Steroids in exacerbations of asthma: tablets or inhalers?

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How should we treat exacerbations of asthma in general practice? The innovative study reported by Levy and co-workers on pp 1087-92 of this issue of *Thorax* raises some interesting questions.¹ In a double blind, double dummy, randomised parallel group study of patients with mild to moderate exacerbations of asthma in general practice they could find no difference between the effects of a reducing course of prednisolone and 2 mg daily of inhaled fluticasone propionate. The study was well conducted, with measurements of both lung function and symptoms. No patients experienced more than minor adverse effects with either medication. The authors suggest that inhaled fluticasone propionate may be considered as first line treatment for mild exacerbations of asthma in general practice.

Does this study mean we should change our practice? What of any methodological problems? Firstly, the authors acknowledge that their choice of prednisolone dosing (40 mg, tapering by 5 mg every other day) could be sub-optimal. In a double blind study Webb² found a two week non-tapering course of 0.6 mg/kg prednisolone (equivalent to 42 mg daily for a 70 kg patient) to be more effective than lower doses. Rowe *et al*, in a meta-analysis of studies of steroid treatment in asthma exacerbations, found greater benefit with higher doses of prednisolone.³ New treatments are best compared with a "gold standard"; whilst it is difficult to define this for oral prednisolone in exacerbations of asthma, a larger dose without tapering⁴ would have been more appropriate for comparison.

Secondly, the authors found it difficult to recruit patients to the study and ended with only 57% power to detect a difference between treatments. As Altman and Bland⁵ point out, absence of evidence is not evidence of absence. Lack of power here means danger of a type 2 error – we may be missing a difference between the two treatments. This is important since there was a trend towards greater improvement in the group treated with oral steroid.

What of the safety aspects? An underlying assumption by the authors of this paper is that 2 mg of fluticasone propionate by inhalation is superior, in terms of potential adverse effects, to a tapering regime of oral prednisolone. While this is almost certainly true, 2 mg of fluticasone propionate represents a substantial dose of a very potent topical steroid. Whilst gastrointestinal absorption of fluticasone propionate is minimal, pulmonary absorption is significant, producing effects on the hypothalamo-pituitary-adrenal axis which, on a microgram equivalent basis, are greater than or equal to those of other inhaled steroids.⁶⁻¹⁰

Avoiding the use of oral steroids where possible is attractive to doctors and patients alike. The superior safety record of inhaled corticosteroids over chronic oral steroid treatment is well established.¹¹ Whether occasional use of rescue oral steroids in patients maintained on inhaled steroids has any clinically significant adverse effects is less clear. Patients recruited to this study had mild to moderately severe asthma (three quarters were on less than 1 mg daily of inhaled steroid and had experienced between zero and two exacerbations in the last year). The study addressed relatively mild exacerbations (all but 11 of over 400 patients at entry to the study had peak expiratory flow rates after bronchodilator of >60% of best or expected).

It seems unlikely that such infrequent short courses of either oral steroids or high dose fluticasone propionate in these patients would provoke long term harm. Gathering data on adrenal function in a general practice based study such as this would have been difficult, but the results would have been of considerable interest.

What of cost implications? A two week course of fluticasone propionate treatment in this context costs about 70 times that of a course of oral prednisolone.¹² In the management of chronic stable asthma there seems little to choose between the efficacy of fluticasone propionate compared with beclomethasone dipropionate and budesonide,⁶⁻⁹ while relative safety aspects are still being debated.¹³ Switching patients established on inhaled beclomethasone dipropionate or budesonide to fluticasone propionate to manage an exacerbation could easily lead to them remaining on the more expensive but no more effective preparation afterwards. With an average general practitioner seeing over 30 exacerbations a year, this has important cost implications for the NHS overall and for general practitioners striving to keep within their prescribing budget limits.

What do we know about exacerbations of asthma in general practice? Firstly, they are common and not always optimally treated by general practitioners¹⁴ (but we may be getting better¹⁵). Secondly, patients often reach hospital without starting oral steroids or increasing their prophylaxis,¹⁶ although many refer themselves rather than seeking out their general practitioner.¹⁷ Thirdly, many general practitioners are poorly equipped to deal with exacerbations, carrying neither peak expiratory flow meters nor spacers/nebulisers.¹⁸ Fourthly, and perhaps most importantly, early use of rescue oral steroids (oral is as effective as intravenous)¹⁹ reduces the chances of admission to hospital. In a high quality meta-analysis Rowe *et al* found that given, for instance, a baseline risk of admission to hospital of one out of every five patients with exacerbations seen in casualty departments or primary care, we need to treat only about 11 patients with rescue oral steroids to prevent one admission.³ With admission rates for asthma running at double the national average in some areas,¹⁹ there is clearly room for improvement in the primary care management of exacerbations of asthma.

Finally, what else does this study suggest we need to know? As the authors point out, we should explore the potential benefits of high dose inhaled steroids in patients with more severe exacerbations. Other groups with exacerbations worth studying are adolescents and children (particularly those at puberty who may be more susceptible to the effects of regular oral steroids²⁰) and adults with more severe chronic asthma. Benefits in the last group are likely to be limited since they will tend already to be on near maximal inhaled therapy, limiting the room for an increase in dosage. We should also compare the efficacy of other inhaled steroids with that of a more appropriate dose of oral steroid in managing asthma exacerbations.

In conclusion, this study provides a promising start but further studies are needed before changing the recommendations for managing moderate exacerbations of asthma in general practice.

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