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Review Article

Obstructive Sleep Apnea (OSA) - Review of Literature

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Abstract

Obstructive sleep apnea (OSA) is one of the six sleep-related disorders classified in the ICSD-3 by the American Academy of Sleep Medicine (AASM). Its prevalence has been on a steady increase in the past decade, making it a key health concern in a global scale. China, the United States, and Brazil are among the countries with the highest number of people suffering from OSA. There are numerous treatment options for OSA, with CPAP being the preferred option. However, some patients have tolerability issues with CPAP, which reduces its efficacy in correcting OSA hence the need to use alternative treatment methods that use oral appliances, such as Mini-Implant Assisted Rapid Palatal Expansion (MARPE) and mandibular advancement device (MAD), which have gained widespread popularity. The two treatment options alongside oral pressure therapy have proved beneficial to non-tolerant patients of severe OSA. The periodontal and oral nature of the treatment options makes the inclusion of dentists in the OSA treatment plans critical.

Keywords: *Obstructive Sleep Apnea (OSA); Dental Sleep Medicine; Obstructive Apneas; Repetitive Hypopneas; Sleep-Disordered Breathing*

Abbreviations

MARPE: Mini-Implant Assisted Rapid Palatal Expansion; ICSD-3: International Classification of Sleep Disorders Third Edition; DSM: Dental Sleep Medicine; MAD: Mandibular Advancement Device; CPAP: Continuous Positive Air Pressure; BPAP: Bilevel Positive Airway Pressure; APAP: Automatic Positive Airway Pressure; nEPAP: Nasal Expiratory Positive Airway Pressure; PSG: Polysomnogram; OSA: Obstructive Sleep Apnea; AASM: American Academy of Sleep Medicine; SRBD: Sleep Related Breathing Disorders; BMI: Body Mass Index; ATS: American Thoracic Society; SDB: Sleep-Disordered Breathing

Introduction

The American Academy of Sleep Medicine (AASM) classifies Sleep Related Breathing Disorders (SRBD's) among the six-known sleep disorders recognized in the third edition of International Classification of Sleep Disorders [fICSD-3] [1]. In a policy statement concerning the management of SRBDs, Addy., *et al*. reckon that "sleep-related breathing disorders impact a significant portion of the population, estimating that 23.5 million of United States adults have undiagnosed or untreated OSA-costing billions. The condition has increased the risk of health complications, such as hypertension, congestive heart failure, atrial fibrillation, coronary artery disease, stroke, and type 2 diabetes, consequently reducing the quality of life for a significant portion of the population" ([2] p25). Sateia asserts that there are five other sleep related disorders in the ICSD-3 namely insomnia, central disorders of hypersomnolence, parasomnias, rhythm sleep wake

disorders, and circadian sleep related movement disorders [3]. SRBD's are classified into four sections namely, central sleep apnea syndromes, OSA, sleep-related hypoxemia, and sleep-related hypoventilation disorders [3]. Frequent collapse or narrowing of the pharyngeal airways during sleep causes OSA.

The clinical diagnosis of OSA subtly differs in pediatric and adult diagnosis. The criterion for adult diagnosis requires either symptoms/signs or associated psychiatric or medical disorders, which combines with five or more critical respiratory events for every hour of sleep during polysomnogram [PSG] [3]. The symptoms might include fatigue, snoring, and associated sleepiness, insomnia, observed apnea or subjective nocturnal respiratory disturbance. The psychiatric or medical disorders associated with OSA might include coronary artery disease, hypertension, congestive heart failure, atrial fibrillation, mood disorders, diabetes, or cognitive dysfunction [4]. Sateia lists major obstructive events accompanying the disorders, including mixed and obstructive apneas, respiratory arousals, or hypopneas.

In contrast, ICSD-3 simplifies the diagnosis criterion for pediatric OSA. For instance, it requires the presence of a single symptom unlike the multiple ones required for an adult diagnosis. Similarly, one obstructive event is enough for a PSG criterion for diagnosis [3]. Numerous researches have studied the disease burden and prevalence of OSA globally. In a literature-based study examining the worldwide prevalence and burden of OSA, Benjafield., *et al*. [7] assert that an estimated 1 billion adults from the ages of 30 to 69 suffer from OSA [5]. However, the scholars trim down the figures to 425 million as those experiencing moderate to severe OSA and who deserve treatment, with China recording the highest number of affected individuals ahead of the United States, Brazil, and India respectively [5]. According to Benjafield., *et al*. the cost of diagnosis and treatment of OSA in the USA in 2015 was US $12.4 billion. Due to its socio-economic impacts, OSA is gaining scholarly attention [5].

Discussions

Pathophysiology

In a study exploring the high prevalence of sleep-disordered breathing in adults, Peppard., *et al*. note that the apnea and hypopnea incidences of sleep-disordered breathing-(SDB) have considerable harmful health implications, with instantaneous effects encompassing "intermittent hypoxia, fragmented sleep, and exaggerated fluctuations in heart rhythm, blood pressure, and intrathoracic pressure" ([6] p1006). Recurrent collapse or obstruction of the pharyngeal airways when one sleeps, leading to a reduction (hypopnea) or ultimate cessation (apnea) of airflow in spite of the continuing breathing efforts, causes OSA [7]. Some of its manifestations include cyclic apneas, hypoventilation, and repetitive hypopneas. The upper airway is adapted to performing various functions, such as swallowing, speech, and air passage for breathing due to its anatomical soft tissues, muscles, and bony/rigid support. Bilston and Gandevia underscore the multifunctionality and complexity of the upper airways besides its neuromechanical systems that requires consistent coordination for patency [8]. The airway contains collapsible portions whose frequency and timing of collapse causes OSA. For instance, its portion between the hard palate and the larynx is collapsible, making it susceptible to collapse during inopportune moments, such as during sleep.

Susceptibility to OSA depends on the size of the victim's narrow airways having higher probability for collapse compared to large/wide ones. During sleep, the tongue, jaws, and throat relax narrowing the airway resulting in a vibration sound (snoring) when one breathes-in [9]. However, a complete blockage of the airway during sleep denies the brain of oxygen triggering the fight or flight mode in the brain that compels the person to wake up and breathe again. The actions could happen multiple times a night for people with OSA, making it a clinical condition that requires diagnosis and treatment [10]. Chen., *et al*. assert that OSA is clinically viewed as an absolute malfunction of airway anatomy resulting in sleep difficulties, snoring, insomnia, associated sleepiness, or subjective nocturnal respiratory disturbance [11]. Physiologically, the upper airway anatomy and collapsibility are the most critical trait in developing OSA, where the critical passive

airway closing pressure-(Pcrit) quantifies the tendency to airway collapsibility [12]. Thus, the physiological traits contributing to the development of OSA should be researched extensively.

Screening and physical examination

Dentists can screen OSA through medical techniques and general examination processes for anatomical abnormalities. Earlier screening helps in establishing a patient's daytime and nocturnal OSA signs/symptoms, such as snoring, sleeping, as well as gasping to ascertain the presence of SRBD. In addition, other popular screening questionnaires, such as "STOP-BANG, Berlin, and Epworth Sleepiness Scale (ESS), have acquired worldwide usage" ([13] p3105, [14]). Amra., *et al*. explain how the STOP-BANG questionnaire functions. The questionnaire contains four subjective and four demographic items [14]. The subjective items include "tiredness, snoring, high blood pressure, and observed apnea whereas the demographic items include age, gender, neck circumference, and body mass index (BMI)" ([15] p287). A "Yes" answer to atleast three of the items indicates a high risk for OSA [14]. The scholars also simplified how the Berlin Questionnaire (BG) works. BQ consists of three sections on snoring, sleepiness, and daytime fatigue, and finally anthropometric measures and medical history, such as BMI and hypertension [14]. A score of two or more in the three categories indicates high risk for OSA. Unlike the BQ, the ESS has eight items to assess daytime sleepiness. It uses a four-point Likert response format with a score ranging from zero to 24 [14]. A score of 11 or more indicates a high affinity for daytime sleepiness hence high likelihood for OSA. Even though these questionnaires are critical in examining OSA, there should not completely replace the need for an objective OSA test since they only help highlight those at risk of the disorder [16]. In OSA, a positive airway pressure is used to phenotype patients' pathophysiologic traits (PTs); the patient should be in a supine position as well as the stage-2 non-rapid eye movement sleep [NREM] [17]. Thus, the patient's daytime and nocturnal symptoms, such as snoring, disturbed sleeping, or gasping, can unveil the likelihood of OSA.

In a study investigating the screening, treatment, as well as management of patients with SRBDs, Levine., *et al*. note that a physical examination by a qualified dentist is vital in accurate diagnosis of OSA at the preliminary stages. In the process, a dentist records vital signs indicating the condition, such as neck perimeter, BMI, as well as blood pressure levels [1]. Thorough and systemic physical examination, with descriptive assessments and visual presentation of craniofacial complexes in the posterior airways and pharyngeal wall, is recommended. Besides, dentists are expected to assess major structures, such as uvula, palatine tonsils, and soft palate, to ascertain the level of infection [1]. In the same way, the nose of the patient should be closely checked for any form of deviation, obstruction incidence, and/or valvular collapse. Observation of any patency with the pharyngeal and nasal airways calls for immediate referral to the ENT clinic [18]. The authors further offer critical insights critical in the examination that hold clues to a possibility of OSA. For example, assessment of the occlusal positioning as well as the size of the tongue size substantially indicates oropharyngeal crowding. The surface texture, shape, color, and tonicity of the tongue also offer valuable clues.

In addition, soft and hard tissues of the oral cavity should be examined. The area consists of the teeth, the hard palate tissues, gingiva, alveolar processes, as well as frenal attachments. The dentist should identify the location as well as the teeth numbers besides their morphological integrity to determine the patient's standing to oral appliances [19]. A periodontal examination can guide dentists in the selection of appropriate appliance. Similarly, some dentists use radiographic imaging foe oral appliance therapy candidacy, often to assess the level of damage to the soft tissue and skeletal presentations. Levine., *et al*. takes note of the close association of the SRBDs and temporomandibular disorders [1]. Therefore, it is critical for the dentists to focus temporomandibular joint section that includes the temporalis, masseter, associated superficial muscles, and sternocleidomastoid muscles [1]. The examination also focuses on the protrusive areas, lateral deviations, and anomalous movements.

A comprehensive dental assessment would encompass angle classification, overjet and overbite, and recording any figures, structures or occurrences that deviate from the norm. There should also be documentation of crossbites, midlines, crowding and intra-arch spacing,

and interproximal and occlusal contacts for reference [1]. When anticipating the use of use of OA, dentists should acquire extraoral and intraoral photographs to justify the pre-management dental condition. A fulfillment of all these mentioned tests and examinations should provide the necessary information concerning the presence of OSA and the most favorable treatment option.

Treatment options for OSA

According to Levine., *et al*. continuous positive airway pressure (CPAP) remain the immediate or the first-line treatment for many OSA patients, although the long-term compliance with CPAP therapy is often a challenge. The choice for treatment depends on various factors, such as the patient's tolerability of the treatment option, their age, ease or comfort of using the appliance, and state of health among other reasons. Some other treatment options include "positional therapy, nasal expiratory positive airway pressure (nEPAP), oral pressure therapy, oral appliances, hypoglossal nerve stimulation, surgeries, pharmacologic treatments, and weight loss and exercise" ([20] p2). Some treatment options, such as the oral appliances like mandibular advancement device, provide a perfect alternative for patients who are non-tolerant to CPAP, BPAP and APAP. Thus, the treatment of OSA should be anchored on the screening results and other physiological factors differing from one patient to the next.

Positive airway pressure: According to the American Thoracic Society (ATS), PAP refers to the continuous positive airway pressure and includes numerous strategies. The organization lists various types of positive airway pressure, such as continuous positive air pressure (CPAP), automatic positive airway pressure, and the Bilevel positive airway pressure (BPAP). The machines/treatment option uses air pressure to open and ventilate the upper airways during sleep. The unhindered breathing due to the open upper airway facilitates free movement of air into the lungs preventing snoring or constantly waking up at night due to obstruction of the airway [21]. According to Calik (in a study exploring the treatment options for obstructive sleep apnea), CPAP is the "is the current gold standard treatment for OSA, as it pneumatically stabilizes the upper airway" ([22] p181). CPAP treatment involves the use of a mask covering the patient's nose and mouth and providing pressured air to keep the upper airway open during sleep facilitating an uninterrupted sleep. Calik asserts that the machine does not breathe for the patient but instead facilitates breathing by opening up the airway while the patient independently inhales and exhales [22]. Thus, the positive airway pressure facilitates free movement of air into the lungs preventing snoring or constantly waking up at night due to obstruction.

Even though CPAP, BPAP, and APAP operate in a more or less similar manner, there are slight variations in their operations. The APAP machines send air through a thin tubular passage mounted in a patient's nose and mouth during sleep. However, unlike CPAP that facilitates ventilation by opening the airway using one inthoracic and alveolar pressure, the BPAP machine delivers "an exhalation (Exhalation positive airway pressure or EPAP) and inhalation pressure (Inhalation positive airway pressure or IPAP)" ([22] p183). In addition, the BPAP machine monitors the patient's effort during exhalation and inhalation and delivers/induces breathing if the patient fails to breathe for a set/programmed period. The programmed timing for breathing acts as a 'back-up rate" that monitors adherence to the recommended breathes per minute (BPM). The recommendation for a CPAP or BPAP machine by the physician or dentists depends on various factors due to the difference in how they operate [23]. For instance, CPAP is often the most recommended for OSA whereas BPAP is best suited to correct COPD, complex sleep apnea and central sleep apnea. BPAP helps reduce the expiration strain that is often associated with CPAP and which makes it intolerable for some patient [21]. Another form of PAP treatment is the automatic positive airway pressure (APAP). According to Calik, APAP consists of software that automatically regulates the amount of air the patient breathes during sleep based on need [1,22,24]. The machine automatically raises the air pressure if it detects a slight narrowing of the airway during sleep to ensure it remains open and does not hinder breathing.

Oral appliances: Oral appliances function to prevent collapse of the upper airway through various strategies, such as raising the soft palate to facilitate increased airflow, advancing the mandible or stabilizing the tongue. All these strategies facilitate free flow of air by

ensuring the airways remain open. According to Aarab and Lobbezoo, the advancement of the mandible helps alleviate obstructive apneas [20]. Sutherland., *et al*. asserts that the use of oral appliances is the second most widespread treatment option for OSA after CPAP [25]. "Oral appliances cover the lower and upper dental arches and have a configuration that ensures the lower jaw is held forward in a more protruded position" ([25] p176). She further admits that the action of advancing the mandible reduces the likelihood of airway collapsibility and increases the pharyngeal airway space. The efficacy and success of oral appliances vary among individuals. However, it remains the best alternative for people with tolerability issues for CPAP [26]. Various factors contribute to the variations in success of oral appliances, such as differences in treatment protocols and devices, obesity, and upper airway and craniofacial features of the patient [25,27]. Examples of an oral appliance in widespread use include the mandibular advancement device (MAD), mandibular repositioning appliances, mandibular advancement splints, and tongue retaining devices.

Mandibular advancement device (MAD): The two versions of MAD namely adjustable advancement and fixed advancement are popular in the management of OSA by ensuring the upper airways remain open during sleep [28]. Lozano., *et al*. posit that MAD conducts an inferior and anterior jaw movement producing anatomical variations in the upper airways creating more space in the pharyngeal area [28]. The movement fixes, aligns, and stabilizes the hyoid bone and the jaw securing these structures from posterorotation during decubitus hence prevent airway blockage [28,29]. The device functions by ventrally displacing the soft palate increasing the capacity of the lateral walls within the velopharyngeal area to drastically reduce or eliminate snoring. MAD's trigger changes in the pharyngeal pressure that enables normalization of the physiological properties of the upper airways. The change in anatomical relationship (mandibular advancement and rotation) triggers a neurosensorial stimulation increase that in turn reduces the collapsibility likelihood by increasing the motor muscular tone [30,31]. The positional change of the hyoid bone that pushes it forward alters the suprahyoid musculature that facilitates an increase in permeability and volume of the upper airway. However, MAD is not effective among some patients such as those with scarce mandibular advancement/deficient protrusive, those with periodontal or dental problems, and those with temporomandibular disorders [28]. The treatment has a 90% to 100% success rate among patients with OSA particularly in reducing or eliminating snoring.

Mini-implant assisted rapid palatal expansion (MARPE): It is often called the Mini-screw assisted rapid palatal expansion, which is a non-extraction and non-surgical treatment option for OSA that expands the upper jaw called the maxilla. The size of the maxilla directly affects the airflow. For instance, a narrow maxilla hinders facial development, causes nasal obstruction, and leads to crowded teeth due to the limited space. MARPE is most effective among young people whose suture is fused. It includes a deliberate effort to expand the maxillary bone and create more room to allow for free flow of air during inhalation and exhalation by increasing the volume of the oral and nasal cavity [32]. The process includes the placement of a custom-designed maxillary expander with mini-screws within the mid-palatal suture [32]. Due to the use of the expander for a period ranging four to six months during which the new bone forms, the suture often splits creating a gap between the front teeth. The dentists can help close the gap and guarantee a stable bite through orthodontic treatment [32]. MARPE is an effective non-surgical treatment option for OSA particularly for youths due to its simple maxillary bone expansion.

Oral pressure therapy: According to Calik, oral therapy pressure includes the application of negative pressure on the upper airway to prevent retro-palatal collapse [22]. The therapy involves the use of the oral pressure therapy device to apply gentle suction superiorly and anteriorly to displace the soft palate and the tongue and facilitate breathing using the nasopharyngeal airway [22]. OPT has a 25% to 37% success rate, which is low compared to other available treatment options for OSA. Belkhode., *et al*. attributes the low success rate to the therapy's focus on pressure application on the upper airway to prevent retro-palatal collapse with zero focus on the collapse of other levels [33]. The therapy helps marginally; reduces the AHI but fails to make a considerable impact due to the relatively high AHI arising from the collapse in other levels and positional apneas. Oral tissue irritation, dry mouth, and dental discomfort are some of the side effects associated with the therapy, hence affecting adherence.

Other treatment options for OSA (Positional therapy, pharmacologic treatment, nEPAP, and weight loss)

Even though qualified dentists can conduct various OSA treatment options on patients such as CPAP, oral appliances such as MAD, MARPE, and oral pressure therapy, there are numerous other treatment options for the condition. According to Yan Li., *et al*. CPAP remains the highly proposed effective treatment for OSA" ([34] p1184). A general physician conducts the remaining alternative treatment options for OSA, such as positional therapy, pharmacologic treatment, nEPAP, hypoglossal nerve stimulation, and weight loss. These alternatives seldom require dental or periodontal services hence the need for a general physician either alone or in collaboration with a dentists. Scholars assert that a person's sleeping position could contribute to OSA hence the recommendation for positional therapy.

Lying in the supine position has numerous disadvantages that make an individual susceptible to OSA. Calik (183) claims that sleeping in the supine position increases the patient's apnea-hypopnea index (AHI) compared to when one is the lateral position [22]. Studies indicate that an estimated 60 percent of OSA patients typically sleep in the supine position, making it a key contributory factor [22]. Calik further asserts that "a drug-induced sleep endoscopy research demonstrated that the upper airway collapses at multiple levels when in the supine position as opposed to a single level sleeping in the lateral position" ([22] p183). Therefore, it is recommended that OSA patients sleep in the lateral position as opposed to the supine position to lower the likelihood of airway collapse and increase passive airway anatomy. Positional therapy includes the use of a device worn by the patient during sleep and which notifies the patient when they slip into supine position so that they maintain sleep in the lateral position hence considerably decrease AHI [35]. Even though compliance to the therapy is relatively low among most people, it is a good alternative for patients who are intolerant to the use CPAP. It also helps alleviate the severity of OSA for users, include those with compliance challenges.

In addition, there is a direct correlation between obesity and OSA. Weight gain reduces the volume of the oral cavity, increasing the likelihood of OSA. Snoring is particularly common among people suffering from obesity. Studies show that a lifestyle change or dieting results in weight loss for people who were previously obese and reduces the severity of OSA [36]. nEPAP is also treatment option for OSA that includes attaching a single-use device to the nostril using an adhesive thereby resulting in an airtight seal. The mechanical valve contained in the device results in a high resistance during expiration as opposed to during inspiration. nEPAP focus on the expiration; prevents upper airway collapse often happens at the end of the respiratory phase due to phasic activation or lack of positive pressure in the upper airway [22]. Calik summarizes the pharmacologic treatment options for OSA. He classifies the drugs according to their role in alleviating OSA [22]. For instance, acetazolamide, progestogens, and theophylline help alleviate OSA by increasing the ventilatory drive while cholinergic and serotonergic drugs expand the upper airways tone. The treatment option for OSA should be pegged on a patient's physiological and pharmacological features.

OSA implications on dental medicine

Contemporary researches about the OSA pathophysiology unveil new ideas about the heterogeneity of the disease. For instance, recent studies on OSA's phenotyping have pathophysiological frameworks discerning the disease at the patient level. It has also exposed the critical role of qualified dentists and physicians in the screening, diagnosis, examination, and treatment of OSA [37]. Dental sleep medicine is an area that requires collaboration between physicians and dentists due to its overlapping nature and numerous treatment options that range from oral appliances, invasive and non-invasive machines like CPAP, pharmacologic treatment, surgeries, and numerous other therapies like positional therapy. However, not all dentists are licensed to offer dental sleep medicine.

The American Academy of Dental Sleep Medicine and the European Respiratory Society underscores the need for collaboration between physicians and qualified dentists in the diagnosis and treatment of DSM. They encourage the training of dentists to practice DSM and helps reduce the public health burden of SRBD (38, 39, 41). Both organisations proposes the use of questionnaires like the STOP-

BANG, Berlin and Epworth Sleepiness Scale designed to collect critical information from the patient that helps the dentists determine the risk, presence, or absence of OSA [40]. The inclusion of dentists in DSM arises from the nature and treatment options for OSA, most of which extensively involve the periodontal and oral cavity. The dental/periodontal nature of these treatment options underscore the importance of incorporating dentists to collaborate with physicians in the diagnosis and treatment of OSA [40]. For instance, MARPE and MAD involve the placement of an oral appliance in the mouth. The placement of such appliances should be done by a dentist since that is their area of expertise hence understands it better than general physicians. Some of the oral appliances, such as MARPE, distort the arrangement of the teeth by creating a gap between the two front teeth as the bone expands. There is need for a dentist to help close the gap through orthodontic treatment. Thus, there is a close relationship between DSM and dentistry in terms of the available treatment options.

Conclusion

The pervasiveness of OSA renders the disorder a critical public health concern, considering its high morbidity rates, societal impacts, and economic burden. For instance, the U.S spent $12.5 billion in 2015 for diagnosis and treatment of OSA, exemplifying the huge financial burden related with the disorder. The pharyngeal collapse typifying OSA causes such symptoms as hypoventilation, cyclic apneas, and repetitive hypopneas. Even though CPAP remains the "gold standard" treatment option for OSA, the use of oral appliances, as is the case in MARPLE and MAD, have gained widespread use since the dentists can adjust/design them to match individual need of every patient. The oral appliances also act as an alternative treatment option for people who have tolerability issues with CPAP reducing its efficacy. Some of the popular oral appliances include the mandibular appliance device and MARPE. The two devices function to ensure the upper airway stays open during sleep to facilitate breathing. However, other treatment options include "positional therapy, pharmacologic treatment, nEPAP, hypoglossal nerve stimulation, and weight loss." These alternative treatment options are primarily performed by physicians since they fall out of the dental domain. For instance, pharmacologic treatment or surgery requires a trained physicians or general surgeon. The American Academy of Dental Sleep Medicine underscores the need for collaboration between dentists and physicians in the treatment of OSA. The organization provides the basic requirements mandatory for a dentist to qualify into providing DSM.

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