**Symposium**

**Korean Academy of Allergy, Asthma and Clinical Immunology: *Severe Asthma***

# Management of Severe Asthma

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## Content Description

Severe asthma presents significant management challenges. Patients can be difficult to control despite use of current standard-of-care therapy. Severe asthma is not homogeneous and is likely made up of multiple known and yet-undefined phenotypes. Identification of these distinct phenotypes with specific biomarkers will likely lead to improved and distinct management strategies. Another important problem is that the vast majority of severe asthmatic patients remain symptomatic despite the use of combined long-acting beta2 agonist (LABA) and inhaled corticosteroid (ICS) therapy. Add-on options to LABA/ICS (e.g. leukotriene modifiers, anti-IgE antibodies and anticholinergics) and targeted options (e.g. anti-IL13 antibodies, anti-CD25 antibodies and bronchial thermoplasty) shed new light on the management of severe asthma. This presentation will be focused on Xenon ventilation computed tomography as a new modality for severe asthma phenotyping and tiotropium bromide, a long-acting inhaled anticholinergic as a promising agent for severe asthma treatment.

## Learning Objectives

- Hurdles for assessing and managing severe asthma properly
- Imaging technique as a new modality for assessing severe asthma
- Emerging medications for managing severe asthma

## Additive role of tiotropium in severe asthmatics and Arg16Gly in *ADRB2* as a potential marker to predict response *(Allergy 2009;64:778-783)*

Recent findings have raised new interests about the use of anticholinergics, especially tiotropium, for the treatment of asthma. This study was performed to determine whether an additional improvement in lung function is obtained when tiotropium is administrated in addition to conventional therapies in severe asthmatics, and to identify factors capable of predict response to tiotropium using a pharmacogenetic approach. A total of 138 severe asthmatics on conventional medications and with decreased lung function were randomly recruited. Tiotropium 18μg was added once a day and lung functions were measured every 4 weeks. Responders were defined as those with a forced expiratory volume in 1 second improvement of ≥ 15% (and 200 ml) that were maintained for at least 8 successive weeks. Eleven single nucleotide polymorphisms (SNPs) in *CHRM1-3* (coding muscarinic receptor 1-3) which were identified by re-sequencing, and Arg16Gly and Gin27Glu in *ADRB2* (coding beta2 adrenoreceptor) were scored in 80 of the 138 asthmatics. Forty-six of the 138 asthmatics (33.3%) responded to tiotropium treatment. Logistic regression analyses (controlled age, gender and smoking status) showed that Arg16Gly in *ADRB2* [P = 0.003, OR (95% CI) = 0.21 (0.07-0.59) in a minor allele dominant model] was significantly associated with response to tiotropium. As many as 30% of severe asthmatics on conventional medications with reduced lung function were found to respond to adjuvant tiotropium. The presence of Arg16Gly in *ADRB2* may predict response to tiotropium.

## Clinical meanings of air trapping within the lungs of severe asthmatics: A promising role of Xenon ventilation computed tomography *(A preliminary result)*

Xenon ventilation computed tomography (CT), in which CT is performed after inhalation of radio-dense xenon gas has shown potential in assessing regional ventilation status in animals and healthy human volunteers. Recent introduction of dual-energy source CT enabling differentiation of xenon gas from lung tissue make it possible to use xenon ventilation CT in clinical practice. In our previous study, we observed that about 30% of severe asthmatics with reduced lung function respond to adjuvant tiotropium. We tried to identify factors capable of predicting response to tiotropium. In this preliminary study with 10 severe asthmatics, we found that a decrease in total number of air trapping on Xenon ventilation CT in wash-out phase after bronchodilator inhalation at baseline (before tiotropium was added) was a potential marker predicting a further increase in FEV1 after 12-week tiotropium treatment, even in patients who showed no increase in FEV1 after bronchodilator inhalation at baseline. Xenon ventilation CT must be an objective and promising modality in measuring asthmatic symptoms and treatment responses, especially in severe asthmatics.

## References

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