EFFECT OF ORAL AND INHALED CETIRIZINE IN MILD ASTHMATIC PATIENTS

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ABSTRACT

Objectives: The effect of an inhaled and oral H1 antagonist has been compared in the same patients.

Material and Methods: We have compared the effect of a single dose of nebulised (1 ml – 10 mg /ml) and oral (15mg) cetirizine to a matched placebo in a double blind double blind double dummy cross over study in 10 atopic asthmatics with moderate airflow obstruction mean (sem) age 52 (5.22) years, mean predicted FEV1 59 (3.9%).

Results: The data was analysed by applying the multiple Regression analyses and chi square statistical methods. There was no significant difference in the baseline FEV1 on three study days. The maximum mean percentage increase in FEV1 after placebo, nebulised and oral cetirizine were 11.7 (2.8); 11.3 (5.5) and 21.8 (3.7) respectively. Significant bronchodilation was observed at 60 (P<0.02) ,120 (P<0.02) and 180 minutes (P<0.05) after oral cetirizine compared to placebo. Four patients developed transient bronchoconstriction after inhaled cetirizine. These results suggest the presence of a local histamine tone in the airways.

Conclusion: Ordinary doses of currently available H1 receptor antagonist have minimal bronchodilator and bronchoprotective activity. In severe persistent asthma, H1 receptor antagonist have no significant clinical effect, however in moderate asthma clinical benefits of H1 receptor antagonist are apparent. The participation of antihistamine in the allergic inflammation including asthma must be reexamined, since the effect of histamine are more widespread and further studies are needed to evaluate its role in the management of asthma.

Key words: Cetirizine, bronchodilation, Histamine receptors H1 and H2.
INTRODUCTION

Patient with asthma shows increase airway hyperresponsiveness to histamine.\textsuperscript{1,2} Histamine acts on bronchial smooth muscle via two distinct H1 and H2 receptors .H1 antagonist have been reported to cause bronchodilation in patients with asthma suggesting an airway tone due to locally released histamine. The effect of an inhaled and oral H1 antagonist has been compared in the same patients.

MATERIAL AND METHODS

- 10 moderately severe patients with atopic asthma mean (SEM) age 52 (5.2) mean predicted FEV1 59.8 (3.9) with documents reversibility of > 20% after 2.5 mg of nebulised salbutamol were enrolled.
- 3 separate study days with at least 3 weeks of wash out period in between .
- None of the patients was on oral steroids, oral bronchodilators, antihistamines or anticholinergic drugs.
- Oral and inhaled cetirizine or matched placebo (water) were given in a double blind fashion.
- FEV1 was measured using Vitalograph spirometer over 4 hour period at frequent intervals.
- The solution are given through wirtgh’s nebuliser (reservoir volume 3m).

Output 0.133ml/min) driven by compressed air at 9l/min (pressure 3.5 Kpa) for 7.5 min.

RESULTS

We have compared the effect of a single dose of nebulised (1 ml –10 mg) and oral (15 mg) cetirizine to a placebo in a double blind study in 10 atopic asthmatics with moderate airflow obstruction with mean predicted
FEV1 59 (3.9) %. The data were analysed by applying multiple regression analyses and chi square tests. There was no significant difference in the base line FEV1 on the three study days. The maximum mean percentage increase in FEV1 after placebo, nebulised and oral cetirizine were 11.7(2.8),11.3(5.5) and 21.8(3.7) respectively. Significant bronchodilation was observed at 60 (p<0.02), 120 (p<0.02) and 180 minutes (p<0.05) after oral cetirizine compared to placebo. Four patients developed transient broncho-constriction after inhaled cetirizine. The lack of bronchodilation following nebulised cetirizine is probably related to the local irritant effect as this has been shown with other H1 antagonist such as inhaled clemastine.

DISCUSSION

Asthma is a chronic inflammatory disease of the lower airways and its cardinal features include smooth muscle spasm, mucosal edema, inflammation and mucus secretion. It has been demonstrated that bronchospasm and mucosal edema can be caused by H1 receptor stimulation, while H2 and H1 receptor activation are probably minor causes of mucus secretion. Histamine act directly with the endothelial cells (EC) and induces permeability, a transient expression of p-selection and secretion of lipid mediators (e.g. PGI2, PAF and LTB4). Moreover histamine induces a significant increase of IL-6 and IL-8 secretion by endothelial cells. Since IL-8 exerts a chemo tactic activity of neutrophils, eosinophils and basophils and IL-6 is involved in endothelial permeability, the secretions of cytokines may be involved in the late reaction of asthma.3,4,5,6

Our study demonstrated a significant increase in bronchodilation at 60 min (p<0.02), 120 min (p<0.02) and at 180 min (p<0.05) after oral cetirizine compared to placebo in a mild asthmatic patients. This was further substantiated by another study by Aubier M; Neukirch C et al7 who demonstrated a protective nasal effect of cetirizine in patients against bronchial hyperresponsiveness measured 6 hours after nasal allergen challenge in patients with allergic rhinitis with asthma. This suggest that cetirizine may be useful in asthma patients with allergic rhinitis.

Second generation H1 receptor antagonist have been studied extensively in the treatment of asthma. Many of these drugs have been reported to inhibit eosinophil and basophil chemotaxis and therefore might have an effect on inflammatory reaction that characterize this disease.8 Antihistamines in addition to inhaled steroids and bronchodilators have been shown to offer partial protection against exercise induced asthma, suggesting a possibility of using a combination treatment to manage patients symptoms.9 Simon FE 10, has also reported that plasma concentration of histamine are elevated during the early and late responses to allergens, and may also increase during spontaneous acute asthma episodes. Ordinary doses of currently available H1 receptor antagonist have minimal bronchodilator and bronchoprotective activity. In severe persistent asthma, H1 receptor antagonist have no significant clinical effect, however in moderate asthma clinical benefits of H1 receptor antagonist are apparent. The participation of antihistamine in the allergic inflammation including asthma must be reexamined, since the effect of histamine are more widespread and further studies are needed to evaluate its role in the management of asthma.

REFERENCES


4 Fireman P. Rhinitis and asthma connection: management of coexisting upper allergic disease and asthma. Allergy Asthma Proc 2000; 21(1): 45.

5 Dubuske LM. The link between allergy and asthma. Allergy asthma Proc 1999; 20(6): 341.


10 Simon FE. Is antihistamine (H1 receptor antagonist) therapy useful in clinical asthma? Clin Exp Allergy 1999; 29(3): 98.

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