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Rupatadine: Novel Antihistamine for the Treatment of Allergic Disease

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Allergic rhinitis (AR) is a highly prevalent disease that markedly affects the quality of life.[1] Current pharmacologic treatment strategy for AR include antihistamines, decongestants, leukotriene modifiers and intranasal corticosteroids. Antihistamines are commonly used as a first-line treatment to alleviate allergic rhinitis and urticaria. First generation antihistamines were proven to be useful but have mainly been associated with significant adverse effects on performance and psychomotor activity mediated by their strong H1 inhibitory effect.[2] Second-generation antihistamines, with a lower potential for H1-receptor occupancy in the brain, are less likely to produce sedation at recommended dosages.

The allergic reaction occurs in two phases. The early phase of the reaction involves a release of preformed mediators such as histamine and proteases, as well as numerous other newly-generated mediators.[3] Early-phase (immediate) inflammatory response initiated within minutes of re-exposure to the allergen. It is primarily caused by mast-cell degranulation and release of mediators such as histamine, proteases, platelet-activating factor (PAF), leukotrienes, etc. These mediators stimulate production, adhesion, and infiltration of circulating inflammatory cells such as eosinophils, basophils, monocytes, and lymphocytes into local tissue. And induce symptoms characterized by sneezing, itching, and rhinorrhea. The late-phase inflammatory response begins 2 to 4 hours after allergen exposure caused by inflammatory cell infiltration, mainly eosinophils. Releasing of further mediators promotes local edema and tissue damage and continues of the inflammatory process characterized by nasal congestion and obstruction.

Histamine is a well-established mediator in the pathophysiology of allergic rhinitis and chronic urticaria, explaining the pivotal role of antihistamines in the treatment of these conditions. However, histamine is not the only mediator involved in the 'allergic cascade'. Platelet-activating factor (PAF) is also an essential mediator of AR. And numerous other mediators have also been implicated in the inflammatory process of allergic disease.[4]

Rupatadine is an N-alkyl pyridinium derivative and classified as a new second-generation antihistamine that shows an affinity for H1-receptor with the advantage of exhibiting additional platelet activating factor (PAF) antagonist activity.[5] The activity has been shown in several in vitro and in vivo studies and more recently in specific PAF nasal challenge in healthy and allergic rhinitis subjects[6], where rupatadine was the distinctive treatment able to decrease overall AUC nasal symptoms compared with placebo. Rupatadine (10 and 20 mg) are effective and well-tolerated for allergic rhinitis[7-9], urticaria[10] with no side effects on cardiac repolarization[11] or central nervous system[12]. Rupatadine has been approved for the treatment of seasonal and perennial AR and urticarial in the EU and Russia. It is also available in most Central and South American countries.[13] Although clinical trials show definite benefit, these studies has been limited to local subjects in the Western continent. Regional and ethnic variations among populations may alter a pharmaceutical compound's safety, efficacy, or dose response. To address ethnic sensitivity of a drug in a new region a bridging study can be executed in the new region to "build a bridge" with the foreign clinical data. We present the results of a bridging study to assess the safety and efficacy of rupatadine fumarate in the treatment of Korean perennial allergic rhinitis (PAR) patients. Furthermore the efficacy was compared to bepotastine which is known to be safe and effective in treating AR.

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