

Review

Modalities of treatment for sleep disordered breathing

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Abstract: Sleep disordered breathing is a spectrum of diseases that includes snoring, upperairway resistance syndrome and obstructive sleep apnea. It occurs more in obese males, resulting in hypertension and cardiac complications if untreated. There are various treatments, conservatively and surgically, starting from simple tonsillectomy to multi-level surgeries and multi discipline. Literature review was carried out on the pathophysiology, clinical presentation, complications, diagnosis and various treatments, using internet Google, search PubMed. Additional information was obtained by cross referencing, using text and journals in the medical libraries.

Keywords: sleep disordered breathing; snoring; obstructive sleep apnea; obstructive sleep apnea hypopnea syndrome

1. Introduction

Sleep Disordered breathing is a spectrum of diseases which includes snoring, upper airway resistance syndrome (UARS), and obstructive sleep apnea (OSA).

Snoring is caused by vibration of soft palate, uvular, tonsils, base of tongue, epiglottis, and pharyngeal walls in oropharynx. Sleep disordered breathing includes simple snorers, where patients snore without daytime somnolence and with a normal apnea-hyponea index AHI. Upper airway resistance syndrome (UARS) are patients with excessive daytime somnolence but a normal AHI. Obstructive sleep apnea (OSA) are patients who snore and have both excessive daytime somnolence and abnormal AHI.

Apnea refers to a pause in respiration for more than 10 seconds, and is seen in both central sleep apnea (CSA) and OSA. They are differentiated by a lack of respiratory effort in CSA versus continued but ineffective respiratory effort in OSA.

Hypopnea is defined as reduction in ventilation of at least 50% that results in a decrease in arterial saturation of 4% or more due to partial airway obstruction (Mabata *et al.*, 2012). Hypopnea is also defined as 50% reduction in normal tidal volume.

Apnea-Hyponea Index (AHI) or Respiratory Disturbance Index (RDI) is an index used to indicate the severity of sleep apnea. It is represented by the number apnea and hypopnea events per hour of sleep (Ruehland *et al.*, 2009).

Obstructive sleep apnea hypopnea syndrome (OSAHS) is associated with repetitive collapse of the upper airway, partial or total resulting in apnea or hypopnea, specially during sleep for more than five times per hour AHI (Mabata *et al.*, 2012) plus daytime sleepiness.

Obstructive sleep apnea hypopnea syndrome can be mild AHI (5-15), moderate AHI (15-30), or severe AHI more than 30 (Marin *et al.*, 2002; Hsu *et al.*, 2001).

In middle aged adults, the obstructive sleep apnea incidence is 4-9% (Leung, 2009), and over 65 years is about 10%. Aging may affect the brain's ability to make pharyngeal muscles stiff during sleep, resulting in collapse of these. OSA is four times more common in men than in women (Crummy *et al.*, 2008). Women are more common when pre-pregnant and menopause, but women who receive hormone replacement therapy has less occurrence, suggesting progesterone and oestrogen may be protective. Postmenopausally also, as fat distribution changes to android type, there is obesity, OSA, and complications especially after 60 years age (Don *et al.*, 1999).

About 25-40% of OSA patients have family history due to inherited anatomical abnormalities (Selim, 2015).

OSA is also more common in African Americans, Hispanics, and Pacific Islanders than in whites. Under 35 it is more common in blacks (Selim, 2015).

2. Pathophysiology

During awake, the airway is kept open by dilating muscles which have higher than normal activity, but during sleep, the muscle tone falls, and airway narrows, snoring occurs followed by blockage and apnea. Several neurotransmitters and modulators have been found that help neurochemical regulation of pharyngeal motor function and airway patency (Dempsey *et al.*, 2010).

The intermittent hypoxia, negative intrathoracic pressure, and arousals which are features of apnea, hypopnea leads to increase in blood pressure at the end of sleep disordered breathing, giving rise to hypertension due to heightened sympathetic nervous system and dysfunction of arterial baroreceptor (Olson *et al.*, 2003). Association of OSAHS with cardiovascular disease is seen within AHI (5-15) events per hour and occurs in 1 in 15 adults (Olson *et al.*, 2003). The features of this condition include hypoxaemia, hypercapnia, large intrathoracic pressure with swings up to (-120mmHg), and systemic pressure up to 250/150mm Hg, and is associated with arousals, sleep fragmentation, up to 100 times per hour (Crummy *et al.*, 2008, Marin *et al.*, 2002). Symptoms include excessive daytime somnolence, nonrefreshed sleep, nocturia, and loud snoring over 80db (Crummy *et al.*, 2008).

3. Predisposing factors includes all the factors which cause narrowing of pharynx eg. obesity. More than 50% of obese patients have body mass index (BMI) greater than 30kg/m² and for Asians 23kg/m². Both obesity and OSA seem to be inflammatory with high levels of cytokines such as interleukin6, C-reactive protein and platelet aggregation (Crummy *et al.*, 2008). In a study, a 20% increase in weight was associated with a 70% increase in AHI, whereas a 20% reduction in weight was associated with a 48% decrease in AHI (Crummy *et al.*, 2008). The pathogenesis of obesity remains unknown, but there is resistance to leptin, an adipocyte-derived hormone that regulates bodyweight through the control of appetite and energy (Lowe *et al.*, 2000). Longitudinal data from the Wisconsin Sleep Cohort Study shows that a 10% weight loss predicts a 26% decrease in the AHI (Olson *et al.*, 2003).

Men with a neck circumference 41.36cm and women with 35.68cm also have a significant risk of OSA (Ahabab *et al.*, 2013) and also others correlate with waist circumference (Foster *et al.*, 2009), and age over 60 years (Don *et al.*, 1999).

Central obesity reflected by waist to hip ratio was similar or better predictor of OAS than BMI (Ip *et al.*, 2000), Pickwickian syndrome (extreme obesity BMI above 40 with obesity-hypoventilation syndrome) (Mokhlesi *et al.*, 2008), where excess fat interferes with chest movement and breathing (Don *et al.*, 1999).

Other factors like retrognathia, jaw shape, deviated nasal septum, low lying soft palate, enlarged uvula, base of tongue (Don *et al.*, 1999), hypothyroidism and acromegaly all predispose to upper airway narrowing predisposing OSAHS. Other modifiable risk factors are alcohol, smoking, nasal congestion and OSA occurs twice as often in patients with nasal congestion at night regardless of the cause (Selim, 2015). This may be due to narrowed airways and estrogen depletion in menopause in women (Young *et al.*, 2002). Patients with COPD have resting hypoxia and hypercapnia and when associated with OSA is known as overlap syndrome (Crummy *et al.*, 2008). OHS Obesity Hypoventilation syndrome is defined by development of diurnal hypercapnia (PaCO₂ more than 45 mmHg in obese individuals in the absence of other reasons for hypoventilation such as coexistent lung or neuromuscular disease OHS is associated with a morbidity and mortality due to cardiac and respiratory compromise.

In children tonsillar enlargement, ie lateral impingement more than 50% of the posterior pharyngeal air space, lateral pharyngeal wall impingement more than 25% without tonsil and adenoids enlargement, dental conditions, birth defects such as Down's syndrome, Pierre-Robin syndrome can cause OSAHS (Olson *et al.*,

2003). It was also found that those with apnea index (AI) more than 20 had a greater mortality than those who has less (He *et al.*, 1988).

4. Associated features

In both OSA and CSA, autonomic profile with profound vagal activity leads to bradyarrhythmias, and ventricular ectopy are observed, resulting in cardiac arrhythmias, and sudden, cardiac death (Leung, 2009). Others being, hypertension, angina pectoris, myocardial infarction, and corpulmonale may occur. Sleepapnea may also worsens cardiac dysfunction in chronic congestive heart failure patients (Leung *et al.*, 2001; Don *et al.*, 1999).

In response to OSA, there may also be a group of humans due to certain genetic predisposition develop systemic hypertension, but, also there are others who do not have it (Leung *et al.*, 2001).

The normal nocturnal BP is reduced to about 15% below daytime levels in patients with essential hypertension ie dippers. But in OSA patients who are said to be nondippers, they have absent fall in nocturnal BP (Leung *et al.*, 2001).

Studies also suggest an increase in the risk of myocardial infarction and stroke in untreated OSAHS (Good *et al.*, 1996; Leung *et al.*, 2001; Leung, 2009), Bblockers have been reported to be the most effective among antihypertensive agents, in lowering daytime BP in hypertensive OSA patients as sympathetic overactivity is involved. However antihypertensive medications have little effect on nocturnal BP in OSA, possibly because they do not reduce OSA (Kraiczi *et al.*, 2000).

Stress hormones may be triggered by frequent decrease in blood oxygen levels (Crummy *et al.*, 2008) and can increase heart rate and worsen the heart failure. In obese patients with type2 diabetes, here is undiagnosed OSA of 86.6% (Foster *et al.*, 2009) and OSAHS is associated with insulin resistance, which is not dependent of obesity (Peled *et al.*, 2007). Severe OSA is a risk factor for fatty liver, with elevated liver enzymes, fibrosis, steatohepatitis independent of body weight. Researchers also found connection between OSA and glaucoma (Selim, 2015) and patients with OSAHS also have increased perioperative risk (Olson *et al.*, 2003).

The most common OSA signs and symptoms include-restlessness during sleep, day time sleepiness, fatigue, trouble concentrating, forgetfulness. There can also be depression, irritability, night sweats, sex problems. Apart from these, waking up suddenly and feeling like gasping or choking, trouble getting up in mornings. In children there may be bedwetting, choking, or drooling, learning and behaviour disorders, sluggishness or sleepiness, teeth grinding, unusual sleeping positions, such as sleeping on prone position, or with neck hyperextended.

5. Diagnosis

History of sleep disordered breathing can be obtained from a person who sleeps together or bedpartner. SDB can originate from different parts of the upper airway, therefore all of the upper airway must be examined during evaluation and must be performed before polysomnography and any treatment planned. Clinical impression of sleep physicians for OSAHS is of little value with a 50-60% sensitivity and a 63-70% specificity (Kountakis, 2007). Otorhinolaryngological status should be examined, by endoscope, including Mullers manoeuvre (Kountakis, 2007). Others being Nasal airflow sensors for rhinometry and resistance, Flexible nasopharyngeal video endoscopy, Orthodontic status, Tonsil size staging after Friedman, Mallampati score of tongue and oral cavity relation (Friedman *et al.*, 1999) BMI, Neck circumference, Polysomnography which can be a full night or half night study based on 120 minutes of sleep, and repeated 4-6 months after surgery (Olson *et al.*, 2003). Diagnosis for allergy, imaging of upper airway, tape recording of snoring by snore microphone, (MSLT) Multiple sleep latency testing which measures how long it takes a person to sleep (Carskadon, 1986). Epworth sleepiness scale is most commonly used to assess daytime sleepiness. The score is calculated out of a total of 24, and the normal score is 4.6 (Standard deviation 2.8). Excessive daytime sleepiness is considered to occur if the score is above 10 on the ESS (Kountakis, 2007). Other tests like Osler's test which is a maintenance of wakefulness test still need evaluation and correlated to the ESS (Priest *et al.*, 2001). Finkelstein test-Patients are allowed to drink water with their heads under a running water fountain, and in case of velum sufficiency, no water enters the nose (Kountakis, 2007).

Cephalometric radiology is measuring various linear and angular measurements with emphasis on posterior airway space of retrolingual level. It is safe, noninvasive, minimal radiation, and easy to perform on an outpatient basis (Nuruntaract, 2003).

The differential diagnosis of OSAHS includes-Insufficient sleep, shiftwork, Periodic limb movement disorder (Kaplan *et al.*, 1993), Restless leg syndrome (Christopher, 2003), Depression, Drugs, Narcolepsy, Idiopathic hypersomnolence (Adrian *et al.*, 2015), Parasomnia (Pressman, 2011), Insomnia (Punnoose *et al.*, 2012).

6. Treatment

Obstructive sleep apnea treatment depends on a number of factors, which includes severity of problem, physical structure of upper airway, patients general condition and medical problems. While, some snorers has pendulous and flaccid uvula, webbing tonsillar pillars and enlarged palatine tonsils, others who have these, but did not snore. Thus, OAS is not only due to anatomic problem, but also, probably is initiated by neural events during sleep.

The treatment options include, conservative and surgery.

6.1. Conservatively, it include-

- Weight loss- loosing 10% of the weight will make a difference
- Exercise- should be done about four or more days a week (Selim, 2015).
- Avoid alcohol and sleeping pills- the airway collapse easily and prolongs improper breathing
- Sleeping on the side - in mild snorers, by pinning tennis balls to a sock to the back to sleep on side.
- Sleeping with humidification – may help dry mouth but may have allergy
- Fancy pillows- are expensive and may not work well. Some use with CPAP and others raise the upper body.
- Nasal sprays may relieve nasal congestion, and easy breath, but nasal strips may improve little as obstruction is elsewhere.
- Modafinil- improves sleepiness, and works by altering the natural chemical neurotransmitter in the brain (Emmanuel, 2012). Others being Protriptyline a non sedating tricyclic antidepressant and Mirtazipine a mixed serotonin receptor antagonist (Kryger *et al.*, 2010)
- CPAP machine-Continuous Positive Airway Machine, with a mask over nose and mouth keeping the airway open, and should be titrated to a level which eliminates snoring, usually 5-20cm Hg. Mean daily use of 4 hours a day is necessary (Marin *et al.*, 2005). Even though some improves, some has irritation and stomach bloating, and 46-83 % of patients, are non adherent to therapy (Camacho *et al.*, 2013). But with technological advancements, lower than 50% achieve apnea index which is less than 10, and apnea is reduced by 50% (Olson *et al.*, 2003).
- Oral devices- These are fitted by dentist or orthodontist and worn in the mouth at night. These prevent tongue falling back and advance lower jaw forward. Keeping airway open but it needs to change every 2 years (Lowe *et al.*, 2000).
- Mandibular advancement devices (MAD) or mandibular repositioning appliance (MRA) is widely used and is like a mouth guard in sports and lower jaw eased forwards. It increases velopharynx airway and posteriorinferior displacement of hyoid (Hiyama *et al.*, 2003). Another is Tongue retaining device (TRD). Complications like salivation, altered bite and teeth movement, pain and dry mouth can occur
- Boil and Bite devices- A thermoplastic heat sensitive to enable molding in hot water and bite to fit in mouth, and moves jaw forward (Pressman, 2011)
- Playing the Didgeridoo, an Australian Aboriginal 130cm long musical instrument (Milo *et al.*, 2006). The AH ratio is reduced due to training of muscles of upper airway in dilating and stiffening with playing 20 mins, 5day a week for 2 months.

6.2. Surgery. CPAP should be tried first before surgery. Surgery is for misshapen or patients with extra tissue that blocks airflow through nose and mouth. Nasal and palatopharyngeal surgeries are the mostly performed procedures to treat OSA.

These include-

- Nasal surgeries, including Functional endoscopic sinus surgery, Submucosa resection, submucous diathermy, polypectomies for polyps, deviated nasal septum, hypertrophic turbinates (Poirier *et al.*, 2014)
- Tonsillectomy, Adenoidectomy. This is often the first line treatment for children, as these enlargement causes obstruction, giving sleep apnea. Others being arytenoids reduction, epiglottectomy, epiglottopexy, epiglottoplasty (Punnoose *et al.*, 2012).
- Upper airway stimulator, Hypoglossal nerve stimulation of genioglossus muscle (Eisele *et al.*, 1997). In the device call Inspire, it has a small pulse generator placed under skin on the chest. One wire detects breathing, and another to neck to twelfth cranial nerve to targeted muscle genioglossus, to keep it open during inspiration. It can be remotely controlled (Boon, 2015) and good for moderate to severe OSA (AHI 20-65).

- Injection Snoreplasty- Injection of Sodium tetradecyl sulphate (STS) as sclerosing agent is used to fibrosis and stiffen the palate, for mild OSA (AHI less than 15). Its action is like radiofrequency ablation, but the latter causes thermal injury (Botti *et al.*, 2010). Other sclerosing agent used is 50% ethernol. Advantage is simple, lowcost, and less painful (Brietzke *et al.*, 2001).
- Caustery assisted palatal stiffening operation (CAPSO), where cautery causes fibrosis and palatal stiffening (Punnoose *et al.*, 2012). Mean AHI improve from 25.1- 16.6 (Wassmuth *et al.*, 2000).
- Palatal Implants- The Pillar procedure. These are synthetic polyethelene terephthalate (PET), 18mmx1.8mm porous cylinder rods, and three are implanted in soft palate, making it stiffer. They are good for snoring, but not for severe OSA, (AHI more than 35), or short palate less than 20mm. It is painless simple but occasional pain, foreign body sensation and extrusion can occur (Kuhnel *et al.*, 2005).
- Uvulopalatopharyngoplasty (UPPP)- In 1964, the first pharyngeal surgery for snoring was published in Japan by Ikematsu (Bottiet *et al.*, 2003) with 82% of snorers improve. UPPP was first mentioned in 1981 by Fujita *et al.* who modified Ikemasu technic and become the most common surgery to treat OSA (Botti *et al.*, 2003). It removes redundant palatal and pharyngeal tissues and uvula and widens oropharyngeal inlet, and better results if with tonsillectomy. For AHI less than 25, or moderate to severe OSA as part of multilevel surgery. Complications like wound dehiscence, nasopharyngeal stenosis, speech disorder, and continued obstruction at palate can occur (Woodson *et al.*, 1993).
- Lateral Pharyngoplasty. This technic was described by Cahali in an attempt to increase the lateral space of pharynx and improve the outcome of UPPP preserving uvula and soft palate. It includes tonsillectomy and section of constrictor muscles, and closure of mucosa. Cahali compared with UPPP and the result was found to be better (Botti *et al.*, 2003).
- Z-Palatoplasty is for post tonsillectomy scarring patients, failed UPPP or absence of posterior pilla. It widens space between palate and posterior pharyngeal walls, but has risk of permanent velopharyngeal insufficiency. Although the cure is 67.7% (Friedman *et al.*, 2007), there can be failures and need CPAP.
- Transpalatal Advancement Pharyngoplasty (TAP). It removes the posterior hard palate, and advancing the soft palate into the anterior defect. Simillar to maxillary advancement, but there is no need to move the dentition. Success rate is 67% for patients who have respiratory disturbance index RDI lower than 20 per hour. Thou, globus, aspiration and salivation can occur, it may be appropriate in selected patients as part of OSA treatment (Woodson *et al.*, 1993).
- Laser assisted uvulopalatoplasty (LAUP). For mild to moderate sleep apnea, it reduces the excess tissue of soft palate and uvula by carbonisation and can be performed under local (Botti *et al.*, 2003). LAUP has slight advantage over radiofrequency, but with more discomfort postoperatively (Terris *et al.*, 2002).
- Tongue based suspension can be considered when tongue base collapse more than 50% of airway, and failed UPPP. But over correction may result in tongue thrusting, dysarthria and dysphagia. To prevent tongue from falling back a submucosal polypropelene suture in tongue is attached to genial tubercle. A repose tongue suspension method (Vicente *et al.*, 2006), with UPPP has success of 78% for severe OSA, and BMI less than 35kg/m² (Vicente *et al.*, 2006). But in Frank R Miller study surgical cure rate was 20% (Miller *et al.*, 2002).
- Midline glossectomy, Lingualplasty, and submucosal minimally invasive lingual excision (SMILE) removing tissue from back of tongue and making it smaller, it is less use now (Camacho *et al.*, 2013).
- Radiofrequency ablation (RFA) Somnoplasty. This reduces the tongue base and palate RFPalatoplasty. Mainly for mild cases and uses temperature controlled RF bipolar and plasma mediated ablation (coblation). It causes thermal fibrosis and done under local. There is no tissue resection (Poirier, 2014) and reduce snoring by 60-100%, thou nasal regurgitation and velopharyngeal insufficiency can occur.
- Hyoid suspension and hyoid myotomy. A decrease in airway length can reduce airway resistance, thus hyoid suspension was done with release of inferior attachments under LA (Friedman *et al.*, 1999), or GA, and fixed to mandible or thyroid cartilage using a steel wire as in Hormann hyoid suspension (Hormann, 2009). Ottavio Piccin followed a modified form and AHI reduced from 43.1-10.9/h.no complications were noted (Piccin *et al.*, 2014). When multi level management was done success was 71% (Punnoose *et al.*, 2012).
- Genioplasty or genioglossus muscle advancement (Lee *et al.*, 2000) widens the space of posterior airway in the area of hypopharynx and tongue base. The UPPP, mortised genioglossus advancement is

also effective for OSA. Kezirian & Goldberg (Kezirian *et al.*, 2006) demonstrated success rate of more than 60%, with AHI decreasing from 60-29/h.

A combination of genioadvancement, UPPP, maxillomandibular advancement can be done to avoid multiple procedures (Hendler *et al.*, 2001).

- Maxillomandibular advancement MMA- David J Dattilo noted that comparing Phase 1 surgery (hyoid suspension, palatal surgery, genioglossus advancement) with Phase 2 (maxillomandibular advancement) the latter is more effective (Dattilo *et al.*, 2004, Wagner *et al.*, 2000). It is considered when phase 1 surgery fails, or facial deformities or retrognathia, moving upper and lower jaw to increase size of airway. It achieved respiratory disturbance index of 20 and 50% reduction from preoperative values (Li *et al.*, 2000).
- Maxillomandibular widening by distraction osteogenesis method uses an intraoral distraction device, and bone lengthening is due to that of natural bone healing in the gap of osteotomy, for mild to moderate OSA (Guerrero *et al.*, 1997). The appliance was activated seven days after osteotomy once each day at the rate of 1mm per day and stabilise for 30-60 days after distraction.
- Transoral robotic surgery (TORS) for lingual tonsils, epiglottis, and tongue base reduction (Friedman, 2012). Success was 66.7%.
- Multiple level pharyngeal surgery-because obstruction occurs in multiple levels, multiple sites are needed to operate. Uvulopalatopharyngoplasty, tonsillectomy, mandibular osteotomy, with genioglossus advancement is to increase the oropharyngeal inlet. Modified hyoid myotomy and suspension is to increase the retrolingual area. The authors claim 76.9% achieve more than 50% reduction in AHI with postoperative AHI of less than 20. (average pre and post operative AHI of 52.8 and 15.6 respectively.) (Hsu *et al.*, 2001).
- Bariatric surgery- Of the bariatric surgeries, (Roux-en-Y gastric bypass, laproscopic sleeve gastrectomy, biliopancreatic diversion {BPD}), over 75 % shows improvement. BPD was most successful for OSA, with laproscopic gastric banding, the least (Sarkhosh *et al.*, 2013).
- Tracheostomy is done when others fails. Thou it cures sleep apnea, chances of apnea resolution with decannulation is a problem (Thatcher *et al.*, 2003).

7. Conclusions

It should be noted that there is no single method which is totally effective in treating all OSA patients. Treatment should be tailored according to patients need and desires, preferences and health status, risks and benefits with multilevel surgeries and multidiscipline approach. Surgery is considered when CPAP fails. Surgery should be minimally invasive and avoiding more aggressive methods. Early recognition and appropriate intervention will reduce the mortality and the quality of life can be improved.

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Conflict of interest

None to declare.

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