A Pilot Evaluation

A Unique Internal Nasal Dilator Device (Brẽz® by AirWare®) for the Treatment of Primary Snoring

Barbara A. Harris, PhD,[1] Michael J. Breus, PhD, Thomas Minor, MD, & Yiran Hu, MS[1]

PsyPharma Global, Phoenix, Arizona

Introduction

Snoring is defined as the sound made by the vibration of tissue residing in the naso and oropharynx during inhalation or exhalation while sleeping. The vibration is often due to obstructed air movement due to deviations in the septum or a relaxation of tissue during breathing while sleeping. The pathogenesis of snoring can be related to the combination of physiological, environmental and gender causative factors. Epidemologic data on snoring suggests at least 30% of adults and perhaps as many as 50% of people in some demographics snore. (1) The nose accounts for 50% of nasal breathing resistance while the remaining resistance is associated with upper sinus and throat tissue and tissue relaxation. Snoring is a sign of increased upper airway resistance, and it is an auditory reminder that obstruction of the airway is occurring.

Snoring has been linked to increases in blood pressure, heart attack, and stroke (5,6,14,16,24,28). Not only can snoring be a health risk for the snorer, but research now indicates that individuals sleeping next to a snoring bed partner could lose between 1 and 2 hours of sleep each evening themselves (3). Although snoring is often considered a minor affliction, snorers can sometimes suffer severe impairment of lifestyle (16). In a between-subjects trial, Armstrong and colleagues discovered a statistically significant improvement in marital relations after snoring was surgically corrected, and that snoring strains interpersonal relationships; concerns for its effects were often voiced above a medical malady (4).

Many of the treatments for snoring revolve around opening the breathing passage. This is the reason snorers are advised to lose weight (to stop fat from pressing on the throat), stop

smoking (smoking inflames mucosal tissue and lining narrowing the airway), sleep on their side (to prevent the tongue from blocking the throat), use mandible advancement dental devices (to open the posterior airway space), avoid alcohol (a muscle relaxant) and surgery (to remove structures and tissue) [4, 8].

All of these treatments have significant obstacles for successful adoption as indicated by adherence research in the areas of alcohol consumption, smoking cessation and weight loss. In addition, surgical treatments, while effective in some cases, can be painful, have significant side effects and eventual tissue re-growth. Dental devices can also have side effects including tooth movement and jaw pain [4].

The economics of snoring treatments can include high costs such as non-reimbursed surgery, appropriate dental evaluation and correction, device expense and implementation, and follow-up care can be expensive [18]. There is clearly a need for an economically feasible, reliable and effective solution for simple snoring with few side effects.

The present study tests the hypothesis that use of this unique internal nasal dilator will reduce snoring and improve the sleep quality and quantity of the bed partner.

The Device

The device under study is an intra-nasal dilator. (See picture below) The unique patented shape opens nasal passages to make breathing easier. The device is molded with a soft, FDA approved, food-grade, hypoallergenic plastic. It comes in three sizes to accommodate most human nasal structures. It is free of drugs and latex, disposable and recyclable.

Picture 1

The Brẽz® by AirWare® intra-Nasal Dilator

Study Design

A within-subjects design was used, sample size was determined to be statistically powered to significance at <0.05. The required number of participants was determined via power analysis to be 25.

Methods and Statistics

26 primary snorers with AHI < 6 (12 men and 14 women) and ages ranging from 18-70, (mean age 41) with bed partners, were recruited from the community to participate in this within-subjects design study.

Participants underwent two (2) nights of pre-treatment in-home snoring evaluation with a validated three (3) channel home sleep-testing device (ApneaLink™). These nights were to rule out sleep apnea and obtain a baseline snoring event number. If the snoring participant had a prior PSG study in the previous 3 months that ruled out apnea (AHI<6), then one night of baseline snoring was performed. Snoring events were defined as >0.3 second vibration, with an amplitude deviation from baseline = 1.5-10%.

Pre-treatment and post treatment questionnaires (Bed partner rating scales [1-5]) were used to measure sleep quantity and quality of the bed partners. The snoring participants completed pre and post treatment Epworth Sleepiness Scales. Baseline measurements were recorded and all measurements were conducted for an additional two nights with snoring participants wearing the treatment device. Adverse events were collected.

The outcome variables include snoring events, bed partner's subjective quantity of sleep, bed partner's subjective quality of sleep, and the Epworth Sleepiness Scale (ESS) for the snorers. The self-reported bed partner's quality of sleep disturbed by the snorer contained five levels of snoring effect: (1) - not at all to, (5) – more than anything else. The bed partner's quantity of sleep disturbed by the snorer contained five levels; (1)- not at all, to (5) – greatly disturbs. The Epworth Sleepiness Scale score contained four levels: no chance of dozing (0), slight chance of dozing (1), moderate chance of dozing (2), to heavy chance of dozing (3), all levels were listed in an increasing order.

The primary variable is the study treatment, which has two levels: wearing the treatment device and no treatment device. A comparison of the pre-treatment and post-treatment observations for the above-mentioned outcome variables was performed with adjustment for participants' demographic information (i.e., age and gender). The mean value of two post-

treatment measurements of snoring events was used in comparison with pre-treatment measurement.

Due to participants' improper sizing or manipulation of the device, 74 of 78 observations for snoring events were used, and 50 of 52 observations for ESS scores were used. An α-level of 0.05 was used to determine significance of all statistical tests.

Results

Descriptive statistics of variable snoring events are given below in Table 1. We observed that the snoring events after the treatment had a smaller mean value (decreased by 52%) as well as a smaller standard deviation than the snoring events before the treatment.

Table 1

Variables	Pre-treatment				Post-treatment			
	mean	Stand deviation	Min	Max	mean	Stand deviation	Min	Max
Snore events	1247	830	3	2719	654	495	44	1764

Table 1 - Descriptive statistics of variable snoring events

The graph below also shows that the median post-treatment snoring events are lower than the median pre-treatment snoring events; there seems to be some but not severe variability between pre-treatment and post-treatment groups. No outliers were statistically observed. Assumptions for Analysis of Variance were examined and no violation of the assumptions was found.

Figure 1

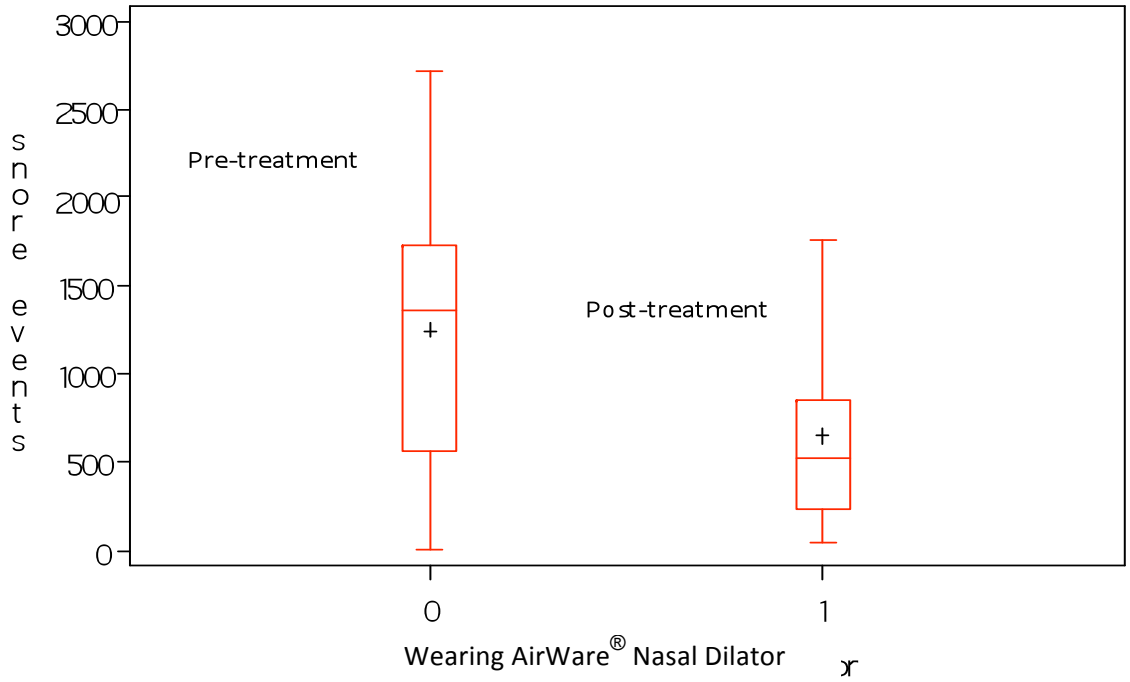

Figure 1 - A box plot of snore events by position. + indicates the value of the mean, the horizontal line within the box indicates the value of the median, the extremes of the boxes indicate the upper and lower quartiles, the ends of the intervals represent the largest and smallest values; there are no outliers.

With adjustment for the participants' demographic information (i.e. age, gender), the analysis indicated that there is strong evidence of a post treatment effect of the intra-nasal dilator on reducing snoring events with a P-value of 0.0037, < 0.05.

Logistic regression analysis was performed to test the effect of wearing the treatment device on the bed partner's subjective *quantity* of sleep. Particularly, with participants' demographics adjusted, analysis showed that participants wearing the treatment device had only a 22.4% likelihood of persistent snoring and bothering their bed partner's sleep compared to their pre-treatment snoring quantity, with a P-value of 0.0217 < 0.05

Table 2

Frequency (%)	Occasional soft snoring: not bothersome to partner	Persistent snoring: bothersome to partner
Pre-treatment	13 (25%)	21 (42 %)
Post-treatment	13 (25%)	5 (10%)

Table 2 - Table of bed partner's quantity of sleep effect before and after the study treatment; the number in each cell is the number of observations that fall into each situation. Percentages are calculated by dividing the number in each cell by the total number of observations (52).

In testing of the effect of snoring participants wearing the treatment device on the bed partner's *quality* of sleep, logit analysis for ordered outcome categories showed their sleeping quality as improved compared to before the subject received the treatment with a P-value of $0.0006 < 0.05$.

Table 3

Frequency (percent)	Great improvement	Moderate improvement	Slight improvement	No difference
Pre-treatment	3 (6%)	3 (6%)	9 (18%)	11 (22%)
Post-treatment	9 (18%)	11 (22%)	3 (6%)	3 (6%)

Table 3 - Table of improved sleeping quality of the bed partner against the study treatment; the number in each cell is the number of observations that fall into each combined situation. Percentages are calculated by dividing number in each cell by the total number of observations (52). In addition, summation of the total "improved" observation divided by the total number of observations (23 / 26) shows that 88% of the bed partners reported some improvement in their quality of sleep.

Descriptive statistics of ESS total scores are given below in table 4. We observed that the ESS total scores after the treatment had a slightly smaller mean value as well as a smaller standard deviation than the ESS total scores before the treatment. However, this difference was not statistically significant.

Table 4

Variables	Pre-treatment				Post-treatment			
	mean	Stand deviation	Min	Max	mean	Stand deviation	Min	Max
ESS total scores	9	4.36	2	16	8	3.76	1	16

Table 4 - Descriptive statistics of ESS scores

There were two adverse events recorded: Mild irritation of the nares (probably related to the device), and head congestion (not related to device).

Discussion

It was found that the Brẽz® by AirWare® had a significant effect on objectively measured snoring in a selected group of non-obese primary snorers (AHI<6). The number of snoring events was reduced. It is assumed that the mechanism of action for the reduction in snoring events was that the placement of the device inside the nostrils decreased nasal resistance during sleep. Historical data have shown that nasal dilation in general does in fact reduce nasal resistance (Hornung et. al. 2001). However, this hypothesis cannot be proven since nasal resistance was not evaluated during sleep or wake. A reduction in snoring with internal nasal dilation appears to depend upon individual patient characteristics, that is to say non-obese, normal airway individuals. Thus, those patients with snoring etiology other than nasal resistance (i.e., obesity, tonsilar hypertrophy, redundant palate, etc) may have a positive reaction to treatment, *only* if their snoring etiology is in combination with nasal resistance.

Bed partner ratings of sleep quality and quantity were also effected post treatment with Brẽz® by AirWare®. Bed partner subjective sleep quality and quantity was overwhelmingly reported as improved, when snorer was using the treatment device. It is assumed that the reason for improved quantity and quality of bed partner sleep was the observed reduction in snoring events since environmental conditions, other than snoring, were constant, as described by the bed partners. However, since this was an in-home study, it cannot be assumed that environmental factors other than the reduction in snoring contributed to these effects. Some of the partner comments post-treatment include: the nights were so much better, the partner didn't have to leave the room, snoring was eliminated, usually wears earplugs and sleeps in another room but not with Brẽz®, and the partner kept waiting for snoring which didn't occur.

Epworth Sleepiness Scale scores were equivocal in snorers while using Brẽz® by AirWare® during the study. Multiple reasons for these results can be put forth including: insufficient

duration of use of treatment device, accumulated sleep debt, or sleepiness due to something other than snoring. Further study is required.

Further clinical studies should include an evaluation of sleep quality in snoring participants and bed partners over a longer treatment period, decibel level reduction in snoring when using the device, evaluation of nasal resistance both during wake and sleep, full-nighttime polysomnography while wearing treatment device and further evaluation of the mechanism of action for this unique and effective device.

References

1. Fitzpatrick, M.F., Martin, K., Fossey, E et al. Snoring, asthma and sleep disturbance in Britain: a community-based survey", (1993) Eur. Respir, J. 69, 531 535, (1993]
2. Gall, R., Isaac, L., Kryger, M.,"Quality of life in mild obstructive sleep apnea", (1993) Sleep, 16, S59 S61 (1993]]).
3. Cartwright, R.D. & Knight, S. "Silent partners: the wives of sleep apneic patients", 1987) Sleep, 10, 244 248. (1987]]).
4. Armstrong, M. W. J. Wallace C. L. & J. Marais, The effect of surgery upon the quality of life in snoring patients and their partners: a between-subjects case-controlled trial", Clinical Otolaryngology & Allied Sciences 24 6 Page 510 (1999-01-12]]).
5. Lugaresi, E., Cirignotta F., Coccoagna G. et al. Some epidemiological data on snoring and cardio circulatory disturbances", (1980), Sleep 3, 221–224
6. Lee Sharon A [1,2]; Terence C. Amis, PhD[1,2,4]; Karen Byth, PhD[2,4]; George Larcos, MBBS[3,4]; Kristina Kairaiti, Heavy Snoring as a Cause of Carotid Artery Atherosclerosis, Sleep, 31(2008).
7. Hoffstein, V. S. Mateika and D. Anderson, Snoring: Is It In The Ear Of The Beholder?, Sleep, 17(1994),
8. Hoffstein, Victor, Is Snoring Dangerous To Your Health? Sleep, 19(1996)
9. Neil, G., Thomas, PhD[1]; CQ Jiang, MD[2]; XQ Lao, MD[1,2]; Sarah M. McGhee, PhD[1]; WS Zhang, MD[2]; C Mary, Snoring and Vascular Risk Factors and Disease in a Low-Risk Chinese Population: The Guangzhou Biobank Cohort Study, Sleep, 29(2006).
10. Hoffstein, V., S. Mateika and A. Metes, Effect of Nasal Dilation on Snoring and Apneas During Different Stages Of Sleep, Sleep, 16(1993)
11. Wiggins, Charles L. [‡]Wolfgang W. Schmidt-Nowara, [*†‡§]David B. Coultas and [*†‡§]Jonathan M. Samet, Comparison Of Self- And Spouse Reports Of Snoring And Other Symptoms Associated With Sleep Apnea Syndrome, Sleep, 13(1990).
12. Perez-Padilla, J. Rogelio, Peter West and Meir Kryger, Snoring In Normal Young Adults: Prevalence In Sleep Stages And Associated Changes In Oxygen Saturation, Heart Rate, And Breathing Pattern, Sleep, 10(1987)
13. Josephson, Stephen C. and [†]Raymond C. Rosen, Response-Contingent Awakening In The Modification Of Chronic Snoring, Sleep, 06(1983).
14. Mateika, Jason H. PhD[1, 2] and George Mitru MSc Cardio respiratory and Autonomic Interactions During Snoring Related Resistive Breathing, Sleep, 24(2001)
15. Hoffstein, Victor, Susan Mateika, and Patrick Hanly, Snoring and Arousals: A Retrospective Analysis, Sleep, 18(1995).
16. Dunai, Andrea MD[1]; Andras P. Keszei, MD, PhD[2]; Maria S. Kopp, MD,PhD[1]; Colin M. Shapiro, MBBCh, PhD, FRCPC, Cardiovascular Disease and Health-Care Utilization in Snorers: a Population Survey, Sleep, 31(2008).
17. Telakivi, T., *S. Kajaste, [†]M. Partinen, [‡]M. Koskenvuo, [†]T. Salmi and [‡]J. Kaprio, Cognitive Function in Middle-Aged Snorers and Controls: Role of Excessive Daytime Somnolence and Sleep-Related Hypoxic Events, Sleep, 11(1988).
18. Strollo, [*]Patrick J. Jr. and [†]Mark H. Sanders, Significance And Treatment Of Nonapneic Snoring, Sleep, 16(1993).
19. De Groen, JHM, †W. Op den Velde, [†]J.E. Hovens, [‡]P.R.J. Falger, [‡]E.G.W. Schouten, Snoring And Anxiety Dreams, Sleep, 16(1993)
20. Mateika, Jason H (PhD)[1,2], Neil B. Kavey (MD)[3] and George Mitru (MS), Spontaneous Baroreflex Analysis In Non-Apneic Snoring Individuals During NREM Sleep, Sleep, 22(1999).
21. Van Brunt, David L. Kenneth L. Lichstein, Sharon L. Noe, R.N. Aguillard and Kristin W. Lester, Intensity Pattern Of Snoring Sounds As A Predictor For Sleep-Disordered Breathing, Sleep, 20(1997).
22. Kryger, Meir H., Is Snoring a Killer? , Sleep, 19(1996)
23. Janszky, Imre MD, PhD[1,2]; Rickard Ljung, MD, MPH, PhD[1,3]; Morteza Rohani, MD[4]; Johan Hallqvist, MD PhD, Heavy Snoring Is a Risk Factor for Case Fatality and Poor Short-Term Prognosis after a First Acute Myocardial Infarction, Sleep, 31(2008).
24. Tan, Michael MA, MSc[1]; Carlo Marra, PharmD, PhD[1], The Cost of Sleep Disorders: No Snoring Matter, Sleep, 29(2006)

25. O'Connor, George T. MD, MS; Bonnie K. Lind, MS; Elisa T. Lee, PhD; F. Javier Nieto, MD, PhD; Susan Redline, MD, MPH; Jonathan M. Samet, MD, MS; Lori L, Variation in Symptoms of Sleep-Disordered Breathing with Race and Ethnicity: The Sleep Heart Health Study, Sleep, 26(2003).
26. Berg, Soren †Susan Nash, †Philip Cole and †Victor Hoffstein, Arousals and Nocturnal Respiration in Symptomatic Snorers and Nonsnorers, Sleep, 20(1997).
27. Leineweber, Constanze MSc[1]; Göran Kecklund, PhD[2]; Imre Janszky, MD[1]; Torbjörn Åkerstedt, PhD[2]; Kristina Or, Snoring and Progression of Coronary Artery Disease: The Stockholm Female Coronary Angiography Study, Sleep, 27(2004).
28. Kapuniai, Linda E, *David J. Andrew, *‡David H. Crowell and *§James W. Pearce, Identifying Sleep Apnea From Self-Reports, Sleep, 11(1988).
29. Han[1] Fang [,2], Erzhang Chen[1], Hailing Wei[1], Xiaosong Dong, Quanying He[1], Dongjie Ding[1], Kingman P, Childhood Narcolepsy in North China, Sleep, 24(2001).
30. Whitney, Coralyn W. [1] Paul L. Enright, [2] Anne B. Newman, [3] William Bonekat, [4] Dan Foley, [5] Stuart F, Correlates Of Daytime Sleepiness in 4578 Elderly Persons: The Cardiovascular Health Study, Sleep, 21(1998).
31. Erman, Milton, Stewart, D., Einhorn, D., Gordon, N., and E. Casal, Validation of the ApneaLink for the Screening of Sleep Apnea: a Novel and Simple Single-Channel Recording Device, Journal of Clinical Sleep Medicine, 3 (4), 2007