LETTERS TO THE EDITOR

Predictors of therapy resistant asthma

We read with interest the report by Heaney et al that the use of a systematic protocol for therapy resistant asthma resulted in control of asthma in 53% of patients who were previously poorly controlled. However, we suspect that a significant proportion of the remaining 47% of patients who were classified as having therapy resistant asthma actually had underlying gastro-oesophageal reflux disease which was either not adequately investigated (by 24 hour pH monitoring alone) or, once diagnosed, was not adequately treated (with standard dose proton pump inhibitor).

A large northern European study of 2661 subjects found that people with gastro-oesophageal reflux had a significantly higher rate of physician diagnosed current asthma and that those with reflux and asthma had more nocturnal cough, morning phlegm, sleep related symptoms, and more peak flow variability than those with asthma alone. Pathological gastro-oesophageal reflux, which is often clinically silent, has been found on pH monitoring in 53–65% of asthmatics and has been shown in various studies to cause increased capsaicin cough sensitivity, increased airway hyperresponsiveness, increased respiratory resistance, and increased respiratory symptoms. Certainly, in the case of chronic cough, gastro-oesophageal reflux should be sought as one of the most frequent underlying causes.

Heaney et al state that 17 patients with positive oesophageal pH monitoring were classified as having therapy resistant asthma because their respiratory symptoms did not improve with standard dose proton pump inhibitors. However, proton pump inhibitors have only a minor effect on the reflux of gastric contents; they alter the pH of the refluxate. This mode of action is effective in diseases such as oesophagitis where acid plays a vital role in pathogenesis. However, in airways disease non-acid reflux may be a major problem. It therefore seems surprising that other anti-reflux treatments such as alginates were not tried in this group of patients with asthma.

Therapy resistant asthma may actually have had undiagnosed gastro-oesophageal disease. In addition, more intensive management of subjects with positive oesophageal function tests would have resulted in improved respiratory symptom control, which was an important factor in defining therapy resistant asthma in this paper.

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References


Authors’ reply

In response to the letter from Professor Morice and colleagues, we welcome the growing interest in the role of the oesophageal-lung axis as evidenced by recent publications by both them and us in this journal. We agree with many of their comments regarding the frequent coinciding of gastro-oesophageal reflux and asthma, but we would suggest that this is not necessarily imply a causal association.

Four issues of substance arise from their letter concerning our paper:

- Were our subjects adequately investigated?
- What is the role of oesophageal dysmotility?
- Were they adequately treated?
- Was our definition of therapy resistant asthma appropriate?

Regarding oesophageal investigation, we would maintain that ambulatory pH monitoring remains the single best test with regard to sensitivity and specificity in the diagnosis of gastro-oesophageal reflux. We therefore believe it highly unlikely that we failed to diagnose reflux in such a large percentage of patients resistant to therapy (12 of 29 (41%) had pH profiles within normal limits). In addition, our pH probes are placed manometrically and all our subjects undergo a limited manometric study (limited in that, after assessment of the lower oesophageal sphincter, if five water bolus swallows were not made we did not record the full 10 swallows). In only one subject was an abnormality detected (that patient was in the therapeutic responsive group and the diagnosis was previously unsuspected achalasia).

We do not believe this supports a prominent role for undiagnosed oesophageal motility disorders in the therapy resistant group.

The authors suggest that inadequate acid suppression may relate to resistance to treatment. We did not repeat oesophageal pH monitoring when patients were treated with standard dose proton pump inhibitors.
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References


