

THE JOURNAL OF Allergy AND Clinical Immunology

February 1999, part 1 • Volume 103 • Number 2

Safety of intranasal steroids

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To the Editor:

The recent article by Wilson et al (J Allergy Clin Immunol 1998;101:470-4) rather startled me, and I was concerned that the hitherto good safety record of intranasal steroids might have come into question. The authors fail to take into account, or discuss, the large body of contrary evidence that exists in the literature.

The "headline" finding that intranasal steroids reduce urinary cortisol levels by between 21% and 43% is misleading because this is an inappropriate method with which to assess this sort of effect. In fact the authors' own findings with creatinine-corrected cortisol levels and low-dose adrenocorticotrophic hormone challenge rather confirm the safety of intranasal steroids. It is curious that an apparently more sensitive method of assessment (creatinine-corrected data) has in fact shown no statistical differences, whereas the uncorrected and more variable data did achieve significance.

The authors cite 2 published references to add weight to their contention. The article by Knutsson et al ¹ was flawed in its design in that it did not include a placebo group. The changes that were observed are consistent not with a systemic effect of nasal steroids but

with changes over time. The study by Foresi et al² also does not provide support for a systemic effect of steroids as speculated. The effects attributed to fluticasone propionate (FP) are consistent with an effect of a topical steroid, having a *topical* anti-inflammatory effect and subsequently diminishing the signal to the bone marrow,³ which *indirectly* diminishes the level of circulating eosinophils.

The topic of systemic effects of inhaled steroids has been the subject of study in the past by the authors and their colleagues. By using their data on FP and that of others, it is possible to calculate the approximate plasma levels of fluticasone that would be required (as it is a sine qua non that to influence plasma cortisol levels an appropriate concentration of an exogenous steroid must be present in the plasma) to cause a fall of approximately 50% in plasma cortisol levels. The approximate 24-hour area under the curve of FP to achieve a mean fall of 50% in plasma cortisol levels is 3200 pg·h/mL. The highest blood level that has been reported after intranasal dosing is 68 pg·h/mL.⁴ The level after 500 µg FP twice daily in the lung is approximately 1000 pg·h/mL, and this is approximately the level in volunteers at which one sees the threshold of a change in plasma cortisol levels.

It appears that even to detect the threshold of change in plasma cortisol levels after intranasal dosing, approximately 50 times the therapeutic dose of FP would have to be given as a single dose. To achieve the approximately 50% reduction in cortisol levels reported by the authors, the whole contents of 12 bottles would have to be administered as a single dose!

I am concerned that other readers of this journal might, like me, take this data at its face value initially, and I would urge caution and care in the interpretation of it. I remain convinced of the safety of the intranasal corticosteroids when used at recommended dosages.

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Journal of Allergy and Clinical Immunology, The

March 2005, Supplement • Volume 115 • Number 3

Elizabeth F. Juniper, Elisabeth Ståhl, Richard L. Doty, F. Estelle R. Simons, David B. Allen, Peter H. Howarth

[ABSTRACT](#)

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Systemic effects of intranasal steroids: An endocrinologist's perspective

Journal of Allergy and Clinical Immunology, The

October 2000, part 2 • Volume 106 • Number 4

David B. Allen, MD

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