Laryngoscope Investigative Otolaryngology

Hypoglossal Nerve Stimulator Implantation in a Non-Academic Setting: Two-Year Result

Brian Weeks, MD; Gao Bao, MD; Tina M. Gilbert, RPSGT, RST; Larry Emdur, DO, PhD

Objectives/Hypothesis: Upper Airway Stimulation (UAS) is an FDA approved treatment option for patients with moderate-to-severe obstructive sleep apnea (OSA) who could not adhere to continuous positive airway pressure (CPAP). Previous studies have shown UAS reduced apnea-hypopnea index (AHI) in controlled clinical trials and from academic institutions. We report patient outcomes and therapy adherence of UAS in a non-academic hospital and clinic setting.

Study Design: Case series of consecutive patients.

Methods: Consecutive implants completed at a community hospital between January 2015 to Feb 2017 are included in this report. All patients underwent baseline polysomnography (PSG) recording and drug-induced sleep endoscopy (DISE) prior to the implant. All patients had returned for standard post-implantation titration PSG at a community sleep clinic to validate and adjust the stimulation setting for optimal response. Results were in mean ± SD, and pre- and post-implant data were compared using a paired student t-test.

Results: A total 22 patients undergoing UAS implant were overweight (BMI of 28.9 ± 5.0 kg/m2) and middle aged (63.2 ± 11.1 years), and had severe OSA (AHI of 35.9 ± 19.1). The AHI from the entire night of the titration study was 16.0 ± 10.4 ($P < .01$, compared with baseline), and the treatment AHI from the sleep period when the optimal setting was programmed was 1.2 ± 1.1 ($P < .001$, compared with baseline), and 90% patients had titrated AHI less than 5. The lowest SpO2 increased from 81% ± 8% at baseline to 91% ± 3% at the titrated setting ($P = .001$). After an average follow up of 95 ± 28.5 days, the therapy use per night was 7.0 ± 1.9 hours per night. The average postoperative ESS was 6.7 ± 5.3 of 18 patients, a reduction from the baseline of 10.9 ± 4.8. A total of 13 of 18 patients with postoperative ESS < 10, a measure indicated normalization of daytime sleepiness.

Conclusion: Patients who elected to receive UAS implant surgery at a non-academic hospital and followed at a sleep clinic showed significant reduction in OSA severity with strong adherence to treatment. These results supported that UAS as a valid treatment option for OSA can be successfully implemented in the non-academic hospital and clinic settings.

Key Words: Hypoglossal nerve stimulation, obstructive sleep apnea, surgery.

Level of Evidence: 4

INTRODUCTION

Obstructive Sleep Apnea (OSA) is recognized as the most common disease of sleep disorder breathing affecting 10% to 17% of males and 3% to 9% females with an apnea-hypopnea index (AHI) of greater than 15 events per hour.[1,2] Symptoms include morning headaches, fatigue, daytime somnolence, difficulty concentrating, and restless sleep. Patients often complain of waking up gasping for air and or dreaming of drowning. Bed partners often complain that the patient is a loud snorer or restless sleeper.[3–5]

OSA is defined as someone having greater than 5 to 15 hypopneas/apneas (AHI) per hour (mild disease), 15 to 30 hypopneas/apneas per hour (moderate disease), and greater than 30 hypopneas/apneas per hour (severe disease).[6] OSA is associated with many comorbid conditions including type II diabetes, nonalcoholic fatty liver disease, hypertension, coronary artery disease, and increased mortality.[7–11]

There are multiple surgical treatments for OSA including tongue base reduction via radiofrequency ablation therapy, hyoid resuspension procedures, uvulopalatopharyngoplasty (UPPP), uvulectomy, septoplasty, mandibular advancement procedures, and upper airway stimulation therapy (UAS).[12,13] A recent study comparing UPPP to UAS showed that UAS is actually a more effective treatment than UPPP with better outcomes.[14] Noninvasive treatments for OSA include weight loss therapy, oral appliances, upper airway strengthening exercises, oral appliances, body positioning devices, nasal EPAP, nasal insufflation, medications, and the gold standard of therapy, positive airway pressure (PAP).[15]

The problem with PAP therapy is one of adherence. Patients self-report adherence rates of only 60%. This is

From the Department of Otolaryngology (B.W.), SENTA Clinic, San Diego, California, U.S.A.; American Sleep Medicine (G.B., T.M.G.), San Diego, California, U.S.A.; and the Department of Pulmonary (L.E.), Alvarado Hospital, San Diego, California, U.S.A.

Editor's Note: This Manuscript was accepted for publication 23 April 2018.

Conflict of Interest: TMG and LE received lecture honorarium from Inspire Medical Systems. No conflict of interests to declare from others authors. This study is not sponsored by Inspire Medical Systems.

Send correspondence to Larry Emdur, DO, PhD, Department of Pulmonary, Alvarado Hospital, San Diego, CA 92120. Email: lemdur@gmail.com

DOI: 10.1002/lio2.176

defined as greater than 4 hours per night for 5 nights per week usage. Objective measurement of PAP usage is as low as 34% with a range of 34% to 83%.[16,17] This poor patient adherence may explain why there was no improvement in cardiac events for congestive heart failure patients (CHF) treated with CPAP therapy compared to sham controls.[18] Adherence in that study was only 3.3 hours per night. A treatment that has better adherence could possibly show a reduction in cardiac events.

The STAR trial describes the successful treatment of OSA with UAS at multiple academic settings using the hypoglossal nerve stimulator (HNS).[13,19] AHI decrease from baseline of 29.3 to 6.2 at 3 years. FOSQ scores increased from 14.6 to 18.8, ESS dropped from 11.0 to 6.0. 81% patients reported nightly therapy use after three years.[19]

This paper describes the patient outcome and objective measures of adherence from one dedicated sleep specialist team comprised of a sleep physician, sleep technician, and surgeon over a two-year period with all procedures performed in one non-academic hospital setting.

METHODS

This study was designed as a retrospective case series with medical record review of consecutive patients who underwent implantation at a single institution by a single surgeon (B.W.) between January 2015 and February 2017.

Patients were selected for UAS implantation as a part of routine clinical practice based on selection criteria established in previous studies.[13] Qualified patients all had a history of moderate to severe OSA from the most recent polysomnography or home sleep apnea report. All patients were unable to adhere to PAP. Most qualified patients had a BMI $\leq$ 32 kg/m2. For patients with a higher BMI, we discussed that previous clinical studies have not included BMI $>$ 32 kg/m2. All candidates for implantation underwent drug-induced sedated endoscopy (DISE) to evaluate the site and pattern of collapse. Patients with a primary pattern of complete concentric collapse at the level of soft palate were disqualified. These patients were offered other forms of medical or surgical OSA treatment.

The Inspire UAS system (Inspire Medical Systems, Minneapolis, MN) was implanted in accordance with standardized surgical techniques[20] and recent updates,[21] which was a part of the Inspire surgical training program. All implantation procedure was performed as outpatient surgery at a single community hospital.

All patients were discharged with over-the-counter pain medication as needed for incisional discomfort in the immediate postoperative period. Clinical follow-up after device implantation included a wound check within one to two weeks, device activation and initiation of therapy one month after implantation. After one month of home use for acclimation, all patients completed a follow-up clinical assessment and polysomnography testing and device adjustment if needed two to six month after implantation.

Data collection from the chart review included demographic information, history of OSA treatment and procedure and therapy-related complications. Epworth sleepiness scale (ESS) were collected at the postoperative visit from all patients and those available at preoperative visits. Sleep study data include AHI from the most recent in-lab PSG study report. Postoperative study report included AHI and lowest oxygen saturation. The objective therapy adherence was registered by the implanted device and available through device interrogation.

TABLE I.
Preoperative Characteristics

Characteristics N = 22	Value
Age, yrs	63.2 ± 11.1
Sex, male vs. female ratio	17/5
Race (White/Hispanic/Other)	19/2/1
BMI, kg/m2	28.9 ± 5.0

Results are in mean ± SD.
BMI = body mass index; SD = standard deviation

RESULTS

Twenty-two patients underwent UAS implantation between January 2015 and January 2017. All patients had a history of nonadherent use of CPAP. Among the 22 patients, 10 patients had previous soft tissue surgeries for OSA, including uvulopalatopharyngoplasty or uvulectomy. One patient received maxillary mandibular advancement. See Table I for a summary of baseline characteristics.

All implantations were completed without complication. One patient had a seroma that required drainage without sequalae. The average operating room time from incision to closure was 171 ± 40 minutes. The mean surgical time reduced from the first ten cases (January–December 2015) of 191 ± 47 minutes to the most recent eleven cases (January 2016–January 2017) of 155 ± 25 minutes ($P = .03$).

Mean postoperative sleep laboratory testing was completed 95.0 ± 28.5 days, ranged from 56 to 141 days post-implantation. The baseline AHI was 35.9 ± 19.1 prior to UAS implantation. Of the 21 patients completed the titration sleep study (one patient did not complete the titration at the time of the study data collection), mean AHI during the entire study was 16.0 ± 10.4 ($P < .001$ vs. baseline). Once the optimal programming settings were determined, the average AHI of the remaining time of sleep was 1.2 ± 1.8 ($P < .001$ vs. baseline), and 90% patients had titrated AHI less than 5. The lowest SpO2 improved from 81% ± 8% at baseline to 91% ± 3% at the titrated setting ($P = .001$).

The average postoperative ESS was 6.7 ± 5.3 of 18 patients, a reduction from the baseline of 10.9 ± 4.8. A total of 13 of 18 patients with postoperative ESS $<$ 10, a measure indicated normalization of daytime sleepiness. After an average of 95 days of follow-up, the mean therapy use was 7.0 ± 1.9 hours per night (n = 18).

Patients with a history of previous OSA surgery had similar demographics and similar improvements in their AHI compared to patients without previous OSA surgery.

DISCUSSION

In this study, OSA patients were screened and implanted with the UAS between January 2015 and

TABLE II.
Comparison Between Patients With or Without Previous OSA Surgery

	Age (years)	BMI (kg/m^2)	Baseline AHI (events/hour)	Treatment-total AHI (events/hour)	Treatment-titrated AHI (events/hour)	*P*-value titrated AHI vs. baseline
Without previous OSA Surgery (n = 11)	65.4 ± 9.0	30.0 ± 5.5	36.4 ± 19.8	17.7 ± 11.0	0.8 ± 1.4	<.001
Previous OSA surgery (n = 10)	60.5 ± 13.3	27.5 ± 4.3	35.2 ± 19.2	14.1 ± 9.9	1.7 ± 2.2	<.001
Total (n = 21)	63.2 ± 11.1	28.9 ± 5.0	35.9 ± 19.1	16.0 ± 10.4	1.2 ± 1.8	<.001
P-value with vs. without previous OSA surgery	.31	.26	.89	.44	.30	

AHI = apnea-hypopnea index; BMI = body mass index; OSA = obstructive sleep apnea.

February 2017 using a dedicated sleep therapy team consisting of a sleep specialist, dedicated sleep technician, and surgeon in one non-academic hospital. The criteria for inclusion in this study were moderate to severe OSA, BMI < 32, no evidence of the concentric collapse of the velopharynx during a DISE, and a history of having failed CPAP therapy.

Statistical analysis compared data with paired t-test. Comparative groups consisted of patients who had previous surgery, no previous surgery, and all patients. The results demonstrated significant improvement of AHI from baseline at a *P* value less than .001 in all study groups. AHI at baseline was 35.9, 36.4, and 35.2 in the three groups, respectively decreasing to 16.0, 17.7, and 14.1 when the UAS was initially tuned on in one month. After optimum titration of the UAS, the AHI improved even further to 1.2, 0.8, and 1.7 for the patients with previous sleep surgeries, no previous surgeries, and the combined group, respectively. Implantation time decreased from 190 minutes to 160 minutes with experience. Epworth Sleepiness Scale decreased from 11.3 to 6.4 post-titration. Post-implantation nadir

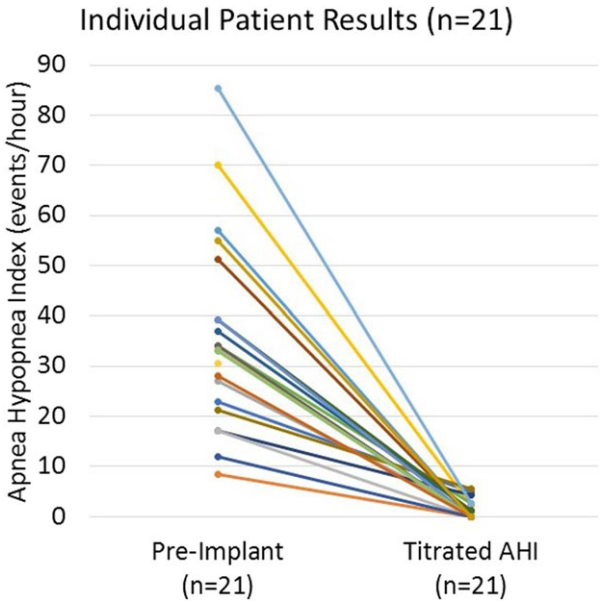

Fig. 1. Individual patient outcome measures of AHI. The pre-implant AHI was measured in the baseline screening sleep study. The post-implant AHI was measured during the postoperative titration sleep study at the optimal programming setting.
AHI = apnea-hypopnea index

O2 saturation increased to 91% ± 3% compared to the baseline value of 81 ± 8%. Adherence to treatment was an excellent 7.0 ± 1.9 hour, similar to what was seen in other post implantation study previously reported.[22,23]

The mechanism of action of the UAS is electrical stimulation of the genioglossus muscle causing the tongue to thrust forward. Multiple studies now indicate that the area of obstruction in OSA is at the level of the velopharynx and tongue base.[24,25] Studies demonstrate that the volume of the air column increases both anterior-posterior and laterally at the level of the palatelingual pharynx and anterior and posteriorly at the level of the velopharynx.[24]

Otolaryngologists have been involved in the care of OSA patients at variable levels, with surgical procedures often seeming like salvage or last option treatments. The introduction of UAS therapy provides the otolaryngologist with an effective surgical treatment for appropriate patients. Additionally, there is direct involvement in both the diagnostic (DISE) procedure as well as the definitive surgical intervention. This has greatly improved the satisfaction of treating these patients in the first author's practice experience. Additionally, many untreated OSA patients have pursued further evaluation due to these newer treatment options

The UAS improves sleep architecture without having to surgically change the anatomy of the upper airway. When the device is turned off, host anatomy and physiology returns to baseline. Patients have complete control over the therapy. This may explain the exceptionally high adherence rate, with average usage at 7 hours per night. Of note, is that the UAS therapy was a successful treatment in patients (10 out of 21) that had previous surgeries including mandibular advancement, uvulectomy, and UPPP. All of these procedures had permanently altered the host anatomy.

There are currently challenges with patient and physician awareness of the benefit of this type of this procedure. Other challenges include insurance company's reluctance to cover the operation. All patients implanted at our practice received coverage by their insurance companies. Currently, most patients need to obtain prior authorization for insurance coverage. The reality, however, is that all the patients in this study had excellent results without any significant complications. The procedure can be performed in non-academic centers with the appropriately trained team that can achieve 91% successful implantation resulting in 90%

adherence to the therapy. Outcomes such as these suggest that it is time to include UAS therapy as a standard first line therapy for moderate to severe OSA in PAP non-adherent patients.

BIBLIOGRAPHY

1. Young T, Paita M, Dempsey J, et al. Burden of sleep apnea: rationale, design, and major findings of the Wisconsin Sleep Cohort Study. *WMJ* 2009;108:246–249.
2. Peppard PE, Young T, Barnet JH, et al. Increased prevalence of sleep-disordered breathing in adults. *Am J Epidemiology* 2013;177:1006–1014.
3. John MW. Daytime sleepiness, snoring, and obstructive sleep apnea. The Epworth Sleepiness Scale. *Chest* 1993;103:30–36.
4. Hossain JL, Ahmed P, Reinish LW, et al. Subjective fatigue and subjective sleepiness: two independent consequences of sleep disorders? *J Sleep Res* 2005;14:245–253.
5. Chervin RD. Sleepiness, fatigue, tiredness, and lack of energy in obstructive sleep apnea. *Chest* 2000;118:372–379.
6. Kline LR, Collop N, Finlay G. Clinical Presentation and diagnosis of obstructive sleep apnea in adults. *UpToDate* 2017;1–26.
7. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and Type II diabetes a population-based study. *Am J Respir Crit Care Med* 2005;172:1590–1595
8. Musso G, Cassander M, Olivetti C, et al. Association of obstructive sleep apnea with the presence and severity of non-alcoholic fatty liver disease. A systematic review and meta analysis. *Obes Rev* 2013;14:417–431.
9. Bradley TD, Flores JS. Obstructive sleep apnea and its cardiovascular consequences. *Lancet* 2009;373:82–93.
10. Friedman O, Logan AG. The price of obstructive sleep apnea-hypopnea: hypertension and other ill effects. *Am J Hypertension* 2009;22:474–483.
11. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep disordered breathing and hypertension. *N Engl J Med* 2000;342:1378–1384.
12. Pushkanr M, Wilford L. Surgical management of obstructive sleep apnea. *Proc (Bayl Univ Med Cent)* 2000;13:338–342.
13. Strollo P, Ryan J Soose, Mauer JT, Nico de Vrie. *N Engl J Med* 2014;370: 139–149
14. Boon M, Hutley C, Chou D, Doghramji K. Comparing upper airway stimulation to uvulopalatopharyngoplasty: A single university experience. Poster Presentation. *Sleep* 2017;40(Suppl 1):A216.
15. Epstein LJ, Kristo D, Strollo PJ, et al. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med* 2009;5:263–276.
16. Platt AB, Field SH, Asch DA, et al. Neighborhood of residents is associated with daily adherence to CPAP therapy. *Sleep* 2009;32:799–806.
17. Weaver TE, Grunstein RR. Adherence to continuous positive airway pressure therapy: the challenge to effective treatment. *Proc Am Thorac Soc* 2008;5:173–178.
18. McEvoy RD, Antic NA, Heeley E, et al. CPAP for prevention of cardiovascular events in obstructive sleep apnea. *N Engl J Med* 2016;375:919–931.
19. Woodson BT, Soose RJ, Gillespie MB, et al; on behalf of STAR Trial Investigators. Three-year outcomes of cranial nerve stimulation for obstructive sleep apnea: the STAR trial. *Otolaryngol Head Neck Surg* 2016;154: 181–188.
20. Maurer JT, Van de Heyning PH, Lin HS, et al. Operative technique of upper airway stimulation: an implantable treatment of obstructive sleep apnea. *Oper Tech Otolaryngol Head Neck Surg* 2012;23:227–233.
21. Heiser C, Thaler E, Boon M, Soose, RJ, Woodson BT. Updates of operative techniques for upper airway stimulation. *Laryngoscope* 2016;126:S12–S16.
22. Kent DT, Lee JJ, Strollo PJ Jr, Soose RJ. Upper airway stimulation for OSA: early adherence and outcome results of one center. *Otolaryngol Head Neck Surg* 2016;155:188–193.
23. Heiser C, Knopf A, Bas M, Gahleitner C, Hofauer B. Selective upper airway stimulation for obstructive sleep apnea: a single center clinical experience. *Eur Arch Otorhinolaryngol* 2017;274:1727–1734.
24. Safiruddin F, Vanderveken OM, de Vries N, et al. Effect of upper-airway stimulation for obstructive sleep apnoea on airway dimensions. *Eur Respir J* 2015;45:129–138
25. Ong AA, Murphey AW, Nguyen SA, et al. Efficacy of upper airway stimulation on collapse patterns observed during drug-induced sedation endoscopy. *Otolaryngol Head Neck Surg* 2016;154:970–977.