

## Advanced and novel therapy of Allergic rhinitis: Monterizine

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Clinical experimental studies shows that asthma and allergic rhinitis share many aspects in pathogenesis. Allergic inflammation is a crucial pathogenesis for these two diseases and these two are aggravated with same factors, such as cold dry air, upper respiratory infection, out door or indoor air pollution, stress and aeroallergens. Epidemiology studies also reveal that most asthma patients have allergic rhinitis and allergic rhinitis is the high risk factor for development of asthma.

Mast cell and basophils play as the key terminal actor in allergic inflammation, and histamine and cysteinyl leukotrienes (cys-LTs) are the most important inflammatory mediators from these cells. Although both histamine and cys-LTs are smooth muscle contractor and vasodilator, the physiology potency of two mediators are quite different in each functional aspects. Cys-LTs are about 1,000 time stronger than histamine for smooth muscle contraction, and histamine plays more important role for vasodilation and enhanced vascular permeability than cys-LTs. That is the basic reason why anti-histamines and cys-LTs receptor antagonist have different indications for management of allergic diseases. Second generation antihistamine has been recognized as the first line treatment for allergic rhinitis, but not asthma. Cys-LTs receptor antagonist has equivalent efficacy to inhaled corticosteroid for management of mild persistent asthma, and equivalent efficacy to inhaled long acting beta2 agonist as an additive prescription to inhaled corticosteroid for management of moderate persistent asthma.

When we prescribe to allergic patients, we have to consider how to increase the adherence of patients to the prescription. Among the factors which affect adherence, adverse drug reactions, convenience of the prescription, and cost are the most important determinants. Adherence to inhaled corticosteroid (ICS) is unsatisfactory, even though KAAACI has done huge devotion to the increment of adherence. The main reasons for the discouragements might be local adverse reaction, inconvenience for use of ICS, and reimburse program of Korean Health Insurance System. Recently, Hanmi Pharm developed Monterizine. It is

the combination of montelukast and levocetirizine, which are the most popular prescription as cys-LTs receptor antagonist, and second generation anti-histamine in Korea, respectively. Phase 3 clinical trial was done for evaluation of efficacy of Monterizine with 210 patients with allergic rhinitis and mild to moderate persistent asthma. The clinical trial consisted of 1:1 two arms: Monterizine vs. montelukast monotherapy. Primary end point was mean daytime nasal symptom score (DNSS) at 3-4<sup>th</sup> week, and secondary endpoints were each symptom score of DNSS at 3-4<sup>th</sup> week: nasal discharge, nasal obstruction, sneezing and nasal itching sensation. The trial met the primary endpoint: Monterizine decreased mean DNSS by 20% compared to montelukast. In detail it decreased domain of sneezing and nasal itching sensation compared to montelukast monotherapy. There was not any difference in adverse events between two arms.

In conclusion, Monterizine is safe and more effective for management of allergic rhinitis with mild to moderate persistent asthma patients compared to montelukast monotherapy. Furthermore it has several advantages in simplicity of prescription and cost, which are also the important determinants for adherence to prescription.