Abstract
Nasal EPAP (Provent Therapy) represents an important novel treatment option for obstructive sleep apnea (OSA). Published clinical studies and case series of nasal EPAP have demonstrated impressive initial patient acceptance and ongoing compliance through 12 months of treatment. This summary is intended to review published nasal EPAP compliance to date and provide healthcare providers with an understanding of how to optimize nasal EPAP compliance in their practices.

Introduction
Continuous positive airway pressure (CPAP) has historically been the gold standard of therapy for obstructive sleep apnea (OSA). CPAP has been demonstrated to have excellent efficacy in the in laboratory setting. However, many patients either initially reject CPAP or do not use it as frequently as prescribed within the home setting. It has been reported that between 46 to 83% of patients with OSA are non-adherent to CPAP. As a result, other treatment options are needed.

One such treatment is nasal expiratory positive airway pressure (EPAP). The only FDA cleared nasal EPAP product indicated to treat OSA is known as Provent Therapy (Ventus Medical, San Jose, CA) [See Figure 1]. The device has been evaluated in seven published studies including a 19 center, 250 patient randomized controlled trial. The device has been shown to effectively treat mild, moderate and severe OSA. [See Figure 2]. The device consists of a small valve attached externally to each nostril with hypoallergenic adhesive. The valve acts as a one-way resistor, permitting nearly unobstructed inspiration. During expiration, the airflow is directed through small air channels, increasing the resistance. This increased resistance during expiration creates EPAP which is maintained until the start of the next inspiration. [See Figure 3].

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The exact mechanism through which nasal EPAP treats OSA is still unclear, but several mechanisms appear most likely:

1) Positive end-expiratory pressure (PEEP) leading to increased end-expiratory lung volumes (or FRC) that increases longitudinal traction on the pharynx, making it less collapsible (“tracheal tug”).
2) Dilatation of the upper airway by EPAP which carries over until the start of the next inspiration
3) Mild hypercapnia due to reduced ventilation which would lead to increased respiratory drive to the upper airway

Recommended patients for Provent nasal EPAP include:

1) Patients (mild, moderate or severe) who have rejected or are non-compliant with prescribed CPAP
2) Newly diagnosed mild/moderate OSA patients without significant co-morbidities
3) CPAP compliant patients seeking alternatives for travel

Review of Compliance from Published Nasal EPAP Studies
Provent Therapy has been studied in a series of longitudinal published clinical studies. Several are highlighted below:

A novel nasal expiratory positive airway pressure device for the treatment of obstructive sleep apnea: a randomized controlled trial
– Berry RB, Kryger MH, Massie CA. [SLEEP 2011; 34:479-485]

In this 19 center study, 250 OSA patients were enrolled in this prospective, multicenter, parallel-group, sham controlled, randomized double-blind trial with three month follow up. Treatment effect by severity is shown in Figure 2. Provent nasal EPAP reduced the median AHI from 8.8 to 3.9 in mild OSA patients (p<0.001), from 20.5 to 8.4 in moderate OSA patients (p<0.001) and from 48.2 to 18.9 in severe OSA patients (p<0.001).

Based on patient self report, the median percentage of nights the EPAP device was used for the entire night was 88.2%.

Long term use of a nasal expiratory positive airway pressure (EPAP) device as a treatment for obstructive sleep apnea

This 13 center study was an extension of the three month (Berry et al) study and designed to evaluate the long-term effectiveness of Provent nasal EPAP after 12 months of follow-up. 41 patients from the Provent arm of the three month study who met adherence and efficacy criteria were continued on therapy and returned for in-lab PSG after 12 months of treatment. The median percentage of nights patients reported using the device the entire night was 89.3%.

A convenient expiratory positive airway pressure nasal device for the treatment of sleep apnea in patients non-compliant with continuous positive airway pressure

This study focused on OSA patients who were non-adherent to CPAP. Most patients had moderate to severe OSA, with over half of the patients having a baseline AHI ≥30. A total of 59 patients with OSA who refused CPAP or used CPAP for less than 3 hours per night were provided the Provent nasal EPAP device, of which 47 patients (80%) tolerated the device. Device use was reported an average of 92% of all sleep hours.

A multicenter, prospective study of a novel nasal EPAP device in the treatment of obstructive sleep apnea. Efficacy and 30-day adherence

This multicenter prospective study was specifically designed to assess adherence over a 30 day period, and also evaluated efficacy based on serial in-lab PSG studies. A total of 34 patients with OSA underwent a 30 day trial of the Provent nasal EPAP device. Participants reported using the Provent nasal EPAP device all night long for 94.4% of the possible nights during the in-home trial.

Retrospective cases series analysis of a nasal expiratory positive airway pressure (EPAP) device to treat obstructive sleep apnea in a clinical practice
– Adams, G. [SLEEP Abstract Supplement, 2011 (34):A146]

This retrospective analysis was completed to evaluate patient acceptance and AHI reduction using Provent nasal EPAP in a real world clinical practice. OSA patients (with AHI >10) received 10 nights of EPAP devices for in-home evaluation. Patients that acclimated returned for efficacy confirmation using standard in-lab PSG. 151 patients sampled nasal EPAP and 131 were in the analysis group. Of the analysis group, 75% acclimated to the device.

Nasal EPAP in the “Real World”
Acceptance and compliance with Provent Nasal EPAP in clinical practice may be more variable than that reported in the published literature. Patients in clinical studies may be more motivated and the level of training provided to them may be more rigorous and standardized than in normal clinical practice. That being said, a recent retrospective case series of 131 real world patients within a community practice demonstrated an impressive 75% acceptance of nasal EPAP after a 10 day trial.

The healthcare provider plays a critical role in educating and motivating the patient to use and acclimate to nasal EPAP. Physicians, respiratory therapists, lab managers, PSG technologists and others that have direct patient contact should be familiar with how to counsel patients about nasal EPAP use and acclimation. A short learning curve is expected for most healthcare providers that begin prescribing nasal EPAP, as expectation setting and acclimation support for nasal EPAP is different from CPAP.

Perhaps the most important messages to provide to the patient is that they need to make sure the device is sealed against the nostril, that they should breathe through the mouth while awake, and that it may take up to a week or longer to adjust to wearing Provent nasal EPAP. Best practices for use of Provent nasal EPAP include:
Set proper expectations while the patient is in the healthcare provider's office:

1) Have the patient apply and then breathe through a Provent EPAP device if available
2) Explain to the patient why Provent works (and reassure that the feeling of expiratory resistance is normal)
3) Instruct the patient to breathe through the mouth (and not the device) while awake to allow comfortable breathing
4) Review all the patient instructions in Figure 5
5) Encourage the patient to read the instruction booklet (included in the box) in its entirety before first at home use of Provent
6) Let the patient know that the first several nights may be uncomfortable, but this should resolve over the next several days. The patient should not give up after a night or two
7) Remind the patient that OSA is a chronic condition that requires treatment every night
8) If the patient is having difficulty, have him/her call the support number on the box to receive individualized training from an acclimation specialist

Other tips

• Cleaning of skin just prior to device application can improve device seal. If skin is oily, apply isopropyl alcohol or witch hazel (an astringent) to ensure good skin contact
• Use a mirror while applying devices
• Prior to applying the device, draw down upper lip over top teeth to stretch out skin under nostril to enable a proper seal
• If a leak is discovered or there are folds or creases present, remove device and re-apply. If this occurs again, remove device and apply new one
• Try briefly breathing out through the device. Notice the resistance. This is normal and means the device has been applied properly
• It may take up to a week or longer to adjust to using the device
• If the patient wakes up during the night and feels uncomfortable, remove the device and try again the next night. This may happen for several nights until they are used to wearing nasal EPAP

Key Patient Instructions for Wearing Provent Therapy

Provent Therapy may require an acclimation period. The device works by making it harder to breathe out through your nose, which helps create the pressure needed to treat your obstructive sleep apnea. It will take up to a week or more of use to feel comfortable breathing with the device. These tips will help you get used to wearing the Provent Device before and during sleep.

1. INHALE
   • Inhale through your mouth or through the device - whichever is more comfortable for you to fall asleep.

2. EXHALE
   • Breathe out through your mouth while awake and trying to fall asleep.
   • If you try breathing through your nose (to check the seal of the adhesive, for example) notice the significant resistance. This is normal and tells you the device is working.
   • Generally, people switch to nasal breathing once asleep, effectively “turning on” the device.

3. RELAX
   • Simply apply the device and go to bed.
   • Do not engage in any activity while wearing the device—just try to fall asleep.
   • Keep a glass of water near your bedside, in case you wake up with a dry mouth.

4. REPEAT
   • If you wake up feeling uncomfortable, just take it off and try again tomorrow.
   • Take time to get used to wearing Provent Therapy.

5. COMMIT
   • Use all devices provided in the pack.
   • The first few nights may be uncomfortable, but you should get used to it.

Figure 5: Key patient instructions

References

8 Adams, G. Retrospective cases series analysis of a nasal expiratory positive airway pressure (EPAP) device to treat obstructive sleep apnea in a clinical practice. SLEEP Abstract Supplement, 2011 (34):A146.