Neither anti-inflammatory nor antibiotic treatment significantly shortens duration of cough in acute bronchitis compared with placebo

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Context

Respiratory tract infections exert a significant burden on society through resultant school and employment absences and demand on primary care services. Most episodes are caused by respiratory viruses such as rhinovirus. Not only are there no effective antiviral drugs available to treat such infections, but our ability to manage their symptoms, especially cough, remains poor. Antibiotics are widely prescribed for acute bronchitis in primary care settings, even though their use demonstrates negligible effects on illness duration and correlates poorly with the presence of bacterial infection.1 2 Ineffective antibiotic use results in unnecessary cost and exposure for patients, and leads to greater bacterial resistance to antibiotics. Llor and colleagues hypothesise that airway inflammation in acute bronchitis may respond to non-steroidal anti-inflammatory drugs (NSAIDs). Although one study found no evidence that they reduce the duration of cough in the common cold,3 NSAIDs are often used for symptomatic benefits. A robust study to assess their effect on cough symptoms has not previously been reported. This study took the novel step of comparing the effect of NSAIDs against the broad-spectrum antibiotic co-amoxiclav and placebo.

Method

This was a single-blind, placebo-controlled, parallel group study conducted in nine primary care centres in Spain. The study assessed acute bronchitis, defined as a respiratory infection of less than 1 week in duration with cough, discoloured sputum and at least one other lower respiratory tract symptom, such as breathlessness, wheezing and chest pain and/or discomfort. Patients were aged 18–70 years. The key exclusion criteria included the presence of radiologically confirmed pneumonia; ‘severe illness’, according to the predefined clinical criteria; and a significant comorbidity (including asthma, chronic obstructive pulmonary disease and immunosuppression). Patients were randomised to thrice-daily treatment groups of either amoxicillin-clavulanic acid 500/125 mg, ibuprofen 600 mg or placebo for 10 days. Patients were blind to the intervention. The primary outcome was the number of days following randomisation that cough was still recorded by the patient on a daily diary card. The power calculation determined a clinically significant change in the cough duration as a difference of 2 days from placebo.

Findings

A total of 416 patients were randomised into the three treatment arms. Fifty-six per cent were women, while the mean age was 45.1 years (with SD of 14.3). The overall mean duration of cough was 10 days (95% CI 9 to 11). The mean duration for the ibuprofen group was 9 days (95% CI 8 to 10), versus 11 days for co-amoxiclav (95% CI 10 to 12) and 11 for placebo (95% CI 8 to 14). A logrank test result was 0.25.

The overall absence of clear benefit was similar across adjusted models and various secondary outcomes, including overall symptom duration and a measure of ‘clinical success’. Adverse events were significantly more common in the antibiotic group (12%) compared with the ibuprofen arm (5%) and patients receiving placebo (3%; p=0.008).

Commentary

This study adds to the weight of evidence against using antibiotics for self-limiting acute bronchitis and also provides evidence that the use of NSAIDs will not reduce the duration of cough in this condition.

The most important limitation is the exclusion of patients with comorbidities, those aged over 70 and those in residential care—groups presenting commonly and in whom, perhaps, any benefit might be greatest. The usefulness of the complete absence of cough as the primary endpoint is questionable. The duration of symptoms is likely important to patients but a reduction in symptom intensity might also allow an earlier return to usual activity. Assessing symptoms is challenging, with overall burden representing a complex composite of severity and duration. Perhaps, also, the treatment was started too late; there was a 4-day average delay between the symptom onset and the start of therapy. Moreover, the authors note that NSAIDs may be prescribed to reduce other symptoms such as chest discomfort—the decision not to collect data examining this perhaps represents a missed opportunity.

The study was single-blind, therefore the investigators were aware of the treatment allocation. This reflected the expense of manufacturing identical preparations in investigator-led studies and does not appear to have led to bias, given the similar outcomes between treatment arms.

In conclusion, it is clear that antibiotics and NSAIDs should not be used routinely to treat cough in acute bronchitis in patients under the age of 70 without comorbidity. That is not to downplay the importance of such circumstances; there remains a real and urgent need to develop effective therapies to reduce the burden of acute bronchitis and other viral infections of the respiratory tract.

Competing interests None.

References