

A Novel Non-Prescription Nasal EPAP Device (Theravent) to Treat Snoring

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Abstract

Primary snoring, defined as snoring in the absence of obstructive sleep apnea/hypopnea (OSA), is a very common problem that can significantly worsen the sleep quality of the bed partner and has been linked to important medical conditions. Healthcare providers are frequently asked by their patients for snoring treatment recommendations. Unfortunately, although there are a variety of over-the-counter therapies available that claim to treat snoring, few if any have demonstrated objective clinical efficacy. This report introduces a novel, FDA-cleared device called Theravent™ Snore Therapy, which represents an important new class of snoring therapy utilizing nasal expiratory positive airway pressure (EPAP). This report summarizes the device's mechanism of action and available clinical data.

Background

Snoring is a ubiquitous complaint of bed partners worldwide and leads to many patient requests for treatment recommendations. Snoring is the audible signature of increased resistance to airflow during sleep, and is part of a spectrum of sleep-disordered breathing conditions that includes OSA.

The sound of snoring is created by turbulent airflow-induced vibration of tissues in the collapsible portion of the upper airway. Any unsupported tissue lining the upper airway down to the vocal cords can vibrate and make noise. This includes the soft palate, uvula, pharyngeal walls and tongue – a diffuse sound generator that renders successful local treatment difficult.¹ Sleep normally reduces the activity of the dilating musculature that otherwise opens and stabilizes the pharyngeal passageway during inspiration.² If the pharyngeal passageway is abnormally narrow or floppy, then airflow into the lungs must speed up, further lowering the pressure in the airway, creating a turbulence which vibrates soft tissue.³ The vibrating tissue creates the harsh noise of snoring.

Epidemiology

In the United States, habitual snoring has a reported prevalence of 34% to 44% in men and 15% to 28% in women. Higher prevalence of snoring was reported in two Canadian studies, in which 71-86% of men and 51-57% of women were found to snore.¹ These differences in reported prevalence reflect the subjective nature of reported snoring and different methods used to gather the information. The correlation between self-reported snoring and objectively measured snoring can be poor.⁴

Studies by Young⁵ and Bliwise⁴ were rigorous and large, so their estimate that about one third of the adult popula-

tion in the United States snores most nights of the week is widely accepted. However, a recent prevalence report in the United States suggested a higher rate of snoring: 59% of 1506 respondents (both sexes) snored, 54% at least 3 nights per week, and 40% every night or almost every night.⁶ This apparent increase in snoring prevalence might reflect the increase in obesity prevalence in the United States as obesity is a risk factor for snoring. Indeed, this trend could be expected to continue.

Snoring is more prevalent in men for reasons that are still not fully explained. The major risk factors for snoring are similar to those for OSA, such as obesity and increased neck circumference. In addition, a number of studies have reported that the prevalence of snoring decreases after the age of 70, a finding that is somewhat counterintuitive. Poor hearing acuity in the elderly, fewer elderly with bed partners, or diminished survival of snorers have been offered as possible explanations.

The Basis for Treatment

Healthcare providers may need to decide whether snoring should be treated. Many patients may ask for therapy to appease a bed partner whose sleep may be disturbed. Frequently, snoring can contribute to relationship problems. Further, there are studies that suggest that snoring should be treated for other reasons beyond trying to improve the sleep of the bed partner.

Daytime Sleepiness

In some individuals, snoring may be associated with episodes of airway obstruction that increase the drive to breathe and cause frequent arousals, but do not cause enough desaturation to meet the usual definition of a hypopnea. This has been called the upper airway resistance syndrome, and the events termed “respiratory effort related arousals” (RERAs) or “flow limitation events” (FLEs). In these patients, snoring may be associated with excessive daytime sleepiness and prescribed treatment with PAP (positive airway pressure) can improve sleepiness and daytime function.

Hypertension

In an extensive review, Hoffstein documented that 14 of 19 studies examining the association between snoring and hypertension found that snoring was not an independent risk factor.⁷ The recent Sleep Heart Health Study of over 6000 individuals found no significant association between self-reported snoring and hypertension.⁸

Coronary Artery Disease

In spite of the scarcity of evidence linking non-apneic snoring to hypertension, a possible association between habitual snoring

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and coronary artery disease is not easily dismissed. A recent, large (>12,000 patients) Hungarian study found that reported loud snoring *with breathing pauses*, but not quiet snoring, was a significant independent risk factor for acute myocardial infarction, as well as hypertension and stroke.⁹

Cerebrovascular Disease

For years the epidemiologic data suggesting an association between habitual snoring and cerebrovascular disease was explained by assuming that self-reported snoring was just a surrogate for OSA. The report by Lee and colleagues in 2008 that heavy snoring independently increases the risk of carotid artery atherosclerosis, likely due to direct tissue vibration, has challenged the old explanation.¹⁰ The finding that peri-carotid tissue vibrations similar to that resulting from loud snoring damaged the lining of the carotid arteries in rabbits supports the hypothesis that snoring-induced vibration is the culprit.¹¹

Treatment Options

Several non-prescription treatments have been proposed for snoring, including position-limiting devices (to keep patients off their back), various drugs, oral sprays, nasal dilators, chin straps and, more recently, snore-activated alarms. The efficacy studies of these are often characterized by enthusiastic subjective reports but poor objective verification.

Behavioral Therapy

Obesity is a major risk factor for snoring, so for overweight and obese snorers, diet and exercise should be the first treatment recommended. Unfortunately, dietary weight loss is seldom maintained and there is little non-anecdotal evidence that weight loss reduces snoring. Because the supine position promotes upper airway collapse, and changing from the supine to a non-supine sleep position may decrease snoring, position restriction devices including head positioning pillows have been popular. The evidence that these devices work or that patients continue to use them over time is sparse. Alcohol consumption can promote snoring so avoidance prior to bedtime should be recommended.

Medical Therapy

Two endocrine diseases, hypothyroidism and acromegaly, can cause sleep apnea and snoring, and should be treated if identified. Nasal decongestants/steroids/lubricants are available over-the-counter and are touted as treatments for snoring. There is evidence that allergic nasal congestion can cause snoring, and presumably other causes of nasal mucosal inflammation can do the same. A brief trial of nasal spray decongestant or steroid is reasonably safe and relatively inexpensive to try. There is little objective evidence that nasal lubricants work nor is there reliable evidence that dietary supplements improve snoring.¹²

Nasal Dilators

Perhaps the most popular non-prescription therapy for snoring is nasal dilators. Traditional nasal dilators can expand and hold open the nasal valves reducing inspiratory flow resistance in a way that is quite noticeable to the awake wearer. External nasal dilator strips (ENDS) and internal nasal dilators (IND) have only equivocal evidence of efficacy.^{12,13}

Oral Appliances

Oral appliances are a recommended prescription treatment for non-apneic snoring. Almost without exception, studies where some objective measure of snoring change is reported confirm a significant improvement in snoring.¹⁴ However, such appliances can lead to excessive salivation and dentition change that can limit their use and require regular follow up with the dentist. Oral appliances do not completely eliminate snoring in everyone and because they may require custom fitting by a dentist, they can be expensive to try.

Continuous Positive Airway Pressure (CPAP)

CPAP eliminates snoring in the vast majority of users but is viewed as being very cumbersome by many users. CPAP acceptance and adherence can be low in patients with OSA, and considerably worse in patients with simple snoring.

Surgical Therapy

Though invasive and painful, surgery can be attractive to some patients because it offers the chance for a “permanent” cure, and some patients do benefit from this treatment. Surgery for snoring is essentially the same as surgery for OSA, and can involve the nose, palate, tongue, and pharyngeal walls but usually not the facial skeleton. Nasal surgery improves snoring only in a minority of patients.¹ Pharyngeal surgery, such as uvulopalatopharyngoplasty alone or with tongue base reduction has had mixed success with reported improvement varying from 22% to 92% depending on the length of follow-up. A recent systematic review of surgery for snoring found that there was limited reliable evidence of a beneficial effect.¹⁵

About Theravent (Nasal EPAP)

The newest class of snoring treatment is nasal expiratory positive airway pressure (EPAP). It is available over-the-counter under the tradename Theravent Snore Therapy (Ventus Medical, Inc., San Jose, California). Theravent is FDA cleared with the intended use of reducing or eliminating snoring. Theravent utilizes proprietary microvalves set within a medical-grade hypoallergenic adhesive patch which surrounds the user's nostrils.

During inhalation, the microvalves open, allowing for relatively unrestricted airflow. However, during exhalation, the microvalves close, creating resistance to airflow and thus creating EPAP (Figure 1, Figure 2).

Nasal EPAP Precedent

Nasal EPAP was demonstrated to treat sleep disordered breathing, namely OSA, as early as 1983 by Mahadevia.¹⁶ Yet, it was not until 2008 that the first EPAP device was FDA cleared and became commercially available to treat OSA, under the tradename Provent[®] Therapy (Ventus Medical, San Jose, California). This prescription-only device has been evaluated in seven published studies¹⁷⁻²³ and has been shown to be clinically effective in treating mild, moderate and severe OSA and in reducing snoring in patients with OSA. Physiologically, EPAP, when provided at resistance levels that can treat OSA, has been shown to increase pressure in the airway until the start of the next inspiration.²⁰



Fig. 1. Theravent nasal EPAP device

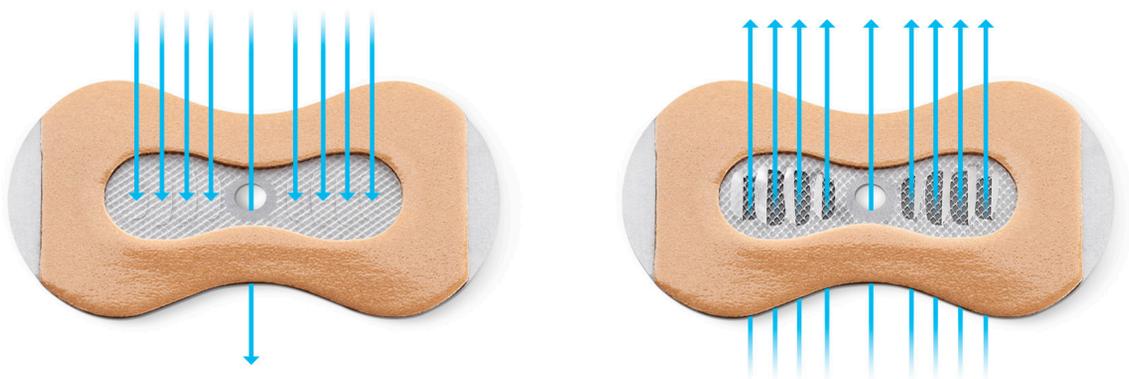


Fig. 2. Theravent microvalves during expiration and inspiration respectively

Though the exact mechanism of action is still not certain, three likely mechanisms have emerged in clinical studies in patients with OSA:

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”).²⁰
2. Dilatation of the upper airway that carries over until the start of the next inspiration.²⁰
3. Mild hypercapnia due to reduced ventilation leading to increased respiratory drive to the upper airway.²³

Importantly, in three studies of the Provent EPAP device in patients with OSA, the percentage reduction in snoring duration was 65%, 58% and 74% using objective measures (vibratory probe on the neck or a decibel meter).^{17,18,22} One study demonstrated that 83% of OSA patients had a reduction in snoring, assessed using an vibratory probe on the neck.¹⁷ Several of these patients had a complete elimination of their snoring.

As described earlier, a novel over-the-counter device has become available for the treatment of snoring, utilizing EPAP, albeit at a much lower resistance than the Provent EPAP device

for OSA. This device, known as Theravent Snore Therapy, has been studied in three separate clinical studies in multiple resistances, which have demonstrated both objective and subjective improvements in snoring.

Clinical Studies Studying Theravent nasal EPAP for the Treatment of Primary Snoring

Objective Clinical Study

A prospective, randomized, single-center trial used decibel meters to evaluate the effectiveness of the Theravent device in a population of primary snorers (without OSA). Forty-nine patients were evaluated on control nights (with no therapy), as well as on Theravent and on commercially available external nasal dilator strips. In addition, patients and their bed partners maintained daily logs and completed a survey at the conclusion of the study.

Methods

Inclusion criteria included age of at least 18, presence of a bed partner, and nightly snoring. Exclusion criteria included diagnosis of OSA, witnessed cessation of breathing or gasps for air

Table 1. Patient Demographics for Objective Clinical Study

	Total (n = 49)
Mean age (years)	44.1
Mean body mass index	28.1
Gender	
Male	39 (79.6%)
Female	10 (20.4%)

while sleeping, diagnosis of insomnia, history of respiratory failure, history of any other unstable and/or untreated serious medical conditions, and history of allergic reaction to acrylic-based adhesives (such as those found in BAND-AIDS). Patients judged to have a high risk for OSA were screened out of the study either during the phone screening or at physical exam. Patient demographics are summarized in Table 1.

During each night of the study, the patient wore the ARES Unicorder portable device (Advanced Brain Monitoring, Carlsbad, CA), a validated portable monitor for sleep disordered breathing.^{24,25} The portable monitor recorded snoring duration (minutes spent > 40 decibels (dB)), pulse rate, SpO₂, head position, and respiratory effort. The snoring microphone was located in the recording device on the forehead, placing it at a fixed distance from the source of snoring. Scoring of time spent snoring > 40 dB was accomplished using the automated ARES software. The choice of > 40dB as a snoring threshold was made because that level was in the mid-range (>30, >40, >50 dB) of the reported snoring loudness levels reported with the ARES microphone, and these levels seemed consistent with the Leq levels reported in snorers by Wilson et al.²⁶ Prior to the generation of the final sleep report for each night, the studies were examined for anomalies such as excessive background noise and off-head alarms. A minimum of a 50% reduction in the percent of time spent snoring > 40 dB (compared to the control night) was used as the primary objective measure of device success. Paired t-test comparison between groups was achieved by comparing the percent time snoring.

Two bed partner reported outcome measures were also used to gauge effectiveness of the snoring treatments. Every morning, in their daily logs, bed partners were asked to assess the volume and duration of their partner's snoring the night before. Answers were provided by visual analog scale (VAS) and later converted to a scale of 0-100. A score of 0 indicated very loud or constant snoring and a score of 100 indicated no snoring.

Results

Forty-nine patients were enrolled in the study. Objective snoring analysis was completed on the 46 patients with sufficient portable monitoring data during both control and treatment nights. Subjective (bed partner) analysis was completed on 48 patients whose daily log data were available.

The mean percent of sleep time snoring > 40 dB, the primary endpoint of the study, was significantly reduced for Theravent compared to control from 19.7% to 12.3% (p<0.001). For the external nasal strips, snoring was reduced from 19.7% to 18.2% which was not significantly different compared to control (p=0.309) (Table 2). Fifty percent (23 of 46) of patients using Theravent had their snoring duration reduced by at least 50%. Among these responders to Theravent, the mean reduction in snoring was 76% according to the decibel meter (Table 3). Only

Table 2. Percent of Time Spent Snoring >40 dB on Theravent and Nasal Strips Versus Control Using a Decibel Meter

		Mean % Number Time Snoring	Median % SD Time Snoring Vs. Control	P-Value	
Control	46	19.7%	14.2%	15.9%	N/A
Nasal Strips	46	18.2%	12.8%	17.0%	0.309
Theravent	46	12.3%	12.9%	9.2%	<0.001

9 of 46 (20%) of patients using external nasal strips achieved at least a 50% reduction in snoring.

Data reported in daily logs indicated that bed partners experienced significantly less sleep disruption and reported a highly significant decrease in both snoring volume (p<0.001) and snoring duration (p<0.001) compared to control (Table 4).

Eight adverse events (none serious) were reported that were deemed possibly related to Theravent, most relating to difficulties adjusting to breathing through the device.

Conclusion

Theravent nasal EPAP significantly reduced snoring duration compared to control (p<0.001) using a decibel meter in the home setting. Responders to Theravent achieved an average snoring reduction of 76%. Furthermore, bed partners reported highly significant reductions in snoring volume (p<0.001) and snoring duration (p<0.001) compared to control during this in-home trial.

Subjective Clinical Studies

Two subsequent studies of Theravent in a not yet commercially available resistance level demonstrated high levels of bed partner satisfaction and snoring reduction. The first study was a prospective customer preference study with seven nights of in-home evaluation of 43 frequent snorers and their bed partners. The end-of-study survey responses demonstrated that 86% of bed partners found that the device reduced snoring. The second study also was a prospective customer preference study with seven nights of in-home evaluation involving 46 frequent snorers and their bed partners. In this study, 89% of bed partners reported that the device reduced snoring and 83% of all subjects expressed interest in continuing to use the device at the end of the study.

Using Theravent in the Real World: Implications for Healthcare Providers

It may take several days for patients to acclimate to wearing and breathing through the Theravent nasal EPAP device. The healthcare provider should let the patient know:

1. That the first few nights using Theravent nasal EPAP may be uncomfortable for some patients, but that comfort improves over the ensuing days
2. To remove the device during initial nights if he/she has difficulty sleeping and to try again the following night
3. To breathe out through the mouth while awake and falling asleep

Table 3. Analysis of Responders to Theravent and Nasal Strips Using a Decibel Meter

Device	# of Successful Patients (of 46 possible)	Success Rate	Mean Reduction
Nasal Strips	9	20%	68%
Theravent	23	50%	76%

Table 4. Bed Partner Reported Snoring Volume and Snoring Duration Ratings (Based on Visual Analog Scale) [A Higher Score Represents Successful Treatment]

Device	N	Snoring Volume Rating (0=very loud snoring; 100=no snoring)				Snoring Duration Rating (0=constant snoring; 100=no snoring)			
		Mean	SD	Median	P-Value Vs. Control	Mean	SD	Median	P-Value Vs. Control
Control	48	46.6	27.3	43.3	N/A	47.3	23.6	45.7	N/A
Nasal Strips	48	51.5	30.5	54.7	0.076	52.4	30.1	51.6	0.06
Theravent	48	64.3	25.0	67.9	<0.001	66.0	24.4	68.9	<0.001

Further, healthcare providers should exclude patients diagnosed with OSA and those with the following conditions:

- A cold, sinus or ear infection or perforated eardrum
- Severe breathing problems (including emphysema)
- Severe heart problems
- Very low blood pressure

Summary

Snoring is a very common condition that historically has had limited, clinically proven treatment options. The Theravent device is a novel, FDA cleared, over-the-counter treatment option for snoring that utilizes nasal EPAP to maintain patency of the upper airway to reduce or eliminate snoring. Data from a study of 49 patients demonstrated statistically significant improvements in snoring duration based on objective monitoring data from a decibel meter and statistically significant improvements in snoring duration and volume based on bed partner assessment. Theravent represents an important new option for healthcare providers to recommend to their patients to treat snoring.

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