



Correspondence

Adrenal suppression with fluticasone furoate

To the Editor: I read with interest the recent dose ranging evaluation with inhaled fluticasone furoate (FF) in patients with persistent asthma.¹ No significant differences were seen in geometric mean fold mean values for uncorrected 24-hour urinary cortisol comparing FF with placebo, with the 95% confidence interval for the differences including unity in eFig 3. This gives an erroneous impression that FF does not produce systemic adverse effects. The proportion of values for 24-hour urinary cortisol, which shifted from normal at baseline (while taking inhaled corticosteroids) to abnormal after 8 weeks, was 3% for placebo as compared with 7% for FF 300 μg and 1% for FF 400 μg . Pointedly, no mention was made as to what value was used for the lower limit of normal, which is usually <40 nmol/24 hours.² Inspection of eFig 4 reveals an estimated count of $n = 14/75$ (19%), who ended up after 8 weeks on FF 300 μg with abnormal values and $n = 13/72$ (18%) on FF 400 μg . The number of abnormal values is clinically relevant because there is a known individual susceptibility to dose-related adrenal suppression.^{3,4}

The presence of a low urinary cortisol value is a strong predictor of a blunted dynamic cortisol response to low-dose adrenocorticotrophic hormone stimulation, indicating impaired adrenal reserve. In this regard, it is more conventional to also report the urinary cortisol corrected for creatinine excretion to obviate potential problems with incomplete collections, which is more likely with a 24-hour than an overnight sample, is more conventional. Finally, the systemic absorption of FF from the lungs (which avoids first-pass inactivation) will be dependent on airway caliber such that patients with a lower percent predicted forced expiratory volume in

1 second (FEV_1) would be expected to have lower systemic exposure and exhibit less cortisol suppression.⁵ Hence, it is worth noting that the mean baseline value for FEV_1 second was 66%, such that the observed degree of cortisol suppression with FF at a given dose would, for example, be relatively greater in patients with a FEV_1 of 86%.

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References

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