Colchicine for Asthma?

In this issue of *Chest* (see page 985), Kelly and colleagues report that colchicine at usual clinical doses (0.6 mg twice daily) partially inhibits IgE-mediated early and late airway responses and suggest that controlled clinical trials should be performed to examine its possible beneficial effect in asthma.

Why should colchicine, an anti-inflammatory agent with a rather limited spectrum of activity, be effective for the treatment of asthma? Further, considering colchicine’s safety profile and extensive use in patients with gout and other diseases, some of whom would be expected to have coexisting asthma, why is there so little information either from controlled clinical trials or anecdotal reports supporting a role for colchicine in asthma?4,5 A review of the pharmacology of colchicine and its potential effects on airway inflammation is needed to address these questions.

Colchicine, an alkaloid of *Colchicum autumnale* (autumn crocus), was first recognized for its beneficial effects for acute articular pain approximately 1,500 years ago and isolated in the beginning of the 19th century. It is an antimitotic agent which binds to microtubular protein (tubulin), thereby interfering with the function of the mitotic spindle and producing metaphase arrest.6 It causes depolymerization and disappearance of the fibrillar microtubules in granulocytes and other motile cells, which is believed to be how it inhibits migration of granulocytes into areas of inflammation.4,5 Colchicine also inhibits histamine release from rat mast cells, which may not be closely related to its effects on microtubules,6 enhances the release of prostaglandin E in rat peritoneal mast cells,7 and potentiates beta-adrenergic and prostaglandin E stimulation of human leukocyte cyclic adenosine monophosphate levels.8 These effects—inhibition of mediator release, enhanced release of anti-inflammatory prostanooids, and increased cyclic adenosine monophosphate levels—could all have beneficial effects in patients with asthma. However, rat peritoneal mast cells may respond differently to colchicine than human airway mast cells. Colchicine has been reported to increase macrophage production of the inflammatory cytokine IL-1,9 and the effects of colchicine on human eosinophils have not been defined. Further, unlike corticosteroids, which are of proven benefit in asthma and also in many other inflammatory diseases, colchicine is not effective in many diseases. The only other pulmonary disorder in which colchicine may produce a beneficial effect is idiopathic pulmonary fibrosis.10 However, its effectiveness in this condition may relate more to an antifibrotic action than to its ability to reduce the inflammatory reaction in the lung.

Based on the currently available information or lack thereof, I am not especially optimistic that colchicine will have a major role in the treatment of asthma. Nonetheless, there may be some patients who will benefit. Because the protective effect of colchicine in the present study was modest at best, it would seem desirable to repeat this type of study using a randomized, double-blind, placebo-controlled design before moving into a large and undoubtedly expensive clinical trial. If such studies confirm a beneficial effect, and in view of the low cost and safety of the drug when used at recommended levels, I would then agree with the authors’ call for a clinical study exploring its effectiveness in treating patients with asthma.

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REFERENCES


Asthma Education

A Time for Reappraisal

The recognition of the importance of asthma education initially came from studies of mortality, an infrequent but tragic outcome.1-5 Such studies highlighted the failure of the person with asthma and their health-care provider to appreciate the severity of the patient's condition, failure to administer corticosteroids at a useful time before death, and problems in long-term management, ie, prescription and use of prophylactic anti-inflammatory therapy. Recommendations on asthma education have advised that patients should be provided with the following information: What is asthma?; the difference between inflammation and bronchoconstriction; triggers of attacks; identifying symptoms and signs of asthma; medications, what they do, administration, and side effects; and self-management plans.6-8 Consequently, throughout the western world there have been significant resources allocated toward establishing asthma education programs to provide information to patients with asthma and their families.

There are now a plethora of published studies on asthma education. They often show positive outcomes in terms of reducing hospitalizations, emergency room use, and days away from work or school.9-16 Many of the studies, however, have relatively small sample sizes and rely on a select population of volunteers. Preaching to the converted or to those who want to be converted is a useful strategy in proving a point, but the limitations must be recognized. There is no standardized approach for providing asthma education and the amount of information supplied. Approaches have ranged from individual sessions to a series of group sessions to 5 days of in-hospital education. Several studies do not have a control group. When a control group exists, the control is generally the group's usual care. No study has examined a control group where education is given but limited to a brief, perhaps 5-min, basic instruction on medications and how to use them properly. In addition, there is precious little information regarding outcome when asthma severity is stratified.

A study attempting to link the aquisition of knowledge with behavior has noted that there is a link, but the relationship is not linear.17 The investigators concluded that when someone has acquired a modest amount of knowledge, no significant behavior changes occur if further information is provided. Furthermore, those with very mild asthma appear to gain little measurable benefit. A recent study examined the effects of an education program supplied to a cohort of patients in an inner-city HMO.18 All potential subjects were included in the analysis. The inner-city setting has repeatedly been shown to be a location with individuals who rely on emergency room rather than continuous care and who are at high risk of a fatal event.19 Despite the best of efforts by Shields et al,18 their study failed to show any benefit in improving measures of asthma morbidity. The authors noted problems in attendance, desire to participate, the lack of a needs assessment, inclusion of mild asthmatic patients, and the lack of a behavioral component to their program. Howcroft reviewed pediatric programs and concluded that benefits are not apparent in patients with mild disease and that many studies do not stand up to rigorous scientific analysis.20

In June 1994 the American Thoracic Society bulletin outlined the "successes" of the National Heart, Lung, and Blood Institute (NHLBI) asthma education program.21 The successes listed were limited to the widespread dissemination of guidelines for asthma management to health-care professionals. Numerous workshops were also held. The list did not include any mention of changes in patient morbidity, mortality, or quality of life. There have been no economic evaluations to date of this large, costly program. The last few sentences, however, mention...