

Novel options in the nonsurgical management of chronic rhinosinusitis

It is well recognized that surgery alone does not resolve the inflammation associated with well-established chronic rhinosinusitis and that postoperative care and ongoing medical management is critical to the success of these patients. In recent years, 1 area of significant focus has been the off-label use of high-dose, high-volume, steroid nasal irrigations postoperatively, and excellent results have been reported previously in uncontrolled trials. It is my personal impression that such therapy also is effective in the unoperated patient, and has reduced my need for surgical intervention in patients. In this issue of the *International Forum of Allergy and Rhinology (IFAR)*, Harvey et al.¹ report the first multicenter randomized double-blind placebo-controlled trial (RDBPC) of high-dose high-volume postsurgical steroid nasal irrigations. The authors utilized 2 mg of mometasone once daily both in the nasal irrigation and in the active nasal spray. The double-blind was performed by utilizing either a saline nasal spray following the active steroid irrigation, or using a saline nasal irrigation and then steroid nasal spray. A significant improvement in both groups was demonstrated following surgery and medical therapy, but the patients on the steroid nasal irrigation demonstrated a significantly greater reduction in nasal blockage, as well as on both blinded endoscopy scores and on computed tomography (CT) scan. Interestingly, however, there was no difference between the 2 groups in terms of overall SNOT-22 scores. Although the mometasone dosage is significantly higher than typically utilized in the United States, the authors feel that it is safe based upon a prior study demonstrating that only about 5% of nasal irrigation is retained in the sinuses and the systemic bioavailability of mometasone delivered intranasally is much lower than budesonide (0.1% vs 34%, respectively).² A prior study by Soudry et al.³ demonstrated asymptomatic hypothalamic-pituitary axis (HPAA) in approximately 4% of patients on budesonide nasal irrigations alone (0.5 mg once or twice daily) and since many of the patients were also on the other topical steroids the overall incidence was 23%. Accordingly, although the use of high-dose, high-volume nasal irrigations has been



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demonstrated to be effective in this well-designed RDBPC study, given the absence of U.S. Food and Drug Administration (FDA) approval for this therapy, it is still important to have additional studies evaluating for the possibility of asymptomatic HPAA suppression or raised intraocular pressure (IOP) with long-term, high-dose use of topical steroids.

Once a patient has developed significant recurrent nasal polyposis, topical steroids are unlikely to penetrate into the sinuses as well as occurred in the Harvey et al.¹ study. For this situation, Kern et al.⁴ report on a phase 3, blinded, randomized sham-controlled study of biodegradable

mometasone-eluting implants for the treatment of recurrent nasal polyposis who have undergone prior surgery. In the sham procedure, the implants were not left in place, and in the treatment group the implants were removed at 60 days so as to allow for a blinded third-party endoscopic assessment at the 90-day time period. All patients were on topical steroid sprays. At the 90-day time point, patients in the irrigation treatment arm were significantly less likely to be judged as needing revision surgery (61% reduction), and had a significantly less ethmoid obstruction. The treatment group also had symptomatic improvements in both nasal obstruction/congestion and sense of smell. It would appear that the sequential use of implants, followed by the use of high-dose, high-volume steroid nasal irrigations might, in the future, obviate the need for revision surgery in a significant number of patients. Pseudomonal biofilms can also be a significant problem in patients with severe persistent chronic sinusitis following her prior surgery. Cho et al.⁵ performed a small rabbit study evaluating the use of a ciprofloxacin-eluting sinus stent and demonstrated a significant reduction in pseudomonal biofilms and a reduction in opacification on micro-CT, fostering the potential for other novel types of biodegradable stents in the future.

Allergy desensitization principles vary significantly between Europe and the United States. In Europe, desensitization is usually performed only to a very limited number of predominant allergens, relying on the so-called “bystander effect” for improvement of other allergies in polysensitized patients receiving either subcutaneous immunotherapy (SCIT) or sublingual immunotherapy (SLIT). Proof of efficacy of this approach becomes particularly important with the advent of a limited number of different allergens in commercially available SLIT tablets and drops. Ortiz

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et al.⁶ report on a study of polysensitized patients treated with single-antigen SLIT over a period of 9 months. In this small study, there was no difference in symptom improvement between the polysensitized patients treated with single allergens and those treated with multiple allergens. This study highlights the importance of additional larger and longer-term studies comparing the 2 different types of desensitization approaches and further investigation of the bystander effect in polysensitized patients.

Are there differences between chronic rhinosinusitis (CRS) in patients who have early onset of asthma and those who have late onset of asthma? A study by Jones et al.⁷ finds that those with late-onset asthma have more frequent nasal polyposis and required increased treatment for CRS. Is it necessary to perform more than 1 sinus culture during surgery? Miller and Davis⁸ evaluate the necessity to perform more than 1 sinus culture during surgery for CRS. In this study, only 5% of the cohort received clinically relevant benefit from a second culture.

Unfortunately, it is difficult to identify 1 ideal animal model for CRS research. As a resident, my early work on mucociliary clearance at Hopkins was performed on dogs. Subsequently, we utilized rabbits and sheep have also been widely utilized because both of these animals have sinuses that are more akin to humans, but neither of these animal models have tools for genetic manipulation. Rodents have markedly different sinonasal anatomy to humans, but do

have well-developed tools for genetic manipulation, and several rodent models have been utilized. Tharakan et al.⁹ report on a novel campaign-inducible murine model of eosinophilic chronic rhinosinusitis (ECRS), which they report more closely resembles the cytokine profile and innate immune characteristics of ECRS, that they feel lays the groundwork for future mechanistic studies of this disorder.

The revised *IFAR* Interactive Case Learning Series is up and running on the *Journal* website, and I hope that you will enjoy some of these cases and videos, and participate in the blog case discussions. I also hope that you will attend the ARS Summer Sinus Symposium that this year will be held in Seattle on July 12 to 14, 2018—a great time to visit the great northwest! Finally, the American Academy of Otolaryngic Allergy (AAOA) will hold its Basic Course in Allergy & Immunology on July 5 to 7, 2018, at the Diplomat Beach Resort, Hollywood, FL, and in the fall its first independent annual meeting in the city that help found our nation—Philadelphia (and now the city of the Super Bowl Champions!). The meeting will offer a unique blend of clinical content while attendees learn about Philadelphia and its history. I look forward to seeing you at some of these meetings or here in Philadelphia.

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