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REVIEW ARTICLE

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Comparison of Intranasal Corticosteroids and Antihistamines in Allergic Rhinitis

A Review of Randomized, Controlled Trials

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Abstract

For several years there has been discussion of whether first-line pharmacological treatment of allergic rhinitis should be antihistamines or intranasal corticosteroids. No well documented, clinically relevant differences seem to exist for individual nonsedating antihistamines in the treatment of allergic rhinitis. Likewise, the current body of literature does not seem to favor any specific intranasal corticosteroid. When comparing efficacy of antihistamines and intranasal corticosteroids in allergic rhinitis, present data favor intranasal corticosteroids. Interestingly, data do not support antihistamines as superior in treating conjunctivitis associated with allergic rhinitis. Safety data from comparative studies in allergic rhinitis do not indicate differences between antihistamines and intranasal corticosteroids. Combining antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis does not provide additional beneficial effects to intranasal corticosteroids alone.

Considering present data, intranasal corticosteroids seem to offer superior relief in allergic rhinitis, when compared with antihistamines.

Allergic rhinitis is a disease characterized by nasal obstruction, rhinorrhea, sneezing and nasal itch and often accompanied by conjunctivitis. It is elicited by IgE-mediated allergic inflammation of the nasal mucosa. The disease prevalence is 10–20% of the population in industrialized countries[1] and seems to be increasing.[2,3] Although allergic rhinitis is not a life-threatening disease, it can severely affect patients' quality of life[4-6] and can cause comorbidity from other diseases, such as asthma, sinusitis,

otitis media and conjunctivitis.[7] Allergic rhinitis can be either seasonal, i.e. present at certain times of the year such as during the pollen season, or perennial, i.e. present at all times of the year.

Applicable therapeutic initiatives in allergic rhinitis are allergen avoidance, allergen immunotherapy and pharmacological intervention. This review considers first-line pharmacological treatment of allergic rhinitis, in which two main treatment options have evolved, i.e. antihistamines and intranasal corticosteroids. The choice between these options has been extensively discussed since the introduction of intranasal corticosteroid treatment.[8] Evidence presented in this review considers only data obtained in patients with allergic rhinitis. Medical literature including abstracts and randomized trials published in the English language during the period 1966–2001 on antihistamines and intranasal corticosteroids in the treatment of allergic rhinitis were identified using Medline.

1. Antihistamines

1.1 General Considerations

Histamine is the major pathophysiological mediator of allergic rhinitis, almost exclusively exerting its action through stimulation of the H_1 receptor. Whether other histamine receptors have any effect in allergic rhinitis remains to be clarified. Antihistamines in the treatment of allergic rhinitis are, thus, H_1 receptor antagonists.[9,10] An additional anti-inflammatory effect of H_1 antihistamines has been proposed, as some newer compounds seem to influence cytokine production, mediator release or inflammatory cell flux.[11-19] However, other studies have been unable to reproduce such findings.[20-23] Whether antihistamines offer additional and clinically relevant anti-inflammatory effects along with their inhibition of histamine action needs further clarification.

1.2 Oral Antihistamines

Numerous H_1 receptor antagonists have been developed over the years. For oral use, these can roughly be divided into older, first-generation (e.g. chlorpheniramine, diphenhydramine, promethazine and tripolidine) and newer, second-generation antihistamines (acrivastine, astemizole, cetirizine, ebastine, fexofenadine, loratadine, mizolastine and terfenadine). This review deals with the newer antihistamines, as use of the older drugs in allergic rhinitis is limited by their adverse effects, mainly sedation and anticholinergic activity.

All of the newer antihistamines are effective in the treatment of allergic rhinitis by decreasing nasal itching, sneezing and rhinorrhea, but have a poor effect upon nasal congestion.[24-31] They are also effective upon conjunctivitis and recent results seem to indicate some influence on lower airway symptoms which often co-exists with allergic rhinitis.[32,33]

Moreover, the pharmacokinetic profile of these drugs is advantageous when compared with that of the older ones.[34] They have an onset of action within 1–2 hours, lasting for 12–24 hours, except for acrivastine, which has to be given at 8-hour intervals. With the exception of cetirizine and fexofenadine, which are excreted almost unchanged, the drugs in this group are metabolized via the hepatic cytochrome P450 (CYP) system by CYP3A. As a number of other compounds (antimycotic conazoles, macrolide antibacterials and grapefruit juice) are substrates for this enzyme, this obviously provides a theoretical risk for interactions.[35] This is probably a contributing factor to the occurrence of severe cardiac arrhythmias (such as 'torsade de pointes') and deaths, which have been described following treatment with terfenadine and astemizole.[36-38] These effects seem to be enabled through a quinidine-like action, causing a prolongation of the QT interval.[39,40] At present, no clinical evidence has demonstrated cardiac adverse effects from other second-generation antihistamines, when considered at therapeutically appropriate levels. However, in a consensus statement on the treatment of allergic rhinitis the European Academy of Allergology and Clinical Immunology recommends that antihistamines that are metabolized by CYP450 or have quinidine-like actions be avoided in risk groups, i.e. patients with impaired hepatic function or cardiac arrhythmia.[41]

Astemizole can also act as an appetite stimulant and result in increased bodyweight.[42,43] The cause of this action remains obscure, although a CNS-mediated mechanism, such as serotonin antagonism, could be speculated. However, whether this adverse effect is seen exclusively with astemizole remains unclear, as data regarding this parameter are lacking for other second-generation antihistamines.

While CNS-related adverse effects were a major characteristic of the first-generation antihistamines, the piperazine/piperidine-derived structures of the newer generation reduce their CNS penetration, although sedative effects have been described for some of the compounds, e.g. acrivastine[44] and cetirizine.[45] The binding affinity to muscarinic receptors is also decreased. With the exception of cardiac adverse effects, this leaves second-generation antihistamines with a therapeutic index superior to that of first-generation antihistamines.

1.3 Intranasal Antihistamines

Azelastine and levocabastine are two newer H_1 receptor antagonists for topical use. When applied intranasally, both have

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