

Should we be using mucolytic agents in the treatment of COPD?

IC Gleadhill

Consultant Chest Physician, Ulster Hospital, Belfast, Northern Ireland

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AUTHORS Poole P

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Correspondence to IC Gleadhill,
Respiratory Medicine Department,
Ulster Hospital, Dundonald, Belfast
BT16 1RH

tel. +44 (0)28 90 564 763

fax. +44 (0)28 90 561 394

e-mail iain.gleadhill@ucht.nhs.uk

SUMMARY

In this review, the author revisits a 'classic' study from the 1960s on the effect of a mucolytic agent, methylcysteine hydrochloride, in CB, and provides an update of the relevant literature. In 1963, Mann *et al.* studied 22 men with a history of bronchitis. The study outcomes included sputum volume, sputum culture, cough, lung function tests and bronchoscopy. Eight patients improved in the treatment arm, and four in the placebo arm (statistics not provided). The authors were encouraged enough by the results to suggest that methylcysteine might be helpful in reducing symptoms, and/or relapse rates (exacerbations). Other mucolytic agents which have since been studied include NAC, carbocysteine, ambroxol, sobrerol, cithiolone and iodinated glycerol.

Dr Poole also discusses the conclusions of the Cochrane Review, a meta-analysis of 26 trials;¹ there was a small but significant reduction in the number of COPD exacerbations per subject compared to placebo, such that the number needed to treat (for three to six months) to avoid one exacerbation was six; antibiotic usage was reduced; the number of days of disability fell; lung function was not affected. However, a large study (duration three years, n=523) published in 2005, the BRONCUS, showed no overall reduction in exacerbation rate, except in a sub-group of patients not on ICS.² The study found that NAC was safe and well tolerated, and even allowing for the small level of benefit shown, was cost effective.

OPINION

Mucolytics have resurfaced in the past few years as potential agents in our armamentarium. For many years they were blacklisted in the NHS (whereas they were widely used in some European countries). After the Cochrane review, the blacklist status was lifted in 2001, and the 2004 NICE Guideline for COPD states that '[m]ucolytic drug therapy should be considered in patients with cough productive of sputum' (grade B recommendation).³ Mucolytic agents are thought to render sputum less viscous by breaking down disulphide bridges. An additional aspect is that some agents such as NAC appear to act as both a mucolytic and an anti-oxidant.

The 2006 Cochrane Review indicates that mucolytics are beneficial for some COPD patients and reduce exacerbation rates. The findings of the BRONCUS study (not confirmed in other studies) suggest that exacerbation rates are reduced only in the subgroup, and not on ICS, are a bit confusing for the clinician – it is the more severe patient with repeated exacerbations (and who should already be on ICS) who particularly needs a reduction in exacerbations. Mucolytics do not appear to improve lung function. One would like to have more convincing evidence that they improve the target symptoms (cough and sputum) and quality of life. Although safe, well tolerated and reasonably inexpensive, they do require to be taken three or four times a day which is inconvenient for patients. Which mucolytics are

available on the NHS? The British National Formulary 2006 lists only carbocysteine (e.g. Mucodyne) and methylcysteine hydrochloride (e.g. Visclair).

The clinical message is that it would seem reasonable to document in patients with COPD any 'sputum difficulties', including sputum volume, colour and

stickiness (despite full treatment for their COPD). For appropriate patients, a mucolytic should then be prescribed, in conjunction with adequate hydration and chest physiotherapy where required. Ideally after a month, the 'response' should be reassessed, and in those with a subjective/objective improvement, treatment should be continued, at least for the winter months.

REFERENCES

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