

## LETTERS

### The authors reply to: “Systemic absorption of intranasal corticosteroids may occur and can potentially affect the hypothalamic–pituitary–adrenal axis”

We thank Dr. Kline and colleagues for their insightful comments regarding the potential risk of hypothalamic–pituitary–adrenal (HPA) axis suppression in certain scenarios with nasal corticosteroids.<sup>1</sup> We agree that physicians should be aware of possible medication interactions, in particular with cytochrome P-450 3A4 (CYP3A4) inhibitors. At the same time, physicians should not shy away from prescribing these medications for most patients with symptomatic nasal complaints because their safety profile is well established.

We would like to comment on the systematic review citing a 4% incidence of biochemical adrenal insufficiency with nasal steroid use.<sup>2</sup> Broersen and colleagues reference 8 articles regarding this, but on detailed review of this study, we could identify only 5 with intranasal delivery of corticosteroid, the most recent being from 2004. This also included 2 articles that used corticosteroid drops rather than spray, which is well-known to deliver a higher dose of corticosteroid; this form is not available in Canada owing to the risk of HPA axis suppression.

A much more detailed review of adverse effects with intranasal corticosteroid therapy in adults was published in December

2020.<sup>3</sup> Donaldson and colleagues found 28 studies looking specifically at HPA suppression in adults. Of these, 23 reported no evidence of HPA axis suppression, and the 5 studies that did used a corticosteroid delivery method (3 used drops) that was not approved by the US Food and Drug Administration. The same group published a similar systematic review for children<sup>4</sup> in which they identified 23 studies that included information on HPA axis suppression. Of these studies, 17 showed no evidence of HPA axis suppression. Five of the 6 that did report some suppression were using intranasal corticosteroid drops.

Given the comorbidity of asthma with chronic rhinosinusitis or allergic rhinitis, it is important to bear in mind that the effect of using both inhaled and intranasal corticosteroid may be additive and heighten the risk for HPA axis suppression. Indeed, 1 of the cases cited by Kline and colleagues was on concurrent inhaled corticosteroid.<sup>5</sup> As such, we would suggest selecting a second-generation nasal corticosteroid (e.g., ciclesonide hydrofluoroalkane, mometasone furoate or fluticasone propionate) for patients taking inhaled corticosteroids, and, on occasion, to re-evaluate whether the current intranasal corticosteroid dose and treatment is still required for symptom control.

#### Leigh J. Sowerby MD

Associate professor, Otolaryngology–Head and Neck Surgery, Western University, London, Ont.

#### James Fowler MD

Resident, Otolaryngology–Head and Neck Surgery, Western University, London, Ont.

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