H$_1$-Receptor Antagonists in the Management of Allergic Rhinitis
A Comparative Review

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Summary

Allergic rhinitis, the most common clinical expression of atopy, is caused by: (a) the action of various mediators and other cell-derived substances released during the acute phase of the allergic reaction; and (b) the inflammatory response that follows hours later. Histamine, a mediator of major importance in eliciting the signs and symptoms of allergic rhinitis, is known to act via a number of distinct receptors (H$_1$, H$_2$, H$_3$ and possibly H$_4$). It appears that H$_1$-receptors are function-
ally most important in the nose, and hence H1-receptor antagonists have been the mainstay of rhinitis treatment for over 50 years.

Classic first-generation antihistamines freely cross the blood-brain barrier and also exhibit significant anticholinergic activity, causing sedation and other adverse effects that restrict their use. Second-generation non-sedating H1-antagonists have fewer adverse effects, are longer acting, permitting a more convenient dosage schedule, and also exhibit additional antiallergic properties. Such features are probably more important in the chronic forms of rhinitis, where second-generation agents should preferentially be employed.

No single H1-antagonist, old or new, controls nasal blockage adequately. As a consequence, the demand for combining antihistamines with sympathomimetic vasoconstrictors has been more or less constant, despite the introduction of the improved second-generation H1-antagonists. Several of the non-sedating antihistamines are presently available in fixed combinations with pseudoephedrine and might be used in cases of persistent nasal blockage. Combination of H1- and H2-antagonists, even when applied locally, does not appear to alleviate the symptoms of rhinitis more than monotherapy with H1-antagonists.

Caution must be observed when considering H1-antagonist therapy for special groups of patients. These situations include extremes of age, pregnancy, lactation, individuals with impaired renal or hepatic function, and those who are receiving drugs known to interact with particular antihistamines.

Asthma coexisting with rhinitis does not constitute a contraindication for the use of H1-antagonists. Second-generation antihistamines are particularly appropriate in this situation, not only because they are free of anticholinergic adverse effects such as drying of mucous membranes, but also because some of them exhibit additional antiallergic properties and/or mild anti-inflammatory activity.

1. Allergic Rhinitis

1.1 The Magnitude of the Problem

Allergic rhinitis represents the most common clinical expression of atopy. Its high prevalence, estimated to be 10 to 20% in the general population, underlines its major health and socioeconomic importance. Rhinitis is classified among the 10 leading causes of chronic disability. Despite its benign nature, it causes significant morbidity and dysfunction, usually directly or because of paranasal complications, but occasionally because of adverse effects of treatment. In children, rhinitis and related problems constitute the most common cause of school absenteeism. In adults, it can be a handicap for certain professions, for example singers, teachers and reporters.

Seasonal (pollen-induced) allergic rhinitis, or "hay fever", and its perennial counterpart, caused by long term allergen exposure, are typical type I hypersensitivity reactions. Treatment of these disorders is a daily occurrence in the practice of various medical and surgical disciplines such as allergology, paediatrics, internal medicine and otolaryngology. This review on H1-antagonists in the treatment of allergic rhinitis will be approached with due consideration to the needs of such a diverse group of practitioners.

A rational approach to the treatment of allergic rhinitis should, however, start exactly where the problem begins: the inciting allergen. Measures aimed at:

- allergen avoidance, when feasible and realistic (cat dander)
- reduction of the allergen load (mites)

are essential prerequisites for the sound management of allergic patients in general and rhinitis sufferers in particular.