



Apnea Alternative Gains Momentum

With newly published clinical research, Provent Therapy offers physicians and patients another choice beyond CPAP, oral appliances, and surgery.

More than 2 years after bringing Provent Therapy to market, Rajiv Doshi, MD, continues his quest to educate patients and sleep doctors about the benefits of *expiratory* positive airway pressure (EPAP). Considering that obstructive sleep apnea is generally thought of as an *inspiratory* process, this has not always been an easy task.

Despite the challenges, Doshi and a dedicated team at Belmont, Calif.-based Ventus Medical (makers of Provent Therapy, www.proventtherapy.com) have meticulously built their case on a foundation of clinical research, patient choice, and business opportunity for sleep physicians and sleep laboratories. To date, there have been seven published studies attesting to the clinical efficacy of Provent Therapy.

The most influential of the studies, involving 19 centers, 250 subjects, and a 3-month follow-up, appeared in the April 2011 journal *Sleep*. "In this study, roughly half the people were in a sham arm and the other half in the active Provent arm," explains Doshi, a consulting assistant professor of Medicine at Stanford University, Palo Alto. "The study showed dramatic and statistically significant improvements in AHI for the active arm, but not in the sham arm. This benefit was maintained for the full 3 months of the study. At the same time, the Provent arm showed significant improvement on the Epworth sleepiness scale and high compliance rates."

Doshi predicts the study will serve as the defining nasal EPAP study for years to come, with awareness only building among patients and physicians who crave choices beyond CPAP, oral appliances, and surgery. Provent's unobtrusive two devices (that adhere to each nostril) attracted a standing-room-only audience at this year's APSS conference, a testament to burgeoning interest that will only grow as the massive undiagnosed and CPAP non-compliant populations seek more options.

Counter Intuitive

Rigorous clinical studies conducted by highly respected sleep physicians are making it easier to spread knowledge about the admittedly "counter intuitive" technology that fuels Provent Therapy. Many physicians, for example, wonder how an expiratory device can help treat what is commonly known as an inspiratory condition. "When you inhale, the valve opens for normal breathing," explains Doshi, who also serves as the United States executive director of Stanford-India

Biodesign. "When you exhale, the valve partially closes, and in the process it creates a resistance. This resistance generates expiratory positive airway pressure, and that provides a little bit of pressure into the airway right when the airway is most prone to narrowing and collapse—which is at the end of expiration. Because the airway is more open at the end of expiration, it is believed it is less likely to collapse on the next inspiratory effort. It is a little bit counter-intuitive."

For ongoing use, patients can buy packs of 30 (a 10-night trial pack is also available), using each pair for one night, and then throwing them away after use. The device uses a Micro-Valve design that attaches over the nostrils, secured in place with hypoallergenic adhesive. Doshi hopes physicians will understand that beneath the simplicity lies a validated and emerging body of clinical data that they can rely on and confidently offer to patients.

Whether sleep doctors refer to others (such as HME companies or sleep labs) or choose to self dispense, the opportunity to build the practice stems from the crucial element of choice. If patients know that a less intimidating choice exists, they may be more motivated to stick with the process from start to finish. "From the time they are told they have a problem to the time they can get therapy, there are a lot of chances to lose motivation," says Peter Wyles, president and CEO, Ventus Medical. "If patients are aware of other options, they may be more inclined to speak with the sleep specialist and get a sleep test than if CPAP were the only option. If sleep doctors can't convince patients they will be successful with CPAP, they can talk about Provent as a second-line option."

Expanding the Lingo

How big is the acronym awareness challenge? Googling "CPAP" yields about 6.4 million hits, and virtually all selections refer to continuous positive airway pressure. Meanwhile, a search for "EPAP" garners slightly more than 400,000 links. That wouldn't be so bad, but 99% of those refer to countless other acronyms, such as the Egyptian Pollution Abatement Project, that have nothing to do with sleep medicine.

Doshi is not surprised that awareness has a ways to go. While he learned about sleep apnea during his education at Stanford Medical School, the specialized knowledge he has today has largely grown out of his own interest in the physiology of sleep. This knowledge led him to conceive of a solution to tackle sleep apnea through the expiratory process about 7 years ago. With intellectual property safeguards in place, the idea

continues to gain ground in an industry largely dominated by large CPAP manufacturers with sizable marketing budgets.

Friendly Competition

It may seem daunting to introduce something new, but Wyles and Doshi believe that positive outcomes and a patient-first philosophy will steadily build the business. Instead of going head to head with CPAP, Doshi is confident that Provent can peacefully coexist. "We are not trying to be competitive with CPAP. CPAP is an extraordinary therapy and life changing for many patients," he says. "We view Provent as an alternative that gives physicians the opportunity to focus on those who are not being treated with CPAP. I don't think the CPAP companies are viewing us as a competitor. We have a friendly relationship with these companies. In fact, we think Provent will bring many new patients in to be diagnosed and will bring non-compliant CPAP patients back into the system as well."

By most estimates, the pie is growing, with 75% of sufferers still undiagnosed. Doshi points to a presentation at the 2010 APSS conference that estimates about 90% of people who have given up on CPAP are looking for other treatment options. "Those options could be surgery or oral appliances," he says. "However, patients prefer things that are non invasive, and Provent would be a leading candidate in that realm. Right now, there is a treatment dilemma for docs, because CPAP may be overkill for some patients, including those with less severe OSA and without comorbidities."

According to Philip Westbrook, MD, the whole point is to offer something that patients will actually use. "The gold standard of treatment is CPAP," says Westbrook, who serves as chief medical officer for Ventus Medical. "But too many patients do not use it, or do not use it adequately. There is a huge pool of patients already diagnosed, and undiagnosed, and they need treatment. Too many of those folks just do not get any treatment at all. Here we have something that is simple to use, inexpensive to try, and if it works and they use it, it will be terrific."

Stats Don't Lie, Right?

Industry experts agree that statistics point firmly to solid economics for the sleep industry. But despite the numbers, a rough economy can put sleep apnea on the back burner with patients viewing it as a tolerable ailment. Add on the undeniable concerns about CPAP, and Provent officials believe that viable options are needed to bring more people into the fold who may have stayed away.

HME companies and self dispensing labs are feeling the financial strain due to many factors, and Wyles believes they are thirsting for something new. "When you talk to sleep lab officials who say they can't fill their beds, it's an amazing comment when you consider how many people are out there suffering," says Wyles. "It's true that suppliers are getting squeezed by the government. Competitive bidding whacked them by 30%, and everybody in the supply chain is getting hammered. It is sad for the docs who want to treat patients. Even with these economic issues, boosting patient motivation to get diagnosed, treated, and stay compliant can be accomplished."

Far from shunning the cash aspect, Doshi believes patients will readily embrace the upfront money concept primarily because Provent is markedly less expensive than other options. "It's so easy to try that it will certainly be a second-line option that is much more acceptable than surgery," he adds. "The same would apply to oral appliances. If you are going to get a custom oral appliance made, you need to go to the dentist, and then get follow-up care to make sure there are no adverse events. With Provent, patients can try the device for a nominal up front cost—far less than oral appliances. Economically,

Provent should become the dominant second-line therapy quite quickly, and we are seeing that. It could also be a great first-line option, especially in the mild to moderate group without comorbidities. Many physicians believe that CPAP and Provent will be the dominant treatment options of the future."

Expanding the Possibilities

One subset of the sleep disordered population is a group already using CPAP, but even for these devoted patients the bulky machine is not always convenient. "Many people decide not to bring their CPAP when they travel," says Doshi. "They don't want the hassle of taking a CPAP machine through airport security. For those occasions where they are traveling, camping, or during a power outage, Provent represents an opportunity to provide patients and physicians with another therapeutic option."

Westbrook is equally confident that Provent can fill these gaps. However, he also points out that like all other sleep therapies, Provent is not for everyone. "We know that not all patients will use or benefit from Provent," concedes Westbrook. "We can't a priori reliably pick out those who successfully use Provent, but it doesn't make much difference because we can inexpensively and accurately find out whether a patient will use it, and whether or not it works. While right now, we can't accurately predict the people for whom it *won't* work, we are not too much different from other therapies such as oral appliances and surgery. Even with CPAP, we can't really predict who's going to use it and who is not going to use it."

A Competitive Edge

Whether it's in spite of or because of politicians, the historically resilient American economy seems to always make a comeback. If this comeback coincides with a realization of the sleep apnea patient potential, consultants agree that it's wise to prepare now and establish trust and referral bases. "The Provent device, which was cleared by the FDA in 2008 for the treatment of OSA, works differently in different people," says Doshi. "Some may get a huge AHI reduction, and some may not. It is important to test whether the device works, and the ideal means to confirm this is an in-lab PSG or a portable study."

According to Wyles, "With all the proper pieces in place, this is a solid clinical practice builder. For the subset of docs and sleep labs that are dispensing, they can realize the annuity on the sale of Provent as well."

Ultimately, patients want selection, and general practitioners want to send their patients to sleep doctors who get results. "With Provent, physicians are able to market themselves as clinicians who prescribe new and cutting-edge therapies," adds Wyles. "With more clinically validated options, it shows they are among the leading sleep doctors and enhances their reputation, which drives more referrals, and most importantly leads to healthy and satisfied patients."

For more information visit www.proventtherapy.com

Rajiv Doshi, MD, invented the core technology and founded Ventus Medical. Rajiv is a Consulting Assistant Professor of Medicine and a Lecturer of Mechanical Engineering at Stanford University. He is the inventor on over 30 pending and issued patents. Rajiv earned a BS in Chemical Engineering, an MSE in Biomechanical Engineering and an MD from Stanford University.

Peter Wyles, President and CEO.

Peter joined Ventus Medical as President and CEO in June 2010. Peter was most recently with Bayer Healthcare for 15 years where he led consumer, pharmaceutical and medical device businesses in Germany, Japan, Canada and the U.S. He also led the global expansion and integration of Metrika, a former start-up in the diabetes space that was acquired by Bayer HealthCare in 2006.