



## Obstructive Sleep Apnea and Oral Appliances- Review

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### ABSTRACT

*Obstructive sleep apnea is a chronic, progressive and disabling sleep related breathing disorder. It requires long term, multidisciplinary management .Various treatment modalities such as behavioural, medical, surgical options are available. Contribution from various health care specialties could lead to effective treatment benefits when considering treatment for OSA. The most common clinical procedure involves continuous positive airway pressure (CPAP). Orthodontics is not just limited with mere alignment of the teeth and smile esthetics but it has an expanded health care role that has established a new standard of health care for OSA patients. Oral appliances are simple, noninvasive, cost effective and reliable treatment method compare to all other airway pressure therapy and surgical approach in mild and moderate OSA patient.*

**Key word:** Apnea, CPAP, Obstructive Sleep Apnea, Oral appliance, Polysomnography.

### INTRODUCTION

Obstructive Sleep Apnea is a prevalent but under recognized chronic sleep related breathing disorder with associated substantial morbidity and mortality. It is characterized by recurrent episodes of partial or complete upper airway obstruction during sleep.<sup>1</sup> This manifests as a reduction (hypopnoea) in or complete cessation (apnoea) of airflow despite ongoing inspiratory efforts resulting in oxygen desaturations and arousals. There is accumulating evidence that OSA is being considered as an independent risk factor for hypertension, glucose intolerance / diabetes mellitus, cardiovascular diseases and stroke, leading to increased cardio metabolic morbidity and mortality.<sup>2-5</sup>

Obstructive sleep apnoea syndrome, defined as an apnoea/hypopnoea index (AHI) of 5 or more—that is, at least five apnoeic/ hypopnoeic events per hour of sleep—plus reported sleepiness, is a common form of SDB. According to the American Academy of Sleep Medicine recommendations, OSA is defined with AHI >5, and it is classified as mild OSA with AHI of 5 to 15; moderate OSA with AHI of 16 to 30; and severe OSA with AHI > 30.<sup>1</sup> Overweight middle-aged adult men have the highest prevalence of the disease<sup>7,8</sup> yet women and an increasing number of children are also affected by OSA<sup>9</sup> This condition affects 2% to 4% of adults aged from 30 to 60 years;10 prevalence increases with age.<sup>11</sup>

**Table 1.** Definitions of terms used in obstructive sleep apnoea <sup>6</sup>

Term	Definition
Apnoea	Cessation of airflow of at least 10 seconds
Hypopnoea	≥50% decrease in airflow amplitude of at least 10 seconds; or <50% decrease In airflow amplitude associated with either an arousal or oxygen desaturation of ≥3%
Respiratory effort-related arousal	An event characterised by increasing respiratory effort for 1 ≥0 seconds, leading to an arousal from sleep but which does not fulfill the criteria for a hypopnoea or apnoea
Apnoea/hypopnoea index	No. of apnoea + hypopnoea episodes per hour of sleep
Respiratory disturbance index	No. of apnoea + hypopnoea episodes + arousals per hour of sleep

**POLYSOMNOGRAPHY <sup>12</sup>**

The gold standard diagnostic test for OSA is the overnight in-laboratory polysomnography. It involves multi-channel continuous polygraphic recording from surface leads for electroencephalography, electrooculography, electromyography, electrocardiography, nasal pressure transducer (supplemented by thermistor) for nasal airflow, thoracic and abdominal impedance belts for respiratory effort, pulse oximetry, tracheal microphone for snoring, and sensors for leg and sleep position. These recordings will identify different types of apnoeas and hyponoeas during sleep. **Polysomnography (sleep study)** results can reveal the cessation of air flow for 10 seconds even with maintenance of respiratory effort, five or more episodes of apnea per hour and a decreased oxygen saturation of at least 4% during episodes. These findings are indicative of OSA. The ideal OSA treatment,

should aim of normalizing breathing during sleep, consequently eliminating excessive daytime sleepiness and neuropsychiatric and cardiovascular changes with no side effects or risks.<sup>18</sup>

**TREATMENT MODALITIES**

The American Association of Sleep Medicine (AASM) describes continuous positive air pressure (CPAP) as the gold standard. The AASM also describes eight surgical treatment options and five conservative treatment options for the patient with OSA. The general surgical procedures most commonly include bariatric surgery to assist with significant weight loss and pharyngeal surgery to remove adenotonsillar hypertrophy and/or to reduce the size of the uvula . The dental surgical procedures include genioplasty, mandibular advancement, and maxillomandibular advancement (MMA). Oral appliance therapy is among the conservative treatment options listed.<sup>19</sup>

<b>Table-2</b> Various Diagnostic tests for OSA	
<b>Polysomnagraphy</b> - Gold standard	
Nocturnal Pulse oximetry <sup>13</sup>	CT scan <sup>17</sup>
Multiple sleep Latency Test <sup>14</sup>	MRI
Lateral cephalometric radiographs <sup>15,16</sup>	Visualisation of upper airway

**Table 3 - Various Treatment modalities**<sup>20</sup>

Treatment Type	Measures used
Conservative	- Lose weight, sleep in lateral position, avoid alcohol
Medical	- Use Nasal continuous positive airway pressure, auto-continuous positive airway pressure, bilevel positive airway pressure - Use oral appliances - Give medication - Treat associated diseases, eg hypothyroidism, acromegaly, Allergic rhinitis
Surgical	- Tracheostomy - Nasal procedure, eg turbinectomy, polypectomy, septoplasty - Uvulopalatopharyngoplasty - Laser-assisted uvulopalatoplasty - Maxillo-mandibular advancement
Experimental	- Pharyngeal pacing - Radio-frequency ablation - Rapid maxillary expansion

### ORAL APPLIANCES

Oral appliances have been recommended as a treatment option for being simple to use and non-invasive.<sup>21</sup> These devices are intended to increase the volume of the airways through a mechanical maneuver<sup>22,23</sup>. Several authors stated in their studies that oral appliances are a good alternative for the treatment of snoring and OSAS due to their low cost, relative comfort, and ease of use, which can therefore lead to greater patient compliance.<sup>24,25,26</sup>

These devices offer advantages over CPAP in that they do not require a source of electricity and are less cumbersome, especially with travel. Oral appliances are well-tolerated in most patients and therapeutic adherence may be better than CPAP.<sup>27-30</sup>

Several studies demonstrate that oral appliances can be a useful alternative to positive air way pressure with mild to moderate sleep apnea.<sup>31,32</sup> There is also robust evidence of the efficacy of oral appliances for improving polysomnographic indices and modifying the health risk associated with OSA.<sup>33</sup>

Oral device may be helpful in the management of OSA by; improving upper air way potency,

increasing the cross sectional area or decreasing the upper air way collapsibility by increasing the muscle tone.<sup>34</sup> The US FDA approved 16 devices for use in sleep apnea oral appliances as an alternative to CPAP therapy. They are designed to keep upper air way open.<sup>35</sup> The theoretical basis for the potential treatment of Oral appliance therapy is that in the supine position, all gravity dependent tissue tends to fall posteriorly, including the tongue and lower jaw. If the oral appliance can prevent one or both, the airway will remain patent reducing the number of apneic and hypopneic events. Although Mandibular Advancement Device (MAD) has positive effect in treatment of OSAS, it has multiple complications. These may include craniofacial change in maxillomandibular relationship and bony dimensions, overbite alteration, tooth pain and TMJ problems.<sup>36</sup>

Oral appliances are devices intended to protrude and stabilize the mandible to maintain a patent airway during sleep.<sup>37</sup>

A custom OA is “fabricated using digital or physical impressions and models of an individual patient’s oral structures. As such, it is not a

primarily prefabricated item that is trimmed, bent, relined or otherwise modified. It is made of biocompatible materials and engages both the maxillary and mandibular arches.” Non-custom OAs, commonly known as “boil and bite devices,” are primarily pre-fabricated and usually partially modified to an individual patient’s oral structures. In addition to being custom- or non-custom made, OAs are either titratable or non-titratable. Titratable OAs have a mechanism that allows for varying amounts of mandibular protrusion. The increasing protrusion of the mandible is considered analogous to the titration of continuous positive airway pressure (CPAP). Non-titratable OAs hold the mandible in a single protrusive position and no changes are possible over the course of treatment.

#### **ORAL APPLIANCE THERAPY RATIONALE**

The theoretical basis for the potential treatment effect is that in the supine position, all gravity dependent tissue tends to fall posteriorly, including the tongue and lower jaw. If the oral appliance can prevent one or both, the airway will remain patent reducing the number of apneic and hypopneic events. The gold standard assessment requires PSG, and this has been performed in case reports, case series, and prospective non-randomized studies. Limited sample sizes, high dropout rate, lack of controls, short study duration, and other factors make interpretation and application of these investigations difficult.<sup>38,39</sup>

More recently, higher levels of evidence using PSG in prospective randomized control studies have emerged. Okuno<sup>40</sup> demonstrated that oral appliances improved AHI more than control appliances, although less than CPAP. Contrary to previous investigators<sup>41,42</sup> their study group demonstrated similar compliance rates with oral appliances or CPAP.

In a short-term prospective randomized cross-over study, Phillips<sup>43</sup> compared the results of CPAP and a mandibular advancing device (MAD). With over 100 patients completing both arms of the

study, the MAD achieved complete resolution in 40% and partial resolution in another 25% of patients in contrast to CPAP which achieved complete resolution in 75% and partial in 15% of patients.

Nelly et al<sup>44</sup> investigated the efficacy of orthopedic mandibular advancement and/or rapid maxillary expansion in the treatment of pediatric obstructive sleep apnea. A total of 58 studies were identified. Only eight studies were included in the review; of these, six were included in the meta-analysis. Although the included studies were limited, these orthodontic treatments may be effective in managing pediatric snoring and obstructive sleep apnea. Other related health outcomes, such as neurocognitive and cardiovascular functions have not yet been systematically addressed.

Based on a single retrospective study by Holley 2011, however; there was no significant difference in the percentage of mild OSA patients achieving their target AHI/RDI/REI (<5, <10, >50% reduction) after treatment between OAs and CPAP. [For patients with moderate to severe OSA, however, the odds of achieving the target AHI was significantly greater with CPAP than with OAs.<sup>45</sup>

In an RCT conducted by Randerath<sup>46</sup>, the odds of achieving the target AHI of <10 in mild to moderate adult patients was significantly greater with CPAP than OA therapy. OA therapy should be reserved for use in severe OSA patients who did not benefit from CPAP therapy or were intolerant to CPAP<sup>47,48</sup>. In a prospective, randomized crossover trial, Robertson et al.<sup>49</sup> found that changes in the Snoring Outcomes Survey were similar with the OA and nasal CPAP. The authors also observed that the OA was superior to CPAP in improving sleep quality among bed partners. More patients in this trial also preferred the OA over CPAP for long-term treatment of snoring.

Ghazal<sup>50</sup> compared two oral appliances, a modified Herbst appliance (IST) and a prosthodontic (TAP) appliance over several years.

The study utilized 103 consecutively enrolled and randomly assigned middle-aged adults. At 6 months, both appliances improved the AHI, with the TAP having a higher percentage of success. By study end (42 months), both appliance groups showed similar results. Caution must be taken with these results as there was significant patient drop out and loss to follow-up leaving less than half the original study population. Of note, this group was among the first to examine not only the AHI, but also the effects of oral appliances on blood pressure, an important consideration given the recent concern that controlling blood pressure (BP) may be more important than AHI in reducing the adverse health effects of OSA<sup>51,52</sup>

With the increasing number of prospective randomized studies, systematic reviews and meta-analyses have now been performed examining different aspects of treatment. Using 14 of a possible 1475 studies that met their initial search criteria, Ahrens and Hagg evaluated oral appliances (one or two piece) vs. control appliances and each other<sup>53</sup>. They concluded that MAD appliances performed better than controls with two-thirds of treated patient's AHI improving. There was no difference between one-piece MAD designs and also no difference for 50% or 75% maximum protrusion. Comparing one- or two-piece design, there was no clearly superior appliance. Using 7 separate studies with a pooled 399 patients, Iftikhar<sup>54</sup> evaluated oral appliances and their effect on BP demonstrating a modest decrease in systolic, diastolic, and mean arterial pressure, although there was no correlation between the reduced blood pressure and the decreased AHI.

## CONCLUSION

Sleep medicine is obviously a challenging field, evolving with new technology. There have been major new discoveries and growing evidence in clinical research studies, however, a number of key questions remain unanswered. The mechanisms by which overall health improvements in sleep apnea individuals by

means of oral appliance, It should be a focus for future basic and clinical research.

## REFERENCES

1. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. *Sleep* 1999;22:667-89.
2. Peker Y, Hedner J, Norum J, Kraiczi H, Carlson J. Increased incidence of cardiovascular disease in middle-aged men with obstructive sleep apnea: a 7-year follow-up. *Am J Respir Crit Care Med* 2002;166:159-65.
3. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353:2034-41.
4. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. *N Engl J Med* 2000;342:1378-84.
5. Reichmuth KJ, Austin D, Skatrud JB, Young T. Association of sleep apnea and type II diabetes: a population based study. *Am J Respir Crit Care Med* 2005;172:1590-5.
6. Loube DI, Gay PC, Strohl KP, Pack AJ, White DP, Collop NA. Indications for positive airway pressure treatment of adult obstructive sleep apnea patients: a consensus statement. *Chest* 1999;115:863-6
7. Wang Y, Beydoun MA. The obesity epidemic in the United States - gender, age, socioeconomic, racial/ethnic, and geographic characteristics: a systematic review and metaregression analysis. *Epidemiol Rev* 2007; 29 : 6-28.
8. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-

- disordered breathing among middle-aged adults. *N Engl J Med* 1993;328:1230-5.
9. Marcus CL. Sleep-disordered breathing in children. *Am J Respir Crit Care Med* 2001;164:16-30
  10. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middleaged adults. *N Engl J Med* 1993;328:1230-5
  11. Roehrs T, Zorick F, Sicklesteel J, Wittig R, Roth T. Agerelated sleep-wake disorder at a sleep disorders center. *J Am Geriatr Soc* 1983;31:364-70
  12. Jamie C.M. Lam, S.K. Sharma & Bing Lam Obstructive sleep apnoea: Definitions, epidemiology & natural history *Indian J Med Res* 131, February 2010, pp 165-170
  13. Williams AJ, Yu G, Santiago S, Stein M Screening for sleep apnea using pulse oximetry and a clinical score. *Chest*. 1991 Sep;100(3):631-5.
  14. Michael R. Littner ; Clete Kushida ; Merrill Wise ; David G. Davila, ; Timothy Morgenthaler ; Teofilo Lee-Chiong ; Max Hirshkowitz Practice Parameters for Clinical Use of the Multiple Sleep Latency Test and the Maintenance of Wakefulness Test SLEEP, Vol. 28, No. 1, 2005
  15. Alan.A.Lowe. Cephalometric and demographic characteristics of obstructive sleep apnea: an evaluation with partial least squares analysis. *The Angle orthodontist* vol 67 no 2 1997
  16. Bernard Deberry-Borowiecki Cephalometric analysis for diagnosis and treatment of obstructive sleep apnea, *The Laryngoscope* vol 98,issue 2, pages 226-234, February 1988
  17. Haponick EF, Smith PL, Bohlman ME, Allen RP, Goldman SM, Bleecker ER. Computerized tomography in obstructive sleep apnea. Correlation of airway size with physiology during sleep and wakefulness. *Am Rev Respir Dis* 1983, 127 : 221-6.
  18. Epstein LJ, Kristo D, Strollo PJ, Friedman N, Malhotra A, Patil SP, Ramar K, Rogers R, Schwab RJ, Weaver EM, Weinstein MD. Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. Adult obstructive sleep apnea task force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2009; 5:263-76.
  19. Conley R. S. Management of sleep apnea: a critical look at intra-oral appliances. *Orthod Craniofac Res* 2015; 18(Suppl.1): 83-90
  20. DSC Hui, DKL Choy, FWS Ko, TST Li, CKW Lai Obstructive sleep apnoea syndrome: treatment update *HKMJ* june 2000 vol ;6 no:210
  21. Warunek SP. Oral appliance therapy in sleep apnea syndromes: a review. *Semin Orthod*. 2004; 10:73-89.
  22. Chan AS, Sutherland K, Schwab RJ, Zeng B, Petocz P, Lee RWW, Darendeliler MA, Cistulli PA. The effect of mandibular advancement on upper airway structure in obstructive sleep apnoea. *Thorax*. 2010; 65:726-32.
  23. Lee CH, Kim JW, Lee HJ, Seo BS, Yun PY, Kim DY, Yoon IY, Rhee CS, Park JW, Mo JH. Determinants of treatment outcome after use of the mandibular advancement device in patients with obstructive sleep apnea. *Arch Otolaryngol Head Neck Surg*. 2010; 136:677-81
  24. KA, Ono T, Lowe AA, Keenan SP, Fleetham JA. A randomized crossover study of an oral appliance vs. nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. *Chest*. 1996; 109:1269-75.
  25. Almeida FR, Parker JA, Hodges JS, Lowe AA, Ferguson KA.Effect of a titration polysomnogram on treatment success with a mandibular repositioning appliance. *J Clin Sleep Med*. 2009; 5:198-204.

26. Ferguson KA, Ono T, Lowe AA, al-Majed S, Love LL, Fleetham JA. A short term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax*. 1997; 52:362-8.
27. Ferguson, K.A., et al., A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. *Thorax*, 1997. 52(4): p. 362-8.
28. Engleman, H.M., et al., Randomized crossover trial of two treatments for sleep apnea/hypopnea syndrome: continuous positive airway pressure and mandibular repositioning splint. *Am J Respir Crit Care Med*, 2002. 166(6): p. 855-9.
29. Bloch, K.E., et al., A randomized, controlled crossover trial of two oral appliances for sleep apnea treatment. *Am J Respir Crit Care Med*, 2000. 162(1): p. 246-51.
30. Clark, G.T., et al., A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. *Chest*, 1996. 109(6): p. 1477-83.
31. Hoekema A, Van der Hoeven JH, Wijkstra P J: Predictors of obstructive sleep Apnea-Hypopnea Treatment Outcome. *JDent Res*2007 86(21):1181-1186,
32. Krishnan V, Nancy A., Steven C: An Evaluation of a Titration Strategy for prescription of oral appliances for obstructive sleep apnea; *Chest* 2008; 133:1135-1141.
33. Chan, Andrew S.L, Cistulli, Peter A. Oral appliance Treatment of obstructive sleep apnea: an update. *Current opinion in pulmonary Medicine*. 2009; 15 (6): 591 – 596. 40.
34. Chhajed PN, Chhajed T.P. Tamm M, Strobel W. Obstructive sleep apnea: therapies other than CPAP. *JAPI*,2004; 52: 143-151
35. Lim J, Lasserson TJ, Fleetham JA, Wright J. Oral appliances for obstructive sleep apnoea. [Cochran Database]. *Cochran Database Syst. Rev.*; 2006; (1): CD004435.
36. Petit FX; Pepin JL, Bettega G et al. Mandibular advancement devices: rate of contraindications in 100 consecutive obstructive sleep apnea patients. *AM J Respir Crit Care Med* 2002; 166: 274-78
37. Scherr SC, D.L., Almeida FR, Bennett KM, Blumenstock NT, Demko BG, Essick GK, Katz SG, McLornan PM, Phillips and P.R. KS, Rogers RR, Schell TG, Sheats RD, Sreshta FP., Definition of an effective oral appliance for the treatment of obstructive sleep apnea and snoring: a report of the American Academy of Dental Sleep Medicine. *Journal of Dental Sleep Medicine*, 2014. 1(1): p. 39-50.
38. Deane SA, Cistulli PA, Ng AT, Zeng B, Petocz P, Darendeliler MA. Comparison of mandibular advancement splint and tongue stabilizing device in obstructive sleep apnea: a randomized controlled trial. *Sleep* 2009;32:648–53.
39. Lekerud AK, Sand L, Englund AK, Hirsch JM. Treatment of sleep apnoea using a mandibular advancement splint—an open prospective study. *In Vivo* 2012;26:841–5.
40. Okuno K, Sato K, Arisaka T, Hosohama K, Gotoh M, Taga H, et al. The effect of oral appliances that advanced the mandible forward and limited mouth opening in patients with obstructive sleep apnea: a systematic review and meta-analysis of randomised controlled trials. *J Oral Rehabil* 2014;41:542–54.
41. Hoekema A, Stegenga B, Wijkstra PJ, van der Hoeven JH, Meinesz AF, de Bont LG. Obstructive sleep apnea therapy. *J Dent Res* 2008;87:882–7.
42. Lam B, Sam K, Mok WY, Cheung MT, Fong DY, Lam JC, et al. Randomised

- study of three non-surgical treatments in mild to moderate obstructive sleep apnoea. *Thorax* 2007;62:354–9.
43. Phillips CL, Grunstein RR, Darendeliler MA, Mihailidou AS, Srinivasan VK, Yee BJ, et al. Health outcomes of continuous positive airway pressure versus oral appliance treatment for obstructive sleep apnea: a randomized controlled trial. *Am J Respir Crit Care Med* 2013;187:879–87.
44. Nelly Huynh, Eve Desplats, Fernanda, Almeida Orthodontics Treatments for Managing Obstructive Sleep Apnea Syndrome in Children: A Systematic Review and Meta-analysis sleep medicine reviews feb 2015
45. Holley, A.B., C.J. Lettieri, and A.A. Shah, Efficacy of an adjustable oral appliance and comparison with continuous positive airway pressure for the treatment of obstructive sleep apnea syndrome. *Chest*, 2011. 140(6): p. 1511
46. Randerath, W.J., et al., An individually adjustable oral appliance vs continuous positive airway pressure in mild-to-moderate obstructive sleep apnea syndrome. *Chest*, 2002. 122(2): p. 569-75.
47. Qaseem, A., et al., Management of Obstructive Sleep Apnea in Adults: A Clinical Practice Guideline From the American College of Physicians. *Ann Intern Med*, 2013.
48. Epstein, L.J., et al., Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. *J Clin Sleep Med*, 2009. 5(3): p. 263-76
49. Robertson, S., et al., A randomized crossover trial of conservative snoring treatments: mandibular repositioning splint and nasal CPAP. *Otolaryngol Head Neck Surg*, 2008. 138(3): p. 283-288.
50. Ghazal, A., et al., A randomized prospective long-term study of two oral appliances for sleep apnoea treatment. *J Sleep Res*, 2009. 18(3): p. 321-8.
51. Marin JM, Carrizo SJ, Vicente E, Agusti AG. Long-term cardiovascular outcomes in men with obstructive sleep apnoea-hypopnoea with or without treatment with continuous positive airway pressure: an observational study. *Lancet* 2005;365:1046–53.
52. Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005;353:2034–41.
53. Ahrens A, McGrath C, Hagg U. A systematic review of the efficacy of oral appliance design in the management of obstructive sleep apnoea. *Eur J Orthod* 2011;33:318–24
54. Iftikhar IH, Hays ER, Iverson MA, Magalang UJ, Maas AK. Effect of oral appliances on blood pressure in obstructive sleep apnea: a systematic review and meta-analysis. *J Clin Sleep Med* 2013;9:165–74.