NASAL DRUG DELIVERY: WHAT THERAPISTS NEED TO KNOW

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I would be willing to wager that most respiratory therapists have all but forgotten about the nose, or nasal cavity, as an important part of the respiratory system. We are so generally preoccupied with the chest and lungs that it is easy to forget that the nasal cavity is that portion of the respiratory system that makes first contact with the environment. I suspect that we all dutifully recollect that the main function of the nasal cavity is to warm and humidify inspired air but how many of us can truly recall all the anatomical features, or the names and locations of all the paranasal sinuses? Chances are, the nose was rather quickly skipped over in RT school -- unless you went to school back when I did, when I learned how to pass a green 14 gauge oxygen catheter through my nares so that its tip in my hypopharynx was directly adjacent to my uvula. Presumably, if I could do that to myself, I was qualified to do it to a patient. Competency assessment, circa 1965. Inhalation Therapy school was where I first learned, painfully, that I had a deviated septum. But, I digress. The point is: for years that was about all that I really knew about the nose as far as respiratory therapy was concerned. However, as far as pathology is concerned, I, and about 32 million other people in this country, have become quite familiar with the pain and suffering of acute rhinitis and chronic sinusitis. That's more people than asthma and COPD together. Health care costs for sinusitis exceed $5 billion annually. Those afflicted with so-called chronic sinusitis typically have bouts of facial pain, inflammation and infection of the nasal mucosa, discharge, post-nasal drip, cough and other symptoms lasting, by definition, for 8 weeks and longer.

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One of the other features of the nose, which we sometimes recall when we are trying to deliver aerosol to the pulmonary regions of the respiratory system, is that it was designed to keep stuff out of the respiratory system. Keep that in mind and I'll tell you why later. A plethora of irritants and allergens, dust, dirt, pollen, and a myriad of other tiny particles normally encountered during the activities of daily living are routinely trapped in the nasal cavity in order to prevent their delivery to the lower respiratory tract. This also includes bacteria and viruses that hitch a ride into the nose on airborne droplets or some of the other aforementioned particles. Ordinarily, the mucus blanket of the nasal cavity drains to the hypopharynx to remove foreign material, including bacteria and viruses, from the nasal cavity and sinuses. However, when chronic inflammation occurs, normal nasal mucus drainage is interrupted by mucosal edema, excessive mucus secretion and obstruction of the narrow passageways of the nasal cavity. Drainage is blocked, pathogens are not removed in a timely manner, inflammation results and infection takes hold and spreads. If you have chronic sinusitis, it is easy to understand the vicious cycle that quickly develops and the excellent conditions for long-term infection that the sinuses generously provide for pathogens.

In the more serious cases, surgical treatment of chronic sinusitis is generally a last resort, although there are almost 600,000 sinus surgeries performed annually. The surgery is painful and does not always result in permanent resolution of the disease process. Medical treatment with a wide range of available medication is almost always undertaken for a long time before surgery is contemplated. One of the oldest treatments involves irrigation of the nasal cavity with saline or other solutions. This ancient practice, named Jala neti in Sanskrit, means "water cleansing" and is increasingly being recognized by Western medicine as an adjunct in the treatment of sinusitis. If you perform an internet search for the term neti pot, you'll come up with some interesting low tech devices for accomplishing this. However, more recently, a number of medical companies have introduced a variety of nasal humidification systems derived from typical respiratory therapy devices. But the exciting future in treating chronic sinusitis involves the aerosol delivery of intranasal medications.

As with pulmonary disease, topical application of medication is preferable to systemic routes for most of the same reasons. Topically delivered doses are almost always much less than systemic doses thereby reducing the potential for toxicity and side effects. Intranasal drug delivery by aerosol would therefore seem to be the preferred method of administration in order to reduce toxicity and deliver the medication right to the site of the infection in the shortest amount of time. As with pulmonary drug delivery, the idea is to create an aerosol of the correct size particles, containing a nominal dose of medication to be deposited in the appropriate regions of the nasal cavity and sinuses. As with pulmonary delivery, the art and science must converge in order to match an effective drug with an effective delivery device that can reliably and repeatedly deliver the correct dose to the correct target site. The earliest types of intranasal medications, some of which have been in use for decades, include the mucosal decongestants (neosynephrine,

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phenylephrine, oxymetazoline) which act by constricting the small capillaries in the nasal mucosa in order to reduce mucosal edema and swelling. These drugs have typically been administered with relatively "low tech" devices such as manually operated aqueous spray bottles fitted with nasal adapters. These delivery systems rely on the user to squeeze the plastic container to propel the liquid medication through a small orifice thereby producing a spray which is inhaled nasally. Generally speaking, these medications provide only temporary relief at best.

Consequently, a large variety of other drugs for intranasal delivery have been developed and used with varying degrees of success. These include intranasal versions of many of the same inhaled steroids that are used for pulmonary disease, namely flunisolide, fluticasone, beclamethasone, triamcinalone and, more recently, budesonide. Similarly, mast cell inhibitors, anticholinergics and antihistamines are all available for intranasal delivery. One of the challenges of formulating nasal medications is creating compounds that have a rapid enough onset of action that can do some good before being removed by the nasal mucociliary clearance mechanism. Many ENT physicians prescribe antibiotics for intranasal aerosol delivery, and these are generally prepared by compounding due to the absence of specific commercial formulations for this purpose. There are also a variety of delivery systems for these medications, ranging from the simple aqueous spray pump bottles to liquid and powder inhalers that have been adapted for intranasal delivery, to pneumatic nebulizers that have been fitted with nasal administration adapters. As with pulmonary aerosol delivery, the importance of the delivery system is being increasingly recognized and further studied both on the test bench in terms of technical performance, and clinically in terms of outcomes.

Although we sometimes overly trivialize intrapulmonary aerosol drug delivery, it is actually is somewhat more facile and reliable than intranasal aerosol drug delivery owing to the difficulties posed by the unique anatomy of the nasal cavity. Unlike the pulmonary system, inspired air is not "drawn into" the paranasal sinuses in the same manner as it is "drawn into" the alveoli. So that immediately limits the utility of nasal aerosol delivery. Further, the nasal anatomy complicates intranasal drug delivery. Nasally inhaled medication must traverse the anterior portion of the nasal cavity in order to reach the sinuses. In severe disease this can be a mighty challenge. And even when aerosol does traverse the anterior nasal cavity, the factors that influence or enhance deposition and distribution in the various paranasal sinuses are not yet very well understood. Ironically, even though the nose is designed to keep things out of the respiratory tract, as we mentioned earlier, one of the problems with intranasal drug delivery is that some of the drug also passes completely through the nasal cavity and is inhaled. Some companies are working on highly evolved intranasal delivery system to counteract this problem.

It would appear that intranasal aerosol delivery will be an exciting field for many years to come with the potential for many new drugs, devices and approaches for treating chronic sinusitis. It is not inconceivable that respiratory therapists might be called upon to lend their expertise to this type of therapy in the future as new technical developments unfold and as much more clinical outcome experience guide the development of effective aerosolized intranasal drug delivery.

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