Drugs 2001; 61 (1): 79-80
0012-6667/01/0001-0079/$27.50/0

Budesonide/Formoterol Combination

A Viewpoint by Brian J. Lipworth

Asthma and Allergy Research Group,
Department of Clinical Pharmacology,
Ninewells Hospital and Medical School,
University of Dundee, Dundee, Scotland

The rationale behind using the inhaled budesonide/formoterol combination is that the addition of formoterol has a 'steroid sparing' effect on inhaled budesonide. However, the FACET study also showed that a significantly greater improvement in severe asthma exacerbation rates was achieved by optimising the dose of budesonide as monotherapy (800 μg/day) compared with adding formoterol to budesonide 200 μg/day. Although the addition of formoterol reduces exacerbation rates, there are no long term (i.e. >1 year) airway biopsy studies to indicate whether the use of a lower dose of budesonide in conjunction with formoterol is associated with increased airway remodelling. Indeed, the mechanism by which formoterol reduces exacerbation rates is not known, i.e. whether this may be due to putative anti-inflammatory activity or merely stabilising the airway as a result of prolonged bronchodilator activity. Another possibility is that formoterol increases peripheral deposition of budesonide, so enhancing its anti-inflammatory activity. By the same token, increased lung bioavailability could produce increased systemic adverse effects.

The budesonide/formoterol combination has the advantage of facilitating compliance with inhaled steroids as patients perceive the rapid bronchodilator effect of formoterol, which they seem to like. The budesonide/formoterol combination has limited flexibility in terms of being able to double the dose of inhaled corticosteroid for a given strength. Consequently, the maximal dose of budesonide in the combination is 640 μg/day, which may not be enough in patients with more severe asthma. Bronchodilator tolerance was shown in the FACET study where there was an approximate 50% fall in peak flow rate during the first 2 weeks of treatment, but thereafter peak flow remained at a constant residual level. Treatment with regular formoterol and inhaled budesonide is associated with a marked loss of its bronchoprotective activity which may be relevant for patients who are exposed to daily bronchoconstrictor stimuli such as exercise, cold air or allergen.

Thus, although budesonide/formoterol combination is convenient for patients and may enhance compliance with inhaled corticosteroid therapy, it limits the flexibility of inhaled corticosteroid dosing and commits the patient to taking regular long-acting β2-agonist therapy, which they may not need all year round. For most patients with mild to moderate asthma, it is probably more logical to first optimise the dose of inhaled budesonide up to 640 μg/day before considering the addition of formoterol, with the latter used on an 'as needed' basis. For patients with more severe disease, who despite optimised budesonide therapy also require regular formoterol, then switching to the combination product would be a logical next step. In severe asthmatics it would be valuable to have a higher strength budesonide/formoterol combination (i.e. 320/9 μg), which is not currently available.