

Etiopathogenesis and Diagnosis of Obstructive Sleep Apnea: A Literature ReviewDr. Mudit Agarwal^{1*}, Dr. R Muthunagai², Dr. Harleen Bali³¹Senior Lecturer, Department of Oral & Maxillofacial Surgery, Seema Dental College & Hospital, Rishikesh, Uttrakhand-249203, India²Reader, Department of Oral & Maxillofacial Surgery, Seema Dental College & Hospital, Rishikesh, Uttrakhand-249203, India³Private Consultant, Department of Oral Medicine & Radiology, Jammu & Kashmir, India**Review Article*****Corresponding author**

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Abstract: Obstructive sleep apnoea (OSA) is increasingly being recognized as an important health issue in the last two to three decades. It is characterized by frequent episodes of upper airway collapse during sleep, causing recurrent arousals, intermittent hypoxaemia, sleep fragmentation and poor sleep quality. 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 cardiometabolic morbidity and mortality.

Keywords: Obstructive, sleep, apnoea, hypoapnoea, apnea.

INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is characterized by episodes of partial or complete obstruction of the upper airway during sleep, interrupting (apnea) or reducing (hypopnea) the flow of air, followed by transient awakening that leads to the restoration of upper airway permeability [1].

These cycles of apnea/hypopnea are repeated several times every hour, producing fragmented and scantily repairing sleep. Within the upper airway, the pharynx, and particularly the oropharynx and hypopharynx, is the region where most obstructive processes leading to OSAS are found². OSAS has a negative impact on the health and behavior of millions of adolescents throughout the world. It is an independent risk factor for many diseases, such as hypertension, heart failure, heart attack, cardiovascular events and arrhythmias.

Definition

An apnoea is defined as the complete cessation of airflow for at least 10 sec. There are three types of apnoeas: obstructive, central and mixed. In *obstructive* sleep apnoea, respiratory effort is maintained but ventilation decreases or disappears because of partial or total occlusion in the upper airway. *Central sleep* apnoea is defined as reduced respiratory effort resulting in reduced or absent ventilation.

Mixed apnoea is often characterized by starting with central apnoeas and ending with obstructive events. A *hypopnoea* is defined as a reduction in airflow (30-50%) that is followed by an arousal from sleep or a decrease in oxyhaemoglobin saturation (3-4%) [4-6]. Sleep apnoea severity is assessed with apnoea-hypopnoea index (AHI), which is the number of apnoeas and hypopnoeas per hour of sleep. 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[2].

Epidemiology

OSAS is the second disease in order of frequency among the different respiratory disorders, surpassed only by asthma. The syndrome can affect any age group, and is estimated to affect 2-4% of the adult population, though it is more common in middle aged males. One out of every 5 adults suffers moderate OSAS, and one out of every 15 presents moderate to severe OSAS [3].

Risk factors

The major risk factors for OSA include advanced age, male sex and obesity, although the underlying mechanisms remain unclear. It has been proposed that the pathophysiological pathways linking these risk factors for OSA can be explained by anatomical abnormalities, increased pharyngeal dilator muscle dysfunction, lowered arousal threshold, increased ventilatory control instability, and/ or reduced lung volume [7].

Age:

The increased prevalence of SDB breathing in the elderly appears to plateau after 65 yr [4, 8], it is estimated to be 10 per cent. However, when the prevalence is controlled for body mass index, the severity appears to decrease with age [9]. Several studies have attempted to address the cause of age-related impact on sleep apnoea but no conclusions have been reached. Mechanisms proposed for the increased prevalence of sleep apnoea in the elderly include increased deposition of fat in the parapharyngeal area, lengthening of the soft palate, and changes in body structures surrounding the pharynx [10].

Sex

It is not clear why OSA is more common in men than women. It can be attributed to anatomical and functional properties of the upper airway and in the ventilatory response to the arousals from sleep [11].

Imaging studies have revealed that men have increased fat deposition around pharyngeal airway as compared with women [12]. Besides, hormonal differences may play a role in the predisposition to abnormal breathing during sleep [13]. Pre-menopausal women are relatively protected from OSA even if they have other known risk factors for OSA. In a cross-sectional prevalence study, it shows a four-fold higher prevalence of at least moderate OSA in post-menopausal women as compared with pre-menopausal women. And interestingly, in post-menopausal women taking hormonal replacement therapy, the prevalence of OSA is similar to premenopausal women [14]. It would be of great interests to understand why female hormonal status may protect against the development of OSA in premenopausal women.

Obesity

Obesity/visceral obesity is the major risk factor for the development of OSA, it is thought to be associated with anatomic alterations that predispose to upper airway obstruction during sleep, by increasing adiposity around the pharynx and body. Central obesity has been associated with reduction in lung volume, which leads to a loss of caudal traction on the upper airway, and hence, an increase in pharyngeal collapsibility [15].

Subjects with severe obesity, BMI of >40, the prevalence of sleep apnoea was markedly increased to 40-90 per cent [15]. It was well demonstrated that a 10 per cent body weight reduction was associated with a parallel 26 per cent decrement in AHI [16]. Thus, weight reduction is an important conservative treatment for sleep apnoea.

Family history and genetic predisposition

Familial aggregation and genetics factors are thought to play a role in the development of OSA. First degree relatives of those with OSA increases the

relative risk compared to those without OSA by 1.5 - 2.0, and familial susceptibility to OSA increases directly with the number of affected relatives [17,18]. Obesity is closely associated with OSA and itself aggregates in families, so it is possible that familial aggregation of OSA is related to the genetics of obesity. Besides, apolipoprotein E (APOE) is particularly associated with OSA in younger subjects, the odds ratio for subjects with this allele who are < 65 yr of having an AHI > 15 is 3.1 [19]. Craniofacial morphology represents another mechanism by which genetics may influence the development of OSA, the bony and soft tissue structures that are seen from one generation to another in different families, including specific craniofacial disorders, for example, Pierre-Robin syndrome, these patients have micrognathia, glossoptosis, and cleft palate, the tongue tends to prolapse backward, leading to airway obstruction, and hence, they are more prone to suffer from OSA [20].

Craniofacial abnormalities

The structural factors in the upper airway may alter its mechanical properties. Differences in craniofacial morphology may explain some of the variation in risk for OSA in different ethnic groups. Previous studies have shown that craniofacial abnormalities are important in the pathogenesis of OSA, particularly in non-obese patients [21].

Smoking and alcohol consumption

Cigarette smoking and alcohol have been shown to be risk factors for OSA. Smoking is associated with a higher prevalence of snoring and sleep-disordered breathing [22, 23]. In Winconsin Sleep Cohort Study, current smokers had a much greater risk of moderate or worse degree of OSA (odds ratio, 4.44) compared with never smokers [24]. It can well be explained by the cigarette induced airway inflammation and damage which could change the structural and functional properties of the upper airway, and increasing the risk of collapsibility during sleep. Alcohol relaxes upper airway dilator muscles, increases upper airway resistance and may induce OSA in susceptible subjects. Therefore, alcohol intake can prolong apnoea duration, suppress arousals, increase frequency of occlusive episodes and worsen the severity of hypoxaemia[25], however, the underlying mechanisms are not well understood.

Pathophysiology of obstructive sleep apnoea

Three factors that play a significant role in the development of OSA are: (i) a reduction in the dilating forces of the pharyngeal dilators, (ii) the negative inspiratory pressure generated by the diaphragm, and (iii) abnormal upper airway anatomy, the element most effectively addressed by surgery. The multifactorial nature of this condition may explain why surgical procedures in the upper airway often address the sound of snoring but do not necessarily result in the complete elimination of OSA [26].

The most common sites of obstruction are located in the pharynx [27]. The muscles of the upper airway, including the sternohyoid, genioglossus, and tensor veli palatini, work synergistically to dilate or stiffen the extrathoracic airway and to maintain its caliber. Airway collapse often occurs when patients sleep on their back and the base of the tongue abuts the posterior pharyngeal wall and soft palate. Elongated or excessive tissue of the soft palate, a bulky tongue, enlarged uvula, large tonsils, and redundant pharyngeal mucosa are the most common causes of snoring and obstructive sleep apnoea. Along with the narrowing of the airway, an increased inspiratory pressure is needed to maintain adequate ventilation.

Factors in development of OSA

Play an important role in progression of the disease. Additional factors are several factors are implicated in the development of OSAS [28]. The main cause described in the literature is a reduction of the expansion forces of the pharyngeal dilator muscles, as in situations of genioglossal muscle dysfunction, and discoordination between the inspiratory activity of the muscle and respiratory effort [29], which excessive and elongated tissues of the soft palate, macroglossia, tonsillar hypertrophy, and a redundant pharyngeal mucosa [30].

Pae *et al.* found tongue shape in patients with OSAS to be different from that of normal subjects in the supine position this being the first study to evaluate tongue shape in the supine position. Tongue shape therefore may be taken to play an important role in the development of OSAS [31].

Altered upper airway anatomy, conditioned by skeletal abnormalities as in Pierre Robin syndrome, or by alterations of the soft tissues of the neck, particularly in obese patients, with increased adipose tissue in the region of the neck with fat infiltration and edema in the soft palate³², are also implicated in this syndrome.

Although obesity is regarded as a principal risk factor in the occurrence of OSAS, it has been shown that the neck perimeter is more closely correlated to severity of the syndrome than body mass index, though there is usually direct proportionality between obesity and neck perimeter [32].

Adult upper airway abnormalities in sleep apnoea[33]

Enlarged and elongated uvula
Hyperplastic or thick soft palate
Constricted oropharynx

Macroglossia

Enlarged tongue base
Prominent oropharyngeal folds
Skeletal deformities, Maxillary
& Mandibular Retrognathism or
Hypoplasia, Receded chin

Adenoids
Obstructive tonsils
Deviated septum
Enlarged nasal turbinates
Nasal polyps or any other
Obstructive masses

Clinical features

With regard to the major signs and symptoms of OSAS, a distinction can be made between day and night.

Nocturnal symptoms

The most frequent and characteristic nocturnal symptoms of OSAS are snoring and observed apneas, both of which reflect the underlying physiopathological events:

Snoring is the most common symptom of OSAS (present in up to 95% of all patients) [34]. However, it is also very common in the adult general population, affecting 25-30% of all women and 40-45% of all men on a regular basis [35].

This explains why snoring is of little diagnostic value in identifying OSAS [34]. Patients who consult with suspected OSAS tend to have a long prior history of snoring that has become increasingly intense and irregular over time, often in connection with increased body weight, alcohol consumption or muscle relaxant drugs, or with menopause in women [36].

Observed apneas are a frequent cause of consultation, since they often worry the couple of the patient, describing them as respiratory pauses that interrupt snoring while the patient continues to make efforts to breathe. Observed apneas are more predictive of a high apnea/hypopnea index (AHI) than either snoring or excessive daytime sleepiness.

Arousals or awakenings are less frequent than observed apneas. Such situations correspond to “perceived apneas” that end when arousal occurs. They are conscious phenomena and are accompanied by brief and intense dyspnea sensation.

This symptom is related to high blood pressure [37], because repeated arousals are linked to sympathetic discharges that raise blood pressure and heart rate. Choking, diaphoresis, nocturia, restless sleep and somnolence are additional nocturnal symptoms related to OSAS.

Daytime symptoms

Daytime sleepiness is the most important daytime symptom of OSAS, and is due to the fragmentation of sleep caused by recurrent electroencephalographic awakening that usually terminate the apneas and hypopneas [38]. Daytime

sleepiness is of scant diagnostic value, because a number of situations and disease processes can cause the same symptoms [39].

Morning headaches, apathy, depression, concentration difficulties, memory loss and decreased libido are other characteristic daytime symptoms of patients with OSAS, all as a consequence of daytime sleepiness.

Diagnosis

An essential requirement for a correct diagnosis of OSAS is a correct anamnesis, recording the family history (history of OSAS) and personal antecedents (tonsillectomy/adenoidectomy in childhood, alcohol intake, the use of muscle relaxant drugs, obesity, etc). It is also important to establish the profession of the patient, since in some professions OSAS constitutes a medical emergency [39].

A proper physical examination is also required (height, weight, body mass index, cardiovascular evaluation), including exploration of the upper airway [40] (nasal passages, oropharynx and hypopharynx, and larynx). The above data in turn should be complemented by radiological study in the form of either conventional lateral X-rays [41] or a tridimensional X-ray study [42], which will reveal the craniofacial anatomical alterations predisposing to OSAS [43].

Diagnostic test

Many tests are available for evaluating sleep and for diagnosing OSAS. The most widely used technique is polysomnography (PSG) [44], which monitors the sleeping state, respiration, electrocardiogram, movements of the legs, oximetry and snoring. In addition, PSG records the distribution of the stages of sleep, the number of awakenings, the number of apneas or hypopneas, the starting time of sleep, and the hours of efficient sleep (hours asleep/hours in bed). PSG also provides the apnea / hypopnea index (AHI); in this context, apnea is very serious and can only be treated surgically when AHI >30, while AHI 15-30 defines moderate apnea, and an AHI score of < 15 indicates mild apnea.

While PGS provides a lot of information, it is a complex and expensive technique thus limiting its practical applicability to the evaluation and treatment of OSAS. For this reason, simple tests have been developed and are now used in many healthcare systems. While such techniques provide less information, they are cheaper and can be applied in the home of the patient [45].

The goal of treatment for snoring and OSA is to improve quality of life, daytime sleepiness and psychomotor vigilance, and to reduce or eliminate snoring and sleep apnoea. An algorithmic approach to

select the sites as well as modalities of surgical intervention should not only produce more favourable outcomes but may allow patients to avoid procedures that are less likely to be beneficial [33].

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