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EDITORIALS

http://dx.doi.org/10.15331/jdsm.6740

And if You Believe That, I Have a Bridge to Sell You

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Calgary, Alberta, Canada

Dentists are being inundated with outrageous email and print claims regarding dental sleep medicine education. Examples of claims that have hit my inbox include:

"…join the members…producing over $70, 000 a month in oral appliances…"

"…reduce overhead…"

"…the only course that establishes the dentist as primary treatment providers…"

"…get started immediately after one weekend…"

And if you believe these claims, I have a bridge to sell you.

Dental sleep medicine (DSM) is a growing field and there are full time fellowship programs of one to two years emerging at a few dental schools. However the majority of dentists will get their training in DSM through post-dental school continuing education. There is good quality evidence-based education available for those interested in DSM. The courses offered by the American Academy of Dental Sleep Medicine are a leading example of quality, evidence based DSM education. This journal is also a source of evidence-based, peer-reviewed scientific information in DSM. There is no need to partake in educational offerings from questionable sources.

The practice of DSM has features that are uncommon in general dentistry. Although there are technical aspects, it is primarily intellectual work that cannot be done by a dentist working alone. Diagnosis, treatment and follow up of patients with sleep-disordered breathing is a collaborative, interdisciplinary activity. Collaboration with physicians is critical at diagnosis, treatment, follow-up, and—in some cases—years later if oral appliance therapy (OAT) is no longer effective and alternative or additional therapies need to be considered. Courses that aim to educate dentists and physicians together such as the 2018 Sleep Medicine Trends course will be an important component to future interdisciplinary team building.

DSM practitioners treat a chronic disease; this is not a field with "quick fix" treatments. Once you begin OAT the patient is your responsibility for years. Managing inevitable side effects, particularly occlusal changes, continues to be an important challenge in DSM. Despite these challenges, many dentists have found DSM to be a satisfying and rewarding addition to their practices. Many more are beginning to explore the field.

Don't be fooled by outrageous claims of pots of gold. Practicing quality DSM requires a considerable body of knowledge and training. There are good quality offerings out there. Don't cheat yourself—go for quality. Don't buy the bridge.

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ORIGINAL ARTICLES

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A Fully Digital Workflow and Device Manufacturing for Mandibular Repositioning Devices for the Treatment of Obstructive Sleep Apnea: A Feasibility Study

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Study Objectives: The objective of this study was to examine the feasibility and patient preference of mandibular repositioning devices (MRDs) made from (1) a fully digital workflow including patient scanning, bite registration, and device manufacturing using an open platform intraoral scanner (iTero; Align Technology Inc., San Jose, California, United States) and a computer aided design/computer aided manufacturing (CAD/CAM) MRD (MicrO_2 Sleep Appliance; ProSomnus Sleep Technologies, Pleasanton, California, United States), and (2) a conventional workflow using polyvinyl siloxane (PVS) impressions as the source of patient data. The fit accuracy and comfort level of devices from each workflow were compared. A method for capturing a digital scan using a stable open bite technique is tested for accuracy and ease of implementation.

Methods: This prospective feasibility study reports on selected patients (n = 5) recruited from a dental practice (ages 34 to 51 years; apnea-hypopnea index 1–32 events/h). Each patient received two MRDs. The first MRD was manufactured using a conventional workflow model (ie, PVS impressions, PVS bite registration, CAD/CAM of the MRD with quality control on physical stone models). The second MRD was manufactured using a digital workflow model (ie, digital intraoral scanning using an open platform intraoral scanner, digital open bite registration, and CAD/CAM of the MRD). All patients were then followed up using our standard clinical protocol set based on the American Academy of Dental Sleep Medicine guidelines. The dental fit (ie, the accuracy of the fit against the teeth), the occlusal fit (ie, the accuracy of the upper and lower splint fitting together), and the patient preference (ie, which appliance they preferred using) was recorded.

Results: In the conventional workflow 2 appliances required minor dental adjustments and 3 appliances required occlusal adjustments. In the digital workflow, no dental or occlusal adjustments were required. All patients preferred the digital MRDs in terms of comfort.

Conclusions: It is feasible to utilize a fully digital workflow for manufacturing of MRDs for treatment of obstructive sleep apnea with predictable outcomes. Devices from a full digital workflow are preferred by patients compared to the standard process. The full digital workflow using the CAD/CAM MRD required fewer adjustments and patient satisfaction with the device and the process could make for a better experience for the patient and the doctor. Follow-up studies are required using larger sample size and different intraoral scanners and MRDs.

Keywords: bite registration, device manufacturing, digital workflow, intraoral scanning, mandibular repositioning devices, obstructive sleep apnea, oral appliance therapy

Citation: Charkhandeh S, Kuhns D, Kim S. A fully digital workflow and device manufacturing for mandibular repositioning devices for the treatment of obstructive sleep apnea: a feasibility study. *Journal of Dental Sleep Medicine*. 2017;4(4):97–102.

INTRODUCTION

Obstructive sleep apnea (OSA) is a very common chronic disease with many adverse clinical consequences, affecting an estimated 10% to 20% of the United States population.[1,2] The condition remains undiagnosed in most of these patients, and studies show the percentage of undiagnosed OSA could be as high as 80% to 90%.[3,4] Untreated OSA is associated with higher risk of fatal cardiovascular and cerebrovascular events,[5-8] hence, the importance of long-term treatment of patients. Currently, the most commonly prescribed treatment for patients with OSA is continuous positive airway pressure (CPAP) therapy. Although this treatment is efficacious and relatively safe with minor side effects, patient adherence is low and many patients refuse to start CPAP treatment. It is reported that patient adherence to CPAP could be as low as 50%; therefore, an alternative therapy is required.[9,10] Based on published American Academy of Sleep Medicine guidelines, oral appliances are recommended as an alternative for patients with mild to moderate OSA and patients who cannot tolerate CPAP or are not adherent to the therapy.[11] There has been tremendous growth in this area of dentistry over the past decade and many patients are now seeking this treatment modality. It is estimated that approximately 200,000 appliances are being made every year in North America and by the year 2023 this number will reach over 1 million. Although the growth seems to be very fast, it is worth noting that currently fewer than 10% of patients who could respond to oral appliance therapy (OAT) receive a mandibular repositioning device (MRD).[12] Based on meta-analysis, 50% to 60% of all patients with OSA would respond to OAT,[11] but MRDs are only prescribed in 5% to 10% of all diagnosed patients.

The number of patients prescribed an MRD could increase because of many factors, such as the general public's raised

Table 1—Patient profiles.

Patient No.	Age, years	Sex, M/F	Baseline AHI, events/h	Follow-Up AHI, events/h	Height, m	Weight, kg	BMI, kg/m^2
1	51	M	32	8	1.78	109	34.4
2	34	M	1	1	1.88	93	26.3
3	35	M	3	2	1.85	90	26.3
4	34	M	5	2.2	1.88	92	26.0
5	40	M	28	4	1.75	86	28.1

AHI = apnea-hypopnea index, BMI = body mass index.

awareness of the importance of proper sleep, positive health outcomes associated with OAT, and prospective selection of patients who would respond to OAT.[12,13] Although this is great news in terms of growth in the field of dental sleep medicine, the number of patients will increase our current clinical workflow models and device manufacturing may not be able to keep up with the increased demand. Therefore, having more efficient workflow systems and device manufacturing become crucial in delivery of care.

The use of intraoral scanners for digital impressions of the teeth and a fully digital workflow system, including the device manufacturing, could be a way to more efficiently produce MRDs. The use of digital scanners in dentistry is expected to grow by 13.9% (compound annual growth rate) from 2015 to 2022.[14] Digital scanners have been used widely in the dental industry over the past decade and there seems to be a lot of inconsistent results in terms of being able to register the maxillomandibular occlusal relationship, when the teeth are not fully occluding (ie, "digital open bite registration"). This has been the main hurdle for many practitioners to make use of a fully digital workflow, and therefore, they still use a conventional "bite registration." This creates inefficiencies in the workflow, and it has the potential to introduce inaccuracies in device manufacturing. The difference in the degree of accuracy between conventional bite registration using polyvinyl siloxane (PVS) and digital bite registration could result in improper articulation of the models. An additional benefit of a fully digital manufacturing process is the reduced need for physical models.

If a reliable, fully digital workflow can be established, it could improve patient care by providing more efficient and accurate care to the patient. The objective of the current study was to examine the feasibility and patient preference of MRDs made from a fully digital workflow versus the conventional workflow.

METHODS AND RESULTS

Five patients were selected to participate in this feasibility study. The patients' characteristics and data are summarized in **Table 1**. They were all tested for sleep apnea using an at-home level 3 sleep recorder. The patients' baseline apnea-hypopnea indexes are summarized in **Table 1**. After the baseline sleep study, all patients received full orthodontic records (ie, upper and lower PVS impressions, intraoral/extraoral photographs, and cone beam computed tomography). Proper medical history, dental history, and consent forms were signed. All patients were also examined by a dentist to determine the suitability for an MRD.

Each patient went through both MRD manufacturing workflow models. They first went through the conventional workflow (**Figure 1**) using a George Gauge (Great Lakes Orthodontics, New York, United States) to obtain a PVS bite registration. All patients then went through the digital workflow model (**Figure 2**). The digital workflow started with taking upper and lower intraoral scans using the Ortho Software Module on the iTero scanner (Align Technology Inc., San Jose, California, United States). The bite registration was taken using the initial bite and protrusion level as a reference. In order to stabilize the bite at the protruded position and enabling a scan of the "maxillomandibular" relation, the dentist segmented each bite into 3 pieces, using a surgical blade and a heat torch. The blade was used to cut through the PVS material, to minimize the chipping of the material and distortion of the bite. The heat torch was used to enable cutting through the plastic fork of the George Gauge without creating any distortion in the bite (**Figure 2**). The bite was then stabilized by asking the patient to bite into 2 out of the 3 pieces for each bite scan. When scanning the left side, the anterior and the right segments were seated (**Figure 3**). When scanning the right side, the anterior and the left segments were seated in patients' mouths. This stabilization method was used to minimize the amount of distortion and inaccuracies in the bite registration by minimizing the possible cantilever effect and compression of retrodiscal tissue in the temporomandibular joint when no posterior support is present or there is movement of the mandible with respect to the maxilla. All scans were sent to the appliance manufacturer (ProSomnus Sleep Technologies, Pleasanton, California, United States).

Upon receipt by the manufacturer, each physical impression was poured and articulated with the bite. The bite was then inspected to ensure enough vertical gap (> 3 mm) to enable manufacture of the MicrO_2 Sleep Appliance (ProSomnus Sleep Technologies, Pleasanton, California, United States). A technician measured the vertical gap between the upper and lower arches, and determined if any anatomical features are closer to each other than the required specification of 3 mm as described in the manufacturing technical work instructions. This could be the vertical gap between 2 opposing cusps, for example. All technicians were trained to the same work instructions

Figure 1—PVS and digital patient data capture.

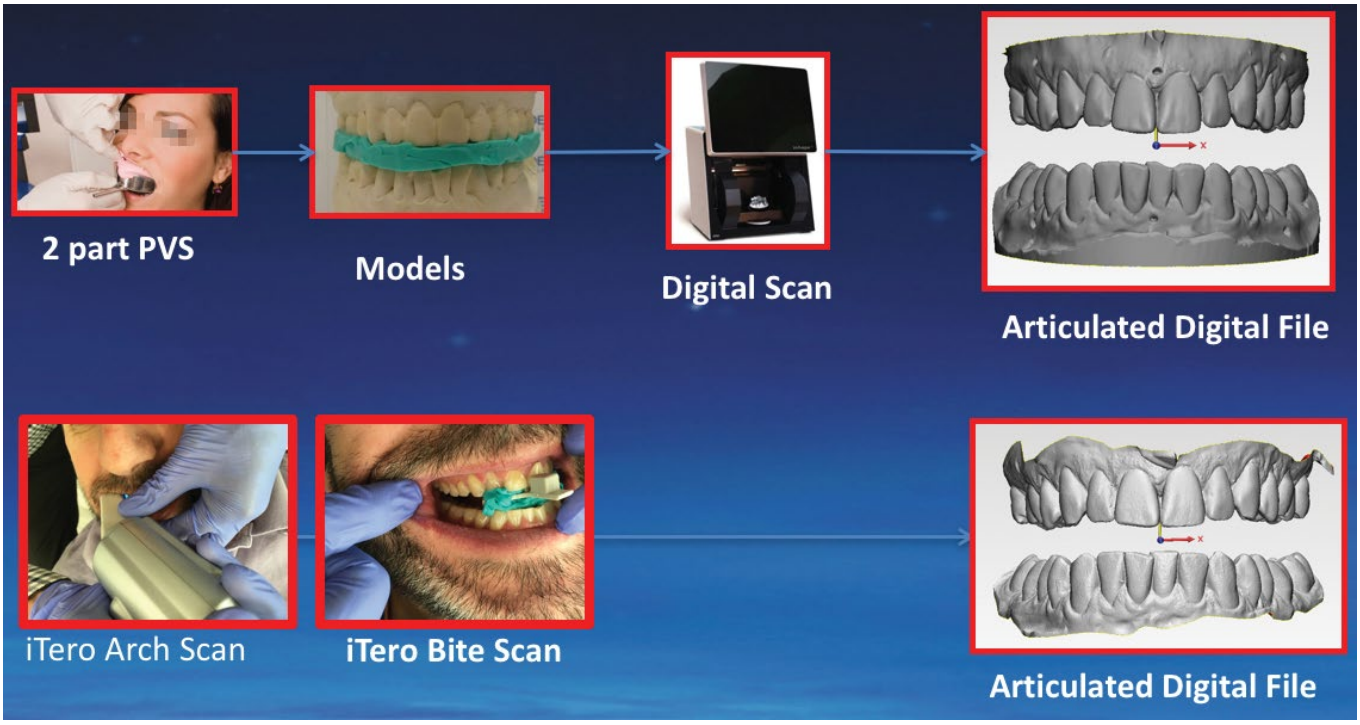
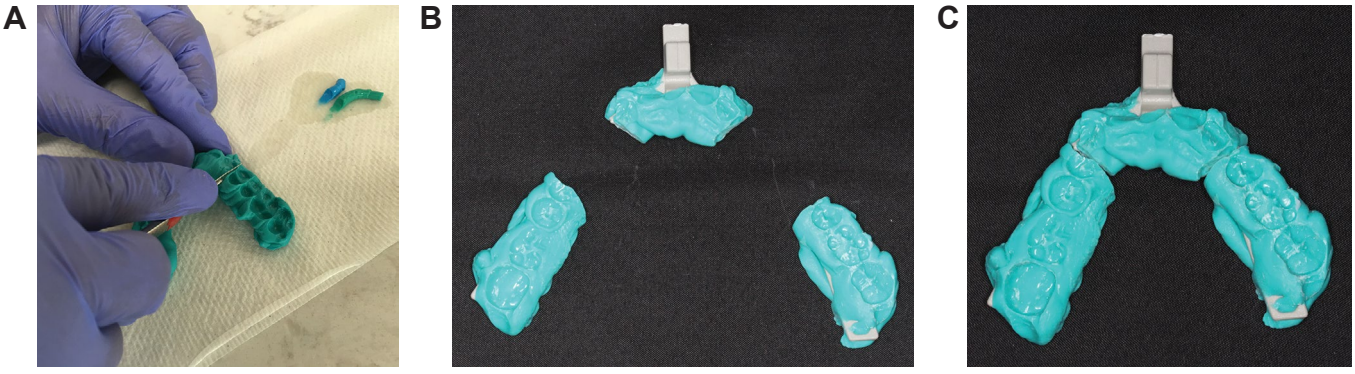


Figure 2—Bite preparation for digital scan.



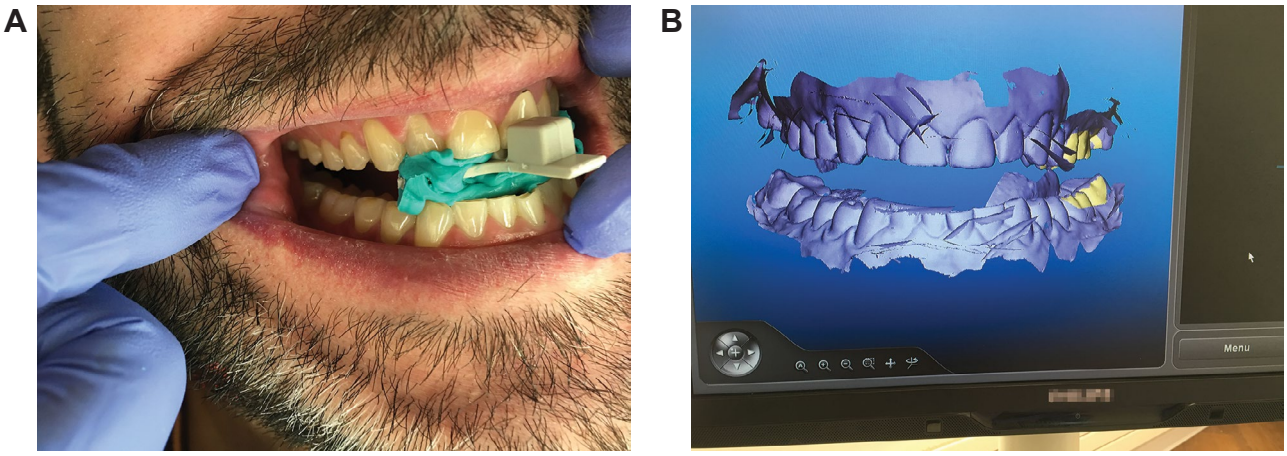
(A) Sectioning the bite-registration. **(B)** Three segments after sectioning. **(C)** Check for any distortion.

and specifications. If the specification was not met, the data would be reviewed by quality personnel to determine if a new bite would be required. The models were scanned separately and together with the bite and the files were imported into the design software. Digital arches and bites were received through the vendor's portal and imported into the design software. Once uploaded, the quality of the scans and bites were inspected digitally. The scan quality specification included evaluating that the digital mesh represents the physical model without holes in the mesh or missing data that would prohibit the manufacture of the device.

To complete the comparison of the physical impressions and digital impressions, both were loaded into the design software and set in place using the same coordinate system. With the models layered (**Figure 4**), a color map was generated showing the distance difference between each surface point for the 2 files. **Figure 4** shows the upper arch overlay on the left and the lower arch overlay on the right, both with a scale of ± 150 microns. The gray reference portions of the overlay represent the scans of the poured impressions; the colorized map shows the delta intersection of the layered digital scan, with red above the reference surface and blue below the reference surface. The green areas describe areas of agreement between the scanned stone model and the iTero scan directly from the patient. However, many areas of deviation are denoted by blues and reds in the 2 images.

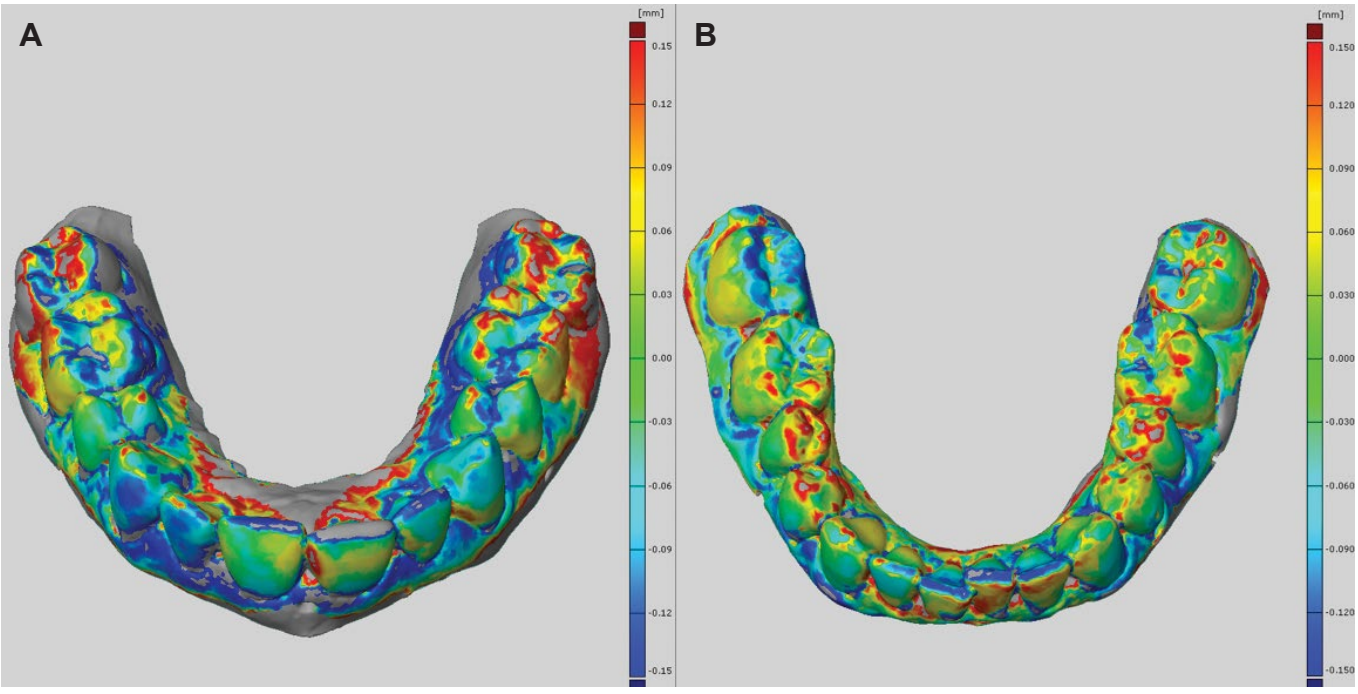
Each patient then received both appliances and wore each appliance for 3 weeks. The dentist also recorded the amount of adjustment needed for each device in terms of adjustment made to the inside surface (to fit the teeth) and adjustment

Figure 3—Bite set for iTero Scan.



(A) Placing sectioned bite registration. **(B)** Digital bite registration.

Figure 4—Overlay of impression and digital data.



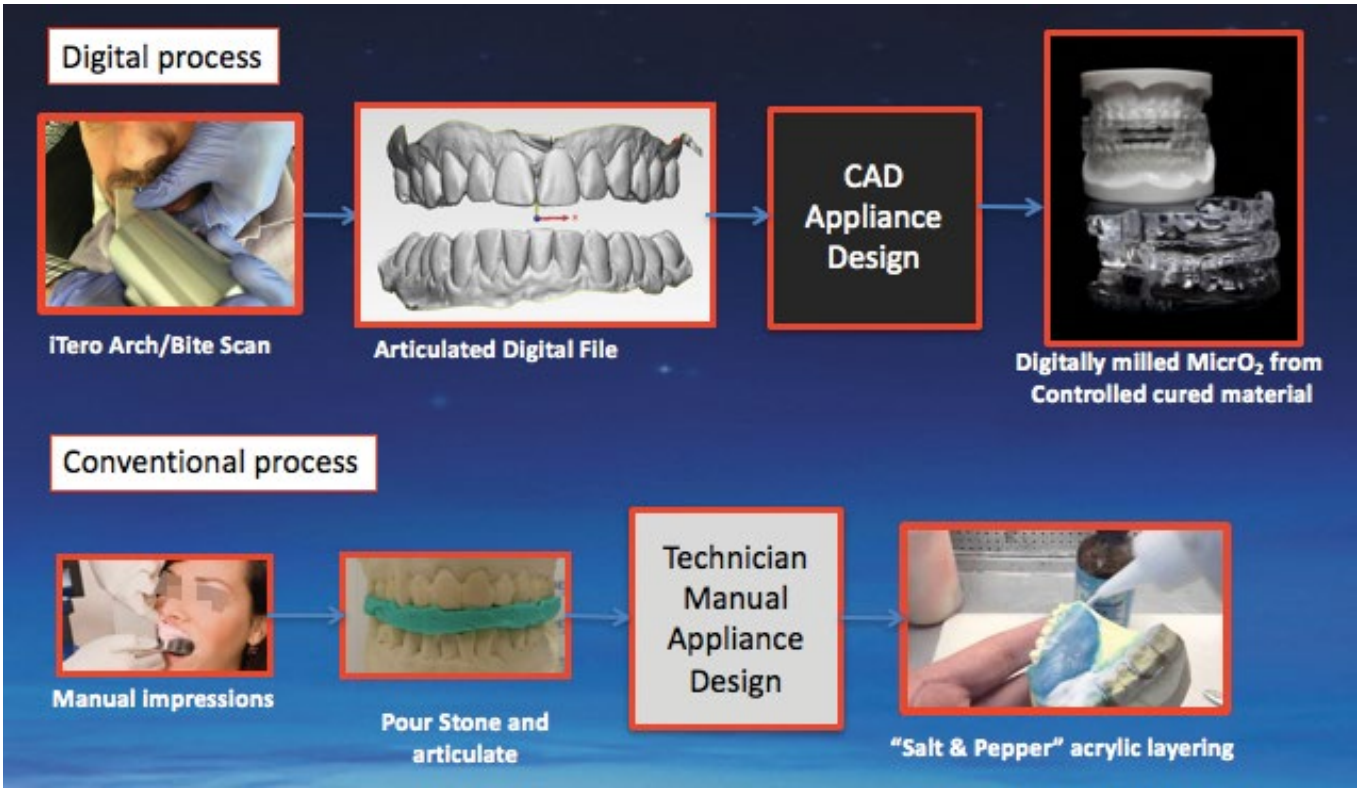
(A) Maxillary Arch. **(B)** Mandibular Arch.

Table 2—Fit adjustments and patient preference for each process.

Patient No.	Device Interior Adjustments		Device Occlusal Adjustments		Patient Preference	
	Conventional	Digital	Conventional	Digital	Conventional	Digital
1			x			x
2	x					x
3						x
4	x		x			x
5			x			x

AHI = apnea-hypopnea index, BMI = body mass index.

Figure 5—Comparison of steps in a digital workflow compared to a conventional process.



to the occlusal surfaces (to achieve properly balanced occlusion). The results are summarized in **Table 2**. After wearing each device for 3 weeks, each patient was asked which appliance they preferred in terms of comfort. The conventional device was worn first, followed by the digital device. There was no washout period between the 2 appliances. The results are shown in **Table 2**. A follow-up sleep study was performed to evaluate the efficacy of the treatment, and the patients' follow-up apnea-hypopnea indexes are summarized in **Table 1**.

DISCUSSION

The results of the study suggest that it is feasible to implement a fully digital workflow using the existing technology in a dental practice and device manufacturing facilities, with no need for physical dental models. The digitally designed and manufactured devices had better accuracy in terms of dental fit and occlusal/bite fit as demonstrated by the digital file overlay and patient preference. All patients preferred the digital devices in terms of comfort. Although the sample size in this study was very small and further controlled double-blinded studies are required to reproduce the results, the possibility of having a fully digital workflow in dental sleep medicine is potentially beneficial for both the patient and the clinician. Digital scans seem to be preferred by most patients in terms of comfort.[15] Dental clinicians using such technologies will minimize the chances of distortion and inaccuracies,and in case of a distorted scan,a full new impression will not be required. The distorted segment can easily be erased and re-scanned. Also,device manufacturing companies prefer the digital workflow due to the consistency,efficiency and in-office inspection of scan quality. **Figure 5** illustrates the reduction in manual steps in a digital workflow. Each manual step adds error due to human touch that varies by technician. Additionally,manually designing and building up the device via the "salt and pepper" method also adds technique and material variance. The monomer/polymer mix, cure time, and resultant properties will also be varied. Milling from a controlled cured material reduces these errors, allowing better translation of data from the patient to the finished device. This results in less time being spent both in terms of the dental clinic and in manufacture of the device. A digital workflow model may also help provide faster turnaround time for the appliance delivery and hence provide more timely care for patients in need of an MRD. Currently,time to efficacious treatment for CPAP therapy can be very quick,whereas that for OAT appears to take more time. This can be caused by many factors such as lack of proper patient selection,subjective titration,and conventional device manufacturing. However,with better methods for patient selection for OAT and efficacious target protrusion,this time can be reduced significantly.

The addition of fully digital device manufacturing could be a significant addition to this model by further reducing the time to efficacious treatment. Also, incorporating digital workflow in dental sleep medicine would allow better long-term monitoring of occlusal changes for patients with an MRD, as the digital scans can be readily stored, retrieved, and compared. As the demand for OAT and MRDs increases, we as clinicians and

practice managers will require workflows and manufacturing technologies that are easily scalable. The full digital workflow model is aligned with the future need to treat the many patients who will soon receive a diagnosis.

In terms of the bite registration and the translation of a conventional bite to a digital bite registration, the investigators found that this procedure is very technique sensitive at this stage and depends heavily on the expertise of the clinician and their level of experience with digital scanners. An important aspect is to have proper stabilization of the protrusive bite to prevent any unwanted movement of the mandible and the dentition during the scanning. Another very important aspect is to maintain the proper vertical dimension both in anterior and posterior region. Failure to provide such posterior support may result in unwanted compression of the soft tissue around the temporomandibular joint, thus resulting in an inaccurate bite registration. Keeping this in mind, a properly designed gauge specifically designed for digital open bite registration could be very helpful in overcoming discrepancies.

The sample size was very small for this study and the process was limited to one type of scanner and device type. Investigators believe more testing with higher numbers of patients and utilizing different scanners and appliance designs would be beneficial. Because of the small number of participants, the statistical significance of the results is unknown and a follow-up randomized study with a larger sample size would be necessary for better statistical analysis of the results. In addition, randomizing the sequence of conventional versus digital MRDs with a washout period added in between would be important for a more accurate comparison. Also, an easier and less technique-sensitive bite registration process needs to be established to avoid segmenting the bite and creating possible issues. With the increasing number of patients requiring MRD, such an approach could result in more efficient workflow models with faster turnaround time, and more accurate and more cost-effective and scalable workflows. More follow-up studies would be useful to understand how such digital workflow, in combination with other available technologies for patient selection, would affect the general efficiency of clinical care delivery for OAT, including time to efficacious treatment, avoidance of OAT nonresponders, number of appointments required for OAT, cost of total treatment, and patient satisfaction.

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This study was funded by ProSomnus Sleep Technologies. Dr. Kuhns is VP of Technology and Sung Kim is VP of Engineering at ProSomnus. Dr. Charkhandeh is the Clinical Director at The Snore Centre and the Chief Dental Officer at Zephyr Sleep Technologies.

REVIEW ARTICLES

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Periodontitis and Obstructive Sleep Apnea: A Literature Review

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Study Objectives: The aim of this literature review was to investigate the possible association between periodontitis and obstructive sleep apnea (OSA) by highlighting hypotheses, probing evidence and current research.

Methods: The PubMed database from 2006 to October 2016 was used to select the eligible articles. Six independent evaluators extracted data from studies investigating the association between periodontitis and OSA and meeting the selection criteria.

Results: Eleven studies were selected for analysis. Three of them only measured the levels of cytokines and collagenases. Five studies found a significant association between periodontitis and OSA, and two studies found no significant association. Different study limitations were observed, thus increasing the risk of bias. A few examples are the lack of standardization for diagnosis of periodontitis and OSA, differences in therapeutic approaches and study design.

Conclusions: A causal relationship between periodontitis and OSA is still debatable due to the heterogeneity of studies and divergence of results. The benefits of periodontal treatment as an adjunct therapy for OSA still need further evaluation in randomized controlled studies with an emphasis on inflammatory plasma and salivary markers linking these two conditions.

Keywords: obstructive sleep apnea, periodontal diseases, periodontitis

Citation: Tremblay C, Beaudry P, Bissonnette C, Gauthier CA, Girard S, Milot MP, Durand R, Huynh N. Periodontitis and obstructive sleep apnea: a literature review. *Journal of Dental Sleep Medicine*. 2017;4(4):103–110.

INTRODUCTION

Obstructive sleep apnea (OSA), a chronic multifactorial respiratory disease, consists of a temporary decrease or cessation of breath for ≥ 10 seconds and leads to a reduction in blood oxygen saturation of more than 3% to 4% and/or neurological arousal.[1–3] OSA involves the upper respiratory tract, and it has been proven that snoring and OSA have systemic consequences in humans.[4] It has been recently suggested that OSA may be related to periodontitis, another chronic multifactorial disease.[5,6] Periodontitis is characterized by chronic inflammation of tooth-supporting tissues.[1,5,6] In addition, these conditions are associated with similar systemic inflammatory responses and involve common inflammatory mediators such as interleukins, metalloproteinases, and tumor necrosis factor (TNF)-α.

Indeed, both conditions have been shown to be associated with the development of systemic diseases including cardiovascular diseases and diabetes.[3,7,8] An association between these conditions could also have repercussions on the practice of dentistry and medicine. In order to guide the health care professional on diagnostic methods, risk factors, and treatments, the research is currently focused on whether there is a causal relationship between periodontitis and OSA. This would not only encourage more comprehensive dental care but also contribute to establish a partnership between the dentist and the physician.

Objective

This review of the literature aimed to evaluate the current evidence regarding the association between periodontitis and OSA and the potential mechanisms involved.

METHODS

Electronic Search

A systematic approach was used to identify articles investigating a potential association between periodontitis and OSA. A detailed search of PubMed electronic literature with a 10-year limit (2006 to October 2016) was applied. The search strategy involved the following keywords: "obstructive sleep apnea" AND "periodontal disease."

Selection of Studies

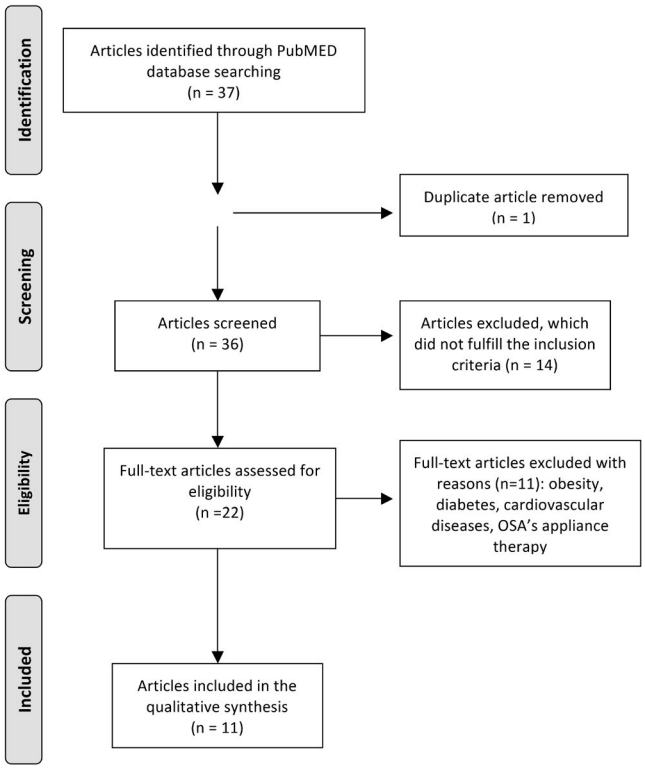
Selection of studies by title and abstracts review was carried out individually by each of the 6 reviewers (CT, PB, CB, CAG, SG, MM). To be eligible, studies had to investigate whether there was an association between the two conditions. Abstracts of articles not covering the subject of association were eliminated. The original article of the incomplete abstracts was revised for further details.

RESULTS AND DISCUSSION

Thirty-six publications were initially selected. However, 25 articles were rejected for lack of emphasis on one or both conditions. For example, the focus for several studies was on obesity, diabetes, cardiovascular disease, and OSA therapeutics. Consequently, only 11 studies were included in this literature review (see **Figure 1**).

In the selected studies, the apnea-hypopnea index (AHI) and the oxygen saturation rate were the objective measures frequently used to diagnose and measure the severity of

Figure 1—Flow diagram (PRISMA).



Detailed research of PubMed electronic literature. The search strategy involved the following keywords: "obstructive sleep apnea" AND "periodontal disease." Limitation of 10 years (2006 to October 2016) was applied. OSA = obstructive sleep apnea.

OSA.[2,3,5–7,9,10] Some authors have, however, relied on more subjective determinants such as the STOP[1] and Berlin[11,12] questionnaires. In regard to periodontitis, clinical parameters including pocket depth, level of clinical attachment, gingival recession, salivary and plasma cytokine levels, and plaque and gingival index were used.[1–3,5–7,10,13] From articles on the association of chronic periodontitis with OSA, the following hypotheses linking these pathologies were described: systemic inflammation, mouth breathing, and common risk factors.[8]

Chronic Systemic Inflammation

First, there is the hypothesis of systemic dissemination of inflammatory markers triggered by the chronic inflammation of periodontal tissues encountered in periodontitis. This inflammation is caused by the host immune response following the exposure to periodontal pathogens such as *Porphyromonas gingivalis*, *Tannerella forsythia*, *Treponema denticola*, and *Prevotella intermedia*. This host response causes an increase in systemic inflammatory factors by destroying the integrity of periodontal tissues.[14,15] In patients with periodontitis, there is an increase in certain inflammatory cytokines and mediators as well as an increase of the C-reactive protein,[2,6,9] an important systemic inflammatory marker. The increase in inflammation mediators in periodontitis can also increase the risk of cardiovascular, cerebrovascular, and pulmonary disease as well as type 2 diabetes, rheumatoid arthritis, osteoporosis, pregnancy complications, osteonecrosis, and even types of cancer.[3,5–7,9,10] In comparison, OSA would promote an increase in adhesion molecules, C-reactive protein, transcription factor (nuclear factor-κB), certain inflammatory cytokines (interleukin [IL]-1B, IL-6, TNF-α), and an activation of circulating neutrophils.[6–8] This inflammatory condition also potentiates several systemic diseases such as certain cardiovascular, cerebrovascular, pulmonary, and neurocognitive diseases as well as type 2 diabetes and rheumatoid arthritis.[1–3,5–7,9,13]

Gunaratnam et al. reported for the first time in 2009 that there may be an inflammatory link between periodontitis and OSA. They noted a high prevalence of periodontal disease in subjects with OSA (77% to 79%) but could not assert a causal link due to a significant lack of correlation of the measures.[6] Nevertheless, they suggested that periodontitis may be one of the co-factors involved in the association between apnea and cardiovascular disease, or that a preexisting OSA could worsen the presence and severity of periodontal disease. Following these hypotheses, several studies (**Table 1**[2,5,6,12,16,17] and **Table 2**[1,10]) have investigated the presence of an association between OSA and periodontitis.

Nizam et al.[9] have shown that OSA does not have a prominent effect on salivary IL-1B, IL-21, and PTX3, inflammatory markers of periodontitis (**Table 3**[3,9,18–20] and **Table 4**[3,21]). However, they found that salivary IL-6 and IL-33 tend to increase in patients with apnea, regardless of severity, whereas IL-33 levels appear to decrease with the evolution of chronic periodontitis. Thus, being in higher concentration during periodontitis, only the salivary IL-6 could be related to the elevation found in OSA.[9] This could then reflect the degree of subclinical inflammation present in the periodontal tissues and partly explain the pathogenesis. This potential cause-effect relationship has unfortunately not been fully demonstrated in another subsequent case-control study by the same authors.[3] Larger population studies with different periodontal disease categories are needed to confirm this link and to test the possibility of a dose-response relationship. No differences were statistically significant with these same cytokines in serum according to the studies by Nizam et al.[3,9] However, some studies have demonstrated a correlation between plasma IL-6 and TNF-α with moderate to severe OSA[22–25] or periodontitis.[26,27] It is suggested that this difference may be related to body mass index, periodontal diagnosis, and demographic status variations between studies.

A third case-control study by Nizam et al.[7] examined the role of salivary and serum collagenases in the association between OSA and periodontal disease (**Table 5**[7,28,29]). The hypothesis was that increased levels of biomarkers in patients with OSA could also affect the periodontal health of individuals. They evaluated the salivary and blood concentrations of neutrophils and their enzymes (metalloproteinases, myeloperoxidases, and elastases), which usually increase during inflammation. Several metalloproteinases (MMP-2, MMP-9) have already been associated with periodontal destruction.[28,30] In this study by Nizam et al., a statistically significant inversely proportional relationship was demonstrated between the severity of OSA and the rate of salivary elastases, salivary proMMP-2s, serum proMMP-9s and the activation degree of salivary MMP-9s.

Table 1—Summary of cross-sectional studies analyzing the association between periodontitis and OSA.

Study	Population	OSA Assessment	Periodontitis Assessment	Results	Limitations	Conclusion
Sales-Peres et al. 2016[12]	• Brazil • n = 108 • Mean age: 40.1 (30–60 years) • Ratio M/F: 23/85 • BMI > 40 or ≥ 35 kg/m^2 (class 3 obesity)	• Bq • ESS	• Periodontal parameters (6 points / teeth; full mouth, clinical attachment, bleeding, calculus and gingival index) • Periodontitis severity scale by AAP and CDC in 2007[16] and modified in 2012[17]	• Periodontitis is not associated with ESS or with Bq • Gingivitis is not associated with ESS or with Bq	• Morbidly obese patients, common risk factor for both conditions • Diagnostic questionnaire for OSA and no PSG (risk of bias at the classification level) • The plaque index was not evaluated	• No significant association between periodontitis and OSA in class 3 obese patients
Loke et al. 2015[2]	• United States • n = 100 • Mean age: 52.6 (28–79 years) • Ratio M/F: 91/9	• PSG • AHI classification ○ Normal ○ Mild (5–15) ○ Moderate (> 15–30) ○ Severe (> 30)	• Periodontal sampling (6 points / teeth; full mouth excluding third molars), recession, clinical attachment, bleeding, plaque %, % of pocket depth ≥ 5 mm, % loss of attachment loss ≥ 3 mm • Periodontitis severity scale by AAP and CDC in 2007[16] and modified in 2012[17]	• AHI: 26 normal, 21 mild, 19 moderate, 34 severe • Moderate to severe periodontitis: 73% • No significant difference in the prevalence of periodontitis between the 4 groups of AHI • A significant association between plaque % and AHI after adjustment for age • Logistic regression to predict moderate / severe periodontitis with AHI, age, and smoking reported a significant association with age only	• High prevalence of periodontitis in subjects, which does not represent the population of the United States (44.7%) • M/F ratio not balanced	• No significant association between OSA and moderate to severe periodontitis except for plaque % and AHI
Seo et al. 2013[5]	• Korea • n = 687 • Mean age: 55.85 ± 6.63 (47–77 years) • Ratio M/F: 460/227	• PSG and questionnaire assessing sleep at home • AHI classification ○ Normal ○ Mild (< 5) ○ Moderate (5–10) ○ Severe (> 10)	• Periodontal parameters (6 points / teeth; Ramfjord's teeth 16, 21, 24, 36, 41, 44), recession, clinical attachment, bleeding, plaque (Silness & Loe) and gingival index • Definition of periodontitis: ≥ 4 teeth with at least 1 site interproximal probing of ≥ 4 mm and attachment loss of ≥ 6 mm on the same tooth	• Prevalence of periodontitis: 17.5% • Prevalence of OSA (AHI ≥ 5): 46.6% • 60% of patients who received a diagnosis of periodontitis had OSA • Compared to the control group, patients with OSA (AHI ≥ 5) are usually associated with periodontitis, pockets of ≥ 4 mm, clinical attachment losses of ≥ 6 mm • Periodontitis is associated with OSA (AHI ≥ 5) in the age group of ≥ 55 years but not in the < 55 years age group*	• Partial periodontal examination; only 6 teeth were evaluated; possibility of underestimating the disease • Some confounding factors have not been evaluated • There is no calculation of the size of the target sample	• Significant association between OSA and periodontitis
Gunaratnam et al. 2009[6]	• Australia • n = 66 • Mean age: 54.9 ± 12.8 (18 to > 75 years) • Ratio M/F: 54/12	• PSG • AHI classification ○ Normal ○ With OSA (> 5) • Only patients with OSA are selected in this study • Patients from a national survey were used as an OSA free control group	• Periodontal parameters (6 points / teeth, full mouth), clinical attachment loss, bleeding, plaque (Silness & Loe) and gingival (modified Lobene) index • Periodontitis severity scale by the AAP and the CDC,[16,17] and the NCHS[6]	• Prevalence of periodontitis: 77% to 79% according to the definition used • Significant association between clinical attachment loss and total sleep time	• The prevalence of periodontitis represents a 4x higher prevalence than the Australian National Survey of Adult Oral Health • Some confounding factors are not assessed • Database for OSA-free controls • Small sample size • Potential examiner bias due to absence of masking	• Association between OSA and periodontitis • Higher prevalence of periodontitis in patients with OSA than in patients without OSA

* = adjusted for age, sex, BMI, alcohol, tobacco, snoring, mouth breathing during sleep, and diabetes. AAP = American Academy of Periodontology, AHI = apnea-hypopnea index, BMI = body mass index, Bq = Berlin questionnaire, CDC = Centers for Disease Control and Prevention, ESS = Epworth Sleepiness Scale, NCHS = National Center for Health Statistics, OSA = obstructive sleep apnea, PSG = polysomnography.

Table 2—Summary of case-control studies analyzing the association between periodontitis and OSA.

Studies	Population	OSA Assessment	Periodontitis Assessment	Results	Limitations	Conclusion
Keller et al. 2013[10]	• Taiwan • n = 7,321 participants with OSA • n = 21,963 controls • Matched for age, sex and socioeconomic status • Mean age: 47.6 (± 15.4 years) • Ratio M/F: 18,232/11,052	• Initial diagnosis provided by the LHID2000 and ICD-9 codes	• Periodontal parameters (6 points / teeth; full mouth), probing depth ≥ 3 mm is considered to be periodontitis • Bleeding index • Gingival color and contour • Tooth mobility • Radiographs to record bone levels	• Prevalence of periodontitis: 33.8% (2,474) cases versus 22.6% (4,960) controls • Logistic regression analysis for the presence of OSA in periodontitis patients compared to controls after adjusting for monthly income, geographic origin, hypertension, diabetes, chronic heart disease, hyperlipidemia, obesity, alcohol, tobacco, chronic obstructive pulmonary disease	• Retrospective study • No adjustment for several confounding factors (eg, family history, tobacco, occupations) • Incomplete definition of chronic periodontitis • Selection bias (patient monitored for chronic periodontitis were more likely exposed to the medical community therefore, more likely to receive a diagnosis of OSA)	• Significant association between OSA and chronic periodontitis diagnosis
Ahmad et al. 2013[1]	• United-States • n = 154 ○ 50 participants with moderate to severe periodontitis ○ 104 controls/ gingivitis or mild periodontitis • Mean age: 61 (18 to ≥ 70 years) • Ratio M/F: 61/93	• STOP screening questionnaire	• Multiple calibrated examiners • Periodontal parameters (6 points / teeth, full mouth), recession, clinical attachment, bleeding, plaque and gingival index • Radiographs to determine bone levels • ADA moderate or severe periodontitis[1]	• Periodontitis prevalence: 32.5% • 60% of moderate periodontitis have a high risk for OSA versus only 28% for controls • Periodontitis cases are more likely to have OSA than controls*	• Subjective OSA diagnosis • Low prevalence of periodontitis compared to national average	• Significant association between moderate to severe periodontitis and an elevated risk for OSA

* = adjusted for age, sex, BMI, alcohol, tobacco, difficult nasal breathing, diabetes, dry mouth, education and income. ADA = American Dental Association, ICD-9, International Classification of Diseases, Ninth Revision, LHID2000 = Longitudinal Health Insurance Database 2000, OSA = obstructive sleep apnea.

This finding contradicts in part the previously described pathophysiological relationship, establishing a proportional relationship between plasma MMP-9 and the severity of OSA.[29,31] Again, these differences may be related to various periodontal diagnostics and demographic status from these studies.

Mouth Breathing

Second, there is the hypothesis that mouth breathing would be indirectly associated with periodontitis through changes it can cause in the oral environment. In a healthy patient with no nasal involvement, mouth breathing accounts for approximately 4% of total ventilation.[5] This percentage tends to increase with aging. In a study by Seo et al.,[5] the prevalence of mouth breathing appeared to be higher in patients with OSA. By generating dry mouth, this type of breathing tends to diminish the self-cleaning and antibacterial effect of saliva. It is then possible to note an increase in bacterial colonization and subsequent gingival inflammation. These two factors may increase the risk of developing periodontal disease or trigger its progression.[5,13] However, in this study, the presence of mouth breathing was subjectively measured using a questionnaire, which limits the interpretation of the results. A case-control study using another type of questionnaire demonstrated an opposite relationship between mouth breathing and periodontitis.[1] It is suggested that a more objective approach (for example, using the AHI) be used in subsequent studies. Confirmation of a bidirectional relationship between OSA and periodontitis through mouth breathing remains to be proved.[13]

Common Risk Factors

Finally, the third hypothesis often presented in the literature is the comorbidity relationship between the two conditions, given that they have several common risk factors such as tobacco use, sex (male), aging, alcohol consumption, obesity, and diabetes.[1,3,5,7,9,10] In periodontitis, we also observe ethnicity (Hispanic and African), stress, social class, and poor oral hygiene.[1,6] The simultaneous presence of periodontitis and OSA in an individual would then be attributable to the common risk factors and would act as a comorbidity link in contrast to the first two assumptions where there is a causal link.[8] It should also be noted that periodontitis is a common disease. According to the National Health and Nutrition Examination Survey, it would affect up to 47.2% of the population in the years 2009–2010.[8] According to a study by Lee et al.,[32] OSA would reach 2% to 4% of middle-aged Caucasian men and women. It is therefore to be expected that these two conditions may very well be present in the same individual without there necessarily being a causal link between them.

As a result of these studies, a systematic review and meta-analysis was published by Al-Jewair in 2015.[8] Including 6 studies, the authors concluded that an association is still

Table 3—Inflammatory cytokines and their association with periodontitis and OSA.

Salivary Cytokines	Role	Statistical Association With Periodontitis ($P < .05$)	Statistical Association With OSA ($P < .05$)
Interleukin-1 (IL-1B)	• Proliferation, differentiation and lymphocyte apoptosis		• No[9]
Interleukin-6 (IL-6)	• T lymphocyte proliferation • Differentiation of B lymphocytes • Stimulation for immunoglobulin secretion • Active bone resorption	• Yes[20]	• Yes, if moderate or severe OSA[3,9]
Interleukin-21 (IL-21)	• Proliferation of NK and cytotoxic T lymphocytes	• Yes[18] • Significant correlation between clinical attachment loss and levels of IL-21[9]	• No[9]
Interleukin-33 (IL-33)	• Production of T helper-2-associated cytokines • Anti-inflammatory activity	• No[19]	• Yes, if moderate or severe OSA[9]
Pentraxin-3 (PTX-3)	• Innate immunity • Control of inflammation • Destruction of apoptotic cells		• No[9]
Tumor necrosis factor-alpha (TNF-α)	• Control of the production of prostaglandins, collagenases, cytokines, cell adhesion molecules, bone resorption factors		• No[3]
Receptor activator of nuclear factor kappa-B ligand (RANKL)	• Osteoclastogenesis		• No[3]
Osteoprotegerin (OPG)	• Osteoclastogenesis		• No[3]

OSA = obstructive sleep apnea.

Table 4—Peptide hormone and its association with periodontitis and OSA.

Peptide Hormone (Serum)	Role	Statistical Association With Periodontitis ($P < .05$)	Statistical Association With OSA ($P < .05$)
Apelin	Physiological respiration		Yes, if severe OSA[3,21]

OSA = obstructive sleep apnea.

possible but that the recent evidence is insufficient to support a causal link, or to assert that the treatment of periodontitis has a significant effect on OSA.[1,2,5,6,9,10] Thus, for the time being, it is preferable to refer to systemic inflammatory pathways common to the two diseases where further studies will be required to fully demonstrate a cause-and-effect relationship.[8,13] As such, a 2016 study by Al Habashneh et al. including 294 men in Jordan evaluated this association link.[11] The Berlin questionnaire was used to assess the risk of OSA. Subjects at high risk of OSA were more frequently and severely affected by periodontitis (odds ratio = 2.3 with 95% confidence interval = 1.03–5.10) than those at low risk of OSA. However, the diagnostic value of the Berlin questionnaire remains debatable in comparison to polysomnography and this study was only carried out with male subjects.

Limitations

There are inevitable limitations in the collection of data and the comparative analysis between several studies. Thus, the research methods and conclusions of the studies often differ from each other. Among others, compared to the study by Gunaratnam et al. where the odds ratio between periodontitis and OSA was almost 4,[6] according to Keller,[10] this ratio would be closer to 1.75. The case-control study of Ahmad et al. also came to the conclusion that there was an association.[1] However, unlike the study by Gunaratnam et al., patients did not receive a clinical diagnosis before they were categorized with OSA. The study used a validated questionnaire (STOP) to obtain an estimate of the risk of OSA.[1] In contrast, Loke et al. concluded that there was a significant association between OSA severity and plaque percentage but no correlation between OSA and the prevalence of moderate or severe periodontitis.[2] These examples of contradictory results demonstrate the importance of the limiting factors present in the studies.

The selection of cases in the studies can be done either by using databases of patients who have responded positively to questionnaires or by means of an examination done clinically. It is evident that an individualized and standardized approach is more accurate for the diagnosis of periodontal diseases.[10] Despite the calibrated classification of the periodontal disease, the case-control division is performed using various measures that can be influenced by the operator. Measurement of plaque

Table 5—Salivary or plasma enzymes and their association with periodontitis and OSA.

Enzymes		Statistical Association With Periodontitis ($P < .05$)	Statistical Association With OSA ($P < .05$)
ProMMP-2	Salivary		Inversely proportional and statistically significant association[7]
	Plasma		No[7]
MMP-2	Salivary	Yes[28]	
	Plasma	Yes[28]	
ProMMP-9	Salivary		No[7]
	Plasma		Inversely proportional and statistically significant association with severe OSA[7]
MMP-9	Salivary	Yes[28]	Inversely proportional and statistically significant association with severe OSA[7]
	Plasma	Yes[28]	Proportional and statistically significant association[29]
Neutrophil elastase	Salivary		Inversely proportional and statistically significant association[7]
	Plasma		No[7]
Myeloperoxydase (MPO)	Salivary		No[7]
	Plasma		No[7]

OSA = obstructive sleep apnea.

level, bleeding, mobility, furcation defect, and loss of attachment by several operators using different techniques may create a certain variance and a margin of error.[1,10] In addition, not all studies used the same definition of periodontitis, which could lead to underestimation or over-estimation of prevalence.[8] In addition, the geographical location may vary from one study to another, which leads to the lack of uniformity in the prevalence and severity of the disease.[8]

Being aware of the initial hypotheses, the objectivity of the examiner may be biased during the periodontal data collection, hence the need for a blind approach.[6] In addition, some studies are limited to a partial periodontal evaluation of the mouth[5] compared to others with 6 measurement points for each tooth.[2] In order to make an objective diagnosis of OSA, in contrast to the rather subjective approach of the STOP[1] or Berlin[11,12] questionnaires, polysomnography assessing rapid eye movement, oxygen saturation index, and AHI were used.[2,3,5–7,9,10]

The often unequal proportion between the case-control groups and the therapeutic irregularity in patients with OSA also affects the results. In addition, untreated OSA is usually associated with mouth breathing. This causes both dry mouth and a decrease in the self-cleaning effect of the saliva, which ultimately promotes bacterial colonization. Patients treated with continuous positive airway pressure (CPAP) or bilevel positive airway pressure (BPAP) will have less of this type of breathing. As a result, a mixture of treated and untreated patients in the same group affects its uniformity and thus, the potential correlation with periodontitis.[13] Similarly, the possibility of having members of the control group with an asymptomatic, undiagnosed OSA or other sleep disorder (eg, snoring) may also lead to a lack of uniformity in the control groups.[13]

Studies that did not distinguish smokers from nonsmokers included a limitation because smoking affects not only the salivary levels of cytokines but also the risk of OSA or chronic periodontitis.[7,9,10] The absence or variation of the AHI is another cited factor that can obscure the uniformity of the observed cases.[2,8] The standardization of study groups according to each of these categories is therefore necessary in order to improve the internal validity of the studies. It is also important to note that some studies had a limited number of participants.[7,9] Severe inclusion criteria and lack of patient availability are reasons.[6,7] In general, it is also possible that in a patient treated for periodontitis, OSA is more likely to be diagnosed in comparison with a person unaware of having this condition. This might again increase the correlation rate.[10]

Future Research and Current Practice Suggestions

Carra et al.[13] recently published a study on the potential improvement of periodontitis with CPAP and/or BPAP. This treatment with a facial mask, a novel therapy for OSA, may include a humidification device, which reduces dry mouth. Even if the link between mouth breathing associated with OSA and periodontitis is still debated to this day, this device opens several avenues of research. This study failed to observe a difference in inflammation, plaque, calculus, number of missing teeth, or masticatory function between individuals using these devices and those who did not use them. However, this study has some limitations. Patients using the CPAP/BPAP could have been particularly motivated to maintain their oral hygiene and receive regular medical follow-ups. Also, the controls were subjectively selected using a questionnaire and the adhesion to the CPAP/BPAP could not be measured. The potential presence of patients with asymptomatic or undiagnosed OSA in the control group is another limitation. Thus, one cannot conclude if this OSA therapy has a beneficial effect on the periodontitis, even if it succeeds in decreasing mouth breathing.

In light of recent studies, a diligent dentist could incorporate new OSA front-line detection techniques into his or her clinical evaluation. According to Ahmad et al.,[1] on average, a patient visits the dentist more often than his or her physician. Having

the responsibility to promote oral health and hygiene,[33] it was suggested that the STOP questionnaire (Appendix 1, supplemental material) be included in the dental examination. As a rapid and effective method, this self-reported questionnaire identifies patients at risk for sleep apnea without, however, providing a categorical diagnosis. The integration of this questionnaire could thus intercept systemic diseases. Collaboration and possible exchange of results between the dentist and the family physician would then be necessary in order to carry out a more objective examination such as polysomnography or polygraphy.

CONCLUSIONS

To date, association studies between OSA and periodontitis are often based on different diagnostic criteria and show conflicting results. The many limiting factors and the difficulty in recruiting high numbers of participants preclude scientists and clinicians from drawing any conclusions. However, there seems to be a possible link between periodontitis and OSA syndrome via plasma and salivary inflammatory markers. Despite recent awareness, few studies have specifically focused on these aspects. Thus, well-structured, randomized control trials are needed to confirm this association and to clarify the mechanism of interaction between the two conditions.

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SPECIAL ARTICLES

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Management of Side Effects of Oral Appliance Therapy for Sleep-Disordered Breathing

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As the field of oral appliance therapy (OAT) to manage obstructive sleep apnea has evolved over the past 30 years, side effects of therapy have become increasingly recognized. Although the most commonly observed side effect is unwanted tooth movement, a number of other side effects have been reported through anecdotes, case reports, and observational studies. Members of the American Academy of Dental Sleep Medicine developed a set of consensus recommendations to guide dentists in the management of side effects as a consequence of OAT. Thirteen expert clinicians were appointed to the panel, which used the modified RAND/UCLA Appropriateness Method to review the body of evidence on OAT side effects and to establish the recommendations. Clinicians are encouraged to use these recommendations in conjunction with their clinical expertise to minimize the side effects of OAT. The recommendations are based on knowledge to date and are expected to evolve over time. Future research should aim at timely identification of these side effects for positive treatment outcomes.

Keywords: malocclusion, mandibular advancement, mandibular repositioning, mouth diseases and therapeutics, oral device, orthodontic appliance, sleep apnea (obstructive and snoring), tooth disease

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INTRODUCTION

The American Academy of Dental Sleep Medicine (AADSM) and American Academy of Sleep Medicine recently updated their clinical practice guideline for the treatment of obstructive sleep apnea (OSA) and snoring with oral appliance therapy (OAT).[1] The guideline included the following recommendation: "We suggest that qualified dentists provide oversight—rather than no follow-up—of oral appliance therapy in adult patients with obstructive sleep apnea, to survey for dental-related side effects or occlusal changes and reduce their incidence."

The management of side effects is essential to maximize treatment adherence and the clinical effectiveness of oral appliances. The guideline further states that although multiple manuscripts refer to side effects, the overall evidence is limited and of low quality.

The field of dental sleep medicine lacks a set of published guidelines that clinicians and dentists can refer to for the management of side effects associated with OAT. Most of the information available to clinicians is derived from individual lecturers and is anecdotal. In an effort to begin to address this gap in knowledge, the AADSM Board of Directors convened a panel of experts to develop consensus-based recommendations for managing the most common side effects encountered in OAT.

BACKGROUND

OSA has a reported prevalence of 2% to 8% in older literature, with more recent estimates suggesting that more than 18 million adults in the United States have sleep apnea, a leading cause of excessive daytime sleepiness. An oral appliance, while effective in ameliorating the respiratory events of OSA, often causes alterations in occlusal (tooth) contacts and mandibular positioning as well as other side effects. During the Advanced Course in Oral Appliance Therapy in 2009, the AADSM first catalogued some of these side effects and proposed solutions for their management. This was originally published in *Dialogue* and was considered a work in progress.[2]

The purpose of this consensus paper is to update those recommendations and to develop a touchstone reference for practitioners and researchers seeking guidance on the management of side effects of OAT for sleep-disordered breathing.

METHODS

Expert Panel Selection

In accordance with the recommendations of the RAND Appropriateness Method,[3] the Consensus Conference panel comprised 13 voting members. All panel members were dentists who were trained and experienced in the overall care of oral health, the temporomandibular joint (TMJ), dental occlusion, and associated oral structures with focused emphasis on the proper protocol for diagnosis, treatment,

and follow-up of patients being managed with OAT for sleep-disordered breathing. All panelists were required to complete conflicts of interest disclosures before being officially invited to participate.

In addition, the American Academy of Sleep Medicine, the American Dental Association, and the American Dental Education Association were invited to identify a representative of their respective associations to attend the consensus conference as nonparticipating observers. These observers were permitted to pose questions during the conference but did not participate in the voting or the development of the recommendations.

Literature Search and Review

A literature search was performed using a combination of keywords and Medical Subject Heading terms in PubMed. Disorder-related keywords used were *sleep apnea, obstructive and snoring, tooth disease, malocclusion, mouth diseases,* and *therapeutics*. These were combined with treatment keywords including *mandibular advancement, mandibular repositioning, oral device,* and *orthodontic appliance*. The search strategy was limited to humans and articles in English. Search results were retrieved for literature published through February 23, 2016, resulting in a total of 181 articles. The panelists reviewed the abstracts to identify articles that included side effects of OAT for sleep-disordered breathing and treatment options to manage side effects. Articles that were not relevant were discarded. The panel also conducted a "spot check" of the literature in June 2016 to identify missing publications. The final number of articles accepted in support of this endeavor was 143.

The full text of all accepted publications was made available to the panel members for review.

Survey of American Board of Dental Sleep Medicine Diplomates and AADSM Committee Members

Concurrent with the literature review, a comprehensive list of the side effects and possible treatment options was developed. Because knowledge about oral appliances varies among providers, an online survey of dentists was conducted to ensure that common side effects and possible treatment strategies were not overlooked.

The survey was designed to capture the percentage of patients in each respondent's practice who were managed with OAT, the common side effects encountered with OAT, the frequency of each of these side effects, and commonly used treatment options to manage each side effect.

In late summer of 2016, the survey was sent to all Diplomates of the American Board of Dental Sleep Medicine and all AADSM committee members: 149 of 295 (51%) responded to the survey; 113 (76% of respondents) submitted complete responses and 36 (24% of respondents) submitted partial responses. All responses were reviewed, whether or not the entire survey was completed.

Survey responses were used in conjunction with relevant literature to inform the panel during the voting process (described in the next paragraphs). To facilitate the literature review, panel discussion, and voting, the side effects were assigned to 1 of 6 groups: (1) TMJ-related side effects, (2) intraoral tissue-related side effects, (3) cephalometric changes, (4) occlusal changes, (5) damage to teeth or restorations, and (6) appliance issues.

Modified RAND Appropriateness Method

The RAND Appropriateness Method[3] uses a detailed search of the relevant scientific literature, followed by 2 rounds of anonymous voting by panelists, to arrive at consensus on the appropriateness of a treatment. For this conference, panelists voted on the appropriateness of each treatment recommendation proposed for all side effects. The first round of voting was conducted via email prior to the face-to-face conference. The second round of voting occurred at the conference after discussion of the available evidence and round 1 voting results. In a modification of RAND Appropriateness Method, the panel completed a third round of voting to rate the priority level of all treatment options that the panel agreed were "appropriate" in round 2 voting.

Round 1 Voting

Prior to the conference, panel members independently reviewed the accepted publications and the results of the online survey. Based on their review of this material and their clinical expertise, each member voted to indicate level of agreement with the following statement: *"Based on the available evidence, [Treatment option] is appropriate to manage [Side effect] in patients using oral appliances."* Each panel member expressed their level of agreement with each statement using a 9-point Likert scale where 1 meant "strongly disagree," 5 meant "neither disagree nor agree," and 9 meant "strongly agree."

Median values of panel scores were calculated for each treatment option according to the following categories: scores of 1–3 indicated *inappropriateness* of the treatment option, scores 4–6 described *uncertainty* about the appropriateness of the treatment option, and scores 7–9 signified *appropriateness* of the treatment option. Panel agreement occurred when at least 10 panelists voted within a single category.

For this initial round of voting, panel members were instructed not to discuss the evidence or their votes with one another to ensure independence and anonymity.

Conference Proceedings: Voting Rounds 2 and 3

At the conference, panelists reviewed the results of round 1 voting for each treatment option proposed for each side effect and discussed the available evidence and their clinical experience in treating each side effect. During these discussions, panelists agreed that Cephalometric Changes should be dropped as a category of changes. The 2 side effects included in this category were "increased facial height" and "altered mandibular position." The results of the online survey conducted prior to the consensus conference suggested to the panel that few practitioners note these side effects, and panelists speculated that clinicians do not routinely obtain or analyze lateral cephalograms. Furthermore, the cephalometric changes documented are most likely a manifestation of occlusal changes that result from OAT, rather than separate and independent side effects.

At the conclusion of each discussion, panelists completed round 2 voting for all treatment options proposed for each of the side effects, following the same procedures as round

1 voting. Only those treatment options for which the panel agreed was appropriate in round 2 voting were retained in the final recommendations. Panel agreement on treatment options whose median scores fell into the *inappropriate* or *uncertain* categories, were dropped from further consideration.

A third round of voting was conducted to categorize the treatment options retained after round 2 voting as a "first-line," "second-line," or "uncommon but appropriate" treatment option for each side effect. The "uncommon but appropriate" category was created to acknowledge the possibility that, in infrequent circumstances, an "uncommon" treatment option would be indicated only after the other treatment options were either ineffective, exhausted, or not appropriate for that specific patient.

Development of Recommendations

Upon completion of round 3 voting, the panel members discussed the voting results and developed the recommendations. The final recommendations were submitted to the AADSM Board of Directors for endorsement.

In view of the availability of many titratable oral appliances (degree of protrusion and other settings) this document should not be considered a comprehensive or exhaustive list of side effects or corresponding options for treating the side effects secondary to OAT.

It is expected that these guidelines will be most beneficial to the novice practitioner in the field of dental sleep medicine and will serve to highlight the breadth of adverse effects of OAT and to provide strategies for managing them. In developing these recommendations, the panel was careful to consider various clinical scenarios but elected to address the most common situations, rather than the most esoteric, that clinicians would encounter. The panelists stress that this document should be used in conjunction with the clinical expertise of the practicing dentist and that individual patient needs may necessitate deviation from these recommendations.

RECOMMENDATIONS

Prior to initiating OAT, the treating dentist should document pretreatment tooth positions with baseline records including dental casts, intraoral photographs, and a record of occlusal relationships. Patients must be informed of potential side effects prior to initiating treatment and informed consent must be secured.

Side effects must be assessed and recorded at all follow-up visits, including occurrence, management, and/or resolution. The dentist should refer to the baseline records to identify changes in tooth position and should immediately disclose to the patient such changes and their possible consequences. Other patient concerns should be noted and managed accordingly. If the patient expresses discomfort with continuing OAT, discussion regarding alternative treatment options should occur and be documented.

If the recommendation is made to permanently discontinue OAT, this decision should be made in consultation with the local treating physician to ensure that adequate alternative therapy is available to manage OSA.

Table 1—Side effects.

Temporomandibular joint-related side effects
• Transient morning jaw pain
• Persistent temporomandibular joint pain
• Tenderness in muscles of mastication
• Joint sounds
Intraoral tissue-related side effects
• Soft tissue and tongue irritation
• Gingival irritation
• Excessive salivation/drooling
• Dry mouth
Occlusal changes
• Altered occlusal contacts/bite changes
• Incisor changes
• Decreased overjet and overbite
• Alterations in position of mandibular canines and molars
• Interproximal gaps
Damage to teeth or restorations
• Tooth mobility
• Tooth fractures or damage to dental restorations
Appliance issues
• Appliance breakage
• Allergies to appliance material
• Gagging
• Anxiety

The following side effects and their recommended treatment options are grouped according to similarity in type (see **Table 1**).

In addition to the tailored treatment options recommended for each side effect, the panel recognized that a set of common management techniques should be considered as well, often as first-line therapy. These common techniques are summarized in the following paragraphs, and are identified in the following recommendations when appropriate.

Common Management Considerations

A number of treatment modalities have utility across a broad spectrum of known oral appliance side effects. For consistency and clarity, these are described as follows:

Palliative Care

Palliative care is supportive in nature and intended to manage patient discomfort during the healing phase. It may include any/all of the following options: reassurance, rest, ice, soft diet, topical or systemic pain relief products or anti-inflammatory medication, massage and physiotherapy.

Watchful Waiting

Watchful waiting is the ongoing process of careful and diligent observation, with the possibility of additional assessment along the way, in an effort to better understand the side-effect process. Documentation of findings must be included in the patient's record, and follow-up of concerns at subsequent visits should occur and be recorded regarding persistence, resolution, or management of side effects.

Morning Occlusal Guide

Morning occlusal guide encompasses many custom-made appliances and prefabricated devices used in the effort to

reposition the mandible into its habitual pretreatment position. These devices may function by utilizing biting force to re-seat the condyles to help reestablish/maintain the appropriate occlusal relationship in the morning following each night of OAT. Some of these custom devices may function by reversing changes that may have occurred in tooth position or work to exercise or stretch muscles of mastication as well. They are intended to address the occlusal discrepancy noted after removal of the oral appliance each morning.

Before the patient begins using the oral appliance, the morning occlusal guide is fabricated chairside or by a laboratory, and is often made of hard acrylic, thermoplastic, or compressible materials. The guide must be adapted to the patient's maxillary and mandibular teeth in habitual occlusion, or to dental casts in maximum intercuspation.

Intended to address the occlusal discrepancy noted after removal of the oral appliance each morning, morning occlusal guides also help patients to monitor their condition by allowing them to ascertain whether their mandible is correctly aligned every morning. Each morning after the sleep appliance is worn, the patient should bite into the guide until the maxillary and mandibular teeth are fully seated for as long as it takes the teeth to re-establish occlusion. In the event that the patient is unable to attain proper habitual occlusion, the patient should contact the oral appliance provider.

Daytime Intraoral Orthotic

The daytime intraoral orthotic encompasses many custom-made appliances and prefabricated devices that are retained by either the maxillary or mandibular dentition/implants. These devices are intended to deprogram masticatory muscles, re-seat the mandibular condyles, and/or reduce the magnitude and frequency of bruxism events as well as its consequences. Distinctive from the morning occlusal guide, this device is intended for more active therapy of preexisting or iatrogenically created conditions affecting the TMJ or the masticatory musculature.

Verification and/or Correction of Midline Position

Verification and/or correction of midline position describes an effort to ascertain and maintain the appropriate lateral position of the mandible in its forward position, often similar in lateral dimensions to the nonprotruded (non-treatment) position.

Verification and/or Correction of Occlusion

Verification and/or correction of occlusion describes an effort to ascertain balanced occlusal forces on the oral appliance both bilaterally and anteriorly-posteriorly. This balance may be altered as the mandibular position is advanced or as muscles alternatively relax or contract with use. This may also encompass consideration of changes to the vertical dimension of the oral appliance.

Habitual Occlusion

Habitual occlusion refers to the position of closure between the dental arches in which the patient feels the teeth fit most comfortably with minimal feeling of stress in the muscles and joints.

Note: The term "habitual occlusion" refers to the patient's most comfortable position of jaw closure at any specific time. Many terms have been used to describe the interarch relationship of the maxilla and mandible, often with the intent of providing a reproducible position for restorative purposes. Terms such as centric relation, centric occlusion, maximum intercuspation position, bite of convenience, and intercuspation position have also been used. This paper favors the term "habitual occlusion" because as many as 85% of patients using OAT for more than 5 years demonstrate altered occlusal relationships from baseline.[4]

Isometric and Passive Jaw Stretching Exercises

Isometric and passive jaw stretching exercises include instructing patients to move the mandible against resistance both vertically and laterally and to stretch the mandibular range of motion assisted by the fingers, targeting the masticatory muscles. Examples would include instructing a patient to move the mandible against gentle resistance both vertically and laterally within their physiologic range of motion and using finger pressure to stretch the lateral pterygoid, temporalis, and masseter muscles. These have been shown to decrease the level of discomfort and improve adherence to OAT.[5] Duration and frequency of exercises will be dependent on the ease with which the patient is able to reestablish occlusion.

Conservative Titration

Conservative titration refers to the minimum amount of advancement of the appliance required to manage sleep-disordered breathing. Aarab et al. demonstrated that the number of side effects increases as protrusion exceeds 50%.[6] Moreover, research reveals that both 50% and 75% protrusion can be equally effective in groups of patients with mild to moderate OSA.[7]

Side Effects

The following subsections list each side effect, grouped by category, and describe the recommendations that the panel put forth to manage each one.

Temporomandibular Joint-Related Side Effects

Note: Several online survey respondents mentioned the terms "TMJ degeneration" and "myofascial pain" as potential side effects. A careful review of the literature revealed no instances where these side effects were verifiably reported to have occurred. Furthermore, the panel found that oftentimes in the literature, the terms myofascial pain, myalgia, muscle pain, and muscle tenderness were used interchangeably. It must be noted that these terms often have specific diagnostic criteria and are often used with various definitions across disciplines (physical therapy, physical medicine, etc.). Inaccurate or improper use of these terms in the sleep apnea oral appliance literature has led to confusion regarding diagnosis, prevalence, and management of these conditions among oral appliance users.

Transient Morning Jaw Pain

"Watchful waiting, palliative care, isometric contraction and passive jaw exercise, and decreasing the titration rate are considered first-line treatments to manage transient jaw pain."

Transient jaw pain includes pain or discomfort occurring in the morning upon oral appliance removal that disappears spontaneously during the day or with prescribed exercises or techniques. It also refers to pain or discomfort of short duration, generally less than a few weeks, that might occur intermittently during use of an oral appliance but more likely during acclimation and titration stages. It is considered to be mild in nature, originating in muscles of mastication and unlikely to cause OAT abandonment.

First-line treatment is usually conservative. Watchful waiting or active surveillance entails that the dental provider rule out pain or dysfunction originating in the TMJ and monitor the patient for a worsening of symptoms. Palliative care, in addition to the options mentioned in the Common Management Considerations section, will include patient reassurance that symptoms are likely to decrease, muscle massage, application of heat, and relaxation techniques.[8,9] Isometric contraction and passive jaw exercise[9] may be employed in an effort to alleviate muscle tenderness by a variety of techniques. Decreasing the rate of advancement may also be helpful in improving symptoms.[6]

Symptoms of pain or discomfort that continue or worsen through the day, last more than a few weeks, or interfere with a patient's normal daily function should be considered persistent and may hinder long-term adherence to OAT.

Persistent Temporomandibular Joint Pain

"Palliative care, isometric contraction and passive jaw stretching exercises, verifying or correcting midline positions, appliance adjustment, decreasing the titration rate, decreasing advancement, and conducting a temporomandibular disorder work-up and management are considered first-line treatments to manage persistent temporomandibular joint pain. Placing posterior stops or anterior discluding elements, decreasing wearing time and temporarily discontinuing use of oral appliance therapy are considered second-line treatments. If these treatment options are insufficient or inappropriate, using a daytime intraoral orthotic, prescribing a steroid dose pack, recommending a different oral appliance design, referring to a dental specialist or additional health care provider, and permanently discontinuing oral appliance therapy may also be appropriate."

It is important to document the findings at the initial presentation of persistent joint pain and then at each subsequent visit until symptoms resolve. Reassurance to the patient is essential, as most studies have found that TMJ pain and discomfort—both baseline discomfort and discomfort associated with oral appliance use—decrease with continued oral appliance use.[9–12]

Palliative care for persistent TMJ pain includes resting the joints as much as possible, intermittently applying ice to the affected joints and adopting a soft diet until the pain resolves. The judicious use of anti-inflammatory and pain medication may aid with resolution. Isometric contraction and passive jaw stretching exercises may be beneficial.

Maxillary and mandibular midlines may not be coincident when the patient protrudes without the appliance. It is important to verify that the midline relationship when the appliance is fully seated matches the relationship when the patient protrudes without the oral appliance. Oral appliances that have independent right and left side advancement mechanisms may be adjusted if necessary to re-establish the midline relationship or to provide relief of symptoms. If the TMJ pain is unilateral, decreasing the advancement on the affected side may help. If the dentist is not able to resolve the cause of the persistent TMJ pain, it may be advisable to conduct a thorough examination for TMJ disorder to identify the cause of the pain, with documentation of both muscle and joint function and levels of discomfort during palpation, function, and movement.

Decreasing the advancement rate may facilitate TMJ accommodation to the repositioned mandible. If the appliance has already been advanced to maximum protrusive position, reducing the amount of advancement may be beneficial. Aarab et al. reported that tenderness in muscles of mastication was more prevalent at 50% and 75% maximum protrusion than at 25% maximum protrusion. However, this approach must be balanced against decreasing the optimal therapeutic effect.[6]

Second-line treatment includes the addition of posterior acrylic stops that may increase patient comfort in appliance designs whose contact is otherwise limited to the anterior region. An anterior stop that produces posterior disclusion may be added to appliance designs with flat contact of the maxillary and mandibular elements.

Additional second-line treatment includes instructing the patient to decrease their time wearing the oral appliance. Decreased wearing time may mean wearing the appliance fewer hours each night or fewer nights per week. In the case of severe pain that is affecting the patient's quality of life and sleep, temporary discontinuation of the appliance may be indicated.

If TMJ pain persists despite the aforementioned measures, it may be appropriate to recommend a different oral appliance design. If the existing appliance rigidly holds the mandible, a design that facilitates more jaw movement may improve the pain. Conversely, some patients may benefit from a more rigid design if the existing design permits too much freedom of movement. Refractory temporomandibular symptoms related to OAT are uncommon. These patients may sometimes benefit from a daytime intraoral orthotic and/or referral to a dental practitioner with advanced education in facial pain disorders.

Appropriate options in occasional circumstances include the use of steroid packs or permanent discontinuation of OAT. A steroid pack may be recommended for limited use and in accordance with pharmacologic recommendations. The decision to permanently discontinue oral appliance use is a collaborative decision that should include the patient's local treating physician to ensure that adequate alternative therapy is available.

Tenderness in Muscles of Mastication

"Palliative care, watchful waiting, verifying or correcting midline positions, use of a morning occlusal guide, and isometric contraction and passive jaw stretching exercises are considered first-line treatments to manage tenderness in the muscles of mastication. Decreasing oral appliance advancement, vertical dimension, and the rate of forward titration, modifying the acrylic, and temporarily discontinuing use of oral appliance therapy are considered second-line treatments. If these treatment options are insufficient or inappropriate, recommending a different oral appliance design, referring to a dental specialist or additional health care provider, and permanently discontinuing oral appliance therapy may also be appropriate. In very rare instances, increasing oral appliance advancement may be indicated."

Initial care is usually conservative. Palliative care, in addition to the options mentioned in the Common Management Considerations section, includes muscle massage, application of heat, and relaxation techniques. If inflammation is suspected, the application of cold packs to the affected area may be helpful. Watchful waiting may also be an appropriate first-line treatment. The verification and/or correction of midline position may allow for a more comfortable position for the muscles and other soft tissues. Pain or dysfunction may be attributed to an imbalance in the protractive forces particularly when using an appliance where two separate lateral titration mechanisms are utilized. A morning occlusal guide as described under the Common Management Considerations section may also be considered as an adjunctive therapy to help with muscle tenderness. Isometric and passive jaw stretching exercises may be employed in an effort to alleviate muscle tenderness.

If tenderness in the muscles of mastication continues despite the aforementioned measures, second-line treatments include decreasing the rate of forward titration, decreasing oral appliance advancement, reducing vertical dimension, modification of the acrylic, and temporarily discontinuing use of OAT. A decrease in the titration rate may be appropriate if the optimal mandibular position has not yet been attained. Chen et al. investigated side effects of the Klearway appliance and noted that muscle tenderness in the lateral pterygoid region was more common during the active titration phase.[13] Therefore, it may be beneficial to advance the appliance at a rate lower than usually prescribed. For example, if the patient is instructed to advance the appliance 0.25 mm twice a week, it may be helpful to decrease the advancement to 0.25 mm once a week.

If the appliance has already been advanced to maximum protrusive position, reducing the amount of advancement may be beneficial. Aarab et al. reported that tenderness in muscles of mastication was more prevalent at 50% and 75% maximum protrusion than at 25% maximum protrusion. However, this approach must be balanced against decreasing the optimal therapeutic effect.[6]

Another option to consider is to decrease the vertical dimension of the appliance by judicious adjustment of the acrylic on the occlusal surfaces. With the aid of articulating paper, even contact is verified on all occlusal surfaces after the vertical dimension has been reduced. Acrylic modifications to appliances with dorsal "fins" include reducing the lingual aspect of the fins. This may serve to permit more lateral movement and decrease muscle tenderness.

In order to alleviate persistent muscle tenderness, it may be necessary to temporarily discontinue use of the mandibular advancement appliance until inflammation subsides. Palliative measures, as described previously, may hasten resolution of symptoms, after which oral appliance use may be resumed. Upon resumption of wear, it may be useful to decrease the amount of mandibular advancement and proceed at a slower titration rate until therapeutic benefit is achieved.

In rare instances, it may be appropriate to advance the oral appliance. The decision to advance the appliance may come from subjective information such as the patient reporting continued snoring or nonrestorative sleep. Objective data from home sleep apnea testing or polysomnography revealing continued apneas and/or hypopneas may also indicate the need for advancement or further evaluation and treatment planning.

Recommendation of a different oral appliance design may be necessary if the clinician judges that muscle tenderness is a result of an appliance design that maintains the jaws in a rigid relationship. When choosing an oral appliance design, it may be appropriate to consider appliance designs that permit lateral movement of the jaws if a patient has evidence of lateral bruxism.

The practitioner may also consider referral to an additional health care provider such as a physical therapist to help alleviate muscle tenderness. If, after repeating the TMJ examination, the clinician is unable to determine the cause of muscle tenderness, referral to a dentist who has undergone advanced education in facial pain may be appropriate.[14] Additionally, it is important to recognize that some pain conditions are exacerbated by comorbid conditions and/or changes in the effectiveness of medications such as selective serotonin reuptake inhibitors; thus, consultation with the patient's primary care provider, local treating physician, or other medical specialist may be necessary to appropriately manage muscle tenderness secondary to OAT.

If none of the aforementioned options serve to manage the patient's muscle tenderness sufficiently to continue with OAT, permanent discontinuation of OAT may be necessary.

Joint Sounds

"Watchful waiting is considered first-line treatment to manage joint sounds caused as a result of using an oral appliance. If this treatment option is insufficient or inappropriate, temporary or permanent discontinuation of oral appliance therapy may also be considered."

TMJ sounds secondary to OAT are usually transient and resolve with time.[9,15,16] When they occur, first-line treatment is watchful waiting. This involves recording the type and location of the sounds and what movement or activity elicits the sounds. Patient reassurance and counseling includes a frank discussion about the uncertainty of joint sound resolution, either with continued use of the oral appliance or after discontinuation. If the joint sounds are accompanied by persistent TMJ pain, however, temporary or permanent discontinuation of the oral appliance may be warranted.

Intraoral Tissue-Related Side Effects

Soft Tissue and Tongue Irritation

"Palliative care and appliance modification are considered first-line treatments to manage soft tissue and tongue irritation side effects. Temporarily discontinuing use of the oral appliance is considered second-line treatment. If these treatment options are insufficient or inappropriate, orthodontic wax and switching to a different oral appliance design may also be considered appropriate."

Intraoral soft-tissue side effects including tongue irritation related to OAT are usually transient and minor if addressed promptly.[17,18] Mechanical trauma of the soft tissue is not unique to oral appliances used to treat sleep apnea. It commonly occurs with other oral devices such as dentures and orthodontic appliances. Techniques for treating soft-tissue issues and tongue irritation related to these other dental appliances will also be applicable to appliances used to treat sleep apnea. Palliative care, in addition to the options mentioned in the Common Management Considerations section, includes patient reassurance and application of topical medications. Appliance modification should focus on recontouring the appliance material to remove sharp, protruding, or offensive features that may impinge on the soft tissues. It may also involve the addition of material for the purpose of creating a physical protective barrier or more physiologic contour.

In infrequent instances, orthodontic wax may be recommended for use by the patient as needed over intrusive appliance components that cannot be recontoured or removed.

If intraoral soft-tissue side effects persist despite the aforementioned measures, consider discontinuing use of the oral appliance temporarily in order to remove the potential irritant and promote more rapid soft-tissue recovery. The patient should be encouraged to use continuous positive airway pressure or consult with their local treating physician about alternative OSA treatment during the oral appliance holiday. Use of the oral appliance is resumed after the offending tissue irritation has resolved.

In occasional circumstances, a different oral appliance design may be selected that positions device components in a way that interferes less with the soft tissues.

Gingival Irritation

"Modification of the appliance and palliative care are considered first-line treatments to manage gingival irritation. Discontinuing oral appliance therapy temporarily is considered second-line treatment."

Appliance modification refers to removal of or adjustment to appliance material (such as acrylic or hardware) that may impinge on the gingival tissues. In addition to the options mentioned in the Common Management Considerations section, palliative care includes documentation of gingival health and attachment level.

If gingival irritation persists despite the aforementioned measures, it may be beneficial to discontinue use of the oral appliance temporarily in order to remove the potential irritant and promote more rapid gingival healing. The patient should be encouraged to use continuous positive airway pressure or consult with their local treating physician about alternative OSA treatment during the oral appliance holiday. Use of the oral appliance is resumed after the gingival irritation has resolved.

Excessive Salivation

"Watchful waiting is considered first-line treatment to manage excessive salivation/drooling. Modification to the appliance is considered second-line treatment. If these treatment options are insufficient or inappropriate, prescribing medications to decrease salivary input may also be appropriate."

Numerous studies have demonstrated that oral appliances are well tolerated despite excessive salivation/drooling and only rarely preclude use.[19–23] Excessive salivation is reported very often but generally decreases with time. Patients should be informed in advance of possible excessive salivation and helped to understand that it is typically transient over the first few weeks. Hypersalivation has not been associated with any specific appliance design. Reassurance often suffices to manage excessive salivation/drooling.

Excessive salivation/drooling as a side effect of OAT is generally benign and initial care can be very conservative. Watchful waiting entails recognizing the problematic annoyance to patients and reassuring them that in most cases this issue will subside in a matter of days or weeks. In some cases, when the problem is minimal, patients may simply accommodate to it. Documentation of findings should be included in the patient's record and follow-up of concerns at subsequent visits should occur and be recorded.

Modification to the appliance may be considered in certain instances if it appears that the shape or design of the appliance may be contributing to the excessive salivation/drooling. Decreasing vertical dimension may be appropriate when it is deemed that it will allow for more effective lip seal or greater ease in swallowing. In certain cases, a mouth shield or oral obturator can be added to the appliance to prevent seepage of oral fluids.

Certain medications are known to decrease salivation and can be utilized if the practitioner is well versed in the use of such medications and is certain that the patient's medical history does not contraindicate such use. Consultation with the patient's local treating physician is advisable.

Dry Mouth

"Palliative care, watchful waiting, and decreasing vertical dimension of the device to encourage lip seal, are considered first-line treatments to manage dry mouth. Modification of the appliance and techniques for discouraging mouth breathing are considered second-line treatments. If these treatment options are insufficient or inappropriate, avoiding commercial mouth rinses with alcohol or peroxide, mouth-taping, and referring to an additional health care provider may also be considered appropriate."

Many studies have demonstrated that oral appliances are well tolerated despite dry mouth and only occasionally preclude use.[19,20,23] Dry mouth is reported very often and may continue with time. Patients should be informed in advance of possible dry mouth, especially against the background of nasal airway resistance. Dry mouth was not associated with any specific appliance design.

Dry mouth as a side effect of OAT is generally benign and initial care can be very conservative. Watchful waiting entails recognizing the problematic annoyance to patients and reassuring them that in most cases this issue may subside in a matter of days or weeks, or they may simply accommodate to it. When patients are struggling to continue appliance use due to dry mouth, conservative palliative care can be initiated by decreasing vertical dimension of the appliance to encourage lip seal or keeping water by the bed for adequate hydration during the night.

When it is believed that medications are responsible for dry mouth, consultation with the patient's local treating physician may be beneficial to see if medications can be changed. Limiting tobacco, alcohol, caffeine, and sugary/acidic foods prior to bedtime may be effective in preventing dry mouth during sleep. Similarly, avoidance of commercial mouth rinses with alcohol and peroxide may be effective.

Techniques for discouraging mouth breathing can be considered in certain instances. When nasal airway resistance appears to be leading to mouth breathing during sleep, evaluation and treatment by an otolaryngologist may be effective. If the nasal airway is patent and the patient is amenable, suitable medical tape may be placed over the lips to prevent excessive lip separation. It is prudent to place the tape vertically over the lips to allow passage of air around the sides of the tape should mouth breathing become necessary.

Occlusal Changes

Altered Occlusal Contacts/Bite Changes

"Watchful waiting, jaw stretching exercises, and use of a morning occlusal guide are considered first-line treatments to manage altered occlusal contacts or bite changes. Chewing hard gum in the mornings and making modifications to the appliance are considered second-line treatments. If these treatment options are insufficient or inappropriate, discontinuing oral appliance therapy temporarily or permanently may also be appropriate."

A direct relationship has been demonstrated between the amount of protrusion and the magnitude of the forces sustained by the dental structures. Forces to the maxilla from the oral appliance are directed distally and intrusively to the posterior segments. However, forces to the mandible are directed anteriorly and intrusively to the anterior segments. These force vectors help to explain the occlusal and skeletal side effects associated with the use of oral appliances.[24] The clinician should strive for conservative titration of the appliance, because it has been demonstrated that the number of side effects can be larger, starting at 50% protrusion position.[6] Moreover, research shows that 50% and 75% protrusion can be equally effective in groups of patients with mild to moderate OSA.[25]

Development of posterior open bites is a common occurrence with OAT.[9,18,26–30] In a 5-year follow-up study of 45 patients, Ueda et al. noted that the number of occlusal contacts decreased in 67% of patients.[28] Most of these changes occurred in the premolar and molar regions. In a study of 51 patients using oral appliances, Doff et al. recorded a significant decrease in the number of posterior occlusal contacts after 2 years of OAT.[30] Patients tolerate or are even unaware of such changes and do not discontinue treatment as a consequence.[9,26,27,31,32]

Initial care is usually conservative and includes watchful waiting. Although there is very little literature addressing the use of any method to prevent or correct the amount of occlusal changes, the daily usage of the morning occlusal guide is recommended.

Jig exercises and jaw stretching exercises can also be used, as described by Ueda et al.[33] Jaw exercises may relieve masticatory muscle stiffness and accelerate the repositioning of the mandible to the normal position, in addition to preventing or minimizing the occlusal functional changes in susceptible patients.[33] Anecdotal evidence suggests that chewing gum in the morning may help reestablish habitual occlusion and is suggested as second-line therapy because chewing gum has potentially very few side effects.[34]

In other instances, modification of the appliance by strategic acrylic relief can be considered if altered occlusal contacts appear to be caused by an ill-fitting appliance or if the clinician seeks to reduce the pressure on specific teeth to prevent or minimize potential bite changes.

At times it may be appropriate to temporarily or permanently discontinue OAT. Discontinuation of OAT should only be considered if an alternative treatment is acceptable.[12]

In all cases, decisions to accept or to correct the occlusal changes should be guided by the extent of the problem, acceptability of treatment alternatives, and the concerns of the patient.

Incisor Changes

"Watchful waiting, use of a morning occlusal guide and modification to the appliance are considered first-line treatments to manage incisor angulation and position changes. If these treatment options are insufficient or inappropriate, recommending a different oral appliance design and discontinuing oral appliance therapy permanently may also be appropriate treatment options."

Among the earliest and persistently reported alterations in occlusion secondary to OAT were changes in maxillary and mandibular incisor position and angulation.[4,18,35–38] Pliska et al. reported that anterior crossbites of at least 1 tooth, but more commonly of 4 anterior teeth, occurred in 62% of patients followed for an average of 11 years.[39] Changes in incisor angulation are difficult to quantify without lateral cephalograms, but alterations in incisor anteroposterior position can be documented by serial diagnostic casts.

Changes in incisor angulation and position are generally manifested as changes in overjet and overbite that are perceived by patients and clinicians alike. First-line treatment includes watchful waiting. Modification to the appliance may also be considered first-line treatment to decrease pressure on the incisors. Forces from OAT are directed palatally to maxillary incisors and labially to mandibular incisors and increase nearly linearly with increases in mandibular advancement.[24] Relief of the acrylic contacting the labial surfaces of maxillary incisors and lingual surfaces of mandibular incisors may reduce reciprocal forces on the incisors while wearing an oral appliance. For patients with shallow overbites and minimal overjet, similar acrylic modification to Klearway appliances has been recommended.[13]

Occasionally, it may be necessary to change to a different oral appliance design to decrease or eliminate undesirable forces on the incisors. If the incisor changes are unacceptable and previous treatments are ineffective, permanent discontinuation of OAT may be necessary, but not before consultation with the patient's local treating physician to ensure treatment alternatives to manage OSA are in place.

Decreased Overjet and Overbite

"Watchful waiting, isometric contraction and passive jaw stretching exercises, and use of a morning occlusal guide are considered first-line treatments to manage decreased overjet and overbite. Chewing hard gum in the morning is considered second-line treatment."

Studies suggest a likelihood as high as 85.7% of a decrease in overjet and overbite in patients managed with OAT.[4] Although patients are often unaware of and tolerant of these changes, patients must nonetheless be informed of these risks prior to initiating OAT.

Due to patient acceptance of general changes in overjet and overbite, initial management is usually conservative; first-line treatment consists of watchful waiting.

Morning occlusal guides are considered first-line treatment for decreased overjet and overbite and are widely used. First-line treatment also includes the use of isometric and passive jaw stretching exercises, which may facilitate reestablishment of habitual occlusion.[33]

Chewing hard gum, bilaterally, is recommended as second-line treatment. Though only anecdotal evidence supports this recommendation, this may be an effective treatment to accomplish the same objectives as mandibular exercises.[34]

Alterations in Position of Mandibular Canines and Molars

"Watchful waiting and use of a morning occlusal guide are considered first-line treatments to manage altered positions of mandibular canines and molars."

In the early 2000s, mesial shifting of mandibular molars and canines was recognized as a side effect of OAT in follow-up studies of up to 2.5 years.[19,27,40,41] Analysis of plaster study casts,[4,27,42] cephalometric radiographs, and 3-dimensional computer-assisted study model analysis noted mesial shifting of the canines and molars in as many as 27% of subjects.[13,28,43] In most of these studies, oral appliances completely covered the dentition, and yet dental alterations occurred regardless.[4,19,41] In a study of an oral appliance fabricated from either soft elastomeric material or hard acrylic, significant mesial shifting of first molars and premolars occurred in both groups, although the change was greater in the hard acrylic group.[41]

Other alterations in the positions of the molars and canines have been noted and include changes in arch width and canine rotations. Changes varied by arch, right or left side position, and Angle classification.[4,13,41] Alterations in molar and canine position continue with prolonged OAT.[13,39] Although altered canine and molar positioning may develop in many patients, occlusal changes led to patient nonadherence in only 12.4% of patients surveyed at follow-up after an average of 5.7 years.[44]

Watchful waiting is the first-line treatment of occlusal changes, and evaluation of the patient's dental alignment should continue as long as the patient is using the oral appliance. Evaluations are suggested every 6 months for the first year, and reevaluation at least annually thereafter.[45] If the changes are of concern to the patient, alternative therapies should be reviewed with the patient. If the patient declines to continue OAT, the local treating physician should be notified to ensure continued appropriate management of the patient's OSA.

Morning occlusal guides are also considered first-line therapy for management of the mesial shift of mandibular canines and molars. They may also be used as a record of the patient's pretreatment habitual occlusion.

Inter-Proximal Gaps

"Watchful waiting, use of a morning occlusal guide, adjusting ball clasps and making modifications to the appliance are considered first-line treatments to manage interproximal gaps. If these treatment options are insufficient or inappropriate, use of a distal

wrap-around retainer and restoration of contact areas may be appropriate."

Open interproximal contacts serve as food traps and may concern patients. Development of open contacts has been documented with OAT and is associated with longer oral appliance use.[4] They occur with greater frequency in patients who are Angle Class 1 and are more prevalent in the mandibular arch.[4,42]

First-line treatment includes watchful waiting and the use of a morning occlusal guide to prevent occlusal changes.

If the oral appliance relies on ball clasps for retention, adjustment or removal of retentive clasps may decrease the occurrence of interdental gaps, but it is noteworthy that interproximal gaps have occurred even when the device was acrylic retained and did not utilize ball clasps.[42]

Modification of the device may include adding a small amount of base material to strategic areas of the oral appliance in an effort to reposition the teeth to close open contacts and counteract the forces placed on these teeth by mandibular advancement. For example, placement of material on the oral appliance lingual to the maxillary incisors, labial to the mandibular incisors, or distal to the last teeth in the arch are strategies to accomplish this effect. Judicious reduction of interproximal acrylic "fins" that aid in retention may also decrease the occurrence of interproximal gaps by reducing the interproximal forces from the wedging effect of these retentive fins.

Daytime use of a distal wrap-around retainer, such as a vacuum-formed acrylic splint, to maintain or recapture initial tooth position may also be considered. An orthodontic-type retainer with a distal wrap-around spring may also be effective in closing or preventing interproximal gaps.

If appliance modification is not effective and a periodontal problem develops or the patient continues to complain about food trapping, restoration of the contact area may be required to prevent loss of periodontal support of the teeth. However, because continued use of OAT may lead to re-creating the interproximal spaces, a restorative approach may not be an effective long-term solution.[4]

Damage to Teeth or Restorations

Tooth Mobility

"Palliative care and modifying the appliance are considered first-line treatments to manage tooth mobility. Decreasing the titration rate is considered second-line treatment. If these treatment options are insufficient or inappropriate, daytime/fixed splinting of teeth may also be appropriate."

Palliative care may be sufficient for managing discomfort associated with tooth mobility, tooth tenderness, gingival discomfort, and hypersensitivity. Nonsteroidal anti-inflammatory drugs or other pain relievers may be used to manage the pain of mobility.

Modification of the internal surface of the device in the area of tooth mobility may be necessary to alleviate the discomfort as well as to reduce mobility. The use of various fit-checking materials can help identify areas of increased pressure on affected teeth. Decreasing the oral appliance advancement rate during initial calibration may allow adaptation to the forces of protrusion that are transmitted to the teeth.

Temporary discontinuation of OAT may be helpful in alleviating discomfort associated with the mobile teeth. Palliative measures may hasten resolution of symptoms, after which oral appliance use may be resumed. Upon resumption of wear, it may be useful to decrease the amount of mandibular advancement and proceed at a slower titration rate until therapeutic benefit is achieved. The elimination or modification of anterior ramps, if used on the opposing arch, may also be helpful. Tooth mobility that is detected after the appliance has been advanced to the target protrusion may be addressed by temporarily reducing the protrusive position to allow mobile teeth to adapt to the forces and potentially stabilize before resuming gradual return to the target protrusion.

If mobility does not respond to aforementioned treatments, daytime use of a pressure or vacuum-formed clear retainer, or alternatively bonded resin splinting, may be considered in cases of persistent tooth mobility. Changing to a different oral appliance design may ultimately be necessary.

Tooth Fractures or Damage to Dental Restorations

"Modifying the appliance and referral to a general/restorative dentist are considered first-line treatments to manage tooth fractures or damage to dental restorations. If these treatment options are insufficient or inappropriate, recommending a different oral appliance design may also be appropriate."

Fractures and damage to restorations or teeth may be a direct result of the stresses on the teeth and restorations caused by appliance clasps or other forms of retention. These may also occur indirectly from OAT as a result of changes to the bite, causing increased stresses on the dentition, especially on anterior teeth.

Bite changes from long-term OAT include reduction of overjet that may result in an increase in forces on anterior teeth, causing chipping or fractures.[46] Although anecdotal evidence supports the occurrence of occasional fracture of teeth or restorations, no published studies were identified that describe the frequency of this side effect.

If the dental sleep medicine dentist is also the patient's general or restorative dentist, treatment of tooth chipping or fractures may involve conservative recontouring of rough edges, bonding, or more definitive restoration when warranted. When dental damage occurs, particular attention should be paid to possible occlusal prematurities emerging as a result of the changing overjet/overbite relationship. Selective occlusal adjustment may be considered to reduce the risk of additional chipping or fractures.

When damage to teeth is the direct result of stresses from the appliance, the internal surface of the appliance should

be modified to eliminate forces that potentially caused the fracture of the tooth and/or dental restoration. Any clasps or tight-fitting acrylic adjacent to the damaged tooth or restoration should be adjusted to eliminate stress on that portion of the tooth structure or restoration. This area of the appliance should also be modified sufficiently to permit proper restorative treatment and to reduce the possibility of recurrence.

Ultimately, if the dental sleep medicine dentist is not also the patient's general or restorative dentist, the patient should be referred to their primary dental care provider if restoration of the dentition is needed for cosmetic or functional reasons.

If the appliance design or material has contributed to the fracture of a tooth or dental restoration, a different appliance design and/or material may be indicated to redirect force vectors and retention features from the damaged area.

Appliance Issues

Appliance Breakage

"Repairing or replacing the appliance is considered first-line treatment to manage appliance breakage. If these treatment options are insufficient or inappropriate, recommending a different oral appliance design may also be appropriate."

Appliance breakage is a relatively common problem across the field of dental sleep medicine. Some appliances may be more prone to these problems, and it behooves the prescriber to gain experience and knowledge to help avoid and/or mitigate this treatment complication. Several articles describe appliance breakage or broken components (clasps, acrylic flanges, etc.).[32,47,48] In a 2-year follow-up study of patients treated with a Herbst appliance, Battagel and Kotecha reported that 60% had experienced appliance breakage with subsequent repair and 40% required a replacement appliance.[32] Martínez-Gomis et al. noted that most breakages occurred in the telescopic mechanism of the Herbst appliance.[47]

When an oral appliance has suffered wear or breakage due to fatigue or acute stress, the clinician must judge if repair of the defective appliance is feasible or, if not, recommend replacement of the device. If appliance breakage occurs repeatedly, further investigation is warranted to determine if the underlying cause of the breakage is due to patient behavior or anatomic variation that may be incompatible with that appliance design. If so, replacement of the oral appliance with a different design would be appropriate.

Allergies to Appliance Materials

"Removing the allergenic material and temporary discontinuation of oral appliance use are considered first-line treatments to manage allergies to appliance material. If these treatment options are insufficient or inappropriate, referring to another health care provider may also be considered as a treatment option."

It may be difficult at times to recognize that intolerance to OAT may be due to an allergic response to appliance materials. Moreover, a patient may perceive an allergic response when none actually exists. The clinician will need to distinguish if a true allergic reaction has occurred or if the symptoms are caused by pressure irritation or other irritation from the device or its components. Sometimes the patient will report mucosal dryness, redness, or irritation and mistake these conditions as an allergic response to the appliance.[8]

If the offending allergen can be identified, through allergy testing if necessary, the clinician should ascertain if the appliance can be fabricated without the allergenic material, or replace the appliance with a different design that is fabricated with nonallergenic materials. For example, nickel, a common component in stainless steel, may elicit a hypersensitivity reaction within the first week in some patients. Altering the appliance by substitution of nonallergenic metals such as chrome, gold, and titanium should also be considered.

If the allergenic material cannot be identified, the dentist should inquire about the new or ongoing use of adjunctive intraoral products that might cause the reaction. Such products include but are not limited to toothpastes, mouth rinses, or lozenges. Inquiry regarding materials used to clean the device may also lead to identification of allergens, as common device-cleaning agents can be noxious and offensive to the soft tissues.

Note that some tissue reactions might occur that are not true allergies. If these irritations are significant enough, however, they need to be managed in the same manner as an allergen. Methyl methacrylate acrylic is a common substance used in the fabrication of most oral appliances. If a device is manufactured with inadequate curing (heat/pressure), the material is more porous, less dense, and contains more unlinked monomer. In susceptible individuals, methyl methacrylate acrylic may cause irritation, which can be exacerbated by inadequately cured acrylic.

It is always prudent, if simple measures are ineffective at relieving the irritation/reaction, to refer the patient to another health care provider such as an allergist or dermatologist, or where unavailable, an otolaryngologist or primary care physician for clinical evaluation and testing.

Gagging

"Modification to the appliance is considered first-line treatment to manage gagging. Deprogramming the gag reflex is considered second-line treatment. If these treatment options are insufficient or inappropriate, recommendation of a different oral appliance design may also be appropriate."

Initiation of the gag reflex may be elicited by an oral appliance. Some patients describe this sensation as a feeling of bulkiness from the appliance causing "choking" and "difficulty breathing."[49] Difficulty with swallowing might also activate the gag reflex. In addition, appliances that hold the mandible rigidly may precipitate feelings of anxiety, gagging or panic.

First-line treatment to help mitigate gagging symptoms include modifications to the oral appliance acrylic to decrease

its bulk by thinning the acrylic or trimming it back to the level of the cementoenamel junction if this can be accomplished without affecting appliance retention.[50] Second-line treatment includes desensitization techniques. Use of anesthetic rinse, spray, or gel may alleviate the initial sense of crowding or eliminate the soft-tissue triggers that may give rise to gagging. These as well as other desensitizing techniques may be managed directly by the dental provider or with the help of those more specifically trained in these areas. Cognitive behavioral therapy may also be effective, managed by those specifically trained in its use.

If appliance modifications and/or desensitization techniques fail to resolve the gagging, the practitioner may consider different oral appliance designs that are less bulky, provide more tongue space, permit free lateral movement of the mandible, or allow uninhibited opening and closing.

Anxiety

"Watchful waiting and use of desensitization techniques are considered first-line treatments to manage anxiety. If these treatment options are insufficient or inappropriate, recommending a different oral appliance design and referring to a different health care provider may also be appropriate."

If a specific device holds the mandible tightly in an immovable position, feelings of anxiety, gagging, or panic may ensue. A common phrase within the literature to describe anxiety as a side effect of OAT was the sense of a "suffocation" that led to discontinuation of oral appliance use.[44] "Choking" and "difficulty breathing" were also noted by some researchers to yield levels of anxiousness sufficient to discontinue OAT.[49]

When anxiety presents as a side effect of OAT, watchful waiting may suffice in order to provide the patient an opportunity to accommodate to the appliance. Desensitization techniques may also prove helpful. One technique consists of asking the patient to wear the appliance for a specified time, such as 1 hour, prior to bedtime until the patient establishes an acceptable level of tolerance for the appliance.

A different oral appliance design may be necessary as some features may be more tolerable for anxiety-prone patients. Examples include appliances that allow free lateral movement of the mandible or uninhibited jaw opening and closing or appliances with less bulk that may facilitate easier swallowing.

If success is not achieved through any of the preceding recommendations, it would be prudent to work with the local treating physician to consider alternative definitive or adjunctive therapy including surgery.

SUMMARY OF THE LITERATURE

The recommendations of the consensus panel on the management of the side effects of OAT are based on their clinical expertise and experience and a body of literature that included more than 140 articles. The articles included 29 randomized controlled trials in addition to numerous prospective cohort studies, retrospective studies, reviews, systematic reviews, and meta-analyses. The studies spanned a period of more than 20 years of research on OAT from 1992[51] to 2016.[52] The findings represent diverse populations: Europe,[12] North America,[9] New Zealand,[53] Australia,[54] Asia,[55] and South America.[5]

Side effects were recorded from studies comparing one appliance design to another,[17,18,50,55,56] OAT to continuous positive airway pressure,[37,57–60] different protrusive positions in the same appliance,[6,7] OAT versus placebo,[54] and OAT versus uvulopalatopharyngoplasty.[25] The literature included a report on side effects in subjects who had been wearing an oral appliance for a minimum of 8 years[39] and others in whom use of an oral appliance had been at least 2 years.[11,18,30,40,61] Most side effect reports were derived from patient self-report through questions at examination, mail or phone questionnaires, or a combination of these methods. The reporting periods ranged from several days after commencing OAT to several years. Side effects that are quantifiable have been extensively and systematically studied using imaging techniques[27,62,63] or analysis of dental casts.[13,39,41,42]

Although most studies describe the type and frequency of side effects, only a few comment on strategies used to mitigate the side effects, and informative details are lacking.[55,56,62,64,65] Even fewer studies investigate interventions to minimize side effects.[5,29,33]

Reports of discomfort or pain in the teeth, muscles, TMJ, tongue, or other oral structures are common. However, only a limited number of studies describe using structured clinical examination methods to evaluate the prevalence and/or incidence of dysfunction and/or pain in the TMJ, muscles of mastication, and teeth or oral structures.[9,11,12,25,40,61,66–69]

Although research in the field of dental sleep medicine has advanced considerably over the past two decades, more information is needed to develop evidence-based guidelines on the most effective treatment options to manage the side effects of OAT for sleep-disordered breathing.

DISCUSSION AND FUTURE DIRECTIONS

Some side effects of OAT are common, causing permanent alterations in dental occlusion and, less often, soft-tissue or TMJ pain, which may negatively affect long-term adherence with therapy. Although guidelines exist for long-term follow-up of all patients using OAT to treat OSA—a lifelong disease with age-related increase in severity—sparse information is available to guide clinicians on how to address side effects related to OAT. The current literature is rife with descriptions of side effects but is lacking in the clarification of causative factors and methods to minimize these adverse effects. Few published data clarify what interventions are most effective, and the recommendations offered are rarely evidence driven. Available studies suggest that side effects may be related to oral appliance design, materials, and amount of mandibular advancement, and long-term studies describe a progressive increase in occlusal side effects with ongoing use of OAT.

Current evidence supports watchful waiting as the major treatment for OAT-related side effects unless discomfort is

present. Most interventions are palliative, involve modification of the oral appliance, or require no active therapy. Many of the side effects were thought to be best addressed prophylactically with use of a morning occlusal guide to help prevent occlusal alterations or to minimize transient muscle contraction. However, it must be noted that despite the widespread use of this technique, no evidence to date has demonstrated its effectiveness.

At this conference, consensus on recommended treatment options was reached among the panelists based on limited empirical evidence. Decisions were often informed by clinical experience and the results of an online survey of practitioners of dental sleep medicine. It is anticipated that these recommendations will highlight specific questions that need clarification and will encourage researchers to design studies to advance the field.

Standardization of both the definition of OAT success as well as clinical and outcome measures in OAT research would enable meaningful comparison across studies. Investigation is needed to clarify factors that lead to the onset and progression of side effects such as appliance design features, appliance materials, vertical and sagittal mandibular positioning, and duration of OAT. Anthropomorphic and imaging studies may help identify patients at greater risk for the occurrence of side effects.

Ultimately an understanding of how the management of OAT side effects influences OAT adherence will ensure that patients with sleep-disordered breathing are optimally treated. More evidence is needed to identify the most effective strategies for minimizing or preventing the occurrence of untoward side effects. Outcomes of research that focuses on these issues are expected to lead to revisions of these recommendations in the future.

These recommendations have been endorsed by the AADSM.

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