Breathe Out

By
Ramy Mahmoud
at OptiNose

Despite affecting millions of people worldwide, treatments for serious nasal conditions have been limited by their inability to target the required site of action. Could new exhalation technologies hold the answer?

Keywords

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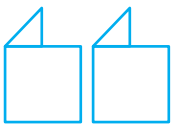
Within the broad category of respiratory technology, innovation focused on the nose, rather than the lungs, has been relatively overlooked. For many years, patients have suffered from a lack of advancement in this space, forced to rely mostly on the existing nasal spray devices that provide unsophisticated treatment delivery that works for simpler and milder applications like seasonal allergies. This often falls short for more serious nasal conditions like chronic sinus disease, or more complex situations, including efforts to deliver drugs to the brain. Though certainly not the only application, one of the most obvious values of improving nasal delivery is to enable better treatment of diseases that reside deep in the nose.

While the limitations associated with current nasal technologies are widely recognised by the patient and healthcare professional communities, solutions for nasal delivery have not been pursued by innovative biopharmaceutical companies in the way that transdermal or inspiratory methods have, resulting in a significant lag in technology development behind other forms of drug delivery. Outside of the patients that struggle with these symptoms every day, and their sympathetic loved ones, there seems to be a stark lack of appreciation for the difficulties faced by those who suffer from nasal-centred diseases.

More than Just a Runny Nose

Among those hardest hit by this oversight are sufferers of moderate to severe chronic rhinosinusitis (CRS), sometimes called chronic sinusitis – a patient population that is 28 million strong. The symptoms of this disease are not widely understood and are therefore frequently misinterpreted. Unless you are suffering from CRS, it is difficult to appreciate the severity of the condition and the impact it can have on daily life. To the outside world, it can sometimes present



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itself simply as a runny or stuffy nose – and who hasn't had a cold? You just deal with it.

But with this disease, the symptoms are more painful and serious. It goes on and on without relief, and patients often cannot breathe, sleep, smell or taste. In some domains, quality of life has been measured to be as negatively impacted as other serious conditions like heart failure, angina or epilepsy.

Good, safe and topical drugs to treat the inflammation at the root of this common condition are available, but it is imperative to get the drug high and deep into the nasal cavity, hitting the affected area – the drugs only work where you put them. Yet, as a consequence of the under-the-radar nature of CRS, there has not yet been a concerted effort to invent ways to deliver drugs further up into the narrow and intricate nasal passages. Current technology is not equipped to do this, and lacks the subtlety or art to get the drug into the crevices where the sinuses normally drain and ventilate.

Meanwhile, this legion of underserved patients have such severe symptoms that recent research found 4.5 million sufferers of CRS had missed 15 days of work or school in the past year due to the disease, and wish they had missed an additional 29 days. Add all of those up, and we are talking about feeling like you need to miss at least one day a week from work for the majority of the year. Needless to say, this is not equivalent to "just a runny nose".

Surgery Challenge

Despite being some of the best available strategies of the moment, surgery and intensive medical therapy – based on high doses of steroid pills – have some real issues. High-dose oral steroids can really help, but symptoms come back rapidly and there is a long list of potential complications when they are used chronically.

Surgery has improved greatly over the last 20 years, and continues to evolve, but is not right for everyone. Some people simply do not want to undergo an invasive procedure, and the surgery can be costly, painful and non-curative. It is a major undertaking, especially when you consider that you might have to do it more than once. In fact, research suggests that of seven million CRS patients, cumulatively, who report having undergone surgery, 16% have had multiple surgeries to attempt to relieve their suffering.

It is important to note that for those with milder symptoms, seasonal allergies or who only experience the occasional acute sinus infection, the current nasal drug delivery technology is often satisfactory. The true unmet need is for those that have more severe, chronic symptoms.

Rethinking Nasal Technology

CRS patients are trying to treat symptoms originating far within the nasal labyrinth, and as a consequence – beyond undergoing surgery or taking steroids – they have struggled with inconvenient and often ineffective equipment to manage their symptoms, like nasal nebulisers or saline flushes. Given the design of these products, which typically require the person to inhale medications, much of the active drug can end up in the lungs, throat and/or the air surrounding the patient or even, in the case of flushes, in the bathroom sink rather than in the nasal passages, where the drug is most needed.

Primary care doctors, allergists and ear, nose and throat specialists that treat these patients are equally frustrated by the lack of effective options – less than 25% report satisfaction with currently available treatments. An overwhelming majority (75%) of these doctors agree that the nasal sprays on the market today fail to deliver the drug far enough inside the nasal cavities to make a difference.

Newer methods may turn this reliance on inhalation on its head by exploring the possibility of exhaling in order to facilitate getting medication deep and high into the nose. Techniques that are predicated on exhalation can produce an air-tight seal of the nasal cavity, closing the nose off completely from the throat and lungs.

When done the right way, air-carrying medicine is able to travel so deeply into one side of the nose that after depositing the medicine, it will escape out the other side.

There is no inhaling or 'sniffing', which creates negative pressures and tends to further narrow the slit-like passages. Instead, a positive air pressure helps to expand them.

This is also unlike pressurised canister nasal devices, which in principle simply 'shoot' medication forcefully into the nose, where it may simply impact harder on the first obstructing surface. The new exhaler technology may seem counterintuitive at first, but it is easy to learn, natural to perform, painless (no pressure builds up in the nasal cavity), and has been shown to 'float' medication much more efficiently into the target sites.

Unlike nebulisers, which carry the drug everywhere you breathe, require durable medical equipment and take minutes to use, or steroid pills that deliver the drugs equally throughout the body and are risky to use for prolonged periods, exhalation devices allow medication to be delivered inexpensively and easily, directly to the affected area. By enabling delivery of topical drugs to the main site of inflammation, the treatment is dramatically more effective and efficient. It is a little like trying to treat your poison ivy with cortisone cream – it works a whole lot better when you put the cream directly on the rash.

A New Era

In spite of its incredible leap forward in the world of nasal drug delivery, exhalation technology is not expensive to manufacture, can be simply paired with many drugs – powder or liquid – and dispensed as part of a regular pharmacy prescription. When applied to medication and diseases where deep and high deposition really matters – and there are quite a few – many new clinical benefits are within reach, even with products we already know about. In a time where drug prices are under intense scrutiny based on effectiveness, necessity to the patients and so forth, this option provides a way to make good medicines great with relatively modest investment. Important innovation does not always need to be so costly.

That is not to say there are no challenges to adopting this technology, as with any medical breakthrough that involves a change in behaviour. After all, the act of using a drug with a particular type of device every day, like other daily activities, becomes an ingrained habit for most people. Therefore, from the user perspective, novel treatments such as an exhaler require a change in mindset – developing the new and opposite habit of exhaling rather than inhaling – to use this type of device.

For this long-underserved patient population, nasal technology is finally experiencing a renaissance of sorts that should help to meet their needs. Companies are starting to pay attention to the unique and specific needs of CRS patients, and the most forward-thinking are committed to bringing exhalation technology to market within the next few years. Subsequently, CRS patients may soon live in a world where they are happy to go to school or work every day of the week.

Exhalation devices can easily be paired with liquid and powder medications

> From the user perspective, new treatments such as an exhaler require a change in mindset

Dr Ramy Mahmoud, President and Chief Operating Officer at OptiNose, joined the company in 2010, and played a key role in establishing its presence in the US. He is responsible for all aspects of the business's operation, including corporate strategy, R&D, manufacturing and supply chain, financial management, and commercial and business development. Ramy previously spent 14 years at Johnson & Johnson, where he was Chief Medical Officer, while holding various other senior roles within the pharma and device sectors. He has also participated in the development, launch and/or commercialisation of dozens of pharmaceutical and medical device products spanning multiple therapeutic categories. Ramy holds a Master's of Healthcare Management and Policy from the Harvard School of Public Health, a Doctor of Medicine degree from the University of Miami, and board certification in both Public Health/Preventive Medicine and Internal Medicine. Email: ramy.mahmoud@optinose.com