Single maintenance and reliever therapy

The paper by Chapman et al reviewing single maintenance and reliever therapy (SMART) in asthma is important in highlighting some of the inadequacies of existing research evaluating this treatment method.

The authors also claim that SMART fails to achieve adequate asthma control as measured by GINA criteria and provide a table detailing seven studies and associated control indices.

While these outcomes are far from ideal, the authors fail to point out that they were no worse than the comparator arm, which varied across the studies from conventional inhaled steroid therapy to fixed dose combination inhaled steroid/long-acting beta-agonist inhalers in high dose (ie, ‘optimal therapy’). This inadequate control therefore reflects the severity of disease in the trial subject group rather than being a specific deficiency of SMART therapy.

It is disingenuous to claim that SMART fails to achieve adequate asthma control without pointing out that in this patient group standard, ‘optimal’, therapy does no better.

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Authors’ response

We thank our colleagues who have forwarded questions and comments to the editors of Thorax, thereby engaging in a discussion of asthma strategy we believe to be long overdue. We must leave the editors of Thorax to respond to comments directed to their principles and policies, but suspect that our review was regarded by the editors and reviewers as a summary of single maintenance and reliever therapy (SMART) outcomes from a traditional yet unexplored perspective that might spark discussion in an important area. In doing so, we believe that the journal has behaved responsibly by encouraging scientific debate. The tenets of single maintenance and reliever therapy of asthma have achieved a marked departure from contemporary asthma management perspectives. These include the following: (1) that a reactive and bronchodilator-driven strategy of asthma care is superior to the prevention of asthma symptoms and disability as long as a small aliquot of inhaled corticosteroid is inhaled at times of acute wheezing and breathlessness; (2) that comprehensive asthma control is no longer needed to evaluate asthma treatment and it is sufficient to measure the time between severe exacerbations; and (3) that rising sputum and biopsy markers of inflammation are of no concern in the choice of maintenance strategies. Until the present correspondence, the absence of discussion and debate concerning these proposals has puzzled us.

Dr Peters and Professor Jenkins have entitled their letter ‘Critical appraisal of Symbicort maintenance and reliever therapy’ to engage in a broad discussion of asthma management principles and not a review of a specific pharmacotherapy; that will be the intended meaning of the acronym in this letter. Peters and Jenkins state that we have implied that fixed dose treatments ‘achieved target levels of control’ in reference to the review of control outcomes by Bateman and colleagues. We can find no mention of fixed dose treatment outcomes in this paragraph of our publication. Elsewhere in the review we have noted that the primary outcome for inhaled corticosteroids/long-acting beta-agonists (ICS/LABA) given in SMART fashion was superior to lower doses of ICS/LABA given in fixed dose fashion and also superior to fixed dose ICS monotherapy.

We thank Drs Peters, Yan, Reddel and Professor Jenkins1 4 5 for highlighting the second relevant Cochrane review.6 A thorough reading will reveal that, in the studies examined by Cates and Lasserson, the dosage of maintenance ICS was reduced during the run-in so that, under these conditions, exacerbations requiring oral steroids (but not hospitalisations) occurred less frequently when patients inhaled ICS/LABA rather than short-acting bronchodilator alone. This finding is consistent with our hypothesis that SMART may allow patients to self-treat exacerbations at home without seeking medical care, and begs the question whether it is better to prevent symptoms and exacerbations entirely by adequate amounts of maintenance anti-inflammatory therapy or to rescue patients once symptoms have occurred.

All correspondents appear concerned that, in the table, we displayed only the SMART trials, but also attempted to discuss the much less frequently mentioned (and often concealed) effect of SMART therapy on asthma control. We have been chastised for highlighting this outcome and commenting on the dearth of discussion around control, but must note that Bateman and colleagues’ manuscript estimating control (on a week-by-week rather than a long-term basis) has only recently been published and was available to add to our review only at the galley proof stage of manuscript production.6 We did not wish to criticise the use of exacerbations as an end point in asthma trials but wished to point out that, by limiting the choice of primary end point to ‘time to severe exacerbation’ in all but one SMART trial (which used peak flow),7 the body of research has concealed the generally poor asthma control outcomes seen with this strategy. Although we referenced in our review the paper by Kuna and colleagues using double-dummy methodology,8 we suspect we are not alone in believing that blinding remains difficult and sometimes impossible when inquisitive and observant asthma patients are given
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