Combined Oral and Intranasal Corticosteroid Therapy: An Advance in the Management of Nasal Polyposis?

Chronic rhinosinusitis with nasal polyposis is a common health problem, affecting 2% to 5% of the general population. Although the condition is not life-threatening, it is costly in terms of health care expenditures, decreased quality of life, and negative effects on lower airway disease (1–3). European guidelines recommend intranasal corticosteroids as first-line treatment for chronic rhinosinusitis with nasal polyps and reserve oral steroid therapy for patients with severe or uncontrolled symptoms and endoscopic sinus surgery for patients with inadequate improvement despite oral steroid therapy (1, 4). After surgery, many patients must continue medical management to prevent relapse (5–7). Yet, these recommendations are largely based on consensus rather than on definitive evidence.

Corticosteroids exert their anti-inflammatory effect by acting on specific receptors present in all human cells, including nasal polyp tissue (8). The reason why some nasal polyp phenotypes are resistant to intranasal corticosteroids is not well understood. However, some investigators postulate that abnormal glucocorticoid receptor expression or a reduced effect of corticosteroids on nasal polyp fibroblast proliferation may explain resistance to topical therapy (8, 9). Other investigations have demonstrated that aspirin-sensitive patients with nasal polyps may develop resistance to steroid treatment (10) without downregulation of glucocorticoid receptors (11), in contrast to observations in in vitro studies (12).

Although randomized clinical trials have demonstrated that intranasal corticosteroid therapy improves nasal symptoms and polyp size before and after surgery (1, 6), data on oral steroids in the treatment of chronic rhinosinusitis with nasal polyps are more limited. In 2007, only 1 study (2) out of 17 initially identified met the inclusion criteria for a Cochrane review on oral steroid therapy for chronic rhinosinusitis with nasal polyps (7). This trial showed a significant improvement in quality of life, nasal obstruction, loss of smell, and polyp size after 2 weeks of treatment with oral steroids compared with no steroid treatment (2). The authors of the Cochrane review called for larger, longer, and more definitive trials of oral corticosteroids for chronic rhinosinusitis with nasal polyps.

Since 2007, only 3 randomized studies in 84, 43, and 33 patients who had chronic rhinosinusitis with nasal polyps, respectively (13–15), have reported a beneficial effect of combination therapy with oral and intranasal corticosteroids. Each of these studies examined different oral steroid strategies that clinicians often use in practice. Benitez and colleagues (10) used prednisone, 30 mg/d, tapered over 2 weeks; Hisaria and colleagues (14) used prednisolone, 50 mg/d, for 2 weeks without tapering; and Van Zele and colleagues (15) used methylprednisolone, 32 mg/d, tapered over 20 days. After oral steroid therapy, the first study (13) used intranasal steroids (budesonide, 400 μg twice daily for an 12 additional weeks); the second study (14) allowed any additional treatment, including intranasal corticosteroids; and the third study (15) did not allow additional treatment. All 3 studies reported an improvement in nasal symptoms and nasal polyp size. Improvement in loss of smell with oral steroid therapy was reported only in 2 studies (13, 14), although this effect did not persist when oral steroid therapy was discontinued (14). In 2 studies, the objective measure of nasal patency was found to have improved (13, 15). Quality of life improved after 2 weeks of oral steroid therapy in 1 study (14) and in an extension of Benitez and colleagues’ study after 48 weeks of treatment (2). Although imaging was used to assess disease status in all studies, only Hisaria and colleagues reported improvement in imaging score after oral steroid treatment (14).

Finally, in a long-term randomized study, Alobid and colleagues (16) reported similar effects in nasal symptoms, polyp size, and quality of life when patients who had severe chronic rhinosinusitis with nasal polyps were treated with oral prednisone for 2 weeks or underwent surgery followed by treatment with intranasal budesonide for 1 year.

Safety is a concern when managing chronic rhinosinusitis with nasal polyps with corticosteroids. Two randomized trials (14, 15) identified clinical adverse events after steroid treatment (insomnia and asthma exacerbation), but they did not assess the effect of these agents on the hypothalamic–pituitary–adrenal (HPA) axis or bone metabolism. Recent studies (albeit lacking control groups appropriately matched for age and sex) suggest that intermittent therapy with oral steroids significantly affects bone mineral density and the HPA axis. In a prospective study of patients with chronic rhinosinusitis with nasal polyps who received more than 3 short courses of oral steroids during the past year (prednisolone, 1 mg/kg of body weight for >21 days of total treatment), Bonfils and colleagues (17) demonstrated that 54.4% of patients had low bone density and 48.8% had asymptomatic adrenal insufficiency. In Rajasekaran and colleagues’ retrospective study of patients with and without nasal polyps who were receiving different oral steroids at dosages of more than 5 mg/d for at least 3 months, 38.6% had low bone density; the effect was greater in postmenopausal women (62.2%; odds ratio, 2.0, 95% confidence interval, 1.2 to 3.3).
In conclusion, this most recent trial is a welcome addition to the evidence about strategies to manage patients who have chronic rhinosinusitis with nasal polyps. Yet, clinicians must temper their enthusiasm for oral therapy with recognition of potential systemic adverse effects on the HPA axis and bone metabolism. These adverse effects are likely to be greatest among elderly patients, postmenopausal women, and those who receive repeated courses of oral therapy. Thus, we believe that oral steroid therapy should be initiated only when patients with chronic rhinosinusitis with nasal polyps have an unsatisfactory response to at least 3 months of treatment with intranasal corticosteroids. We advocate an initial daily dose of 0.5 to 1 mg/kg that is tapered after 2 weeks, followed by intranasal corticosteroid therapy.

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Potential Conflicts of Interest: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M11-0153.

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