

Position Statement

Academy Position Statement: The Use of Antihistamines in Patients with Asthma

November 2002

AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only.

This position statement was originally released in 1988 under the same title. It was updated, reviewed by the membership and the Board of Directors, and published on the Academy Web site in 2002 under the title: "The Use of Antihistamines in Patients with Asthma."

The statement below is not to be construed as dictating an exclusive course of action nor is it intended to replace the medical judgment of healthcare professionals. The unique circumstances of individual patients and environments are to be taken into account in any diagnosis and treatment plan. The above statement reflects clinical and scientific advances as of the date of publication and is subject to change.

Airway hyperresponsiveness to histamine is a hallmark of asthma, and histamine inhalation reproduces acute asthma symptoms. Plasma histamine concentrations are elevated during the early and late responses to inhaled allergens, and may also increase during spontaneous acute asthma episodes^{1,2}.

Although H1 antihistamines are not first line drugs for the treatment of asthma, they should not be withheld from patients with asthma when required for treatment of concomitant disorders such as allergic rhinitis, urticaria, and atopic dermatitis. In 1988, the American Academy of Allergy and Immunology recommended that the traditional labeling for antihistamines, which included the statement, "Antihistamines should not be used to treat lower respiratory tract symptoms including asthma" should be revised to indicate that antihistamines are not contraindicated in patients with asthma³.

H1 antihistamines have, in fact, been demonstrated to increase the threshold for bronchoconstriction after challenge with histamine, exercise, adenosine and, to a lesser extent, allergens, but not methacholine^{1,2,4}. Combined with leukotriene modifiers, they enhance protection against the early and late allergic response⁵, but not against exercise induced asthma⁶. In addition, H1 antihistamines result in modest bronchodilation. Their beneficial bronchoprotective and bronchodilator effects in asthma appear to be dose related^{2,4,7-13}.

Asthma is linked with allergic rhinitis in terms of epidemiology, anatomy, physiology, immunopathology, and response to treatment¹⁴. In patients with mild allergic inflammation throughout the airways, for example, in those with mild intermittent (seasonal) asthma and concomitant allergic rhinitis, H1 antihistamines in manufacturers' recommended doses have been demonstrated to relieve not only the rhinitis symptoms but also to improve the asthma symptoms significantly^{15,16}.

In moderate persistent asthma, some H1 antihistamines have dose related clinical benefits⁷⁻¹³, including steroid sparing effects⁸. These benefits are not worth the potential risks of central nervous system adverse effects from first generation sedating antihistamines. Further, if doses higher than those recommended for allergic rhinitis are required, the benefits may not be worth the risks of many second generation, relatively non sedating H1 antihistamines, as some of the newer drugs lose their non sedating advantage when high doses are given¹⁷. H1 antihistamines combined with leukotriene modifiers may have an enhanced effect in treatment of moderate persistent asthma¹⁸. In severe persistent asthma, however, H1 antihistamines should not be expected to confer significant benefits¹⁹.

There is preliminary evidence from randomized, double blind, placebo controlled studies of one to three years duration that some H1 antihistamines which have prominent, multi faceted anti allergic effects may delay the onset of asthma in some infants who are at high risk for asthma development because of a family history of atopy, atopic dermatitis, and elevated serum IgE²⁰⁻²².

In summary, the role of H1 antihistamines in asthma continues to evolve. With the introduction of new H1 antihistamines with improved benefit to risk ratios which can be used at high dosage with minimal risk of central nervous system adverse effects, this role will likely become more prominent in the future.

REFERENCES

1. Holgate ST. Experimental models in asthma. *Clin Exp Allergy* 1999;29 (Suppl. 3):82-6.
2. Simons FER. Is antihistamine (H1 receptor antagonist) therapy useful in clinical asthma? *Clin Exp Allergy* 1999;29 (Suppl. 3):98-104.
3. Sly RM, Kemp JP, and the AAAAI Committee on Drugs. The use of antihistamines in patients with asthma. *J Allergy Clin Immunol* 1988;82: 481-2.
4. Wood Baker R, Holgate ST. The comparative actions and adverse effect profile of single doses of H1 receptor antihistamines in the airways and skin of subjects with asthma. *J Allergy Clin Immunol* 1993;91:1005-14.
5. Roquet A, Dahlén B, Kumlin M, Ihre E, Anstrén G, Binks S, et al. Combined antagonism of leukotrienes and histamine produces predominant inhibition of allergen induced early and late phase airway obstruction in asthmatics. *Am J Respir Crit Care Med* 1997;155:1856-63.
6. Dahlén B, Roquet A, Inman M, Larssen F, Karlsson O, Hemmings R, et al. The contribution of histamine and leukotrienes to exercise induced airway obstruction in asthmatics. *Am J Respir Crit Care Med* 2000;161:A613.
7. Van Ganse E, Kaufman L, Derde MP, Yernault JC, Delaunois L, Vincken W. Effects of antihistamines in adult asthma: a meta analysis of clinical trials. *Eur Respir J* 1997;10:2216-24.
8. Busse WW, Middleton E, Storms W, Dockhorn RJ, Chu TJ, Grossman J, et al. Corticosteroid sparing effect of azelastine in the management of bronchial asthma. *Am J Respir Crit Care Med* 1996;153:122-7.
9. Gould CAL, Ollier S, Aurich R, Davies RJ. A study of the clinical efficacy of azelastine in patients with extrinsic asthma, and its effect on airway responsiveness. *Br J Clin Pharmacol* 1988;26:515-25.
10. Bousquet J, Emonot A, Germouty J, Molina C, Montané F, Perrin Fayolle M, et al. Double blind multicenter study of cetirizine in grass pollen induced asthma. *Ann Allergy* 1990;65:504-8.
11. Ekström T, Osterman K, Zetterström O. Lack of effect of loratadine on moderate to severe asthma. *Ann Allergy Asthma Immunol* 1995;75:287-9.
12. Spector SL, Nicodemus CF, Corren J, Schanker HM, Rachelefsky GS, Katz RM, et al. Comparison of the bronchodilatory effects of cetirizine, albuterol, and both together versus placebo in patients with mild to moderate asthma. *J Allergy Clin Immunol* 1995;96:174-81.
13. Ratner PH, and the Desloratadine Study Group. Desloratadine improved asthma symptoms and reduced bronchodilator use in 2 studies of patients with asthma and SAR. *Ann Allergy Asthma Immunol* 2001;86:109.
14. Simons FER. Allergic rhinobronchitis. The asthma/allergic rhinitis link. *J Allergy Clin Immunol* 1999;104:534-40.
15. Corren J, Harris AG, Aaronson D, Beaucher W, Berkowitz R, Bronsky E, et al. Efficacy and safety of loratadine plus pseudoephedrine in patients with seasonal allergic rhinitis and mild asthma. *J Allergy Clin Immunol* 1997;100:781-8.
16. Grant JA, Nicodemus CF, Findlay SR, Glovsky MM, Grossman J, Kaiser H, et al. Cetirizine in patients with seasonal rhinitis and concomitant asthma: prospective, randomized, placebo controlled trial. *J Allergy Clin Immunol* 1995;95:923-32.
17. Shamsi Z, Hindmarch I. Sedation and antihistamines: a review of inter drug differences using proportional impairment ratios. *Hum Psychopharmacol Clin Exp* 2000;15 (Suppl. 1):S3-S30.
18. Reicin A, White R, Weinstein S, Finn J A, Nguyen H, Peszek I, et al. Montelukast, a leukotriene receptor antagonist, in combination with loratadine, a histamine receptor antagonist, in the treatment of chronic asthma. *Arch Intern Med* 2000;160:2481-8.
19. Wood Baker R, Smith R, Holgate ST. A double blind, placebo controlled study of the effect of the specific histamine H1 receptor antagonist, terfenadine, in chronic severe asthma. *Br J Clin Pharmacol* 1995;39:671-5.

20. Iikura Y, Naspitz CK, Mikawa H, Talaricoficho S, Baba M, Sole D, et al. Prevention of asthma by ketotifen in infants with atopic dermatitis. *Ann Allergy* 1992;68:233-6.
21. Bustos GJ, Bustos D, Bustos GJ, Romero O. Prevention of asthma with ketotifen in preasthmatic children: a three year follow up study. *Clin Exp Allergy* 1995;25:568-73.
22. Warner JO on behalf of the ETAC® Study Group. A double-blinded, randomized, placebo-controlled trial of cetirizine in preventing the onset of asthma in children with atopic dermatitis: 18 months' treatment and 18 months' posttreatment follow-up. *J Allergy Clin Immunol* 2001;108:929-937.

2002 revision was drafted by:

F. Estelle R. Simons, MD, FRCP, FAAAAI

And reviewed by the membership and the 2002 Board of Directors.

AAAAI Position Statements and Work Group Reports are not to be considered to reflect current AAAAI standards or policy after five years from the date of publication. For reference only. November 2002.