

Building a Better Mousetrap—The Next Generation of Intranasal Steroid Delivery Devices

a report by
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The Treatment of Choice

The development of intranasal corticosteroids (INS) for rhinitis has been ongoing for the past three and a half decades. These medications are the treatment of choice for allergic rhinitis, and are recognized as the most effective agents for providing relief over the spectrum of nasal symptoms.

An Ongoing Improvement Process

As with other evolving classes of medicines, there have been modifications of INS over time. Goals for improvement have included decreased systemic bioavailability^{1,2} and increased glucocorticoid receptor binding affinity and selectivity^{3,4} in the newer products (e.g. fluticasone propionate, mometasone furoate, fluticasone furoate) compared with older products (beclomethasone dipropionate).

Decreased bioavailability is important, not only for minimizing the risk of corticosteroid adverse effects for allergic rhinitis patients, but also for reducing the corticosteroid load in patients with asthma who require intranasal corticosteroids for their allergic rhinitis and inhaled steroids for their lower airway disease. There is a wealth of published scientific research that has clearly demonstrated how, in patients with asthma and concomitant allergic rhinitis, there is immunological and physiological cross-talk because of the upper and lower airway inflammation.⁵ Therefore, it is critical to treat both conditions in these patients to gain optimal disease control.⁶

Taking Into Account the Concerns of Patients when Designing Intranasal Corticosteroids Devices

While efficacy and safety are of paramount importance in the development of new products and formulations, in recent years a number of studies have been published that evaluate the sensory attributes of INS products (e.g. taste, smell, and delivery volume) from a patient's perspective. For

example, in a double-blind cross-over study, 100 allergic rhinitis patients were randomized to mometasone furoate nasal spray (MFNS) or fluticasone propionate nasal spray (FPNS).⁷ At the end of each treatment period, patients rated the study drugs by completing a product sensory attributes questionnaire. Significantly fewer patients perceived scent/odor ($p<0.001$), taste ($p=0.002$), and aftertaste ($p=0.007$) immediately and/or two minutes after administration with MFNS compared with FPNS. Similarly, twice the number of patients preferred MFNS over FPNS for each of these individual assessments ($p=0.0005$ for scent/odor, $p=0.005$ for taste and aftertaste). The consensus of this and other studies^{7,8} is that sensory attributes may influence a patient's preference among INS with otherwise similar safety and efficacy profiles, and that compliance may be compromised with INS products that have unpleasant attributes, such as a noticeable aftertaste, prominent odor, or a spray delivery volume that causes excess medication to run down the back of the throat. As the evidence continues to mount, product sensory attributes will likely play an important role in physician prescribing behavior.

Room for Improvement?

In the words of poet Ralph Waldo Emerson: "Build a better mousetrap and the world will beat a path to your door." This highlights another important facet of the 'experience' of patients that has received little research attention: the design of INS delivery devices. The design of asthma inhalation delivery devices has undergone significant evolution, from earlier 'Rube Goldberg' designs to an array of sophisticated devices that are compact, portable, reliable, and easy to use. Some of the newer devices come equipped with integrated dose counters.⁹ In contrast to asthma delivery devices, evolution in the design of INS delivery devices has not run in parallel with improvements in the INS medications they contain. At a minimum, they are reliable and deliver accurate doses of medication when used properly. However, in light of the emerging importance of product sensory attributes, nasal spray device design may also influence both the preference of patients and the choice of physicians when considering available prescription INS medications with similar safety and efficacy profiles.

Two Categories of Spray Devices

INS nasal spray devices fall into two categories:

- powered aerosol sprays; and
- pump-actuated aqueous nasal spray devices.

Few studies have been performed that compare topical delivery of powered nasal sprays, pump-actuated sprays, and nasal drops. In these,



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the overall results are inconclusive in terms of which mode is superior. In addition, there is likely much inter- and intra-subject variability in administration technique. Furthermore, many studies have been carried out in normal subjects in whom the nasal distribution of study drug is different compared with symptomatic rhinitis patients.¹⁰ The bottom line is that, regardless of delivery, all INS spray products on the market have met the rigors of US Food and Drug Administration (FDA) approval and have been proved to be safe and effective in subjects with allergic rhinitis.

The Importance of a Nasal Spray Device

So why is the nasal spray device important? The same type of question may be asked as to the importance of a manual can opener—one that is comfortable, easy to operate, and does not slip—to a child or an adult suffering from arthritis.

At the time of writing, the two US market leaders for INS prescriptions are mometasone furoate monohydrate nasal spray (Nasonex®, Schering-Plough, Inc.) and fluticasone propionate aqueous nasal spray (Flonase®, GlaxoSmithKline Inc., and generic equivalent). These products come in nasal spray pump devices that are top-down actuated. In February 2007, Schering-Plough announced that the Nasonex device had received the Arthritis Foundation's ease-of-use commendation, making it the first nasal allergy spray to receive this designation. Although this endorsement was based on a survey of Nasonex users, not a well-controlled study using a comparator device from another INS product, it still underscores the need for device design with the patient in mind.

A New Model

At the annual meeting of the American Academy of Allergy, Asthma, and Immunology (AAAAI) in February 2007, there was a presentation on a new, distinctive nasal spray device for a now approved INS product, fluticasone furoate nasal spray (Veramyst™, GlaxoSmithKline, 2007).¹¹ The attention to ergonomic, aesthetic, and functional detail in the design of this novel delivery device is substantial. It was developed for use in diverse patient groups such as children as young as two years, adults, and the elderly, as well as for easier second-party administration. The unique, side-actuated design minimizes nozzle movement within the nose, eliminating the need for a care-giver's fingers to be close to the patient's nose. Once primed, the device remains ready to use, and its cap ensures it remains primed between periods of non-use (up to 30 days).

The device also incorporates a commitment feature to minimize variation in volume during actuation of the mist release button, while consistently

delivering a fine mist to assure dispersion over the nasal mucosa. The mist has been formulated to eliminate ingredients that might cause an unpleasant taste or smell while maintaining a highly effective preservative system. Furthermore, the manufacturers have designed a short nozzle to reduce the likelihood of trauma to the nasal septum. Each dose is delivered in a low volume of 50µl to minimize the amount likely to drip out the nostrils or run down the back of the throat. Another novel feature is a see-through window that enables patients to readily see the amount of remaining medication.

This new device that delivers Veramyst may be a “better mousetrap”; however, as with the Nasonex device, until well-controlled head-to-head

Nasal spray device design may influence both the preference of patients and the choice of physicians when considering intranasal corticosteroids with similar safety and efficacy profiles.

studies are carried out comparing it with other marketed nasal spray devices, no definitive claims can be made as to which is superior in terms of patient preference or ease of use.

Conclusion

It is important to consider INS device characteristics and product sensory attributes, as patients have become more informed and empowered to ask for products that are not only safe and effective, but also pleasant to use and easy to administer. Each allergic rhinitis patient is a unique individual. Considerations when prescribing INS medications should include: the approved INS indications; the efficacy and safety of an agent; the patient's age; the constellation of symptoms; medical history; past response to medications; and presence or absence of concomitant asthma. In addition, it is important that healthcare providers educate themselves on differences in product sensory attributes and delivery device design characteristics, as there is little doubt they can play an important role when choosing among the available prescription INS medications. ■

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