Efficacy of Oral Appliance Therapy in Patients Following Uvulopalatopharyngoplasty Failure

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Objective: Uvulopalatopharyngoplasty (UPPP) is the most common surgical procedure performed to treat obstructive sleep apnea (OSA). This surgery, when performed alone, benefits only a minority of patients. This study was undertaken to determine the efficacy of oral appliance (OA) therapy following unsuccessful UPPP and assess for specific patient and polysomnographic characteristics that may identify those patients most likely to benefit from this combined treatment strategy.

Study Design: Retrospective of clinical outcomes in patients undergoing UPPP followed by treatment with an OA.

Methods: Polysomnographic results (baseline, status post-UPPP, and status post-UPPP with oral appliance use), age, gender, race, and body mass index were subjected to statistical analysis.

Results: The mean apnea hypopnea index (AHI) decreased from 23.6 at baseline to 8.6 following UPPP and oral appliance therapy. The mean O2 nadir increased from 83% at baseline to 89.9% following UPPP and treatment with an oral appliance. Fifty percent of patients (9/18) achieved an AHI <5 and were deemed “cured” of their disease. Seventy-three percent of patients (13/18) achieved benefit with an AHI <20 and ≥50% reduction in their baseline AHI, deemed “successful therapy.” No statistically relevant demographic or polysomnographic differences were found between those who were “cured” and those with persistent disease with the exception that the O2 nadir status post UPPP was found to be lower in the “cured” group.

Conclusion: Oral appliance therapy is an effective treatment option for the majority of patients who have persistent obstructive sleep apnea following unsuccessful UPPP.

Key Words: Obstructive sleep apnea, uvulopalatopharyngoplasty, oral appliance therapy.

Level of Evidence: 4

INTRODUCTION

Obstructive sleep apnea (OSA) is a common disorder, with an estimated prevalence of approximately 4% in men and 2% in women and may be much higher in middle aged men, postmenopausal women, and the elderly. Untreated OSA is associated with excessive daytime sleepiness, decreased quality of life, cognitive impairment, cardiovascular sequelae, and increased mortality. Continuous positive airway pressure (CPAP) is the gold standard treatment for OSA as it is the most likely treatment to yield an AHI <5 when used on a nightly basis. However, acceptance and adherence to CPAP treatment pose major clinical challenges for many patients. Poor compliance with CPAP may decrease the effectiveness of this treatment and other non-CPAP modalities may result in a lower effective AHI when taking into account actual patterns of CPAP use.

Other treatment options for OSA include surgical therapy and use of an oral appliance. Although use of an oral appliance can be highly effective, it is still considered to be a compliance-based therapy requiring a change in patient behavior and many patients opt for surgical treatment instead.

Despite increasing evidence that the majority of patients with OSA have multilevel obstruction, uvulopalatopharyngoplasty (UPPP) remains the most common surgical procedure performed to treat OSA with an overall success rate of approximately 40% in unselected patients. Oral appliance (OA) therapy has become an increasingly common non-surgical treatment for CPAP-intolerant patients, but it has rarely been evaluated in patients with persistent OSA following unsuccessful UPPP. This study was undertaken to determine the efficacy of OA following unsuccessful UPPP and attempt to define specific polysomnographic (PSG) and patient characteristics that may help identify those individuals most likely to benefit from use of an OA after UPPP.

METHODS

The medical records of patients having persistent OSA following UPPP and were subsequently treated with an OA were retrospectively reviewed. OSA was defined as an overall apnea hypopnea index (AHI) of 5 or more events per hour. Patients were eligible for inclusion if they had polysomnographic data at baseline, status post-UPPP, and status post-UPPP with use of an OA. Postoperative PSG was usually obtained between 4 and 6 months following surgery.
PSG following oral appliance therapy was obtained once final adjustments were made by the supervising dentist. Patients were excluded if PSG data from any of the three time periods was unavailable. All study patients attended a multidisciplinary Alternatives to CPAP Clinic at the University of Michigan between December 1997 and October 2015. The Alternatives to CPAP Clinic in which the patients were treated was established to serve those intolerant of CPAP who were highly motivated to seek non-CPAP therapy. This clinic included evaluations by a sleep medicine physician, otolaryngology–head and neck surgeon, oral maxillofacial surgeon, and dentist board certified by the American Board of Dental Sleep Medicine (as of 2004). All patients in this study received their oral appliance from the same dentist via this clinic, whereas UPPP was performed by more than one otolaryngologist. This study was approved by the University of Michigan Institutional Review Board (HUM 00108735).

Demographic information including age, gender, race, and body mass index (BMI) was obtained. Outcomes following UPPP and OA therapy were classified as either: “cured,” defined as an AHI <5 or as “successful therapy,” defined as an AHI <20 and a ≥50% reduction in the pretreatment AHI in order to compare the current study’s results to historical otolaryngologic surgery reports utilizing this definition.5 The term “cured” is used to describe resolution of obstructive events with use of OA therapy. The oral appliance used for patients included in this study was a Thornton Adjustable Positioner at the discretion of the dental provider. Contraindications to OA use included less than nine teeth in each of the upper and lower jaws; discomfort protruding the lower jaw forward greater than 5 mm; discomfort in opening the jaw less than 33 mm; evidence of temporomandibular joint abnormality or chronic joint pain; occlusal wear (>20%) of the clinical crown indicative of severe bruxism; and significant periodontal disease defined as greater than 50% bone loss around the teeth and/or tooth mobility.

Statistical analyses were carried out using SPSS version 24.0 for Windows (IBM Corp.). Characteristics of patients deemed “cured” and those with “successful therapy” were compared to patients with persistent OSA. One-way analysis of variance (ANOVA) was conducted for repeated measures in order to analyze the change in PSG parameters. Unpaired t-tests were used to compare continuous variables (age, BMI, AHI, and SpO2 measures) and chi-square was used to compare dichotomous data (gender and race) between groups. Logistic regression was performed to predict “successful therapy” and “cure” as previously defined.

RESULTS
Between December 1997 and October 2015, 1739 patients were evaluated in the Alternatives to CPAP Clinic. Of these, 417 underwent surgery inclusive of UPPP. Two hundred and fifty-one patients underwent UPPP only. Surgical “success,” as previously defined, was achieved in 151 (60%) of these patients.

Three hundred patients were referred for oral appliance therapy. Twenty-two of those patients had undergone previous UPPP. Eighteen patients following unsuccessful UPPP and subsequently treated with an OA with complete polysomnographic results were identified for study. The majority were male and Caucasian. Demographics are shown in Table I.

| TABLE I. Demographic Data. |
|-----------------------------|
| Gender                      | 83% Male (n = 15) |
| Race                        | 78% Caucasian (n = 14) |
| Mean age (years)            | 47.0 ± 11.7 (range 22.5–71.8) |
| BMI (kg/m²)                 | 30.4 ± 4.2 (range 22.8–30.4) |
| Baseline AHI                | 23.6 ± 17.4 (range 7.7–80.0) |
| Baseline O2 nadir           | 83.3% ± 6.1 (range 70.0–91.0) |
| Post-UP3 AHI                | 21.4 ± 14.3 (range 3.3–81.6) |
| Post-UP3 O2 nadir           | 84.9% ± 8.1 (range 60–98) |

BMI = Body Mass Index; AHI = Apnea Hypopnea Index; O2 = Oxygen Saturation; UP3 = Uvulopalatopharyngoplasty.
Successful therapy was defined as a $50\%$ reduction in AHI or $<20$ and $>50\%$ reduction from baseline AHI.

The mean AHI decreased from 23.6 at baseline to 21.4 following UPPP. The mean AHI further decreased from 21.4 to 8.6 following oral appliance therapy (Fig. 1). The mean O2 nadir increased from 83.0 at baseline to 84.9 following UPPP and further increased to 89.9 following oral appliance therapy (Fig. 2).

Seventy-three percent of patients (13/18) achieved benefit with an AHI $<20$ and $50\%$ reduction in their baseline AHI. Fifty percent of patients (9/18) achieved an AHI $<5$ and were deemed “cured” of their disease. No statistically relevant demographic differences existed between those who had persistent disease compared to those who were either “successfully” treated or “cured” (Tables II and III).

The baseline AHI was higher in those who achieved an AHI $<20$ and $50\%$ reduction in AHI, but this difference was not found to reach statistical significance. In a logistic regression, after accounting age, gender, race, BMI and post-UPPP O2 nadir, the baseline AHI did not predict a successful outcome with the use of an oral appliance. In addition, the AHI and O2 nadir following UPPP, taking into account age, gender, race, BMI did not predict “successful therapy” with an oral appliance.

For those patients who were deemed “cured” versus those who were not, the post-UPPP O2 nadir was found to be significantly lower. No other polysomnographic parameters or patient characteristics were found to be significantly different between the two groups (Table III).

### DISCUSSION

In this study, nearly three quarters of patients benefited from the use of an oral appliance following unsuccessful UPPP and half were cured of their disease. Although the sample size was small, the present series is the largest report to date on the effectiveness of OA use following UPPP. Millman and colleagues in 1998 published the only other study on the use of OA following unsuccessful UPPP in which similar results to the current study were described with an overall response rate (AHI $<20$ and a $>50\%$ reduction in AHI) of $66\%$.6

Historically, surgical treatment for OSA focused on single site surgery of the oropharynx. The UPPP procedure, with or without tonsillectomy, has been the mainstay of surgical therapy following its introduction in the early 1980s. UPPP was designed to alleviate retropalatal collapse in patients with OSA, and has been modified to include the uvulopalatal flap, Z-palatopharyngoplasty and expansion pharyngoplasty in an attempt to improve success rates and prevent postoperative complications.7 In addition, better patient selection utilizing the Friedman staging system has led to improved patient selection and success rates.8 However, despite these improvements, isolated palatal surgery fails to address a potential retroglossal site of obstruction present in many patients with OSA.9–11

Data from the 2006 Nationwide Inpatient Sample, State Ambulatory Surgery Database and State Inpatient Database revealed that of the 35,263 outpatient and inpatient operations performed for the treatment of OSA, more than 75% were limited to isolated palatal procedures, and only 19% involved hypopharyngeal procedures (eg, mandibulotomy with genioglossus muscle advancement, lingual tonsillectomy, hystoid suspension, etc.).12 Failure to perform multilevel surgery may be attributable to lack of training in hypopharyngeal surgery. A recent survey of 103 accredited Otolaryngology residency program directors in the United States revealed high rates of resident surgical competency in oropharyngeal procedures (100% for UPPP) and lesser competency in hypopharyngeal procedures.13 Practice patterns among practicing surgeons self-identified as having a special interest in sleep medicine revealed that only 39% believed their residency training in OSA surgery was of high quality and greater than 40% reported receiving limited training in hypopharyngeal procedures, with the exception of radiofrequency tongue ablation.14

During the past two decades, there has been increased awareness of multilevel obstruction in patients with OSA. In part, this was in response to the fact that non-responders to isolated palatal surgery were frequently found to have additional sites of obstruction, usually at the level of the hypopharynx. Fujita was the first to describe anatomic levels of obstruction in patients with OSA and subsequently created a formal classification system.15 The vast majority of patients were classified as having both oropharyngeal

### TABLE II.
Demographic Data of OSA Participants Subjected to UPPP followed by OA Therapy.

|                | Successful Therapy* | Therapeutic Failure | P-value |
|----------------|---------------------|---------------------|---------|
| Total          | 73% (n = 13)        | 27% (n = 5)         |         |
| Gender (male)  | 77% (n = 10)        | 80% (n = 4)         | 1       |
| Race (Caucasian) | 77% (n = 10)      | 80% (n = 4)         | 1       |
| Mean age (years) | 45.6 ± 12.8      | 50.8 ± 8.1          | .33     |
| BMI (kg/m²)   | 30.8 ± 4.8          | 29.4 ± 2.1          | .39     |
| Baseline AHI  | 26.8 ± 19.2         | 15.2 ± 8.4          | .09     |
| Baseline O2 nadir | 84.0 ± 5.9      | 81.4 ± 6.7          | .47     |
| Post-UPP3 AHI | 20.3 ± 15.4         | 24.4 ± 12.2         | .57     |
| Post-UPP3 O2 Nadir | 84.8 ± 9.3      | 85.4 ± 3.9          | .84     |

*Successful therapy defined as AHI $<20$ and $>50\%$ reduction from baseline AHI.

### TABLE III.
Demographic Data of OSA Participants Subjected to UPPP followed by OA Therapy.

|                | Cured* | Non-cured | P-value |
|----------------|--------|-----------|---------|
| Total          | 50% (n = 9) | 50% (n = 9) |         |
| Gender (male)  | 89% (n = 8) | 78% (n = 7) | 1       |
| Race (Caucasian) | 78% (n = 7) | 78% (n = 7) | 1       |
| Mean Age (years) | 48.9 ± 14.6 | 45.2 ± 8.4 | .53     |
| BMI (kg/m²)   | 29.5 ± 3.8          | 31.4 ± 4.6        | .37     |
| Baseline AHI  | 19 ± 8.5           | 28.1 ± 23.0       | .29     |
| Baseline O2 nadir | 83.1 ± 6.4      | 83.4 ± 6.1        | .91     |
| Post-UPP3 AHI | 24.3 ± 7.4         | 18.6 ± 19.1       | .43     |
| Post-UPP3 O2 Nadir | 81.2 ± 9.2      | 88.7 ± 4.7        | .05     |

*Cured defined as AHI $<5$. 

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and hypopharyngeal sites of collapse. Other studies have similarly reported that the majority of patients with OSA have multilevel obstruction.5,9–11

There are numerous reports documenting the beneficial outcome of multilevel surgery for OSA. In one of the largest reported case series, Riley and colleagues reported an overall success rate of 61% in 306 consecutive patients undergoing phase I surgery (ie, non-maxillomandibular advancement) inclusive of multilevel procedures. Success rates were higher in those with mild and moderate OSA, at 71% and 78%, respectively.10 A more recent meta-analysis of nearly 2000 patients who underwent multilevel surgery reported an overall success rate of 66%, similar to that achieved in the current study combining UPPP and OA therapy.5 The option of OA following unsuccessful UPPP may be of greatest utility to surgeons capable of performing UPPP but without experience in additional hypopharyngeal procedures, but may also be important to more experienced sleep surgeons when considering further treatment following failed UPPP, especially for patients hesitant to undergo additional surgery. Treatment with an OA works by advancing and stabilizing the mandible and genioglossus muscle anteriorly thereby increasing the retroglossal airway. It also leads to an increase in the retroplatal area via mechanical coupling of the palatoglossus muscle and intrinsic tongue musculature.16 Adherence rates for OA use are typically high and have been reported to be better than those with CPAP use.17 Side effects requiring discontinuation of OA use such as occlusal changes and temporomandibular joint inflammation can be minimized with close follow up by a qualified dentist.

The 2015 clinical practice guidelines for the treatment of OSA with oral appliance therapy recommended that physicians consider prescription of an OA for adult patients who are intolerant of CPAP therapy or prefer an alternate therapy.18 This systematic review found that OAs significantly reduce the AHI and increase the oxygen saturation nadir across all levels of OSA severity. In addition, OA use was found to reduce daytime sleepiness and improve disease specific quality of life measures. As found in the current study, no specific patient characteristics, including age, gender, BMI, and cephalometric measurements were identified in this meta-analysis to predict successful treatment.18 Similar findings were observed in the current study with a decrease in AHI from 21.4 to 8.6 and increase in oxygen saturation nadir from 84.9 to 89.9 with the use of an oral appliance following unsuccessful UPPP. Of course, it cannot be determined if similar results would have been achieved with the use of oral appliance alone, since this patient population decided to pursue surgical treatment (UPPP) of their OSA prior to additional treatment with OA. Despite well documented improvement in disease severity and high compliance rates with OA therapy, some patients still prefer surgical treatment and its potential to be a single, discrete intervention as opposed to an alternative compliance-based therapy like OA.

Until recently, predicting the effectiveness of OA therapy prior to use was not feasible. However, in 2013, Remmers and colleagues examined the predictive potential of a remote controlled mandibular positioning device (MATRx, Zephyr Sleep Technologies Inc., Calgary, Alberta, Canada).19 During a titration polysomnogram, a remotely controlled mandibular positioner was attached to disposable dental trays fitted to the patient’s dentition with impression material. Among the study’s 67 patients in this prospective, blinded outcome study, success with use of an OA (defined as AHI <10) was predicted in 32 subjects. Of the 32 patients who were predicted to benefit from OA use, 30 (94%) went on to achieve an AHI <10 with traditional OA use as confirmed by subsequent polysomnography. Patients who were predicted to not benefit with OA treatment failed to reach an AHI <10 in 83% of cases with subsequent traditional OA use. The model’s sensitivity, specificity, positive predictive value, and negative predictive value were 86%, 92%, 94%, and 83%, respectively. The use of an OA pretreatment titration study prior to prescribing OA therapy is currently available at only a few sleep centers around the country. It has only recently been implemented at the authors’ institution, and was not available to patients included in this study.

Despite reviewing data collected over an 18-year period from a clinic specifically created to treat CPAP-intolerant patients, limitations of the current study include its relatively small sample size. This may be, in part, due to limited interest or willingness of individuals following unsuccessful UPPP to undergo further treatment without any further guarantee of success. This reticence may be compounded by the expense of an OA, which may be only partially covered by medical or dental insurance. Another limitation is that some otherwise qualified patients could not be included due to lack of PSG data prior to or following each intervention. Missing or incomplete information is an inherent problem with retrospective studies. In addition to limiting the sample size, it can lead to a no response bias in the results as subjects with missing information may systematically differ from the others. In addition, the majority of patients studied were male and Caucasian which limits the generalizability of the results. Finally, all study patients were selected from a group of highly motivated patients attending a multidisciplinary Alternatives to CPAP Clinic for patients intolerant of CPAP therapy, and as such may not be representative of the larger population of CPAP-intolerant patients. Nonetheless, despite these limitations, this report describes the largest cohort of patients treated with OA following unsuccessful UPPP.

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