used as complementary therapy improves the clinical symptoms and biochemical markers in children with asthma using inhaled corticosteroids.

Patients and methods: In a double-blind, placebo-controlled prospective trial, 85 children with asthma aged 7–15 years were randomly assigned to receive either a daily oral herbal formula of 0.619-g CUF2 capsule of dried aqueous extract with an equal weight of five herbs (*Astragalus mongholius* Bunge, *Cordyceps sinensis* Sacc., *Radix stemonae*, *Bulbus fritillariae cirrhosae*, and *Radix scutellariae*) or placebo for 6 months.

Results: The primary endpoint was the change in steroids dosage; the secondary outcomes included the disease severity score, lung function test, and biochemical markers in blood. Eighty-five (85) children (42 on active treatment and 43 on placebo) completed the 6-month clinical trial. Children randomized to the herbal formula of CUF2 and the placebo showed a similar improvement in clinical symptoms and biomedical markers. The comparison between the CUF2 group and the placebo group showed no significant difference on the dosage of steroids (−2.3 versus −3.1 mg, $p = 0.915$), disease severity score (−2.3 versus −3.1, $p = 0.215$), and lung function test of forced expiratory volume in 1 second/forced vital capacity percent (0.1 versus 0.6%, $p = 0.809$) and peak expiratory flow rate (−7.3 versus −0.6 l/minutes, $p = 0.118$). No significant difference was found between the two study groups in the biochemical outcomes measured. The intervention effect of CUF2 was smaller than the placebo effect.

Conclusions: This study provides no evidence to support the use of the herbal formula of CUF2 in children with asthma. Parents are thus advised to discuss with health professionals before choosing an herbal formula in preference to conventional treatment modes.

Introduction

ASTHMA IS ONE of the most common chronic diseases, and is becoming increasingly prevalent in many countries.¹ Evidence shows that asthma is a multifactorial long-term disease process with genetic, allergic, environmental, infectious, emotional, and dietary influences.^{2,3} The underlying pathophysiology of asthma is associated with allergen-induced chronic airway inflammation and airway hyper-responsiveness, which are caused or aggravated by T-cell and B-cell immune responses.^{3,4} Key areas of management include asthma management plans, day-to-day “preventer” treat-

ments, monitoring for side-effects, and maintaining as far as possible normal daily activity.⁵

Asthma management controls the symptoms using an inhaled β -adrenoreceptor agonist, and reduces acute attacks by avoiding triggers or by the prophylactic use of inhaled corticosteroids, long-acting β -adrenoreceptor agonists, oral corticosteroids, leukotriene receptor antagonists, or theophylline.^{6,7} Although side-effects are unlikely at a low dose of the asthma treatment, they have become apparent at the higher dose.^{5,8} A number of reviews have suggested that inhaling a higher dose of corticosteroid may lead to a reduction in adrenal suppression.^{9–11} Cases with clinical evidence

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of acute adrenal crisis with hypoglycemia have been reported.^{6,8} Given such safety concerns, parents often turn to complementary and alternative medicine (CAM), which they believe is natural and safe and may enable the dosage of conventional medication to be reduced.

A number of surveys have suggested that the use of CAM may be high among children with asthma.^{12,13} A survey done in the United States showed that 89% of parents had treated their child in the past year with CAM.¹⁴ Another self-reported survey in the United Kingdom showed that 80% of participants aged 13–18 years reported using CAM.¹⁵ The most widely used CAM for asthma that was reported in the United Kingdom were herbal medicine, acupuncture, homeopathy, and Ayurvedic medicine.^{16,17} A review by Huntley and Ernst found that herbal preparation was the third choice among CAM options by British asthma sufferers.¹⁸

A number of review articles and clinical trials have reported that treatment with traditional Chinese herbs or formulas has resulted in a significant improvement in lung function and a reduction in the airway hyper-reactivity reaction. However, demonstration of the efficacy of Chinese herbs in the treatment of asthma in these studies was limited by certain methodological flaws, including lack of randomization and blinding, small sample size, and inadequate preclinical studies evidence.¹⁸ In this study, we performed a double-blind randomized trial on a novel herb mixture, CUF2 (*Astragalus mongholius* Bunge, *Cordyceps sinensis* Sacc., *Radix stemonae*, *Bulbus fritillariae cirrhosae*, and *Radix scutellariae*), which was based on classical formulae related to asthma and in-depth literature review by a group of Chinese medical practitioners. The CUF2 is a mild formula and targets lessening the asthma-related symptoms in all patients with asthma. Each of the herbal components could strengthen respiratory function; for instance, *A. mongholius* Bunge invigorates the vital energy to strengthen the body; *C. sinensis* Sacc. invigorates the lung, improves inspiration to relieve dyspnea, and eliminates phlegm; *R. stemonae* nourishes the lung, eliminates phlegm, and relieves cough; *B. fritillariae cirrhosae* nourishes the lung, eliminates phlegm, and relieves cough; and *R. scutellariae* clears away heat from lung and deprives dampness.¹⁹ The CUF2 has been shown to have anti-inflammatory and immunomodulatory activities in both *in vitro* and *in vivo* animal studies.^{20–23} The *in vitro* study showed that CUF2 had an inhibitory effect on the allergic response by regulating the production of cytokines interleukin (IL)-4 and -6 and tumor necrosis factor- α (TNF- α), and by directly affecting gene expression of several key cytokines of HMC-1.^{20,23} The *in vivo* study showed that CUF2 has immunomodulatory effects on Th1/Th2 response in ovalbumin-sensitized rats after allergen challenge and anti-inflammatory activity by reducing the eosinophils and goblet cell hyperplasia.^{21,22} In light of this preclinical evidence, this study aims to determine the efficacy of CUF2 on clinical symptoms and certain biochemical markers of inflammatory response and immunomodulatory activities in children with asthma.

Methods

Study population

Eighty-five (85) children aged between 7 and 15 years with persistent mild-to-moderate asthma according to the Global

Initiative for Asthma guideline,¹ on regular inhaled steroid therapy, and able to perform reproducible spirometry, were recruited between July 2002 and August 2003 in the pediatric clinics of two major government hospitals in Hong Kong. Patients were excluded if they could not swallow capsules or had received parenteral or oral corticosteroids, nedocromil, cromolyn, theophylline, or anticonvulsants in the previous 4 weeks. To detect a 33% difference in the inhaled steroid dosage between the placebo and active groups with 80% power, 36 patients in each study group were needed. At least 80 patients were therefore needed for this study, allowing for a 10% loss to follow-up. Written informed consent was obtained from each patient and from 1 of their parents.

Study design

This was a double-blind, randomized, placebo-controlled parallel group study conducted over a 6-month active study period. The study purpose, details, and rights were explained to all patients and their parents. Since the patients were aged less than 18 years, the written consent would be obtained from the parents in addition to the verbal consent from the patients. Once written informed consent was obtained, patients were provided with a diary and were instructed to make a record of their symptoms and medication use. Participants were then randomly assigned to the active or placebo treatment group according to a computer-generated random list. Researchers, patients, and parents were blind to the allocation until after the final outcome assessment but could thereafter request information directly from the drug producer. A total of 7 monthly follow-up visits were scheduled throughout the 6-month trial period.

Herbal preparation and dispensing

Each capsule contained 0.619 g of dried aqueous extract of equal weights of five herbs. The placebo capsules (of dark-colored cornstarch) were of the same shape, color, smell, and taste (same gelatin shell). All capsules were manufactured by the Shenzhen Research Institute, Hong Kong Polytechnic University, based on Good Manufacturing Practice. The safety of the formula was ensured by the metal screening tests before the clinical trial. In light of advice from Chinese medical practitioners and a review of the relevant literature, the dosage for children above 12 years old was set at three capsules twice daily, and for children under 12 years old at two capsules twice daily. Monthly supplies of the medication or the placebo were provided to the patients during the 6-month treatment period. A research nurse telephoned the family once a month between consecutive follow-up clinics in order to enforce adherence to the treatment regimen, and unused pills were counted at each visit to monitor drug compliance. Patients' diaries on the medication use would be double-checked as well.

Symptom outcome

The severity of asthma symptoms was assessed using a modified Disease Severity Score (DSS).²⁴ DSS values of 1–5, representing increasingly more severe features, were given to six clinical features of asthma observed during the previous month:

1. Number of asthma attacks requiring medical treatment (score 1–5: none, one, two, three or four, five or more);
2. Frequency of attacks of wheezing and/or chest tightness during an average day (score 1–5: none, one, two, three or four, five or more);
3. Frequency of attacks of wheezing and/or chest tightness during an average night (score 1–5: sleep through the night, awakened once, awakened twice, awakened three or four times, awakened by asthma almost hourly);
4. Cough severity on an average day or night (score 1–5: no cough, occasional cough but not disturbing, quite troublesome during attacks only, very troublesome and frequent, or distressing most of the time);
5. Degree of shortness of breath with exertion (score 1–5: no limitation on activity, gets shortness of breath with strenuous exertion, shortness of breath with moderate exertion, such as climbing one or two flights of stairs, shortness of breath with minimal exertion, shortness of breath at rest); and
6. Treatment required to control asthma (score 1–5: none, inhaled β -agonist used less than twice per week, inhaled β -agonist used more than twice per week, inhaled or oral β -agonist used daily, oral corticosteroid use).

The maximum possible score was 30.

Lung function outcome

Children performed spirometry (SpiroPro Jaeger Toennies, Hoechberg, Germany) including peak expiratory flow rate (PEFR), forced expiratory volume (FEV_1), and forced vital capacity (FVC) at the monthly follow-up clinic. The patients were asked to withhold inhaled bronchodilator and steroids for at least 6 hours prior to each clinic visit.

Medication outcome

The dose of inhaled steroids was kept constant for the first 8 weeks of the study. Thereafter the dosage of inhaled steroids would be adjusted in three ways according to the treatment goals of the Global Initiative for Asthma (GINA)/National Institutes of Health (NIH) guidelines as follows:¹

1. If the patient's symptoms were totally controlled in the previous 8 weeks, the dose would be halved or the inhaled steroids would be stopped if the patient was already on the minimal applicable dose (50 or 100 μ g of corticosteroid, depending on the different manufacturers' recommended minimal dosage);
2. If the patient's symptoms were only well controlled at least 6 weeks over the previous 8-week period, the dose would be kept unchanged;
3. If the patient's symptoms were only well controlled less than 6 weeks over the previous 8-week period, the dose would be increased by the physician's clinical judgment. Supplemental doses of oral prednisolone and β -agonist aerosol were given to treat acute exacerbations requiring hospital admission.

According to the GINA/NIH guidelines, "totally controlled" asthma was defined as absence of daytime symptoms, night awakening, rescue β -agonist use, exacerbations, emergency visits, or treatment-related adverse events, and morning PEF $\geq 80\%$ predicted value every day; while "well

controlled" asthma was defined as minimal symptoms, or use of β -agonists < 2 days/week, with morning peak PEF $\geq 80\%$ predicted every day and no night awakening, exacerbations, emergency visits, or treatment-related adverse events.¹

Biochemical outcome

EDTA and clotted blood samples were taken at the baseline and at the end of the study (24th week) for eosinophil counts, immunoglobulin E (IgE) level and cytokine assay. Total serum IgE was measured by the IMX System (Abbott Laboratories, IL) using fluorogenic enzyme substrates and fluorescence polarization techniques, specific IgE against house dust mite (Der p1) by fluoroenzyme immunoassay (Pharmacia and Upjohn, MI) using the specific IgE Pharmacia CAP System. T-helper (Th1) and Th2 cytokines were measured by Human Th1/Th2 Cytokine Cytometric Bead Array (BD Pharmingen, San Diego, CA), thymus and activation-regulated chemokine (TARC) concentration by Quantikine TARC immunoassay (R&D, Minneapolis, MN), IL-18 by Human IL-18 ELISA Kit (MBL, Nagoya, Japan), and TNF- α and interferon- γ levels by high-sensitivity immunoassay kits (R&D). Urinalysis, complete blood count, liver function, and renal function were measured for safety at the baseline and at the end of the study.

In order to understand more about the placebo effect, parents or patients were asked to guess which group they had been assigned to, and to state the reasons for their guess at the end of the study.

Statistical analyses

The primary outcome measure was reduction of inhaled steroid dose. Other outcome measures included reduction of DSS, lung function test, and blood markers.

Data are presented as mean $\pm$ standard deviation (SD). All variables were analyzed for changes from the baseline values and for differences between the CUF2 and placebo groups. The analysis of nonparametric data was performed using Wilcoxon rank sum test and Mann Whitney test for intra-group and intergroup comparisons, respectively. Student's t test was used to analyze parametric data. Chi-square test was used to compare proportions. A p -value of < 0.05 was considered significant.

Results

Enrollment, follow-up, compliance, and adverse effects

A total of 112 patients were screened for enrollment, 22 of whom were excluded because of failure to meet the inclusion criteria, questionable drug compliance, time commitment, and dislike of placebo-control study design. During the treatment period, 1 patient dropped out from the CUF2 group (dislike of swallowing the capsules) and 4 patients dropped out from the placebo group (2 from difficulty in swallowing the capsules, 1 because of time clash, and 1 because of undiagnosed intermittent abdominal pain). Eighty five (85) patients (42 on active treatment and 43 on placebo) completed the 6-month treatment trial period. Baseline characteristics of these patients are presented in Table 1. The only significant difference was in body weight, which was heavier in the CUF2 group. Adherence was similar in the CUF2 and the placebo group both to the study capsules (94% and 93%, respectively) and to inhaled steroid treatment (98% and 94%, respectively). Transient

TABLE 1. BASELINE DEMOGRAPHICS AND CLINICAL CHARACTERISTICS OF STUDY PATIENTS

Characteristic	CUF2 (n = 42)	Placebo (n = 43)	p values
Age (yr)	10.5 (2.3)	9.9 (2.3)	0.628
Sex—no. (%)			
Female	13 (31%)	15 (35%)	0.700
Male	29 (70%)	28 (65%)	
Height (cm)	143.4 (14.2)	138.3 (13.0)	0.413
Weight (kg)	39.8 (15.8)	32.4 (9.2)	0.002
Time since diagnosis of asthma (yr)	3.8 (2.7)	4.3 (2.7)	0.350
Disease severity score	13.1 (1.9)	12.9 (2.0)	0.750
PEFR	298 (82)	272 (60)	0.134
FEV ₁ : % of predicted	96 (15)	96 (19)	0.359
FEV ₁ /FVC: % of predicted	92 (11)	91 (11)	0.388
FEV ₁ after bronchodilator use: % of predicted	101 (15)	99 (18)	0.268
Beclomethasone use (μ g/day): case number			
<250	24	28	0.491
250–500	17	15	
>500	1	0	

All data are expressed as mean (standard deviation) except when otherwise specified.

PEFR, peaked expiratory flow rate; FEV₁, forced expiratory volume in 1 second; FVC, forced vital capacity.

complaints of dry mouth and throat (which resolved themselves spontaneously within a few days) were recorded in 39/42 patients in the CUF2 group and 33/43 patients in the placebo group. Other adverse events included epistaxis (5/42 in the CUF2 group and 11/43 in the placebo group). Blood cell count and liver and renal function tests showed no significant change from the baseline in either group.

Primary outcome

Reduction of steroid dosage. The requirement for steroids decreased after treatment in both groups. Thirty (30) of 42 (71%) children with CUF2 and 37/43 (86%) children with the placebo required a lower dosage of inhaled corticosteroid at the end of the 6-month trial. However, no significant difference was noted between the two study groups ($p = 0.257$) (Table 2). Betamethasone dipropionate was used as a reference for the calculation of steroid dosage. Budesonide and fluticasone were considered to be of equal and double strength, respectively.

Secondary outcome

Asthma symptoms. DSS were significantly reduced both in the CUF2 group (13.1 [SD 1.9]–10.8 [SD 2.8], $p < 0.001$) and in the placebo group (12.9 [SD 2.0]–9.7 [SD 2.4], $p < 0.001$). Most of the reduction in the mean change of DSS occurred in the first month of treatment, and there was no significant difference between the CUF2 and placebo groups in the reduction (–2.3 versus –3.1 mg, $p = 0.915$) (Table 2).

Lung function test. The herbal formula of CUF2 had no effect on the spirometry performed in the clinic. The results for children on CUF2 compared with those on the placebo were 0.1 versus 0.6%, $p = 0.809$ for FEV₁/FVC% and –7.3 versus –0.6 L/min, $p = 0.118$ for PEFR. None of these results changed appreciably after the 6-month trial (Table 2).

Biochemical markers. We found there was no significant effect of the herbal formula of CUF2 on the biochemical markers including eosinophil count, plasma concentrations

of IL-18, TARC, TNF- α , total IgE, and house dust mite-specific IgE compared with the placebo. However, TNF- α was reduced significantly in the CUF2 group (3.8–3.0 IU/mL, $p = 0.004$), the change being significantly greater than in the placebo group (3.1–2.9 IU/mL, $p = 0.245$). However, there was no significant difference between the two study groups. House dust mite-specific IgE was reduced significantly in the placebo group (173.7–139.3 kUA/mL, $p = 0.028$), but there was no significant difference between the two study groups.

Guess on group assignment and placebo effect

At the end of the trial, 83/85 (98%) parents/patients felt able to guess the study group to which they had been allocated and 42/83 (51%) guessed correctly (Table 3). Sixty-one (61) children with asthma believed that they had been assigned to the active study group (74%). The data analysis of the outcome parameters was re-run, and we found to our surprise that there was a significantly larger reduction of steroid dosage in the “CUF2” guess group (53/61 [87%]) than in the “placebo” guess group (13/22 [59%]) ($p = 0.022$) (Table 4).

Discussion

Parents often wish to use herbal therapy to complement conventional medical treatment for their children with asthma so as to reduce the dosage of steroids, and thus to lessen the demonstrable side-effects of steroids on growth and health.¹² Although several methodologically flawed studies of the efficacy of herbal therapy on asthma exist, no systematic review has yet been conducted.¹⁸ In the light of evidence suggesting a potential anti-allergic effect of the herbal formula CUF2 on asthma, we performed the first rigorous clinical trial to assess the effect of CUF2 on children with asthma. The study design was acceptable to the patients, feasible in a primary care setting, and met the highest methodological standards. The study showed that the herbal formula CUF2 had no significant impact on the reduction of steroid dosage, symptom management, lung function, and biochemical markers in children with asthma.

TABLE 2. CHANGES IN SYMPTOM SCORE, LUNG FUNCTION PARAMETERS AND DOSAGE OF INHALED STEROID AFTER 6-MONTH TRIAL

	CUF2 (n = 42)				Placebo (n = 43)			
	Baseline mean (SD)	24th week mean (SD)	Mean (SD) change	p	Baseline mean (SD)	24th week mean (SD)	Mean (SD) change	p (change between groups)
Symptom scores								
Disease Severity Score	13.1 (1.9)	10.8 (2.8)	-2.3 (3.1)	<0.001	12.9 (2.0)	9.7 (2.4)	-3.1 (2.6)	<0.001
Lung function parameters								
PEFR (L/min)	91.7 (17.2)	92.3 (11.0)	-7.3 (20.1)	0.024	87.6 (21.9)	87.0 (18.5)	-0.6 (19.0)	0.844
FEV ₁ /FVC% predicted	92.3 (11.0)	92.5 (10.0)	0.1 (8.8)	0.917	91.5 (10.6)	92.1 (10.4)	0.6 (8.3)	0.644
Dosage of inhaled steroid								
Dosage of steroid	292.9 (151.6)	152.4 (210.1)	-2.3 (3.1)	<0.001	234.9 (137.8)	97.7 (125.8)	-3.1 (2.6)	<0.001
Change of dosage of steroid: case number (%)								
Increase	2 (4.8%)			1 (2.3%)				
Unchanged	10 (23.8%)			5 (11.6%)			0.257	
Decrease	30 (71.4%)			37 (86%)				
Biochemical markers								
Eosinophil count (%)	6.5 (3.2)	6.3 (3.7)	-0.2 (3.5)	0.694	7.6 (3.8)	7.9 (3.7)	0.3 (3.2)	0.557
IL-18 (pg/mL)	279.8 (249.1)	304.1 (270.9)	24.3 (101.5)	0.133	368.5 (340.6)	350.5 (301.6)	-18.0 (277.0)	0.680
TARC (pg/mL)	122.0 (137.9)	125.8 (115.0)	3.8 (92.5)	0.800	100.7 (82.0)	103.4 (72.6)	2.7 (70.0)	0.811
TNF- α (pg/mL)	3.8 (4.2)	3.0 (3.1)	-0.8 (1.4)	0.004	3.1 (2.3)	2.9 (2.0)	-0.2 (1.1)	0.245
Total IgE (IU/mL)	559.4 (632.9)	597.6 (739.0)	38.2 (251.5)	0.349	695.4 (587.6)	761.2 (681.6)	65.8 (251.7)	0.116
House dust mite-specific IgE (kUA/l)	153.1 (214.1)	129.1 (189.0)	-24.0 (88.0)	0.101	173.7 (172.0)	139.3 (152.4)	-34.4 (91.2)	0.028

Bolding indicates significance.

SD, standard deviation; PEFR, peak expiratory flow rate; FEV₁/FVC, forced expiratory volume in 1 second/forced vital capacity; IL-18, interleukin-18; TARC, thymus and activation-regulated chemokine; TNF- α , tumor necrosis factor- α ; IgE, immunoglobulin E.

TABLE 3. PARENTAL/PATIENT'S GUESSES ON THE STUDY GROUP ASSIGNMENT

Guess study group	Correct N (%)	Incorrect N (%)	Total N (%)
CUF2	30	31	61 (73.5%)
Placebo	12	10	22 (26.5%)
Total	42 (50.6%)	41 (49.4%)	83 (100%)

Given the increasing popularity of herbal remedies, CUF2 had a marked placebo effect, which this study has documented. The reduction in steroid dosage (87%) in the "CUF2 guess group" was enhanced by this placebo effect. Another possible explanation that may be attributed to the placebo effect is that the increased nurse-patient interaction (e.g., reminder call and monthly study visit for proper asthma management, which are more frequent than the usual care practice) lead to better patient self-management and thus improve the outcome measures. The clinical trial investigating CAM with minimal placebo effect is very challenging. This study's results were similar to those of another clinical trial using herbs with a double-placebo design by Wen et al.²⁵ In the study by Wen et al., subjects underwent randomization to receive either an herbal capsule and prednisone placebo tablet or an herbal placebo capsule and prednisone tablet. Although the clinical symptoms scores, use of bronchodilators, serum IgE, and lung function were all significantly improved in the herbal group, the efficacy of the herbal therapy was not significantly better than the prednisone group. In addition, a study by Chen et al showed that early intervention using inhaled corticosteroids in children with mild and persistent asthma could improve lung function so as to decrease the use of oral/systemic corticosteroids.²⁶ Therefore, an innovative study design investigating the efficacy of CAM or issues of null additional therapeutic effects of CAM on asthma management needs to be further explored.

The study had several strengths. First, the attrition rate (94%) on the basis of eligible patients and the compliance rate (93%–94%) were very good for a clinical trial, especially one that used herbal therapy. Second, the broad sample source from two major governmental hospitals may not limit the generalizability of the findings.

The study has two limitations. The original study design was to recruit all mild-to-moderate asthma cases; however, the study only wound up recruiting patients with mild asthma. The selection of patients was restricted to children

with only mild asthma and near-normal lung function, who were already on inhaled steroids and in whom a large placebo effect was apparent, so that there may have been little scope for further improvement. By contrast, some previous studies have included subjects with much worse basal lung function.^{1,27} A Traditional Chinese Medicine herbal formula has recently been shown to be effective in the treatment of mild-to-moderate asthma in 5–18-year-old children, but the basal FEV1 of 65%–75% in that study was considerably lower than that in the present study.²⁸

Second, the study did not entirely replicate the approach taken in Chinese medicine therapy. Chinese medicine diagnosis and medication are traditionally based on both the patient's constitution and the presenting features, and it is common to modify the components of herbal preparations as clinical features change during the course of treatment.²⁹ This practice clearly renders their evaluation by randomized controlled trials, which epitomize the Western medical ideal of evidence-based research, impracticably complex. Nevertheless, there is no reason why a predefined presentation of Chinese medicine should not be subjected to such a trial, and a study of this kind might provide further insights into the research methodology involved in clinical trials using herbal therapy.

Conclusions

Although evidence has been presented for the therapeutic effects of CUF2 in both *in vitro* and animal studies, our study was unable to support the efficacy of adjuvant therapy of CUF2 in children with asthma. Although parents understandably wish to give such herbal treatments to children with asthma to complement conventional treatments with undesirable side-effects, our results suggest that CUF2 has no more than a placebo effect. Parents are therefore advised to discuss the scientific evidence for its benefits in asthma treatment with health professionals before choosing it in preference to conventional treatment modes.

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TABLE 4. CHANGES IN DOSAGE OF INHALED STEROID AFTER 6-MONTH TRIAL BETWEEN GUESS ON THE STUDY GROUPS

	CUF2 (n = 61)		Placebo (n = 22)		p (change between guess study group)
	Baseline mean (SD)	24th Week mean (SD)	Baseline mean (SD)	24th Week mean (SD)	
Dosage of inhaled steroid: case number (%)					
Increase		1 (1.6%)		1 (4.5%)	0.022
Unchanged		7 (11.5%)		8 (36.4%)	
Decrease		53 (86.9%)		13 (59.1%)	

*SD, standard deviation.

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Disclosure Statement

No competing financial interests exist.

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