

The way forward for the refractory asthmatic

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Abstract:

Sir,

Ireland has the fourth highest prevalence of asthma in the world. 7.1% of 18+ population and 18.9% of 13-15 year olds have asthma. 38.5% of 13-15 year olds reported wheezing. More than 1 person a week dies from asthma and 29% of asthma patients miss school or work. Despite very safe and effective treatment 5-10% of patients with bronchial asthma do not respond well to their treatment. This group of patients are labelled as refractory asthmatics. Besides compliance, presence of psychogenic and trigger factors and comorbid illness, steroid insensitiveness or resistance may play a significant role in the poorly controlled/responding asthmatics. Type I Steroid resistance is due to lack of binding affinity of steroids to glucocorticoid receptors and may respond to higher doses of steroids while type II steroid resistance is because of reduced number of cells with glucocorticoid receptors, which is very rare and do not respond to even higher doses of systemic steroids and these cases require alternative/novel therapies.

There has been major advances in the research arena. Eosinophilic inflammation is the most focused phenotype because most novel asthma treatments have targeted T-helper type 2 (Th2) pathway. With the discovery of potential biomarkers such as Fractional-exhaled nitric oxide (FeNO), serum periostin and YKL-40, we can see the management of asthma diverging away from other airflow obstructive diseases. Fractional-exhaled nitric oxide (FeNO) is a new method that represents an eosinophilic airway inflammation with a significant correlation with sputum eosinophilia and asthma severity instead of sputum eosinophil count that easily influenced by corticosteroid therapy. YKL-40 is associated with asthma severity and airway remodeling. Serum periostin is a strong serum biomarker for eosinophilic airway inflammation and an indicator of Th2-targeted therapy and airflow limitation. The most promising agents are targeted against cytokines of Th2 pattern and related receptors. Examples are IL-2 (daclizumab) and IL-13 (lebrizumab) or IL-5 in patients with hypereosinophilia (mepolizumab, reslizumab and benralizumab). Other potential drugs have as a target TNF- α or its soluble receptor (infiximab, golimumab and etanercept) or IL-1 (canakinumab), a cytokine with an important systemic proinflammatory action. Finally, the discovery of increased levels of C5a in the airways of asthmatic patients has led to the synthesis of a specific monoclonal antibody (eculizumab). Further help should come from the identification of biomarkers that can guide, in choosing the best treatment for the individual patient, such as IgE for omalizumab or periostin for lebrizumab.

Reflecting on those advances, we can clearly see that the way forward for the refractory asthmatic is likely to be targeted toward cytokines and bronchial thermoplasty.

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References

1. Facts & figures on asthma. Asthma Society of Ireland.<http://www.asthma.ie/get-help/resources/facts-figures-asthma>
2. Luhadia SK. Steroid resistant asthma. J Assoc Physicians India. 2014 Mar;62:38-40
3. Kim MA, Shin YS, Pham le D, Park HS. Adult asthma biomarkers. Curr Opin Allergy Clin Immunol. 2014 Feb;14:49-54.
4. Menzella F, Lusuardi M, Galeone C, Zucchi L. Tailored therapy for severe asthma. Multidiscip Respir Med. 2015 Jan 16;10:1