Oral curcumin supplementation in patients with atopic asthma

Dennis H. Kim, M.D., Joshua F. Phillips, M.D., and Richard F. Lockey, M.D.

ABSTRACT

Oral curcumin is recognized to have anti-inflammatory properties and has been used by ancient traditional medicine for centuries to treat a variety of diseases. In vitro studies have confirmed the ability of curcumin to inhibit allergic inflammatory cytokine responses from lymphocytes; however, there are no in vivo studies of curcumin to treat inflammation associated with allergic asthma. This study was designed to determine the effect of oral curcumin supplementation on patients with stable, persistent, atopic asthma. Adult patients with stable, persistent asthma with evidence of allergic sensitization were randomized to receive 1000 mg of curcumin twice daily or placebo. Subjects were followed for 6 months and performed monthly spirometry (pre- and postbronchodilator); Asthma Control Test (ACT) scoring; and measurements for fractional excretion of nitric oxide (NO), serum eosinophil count, leukocyte count, total IgE, specific IgE to Dermatophagoides pteronyssinus (Der p) and Dermatophagoides farinae (Der f), use of rescue albuterol, and dose of inhaled corticosteroid. Nine patients were randomized into the treatment arm and six were randomized into the placebo group. No differential response was seen in the treatment and placebo groups regarding the primary end point, postbronchodilator forced expiratory volume in 1 second (FEV1). Similarly, all secondary end point evaluations were not significantly different. Despite in vitro evidence that curcumin has anti-inflammatory properties and can inhibit allergic cytokine responses from lymphocytes in vitro, curcumin, 1000-mg, twice daily supplementation did not significantly affect postbronchodilator FEV1, ACT scores, use of rescue bronchodilator, dose of inhaled corticosteroid, exhaled NO, serum IgE, total white blood cell count specific IgE to Der p or Der f, and blood eosinophils in patients with persistent atopic asthma.

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30 days, and a ≥2+ reaction by prick-puncture test (erythema larger than a nickel in diameter with wheal <3 millimeter) to Dermatophagoides pteronyssinus (Der p) or Der f. Subjects were excluded if there was a history of allergy or intolerance to curcumin, other chronic respiratory conditions (chronic obstructive pulmonary disease, pulmonary hypertension, interstitial lung disease, etc.), FEV₁ < 60%, and history of smoking in the past year or cumulative smoking of ≥10 pack-years. Other exclusive criteria included the use of oral corticosteroid in the preceding 1 month, high-dose inhaled corticosteroid for ≥2 weeks during the 4 weeks preceding the screening visit, long-acting β-agonists at screening visit, and use of short-acting β-agonist at ≥4 puffs/day on average during the preceding 2 weeks (other than before exercise). Additional exclusive criteria included the current use of allergen immunotherapy or any immunotherapy in the past year; current use of antileukotrienes; diseases, i.e., medical or psychiatric or social problems that, in the investigator’s opinion, would interfere with participation in the study or place the subject at risk; inability to swallow the study capsule; personal history of alcohol or illicit drug dependence in the last year; and inability to correctly use a peak flow meter.

The study was conducted between November 2008 through January 2010. All study methods and documents were approved by the Institutional Review Board of the University of South Florida, Tampa, FL.

During screening visit 1, subjects underwent baseline spirometry, Asthma Control Test (ACT) scoring, and skin-prick testing to Der f and Der p allergen extracts. Average ACT score for treatment and placebo groups were 19 and 18, respectively. Average postbronchodilator FEV₁ was 82% in the treatment and 78% in the placebo groups.

After a 2-week run-in period to confirm stable disease, subjects were then randomized; nine were entered into the treatment arm (curcumin at 1000 mg twice daily), and six were entered into the placebo group. Mean postbronchodilator FEV₁ at visit 1 for subjects in treatment and placebo arms were 2.29 and 2.87 L, respectively. Subjects also underwent induced sputum collection, exhaled nitric oxide (eNO), another ACT and phlebotomy to measure serum total IgE, total

### Table 1

| Group     | No. of Patients | Variable | Mean (L) | SD (L)  | Median (L) |
|-----------|-----------------|----------|----------|---------|------------|
| Placebo   | 6               | Visit 5  | 3.85     | 8.36    | 3.07       |
|           |                 | Visit 4  | 1.66     | 8.40    | −1.42      |
|           |                 | Visit 3  | 2.89     | 10.42   | 0.11       |
|           |                 | Visit 2  | 4.12     | 7.16    | 0.98       |
| Curcumin  | 9               | Visit 5  | −4.60    | 5.80    | −3.36      |
|           |                 | Visit 4  | −0.57    | 6.49    | −1.45      |
|           |                 | Visit 3  | −4.67    | 8.71    | −2.77      |
|           |                 | Visit 2  | −1.75    | 5.72    | −1.69      |

FEV₁ = forced expiratory volume in 1 s.
blood eosinophil count, and serum-specific IgE to Der p1 and Der f1.

Two subjects in the treatment arm withdrew consent and were not included in the final analysis. The remaining subjects then returned for three follow-up visits, each 1 month apart, at which time they underwent spirometry, eNO, ACT scoring, phlebotomy for measurement of serum total IgE, blood eosinophils, specific antibody to Der f and Der p, and total white blood cell count. Subjects also maintained a daily diary to record the use of their rescue inhaler, symptoms such as coughing and wheezing, peak expiratory flow rates, dose of inhaled corticosteroids, and/or antibiotic or systemic corticosteroid. Bottles containing study drug were weighed to monitor for medication compliance.

Postbronchodilator FEV₁ was chosen to be the primary end point because it measures the best lung function that can be achieved by bronchodilator therapy on the day of the visit and therefore is a more stable measure in asthmatic patients than comparing visit-to-visit baseline FEV₁. Primary end point analysis was done using Wilcoxon sum rank test instead of t-test because the data did not follow a normal distribution. Compared with baseline, the FEV₁ value at visit 5 in the treatment group decreased (mean = 4.6; SD = 5.8), whereas it increased in the placebo group (mean = 3.85; SD = 3.07; p = 0.0562). Overall, there was no statistically significant improvement in median values of FEV₁ among those subjects taking curcumin compared with placebo (Fig. 1; Table 1). Similarly, secondary end point evaluations of eNO, ACT scores, all of the serum analyses, rescue albuterol use, and dose of inhaled corticosteroid were also not significantly different (data not shown).

In conclusion, despite in vitro evidence that curcumin has anti-inflammatory properties and can inhibit allergic cytokine responses from lymphocytes in vitro, curcumin at 1000 mg twice daily supplementation did not significantly affect postbronchodilator FEV₁, ACT scores, use of rescue bronchodilator, dose of inhaled corticosteroid, eNO levels, or levels of serum IgE, total white blood cells, antibody specific to Der p or Der f, and blood eosinophils in patients with persistent atopic asthma. Future studies may benefit from a larger sample size, longer study duration, higher dose of curcumin, and/or improvements in oral bioavailability.

REFERENCES
1. Wong CK, Li ML, Wang CB, et al. House dust mite allergen Der p 1 elevates the release of inflammatory cytokines and expression of adhesion molecules in co-culture of human eosinophils and bronchial epithelial cells. Int Immunol 18:1327–1335, 2006.
2. Wuyts WA, Vanauwenberde BM, Dupont LJ, et al. Involvement of p38 MAPK, JNK, p42/p44 ERK and NF-kappaB in IL-1beta-induced chemokine release in human airway smooth muscle cells. Respir Med 97:811–817, 2003.
3. Kobayashi T, Hashimoto S, and Horie T. Curcumin inhibition of Dermatophagoides farinea-induced interleukin-5 (IL-5) and granulocyte macrophage-colony stimulating factor (GM-CSF) production by lymphocytes from bronchial asthmatics. Biochem Pharmacol 54:819–824, 1997.
4. Ram A, Das M, and Ghosh B. Curcumin attenuates allergen-induced airway hyperresponsiveness in sensitized guinea pigs. Biol Pharm Bull 26:1021–1024, 2003.
5. Baum L, Lam CW, Cheung SK, et al. Six-month randomized, placebo-controlled, double-blind, pilot clinical trial of curcumin in patients with Alzheimer disease. J Clin Psychopharmacol 28:110–113, 2008.
6. National Heart, Lung, and Blood Institute. Guidelines for the diagnosis and management of asthma. Expert Panel Report 3, p. 349, 2007. Available online at www.nhlbi.nih.gov/guidelines/asthma/; accessed May 12, 2010.
7. Enright PL, Lebowitz MD, and Cockcroft DW. Physiologic measures: Pulmonary function tests. Asthma outcome. Am J Respir Crit Care Med 149:S9–S18, 1994.