Cough · 4: Cough in asthma and eosinophilic bronchitis

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Airway eosinophilia and cough may be associated with asthma and with non-asthmatic eosinophilic bronchitis. Whether cough variant asthma and eosinophilic bronchitis are distinct entities or a pathophysiological spectrum needs further examination.

Eosinophilic bronchitis is commonly but not uniformly present in patients with asthma. Asthma and the relatively recently described entity of non-asthmatic eosinophilic bronchitis (EB) are associated with a similar degree of submucosal eosinophilia, as well as thickening of the basement membrane and lamina reticularis. EB can be distinguished from asthma by the absence of reversible airflow obstruction, bronchial hyperresponsiveness to methacholine, and airway smooth muscle infiltration by mast cells. In the subgroup of asthmatics in whom cough is the predominant symptom, spirometric tests may also be normal but bronchial hyperresponsiveness can be demonstrated. Whether EB represents a distinct clinical condition or is a precursor of asthma remains unknown at this time.

COUGH ASSOCIATED WITH ASThma

A number of prospective studies have shown that asthma is one of the most common aetiologies of chronic cough (24–29%) in adult non-smokers. In a subgroup of asthmatics, cough may be the predominant or sole symptom. This condition is referred to as cough variant asthma (CVA).

The diagnosis of CVA often presents a challenge since physical examination and spirometric tests may be entirely normal. Up to 50% of patients with CVA have associated EB, with the degree of eosinophilia being similar to that of other asthmatics. Demonstration of bronchial hyperresponsiveness by methacholine inhalation challenge supports the presence of CVA, but the diagnosis is confirmed only upon resolution of the cough with specific anti-asthma treatment. Although cough due to EB typically responds to inhaled steroid therapy, bronchial hyperresponsiveness is absent.

In general, the therapeutic approach to CVA is similar to that of typical asthma. Symptomatic improvement is often noted after 1 week of inhaled bronchodilator treatment, but complete resolution of cough may require the addition of inhaled corticosteroids for up to 8 weeks. Some patients may suffer a paradoxical exacerbation of cough with the use of inhaled steroids, probably due to a constituent of the aerosol. The more common occurrence of cough with beclometasone dipropionate than with triamcinolone acetonide, for example, is thought to be due to a component of the dispersant in the former. The possibility of inhaled steroid induced cough, as well as improper use of the inhaler device, should be excluded before escalation of treatment.

For cough that is severe or only partially responsive to inhaled steroids, a diagnostic therapeutic trial of oral corticosteroids (prednisone 40 mg or equivalent daily for 1 week) alone or followed by inhaled treatment has been successful. Anecdotal reports initially suggested that the leukotriene receptor antagonists (LTRAs) may be particularly effective in treating asthmatic cough. Subsequently, a prospective, randomised, double blind, placebo controlled trial has shown that the LTRA zafirlukast improves cough and suppresses cough reflex sensitivity to inhaled capsaicin in patients with CVA, including a subgroup whose cough had been refractory to inhaled steroids. The ability of zafirlukast to inhibit cough that had been resistant to bronchodilators and inhaled steroids suggests that LTRAs may more effectively modulate the inflammatory milieu of the afferent cough receptors residing within the airway epithelium in patients with CVA. The mechanisms by which this antitussive effect occurs remain to be elucidated.

Clearly, the LTRAs have earned a place in our therapeutic armamentarium against CVA. Whether these new agents should replace or merely complement inhaled steroids is unclear at this time. At issue is the dearth of information regarding the long term effects of LTRAs against chronic asthmatic inflammation and resultant remodelling of the airway wall. Thickening of the subepithelial layer has been demonstrated in CVA, albeit to a lesser extent than in typical asthma. Chronic anti-inflammatory therapy would therefore seem to be indicated for patients with CVA, but whether monotherapy with LTRAs is sufficient to prevent progression of airway wall remodelling in this setting is unknown. Prospective clinical trials are required to define the role of LTRAs in the chronic treatment of CVA. A stepwise approach to the treatment of CVA is shown in box 1.

Recent data suggest that patients with CVA comprise a very distinct subgroup, rather than simply being asthmatics who cough. For example, subjects with CVA have heightened cough reflex sensitivity to inhaled capsaicin whereas typical asthmatics do not differ from healthy volunteers in terms of experimentally induced cough. Interestingly, despite having increased cough sensitivity, patients with CVA have a lesser degree of bronchial hyperresponsiveness to methacholine than those with the...
CONCLUSION

Airway eosinophilia and cough may be associated with asthma as well as with non-asthmatic EB. EB differs from asthma in that demonstrable bronchial hyperresponsiveness is absent. Although inhaled corticosteroids are beneficial in both conditions, a subgroup of patients with CVA will require more aggressive treatment with systemic steroids. Recent evidence supports the efficacy of LTRAs in the treatment of CVA, but the question of whether these agents alone are sufficient to prevent the complications of chronic asthmatic inflammation remains unanswered. Whether CVA and EB are distinct entities or conditions representing a pathophysiological spectrum awaits further elucidation.

REFERENCES

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