Eur Respir J 2001; 18: 246
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European Respiratory Journal
ISSN 0903-1936

CORRESPONDENCE

Systemic bioavailability of inhaled corticosteroids: appropriate and comparable methodology

To the Editor:

We wish to respond to a recent discussion of systemic bioavailability of inhaled corticosteroids that appeared as a letter to the editor [1]. The authors contend that an estimate of the true systemic bioavailability of inhaled mometasone furoate (MF) cannot be made based on incomplete data and an insensitive assay, and that comparisons with other inhaled steroids certainly cannot be made. The authors then proceed to make those very comparisons *versus* fluticasone propionate (FP) using a number of assumptions, extrapolations, and data normalization, even going so far as to publish a graph showing comparative hypothetical data. This is surprising, considering that the authors have published recent studies or reviews which stress that it is inappropriate to extrapolate from one patient population to another [2, 3]. Comparative claims require comparative studies in the same population under the same conditions.

A careful review of the MACKIE *et al.* [4] indicates that the radioimmunoassay (RIA) method for fluticasone also has a lower limit of detection of 50 $pg \cdot mL^{-1}$ ("The RIA for FP was validated over the range 0.05–0.25 $\mu g \cdot L^{-1}$; interbatch precision varied 13.2–12.7% coefficient of variation (CV) over the assay range and a lower limit of detection was 0.05 $\mu g \cdot L^{-1}$") and not 25 $pg \cdot mL^{-1}$ as quoted by DERENDORF *et al.* [3]. Thus based upon the criteria set forth by them, the assay method for FP is also insensitive. Therefore, the estimated bioavailability of FP using an incorrect lower limit of detection (25 $pg \cdot mL^{-1}$) invalidates the bioavailability estimate.

With respect to comparative pharmacodynamics, the authors reference two studies. In the head-to-head comparison of FP-metered dose inhaler (MDI) 880 μg twice daily *versus* MF-MDI 800 μg twice daily for four weeks in patients with mild/moderate asthma, the authors note that the hypothalamo-pituitary-adrenocortical (HPA)-axis effects of the two comparators were not reported (in the abstract) to be different. In fact, the weekly values of 43–56% cortisol suppression *versus* placebo for FP were significantly greater than the 20–30% values for MF. Moreover, MF at the highest labelled dose (400 μg *b.i.d*) had no HPA-axis suppression relative to placebo [5]. The second referenced claim of HPA-axis suppression was a comparison of intranasal FP *versus* MF at 12 times the recommended dose [6]. The study authors concluded that only minor reductions were observed that were not thought to be clinically significant. This result is consistent with previous reports showing no HPA-axis effects of nasal MF at 20 times the recommended dose [7].

Finally, the claim that mometasone furoate has a number of active metabolites is not supported by the pharmacokinetic and pharmacodynamic clinical data. In summary, we stand by the conclusions of our study.

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