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FILE: ▪Traditional Chinese Medicine
▪Asthma
▪ASHMI

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RE: Clinical Study Shows Safety and Efficacy of Traditional Chinese Herbal Formula in the Treatment of Asthma

Wen M-C, Wei C-H, Hu Z-Q, Srivastava K, Ko J, Xi S-T, et al. Efficacy and tolerability of antiasthma herbal medicine intervention in adult patients with moderate-severe allergic asthma. *J Allergy Clin Immunol*. 2005;116:517-524.

Asthma is a chronic inflammatory condition of the respiratory airways that affects more than 17.3 million people in the United States and 150 million people globally.[1] The current mainstay of long-term asthma treatment is non-specific anti-inflammatory drugs, such as corticosteroids, which are, however, associated with serious adverse events. In an attempt to evaluate the efficacy of alternative treatments for asthma, the researchers conducted a randomized, double-blind, placebo-controlled study at Weifang Asthma Hospital, China.

Ninety-two patients (43 men, 49 women, mean age approximately 45 years) with chronic asthma and atopy (a genetically determined hypersensitivity to environmental allergens) were enrolled in this 4-week study. Inclusion criteria were a history of allergic asthma of duration at least 1 year, serum IgE (marker of atopy) level above 100 IU/mL, daily symptoms of asthma with exacerbations that affect sleep and activities, symptoms that occur at night more than once weekly, forced expiratory volume at 1 second (FEV_1) $\geq$ 59% to < 72%, predicted or peak expiratory flow (PEF; maximum amount of air expired, expressed as a percent of normal for a person's age and sex) $\geq$ 59% to < 72%, PEF or FEV_1 variability > 30%, and use of a $ß_2$-agonist drug (eases respiration during an asthma attack) daily during the previous month, use of corticosteroids twice in the previous 6 months but no corticosteroid use in the previous month, and an understanding of the research protocol with consent to participate. Excluded from the study were subjects with heart, liver, kidney, or other organ disease, as well as allergy or intolerance to any of the herbs in the study's herbal supplement.

Subjects were randomized to receive an antiasthma herbal medicine intervention (ASHMI), a Traditional Chinese Medicine formula (Weifang Pharmaceutical Manufacturing Factory, affiliated with the Weifang Asthma Hospital), or 20 mg oral prednisone treatment taken once daily in the morning plus placebo mimicking ASHMI capsules so that each group received the same number of capsules daily to help ensure blinding. Each ASHMI capsule contained 0.3 g dried aqueous extract of Ling-Zhi (*Ganoderma lucidum* fruiting body), Ku-Shen (*Sophor flavescentis* root), and Gan-Cao (*Glycyrrhiza uralensis,* licorice root). Subjects in the treatment group received 12 capsules per day (3.6 g), which equaled 20 g Ling-Zhi (Ganoderma), 9 g Ku-Shen, and 3 g Gan-Cao (Licorice) for 4 weeks. Outcome measures included symptom scores, use of salbutamol (β_2-agonist medication), and lung function tests. Additionally, concentrations of markers of immune system activation—IgE, interleukin-5 (IL-5), IL-13, interferon gamma (INF-γ), and cortisol levels were tracked.

Symptom scores were calculated in 3 categories—day-time symptoms (cough, chest tightness, wheezing or dyspnea [difficult breathing]), nocturnal symptoms (number of times waking up at night due to dyspnea), and allergic nasal and ocular (eye) symptoms (nasal itching, runny nose, sneezing, itching around the eyes, and tearing)—at weeks 1, 2, 3 and 4 of treatment based on 3 categories of symptoms. They were graded by physicians on a scale from 0 to 3, with a maximum possible score of 9. For day-time symptoms, subjects received a score of 0 for no symptoms, 1 for mild or intermittent symptoms, 2 for moderate symptoms "with frequent occurrence that may affect normal activity at least 1 time," and 3 for "persistent symptoms, affecting all activities." Nocturnal symptom scores were 0 for no night waking, 1 for waking 1 time at night or early morning due to dyspnea, 2 for waking up twice during the night or early morning caused by dyspnea, and 3 for "multiple night awakenings caused by dyspnea." For allergic rhinitis symptoms, subjects received a score of 0 for no symptoms; 1 for symptoms occurring < 4 d/wk and that didn't affect their comfort level, sleep, and daily activities; 2 for symptoms occurring less than 4 d/wk that did affect their comfort level, sleep, and daily activities; and 3 for symptoms > 4 d/wk with effects on comfort level, sleep, and daily activities.

β_2-agonist use was evaluated for 7 days before treatment and during the final week of the study. Lung function was determined by use of spirometry (blowing into a machine that calculates FEV_1 and PEF) the day before treatment began, and 1 day after the stopping treatment. Measurements were repeated 3 times, which is standard protocol for using a spirometer for measuring lung function. Serum markers of immune system activation were tested at baseline and after treatment.

Compared to baseline, after 4 weeks of treatment significant decreases in median symptom scores were detected in the ASHMI group (from 5.0 [4–8] to 2.0 [0–4], $P < 0.001$) and in the prednisone group (from 5.0 [4–7] to 2.0 [0–4], $P < 0.001$). No significant difference in improvement in symptom scores occurred between the 2 groups ($P = 0.47$); however, significant improvements were noted in the prednisone group after 1 week of treatment, but this did not become significant in the ASHMI group until after 3 weeks of treatment. Pulmonary function significantly improved with ASHMI and prednisone treatments, increasing from a median score of 64.9 ± 3.6 at baseline to 84.2 ± 5.0 after treatment with ASHMI ($P < 0.001$), and from 65.2 ± 3.7 to 88.4 ± 8.0 after treatment with prednisone ($P <$

0.001). PEF also significantly improved in both groups compared to baseline, increasing from 64.6 ± 3.5 to 84.8 ± 5.4 in the ASHMI ($P < 0.001$) group and from 65.0 ± 3.5 to 88.1 ± 7.0 in the prednisone group ($P < 0.001$). Significantly greater improvements were noted in the prednisone group compared to the ASHMI group ($P = 0.02$).

β_2-agonist use significantly decreased in both groups, from 4.7 (3.5–5.7) to 0.9 (0.14–2.3) in the ASHMI group ($P < 0.001$), and from 4.7 (3.5-5.6) to 0.6 (0.3–1.0) in the prednisone group ($P < 0.001$). No significant differences in mean change in β_2-agonist between groups was detected ($P = 0.12$). Peripheral blood eosinophil concentrations, a marker of immune system activation to allergens, significantly decreased in both groups from baseline to the psot-treatment measurement (0.52 ± 0.24 to 0.27 ± 0.14 in the ASHMI group [$P < 0.001$], and 0.53 ± 0.24 to 0.21 ± 0.19 ± 0.1 x 10^9/L in the prednisone group [$P < 0.001$]). The difference in improvement between groups was not significant ($P < 0.37$).

At baseline, serum cortisol was slightly depressed in patients in both groups. Depression of cortisol by prednisone treatment is an adverse effect of this drug. Compared to baseline, after treatment with ASHMI, mean serum cortisol significantly increased from 5.4 ± 2.8 to 7.7 ± 2.3 μg/dL ($P < 0.01$), but significantly decreased after treatment with prednisone from 5.1 ± 3.0 to 3.7 ± 2.3 μg/dL ($P < 0.001$). It is important to note that the serum cortisol in the ASHMI group was in the normal range at baseline and after treatment. The difference in the changes in cortisol concentrations between groups was significant ($P < 0.001$).

Significant difference in cytokines occurred in both treatment groups. IL-5 was significantly reduced in the ASHMI group (95.02 ± 43.8 at baseline to 55.2 ± 23.5 pg/mL after treatment [$P < 0.001$]) and in the prednisone group (103.9 ± 49.6 at baseline to 41 ± 19.1 pg/mL after treatment [$P < 0.001$]). IL-13 concentrations were also significantly decreased in the ASHMI group (133.8 ± 25.9 at baseline to 103.0 ± 23.0 pg/mL after treatment [$P < 0.001$]) and in the prednisone group (130.9 ± 24.9 at baseline to 85.8 ± 19.5 pg/mL after treatment [$P < 0.001$]). Changes in these interleukins were significantly greater in the prednisone group compared to treatment with ASHMI ($P = 0.04$ and 0.02, respectively). Unlike treatment with ASHMI, prednisone therapy resulted in a significant decrease in serum IFN-γ, from 403.7 ± 144.1 to 275.7 ± 135.4 pg/mL ($P < 0.001$). On the other hand, treatment with ASHMI resulted in a significant increase in IFN-γ, from 402.8 ± 142.6 at baseline to 585.6 ± 150.8 pg/mL after treatment ($P < 0.001$). An increase in IFN-γ is considered beneficial in asthma patients.[1] IgE levels significantly decreased in both treatment groups, from 950 (552–1349) at baseline to 476 (73–913) U/mL after treatment with ASHMI ($P < 0.001$), and from 948 (368–1356) at baseline to 310 (60–619) U/mL after treatment with prednisone ($P < 0.001$). These changes were not significantly different between the treatment groups ($P = 0.10$).

Both treatments were well tolerated by the subjects. No major adverse events were detected, nor were abnormalities in blood chemistry. Subjects in the prednisone group gained significantly more weight than those in the ASHMI group (2.8 ± 1.3 kg vs. 0.8 ± 1.4 kg, respectively; $P < 0.001$). Gastric discomfort was experienced in 5.08% (3 of 45) subjects treated with ASHMI compared to 15.51% (9 of 46) treated with prednisone.

This study demonstrated the safety and efficacy of an herbal antiasthma formula for the treatment of asthma. Subjects in the botanical formula experienced improvements that were statistically similar to improvements experienced by subjects taking oral prednisone. However, those in the botanical medicine group experienced less side effects and more favorable changes in immune system markers as compared to prednisone. Like many natural therapies, the symptomatic relief obtained from the botanical formula was not as rapid as that experienced with standard drug therapy (e.g. prednisone), but after three weeks of treatment symptomatic relief was not significantly different between groups. For people seeking an evidence-based alternative for the treatment of asthma, the botanical formula used in this clinical trial was shown to be equivalent to conventional oral prednisone treatment.

—John Neustadt, ND

References

[1]Miller AL. The Etiologies, Pathophysiology, and Alternative/Complementary Treatment of Asthma. *Alt Med Rev.* 2001;6(1).

The American Botanical Council has chosen not to reprint the original article.