JOURNAL OF CLINICAL AND HEALTH SCIENCES

REVIEW

Selected Recommendations from International Guidelines on Obstructive Sleep Apnoea

Nurul Yaqeen Mohd Esa, Ahmad Izuanuddin Ismail

Faculty of Medicine, Universiti Teknologi MARA, Sungai Buloh, Selangor, Malaysia

Received
27th August 2017
Received in revised form
24th September 2017
Accepted
22nd December 2017

Corresponding author:
Nurul Yaqeen Mohd Esa
Faculty of Medicine
Universiti Teknologi MARA
47000 Sungai Buloh, Selangor
Tel. no: 016-6905569
Email: ummuqutb@gmail.com

ABSTRACT

Obstructive sleep apnoea (OSA) is increasingly seen as a major health threat globally. However, it is still underdiagnosed mainly among Asian population partly due to lack of understanding on the pathophysiology, and limited access to the diagnostic and management aspect of the disease. Recurring complete and/or partial collapses of the upper airways define OSA. Based on the number of apnoeas and/or hypopnoeas per hour of sleep, OSA is categorized as mild, moderate and severe. Both the American Association of Sleep Medicine (AASM) and American College of Physicians (ACP) has published guidelines regarding the management of OSA in adults. Three recommendations have been suggested by the guidelines which can be used to tailor the management of OSA. The aim of this article is to select relevant recommendations from these guidelines in epidemiology, pathophysiology, diagnostic procedures and treatment for proper management of OSA, while considering specific patient populations, such as hypertensive, diabetic, obese and Asian patients.

KEYWORDS: Obstructive sleep apnoea, sleep disordered breathing, apnoea-hypopnoea index, polysomnography, obesity, excessive daytime sleepiness, continuous positive airway pressure, mandibular advancement devices, metabolic syndrome, Asian population

INTRODUCTION

Obstructive sleep apnoea (OSA) is increasingly seen as a major health threat globally. Affecting approximately 2% of women and 4% of men in Western population [6], it is considered a frequent medical condition.

Recurring complete and/or partial collapses (apnoea and hypopnoea respectively) of the upper airways defined OSA. Based on the number of apnoeas and/or hypopnoeas per hour of sleep, known as the apnoea-hypopnoea index (AHI), OSA is categorized as mild, moderate and severe. Polysomnography (PSG) is the best tool to diagnose OSA [1]. Well known risk factors for OSA include obesity, aging, male sex, smoking and alcohol intake [2-5].

Excessive daytime sleepiness (EDS) or insomnia, nocturia and morning headaches, are common complaints of OSA patients, but some patients may be asymptomatic. Berlin Questionnaire [2] and Epworth Sleepiness Scale (ESS) [3], are examples of clinically helpful questionnaires available to detect high risk OSA patients.

OSA is still underdiagnosed mainly among Asian population partly due to lack of understanding on the pathophysiology, and limited access to the diagnostic and management facility [6]. The aim of this article is to focus on the current state-of-the-art in epidemiology, pathophysiology, diagnostic procedures and treatment selections for proper management of OSA, while considering specific patient populations, such as hypertensive, diabetic, obese and Asian patients.

OSA diagnosis

The diagnosis of OSA is often missed due to its complexity and unavailability of diagnostic modalities in certain centres. In order to standardize the diagnostic criteria for OSA, The American Association of Sleep Medicine (AASM) has come up with a guideline on how to diagnose obstructive sleep apnoea [24].

The document was developed by the AASM committees which consist of renowned authorities in sleep medicine field. The guidelines have outlined six

recommendations, in which four of them were strong recommendations.

First recommendation: clinical tools, questionnaires and prediction algorithms cannot be used to diagnose OSA, even in the absence of PSG. The grading for this recommendation is stated as strong recommendation.

Second recommendation: PSG can be used to diagnose OSA in straightforward cases with signs and symptoms of moderate to severe OSA. The grading for this recommendation is also stated as strong recommendation.

Third recommendation: if a single home sleep apnoea test is negative, inconclusive, or technically inadequate, polysomnography can be performed for the diagnosis of OSA. The grading for this recommendation is stated as strong recommendation.

Fourth recommendation: in patients with significant cardiorespiratory disease, awake hypoventilation or suspicion of sleep related hypoventilation, chronic opioid medication use, history of stroke or severe insomnia and potential respiratory muscle weakness due to neuromuscular condition, PSG is the standard tool to diagnose OSA. The grading for this recommendation is stated as strong recommendation.

Fifth recommendation: for OSA diagnosis, a split-night diagnostic protocol PSG, is preferable compared to a full-night diagnostic protocol if clinically acceptable.

Sixth recommendation: if the first PSG result is negative or inconclusive, a repeat PSG is needed.

Individuals with unexplained daytime sleepiness should be the target for OSA assessment. Appraisal of the common symptoms and risk factors for OSA should be included in the assessment [7-10]. Obesity is the best-documented risk factor for OSA. Accidental sleep episodes during wakefulness, daytime drowsiness, unrefreshing sleep, lethargy, insomnia, and snoring are amongst clinical symptoms for OSA [11-16]. In patients presenting with daytime drowsiness, which is a well-known OSA symptom most responsive to treatment, further evaluation for OSA may be warranted if other causes such as thyroid disease, gastro-oesophageal reflux disease, or other respiratory diseases have been ruled out. In assessing the symptom severity of OSA, sleepiness questionnaires, such as the ESS may assist, but it cannot assess the AHI due to its lack of sensitivity and specificity compared to PSG [22-29].

AASM and the Center for Medicare & Medicaid Services have considered AHI score of at least 15 events per hour or at least 5 events per hour with symptoms (such as daytime somnolence and fatigue) as criteria for OSA diagnosis.

Table 1 Four modes of sleep study available in the market: Type I, Type II, Type III and Type IV

Mode	Definition
Type I	**Type I** is the standard recommended overnight PSG for OSA diagnosis, in which the test was done in a proper sleep lab, attended by sleep technician.
Type II	**Type II** is defined by a test whereby the full PSG with its monitoring devices can be done outside of the sleep laboratory, without the presence of sleep technician.
Type III	**Type III** device channels only measure four physiologic variables which include cardiac variable (eg, heart rate or an electrocardiogram), respiratory variables (eg, respiratory movement and airflow), and arterial oxygen saturation. Signals needed to determine sleep stages or sleep disruption were not recorded by the device.
Type IV	**Type IV** is also known as continuous single or dual bioparameter devices. This device can only record one or two variables and it can work without a technician. The channels usually measure arterial oxygen saturation and airflow.

Type II, III, and IV monitors differ from PSG in terms of AHI estimation. For OSA prediction in various AHI cutoff levels, these monitors have a high positive likelihood ratio and low negative likelihood ratio. Performances are better in monitors with more channels compared to those with fewer channels. Type IV monitors are limited by their inability to distinguish obstructive from central sleep apnoea. Indirect data from studies comparing PSG monitors recommended that performances are better with type III monitors compared to type IV monitors in expecting AHI scores indicative of OSA. 3% to 20% data loss of has been observed for type III and IV monitors [22]. Inadequate clarification of results from the usage of type III monitors has been described in 13% to 20% of the evaluations, resulting from inadequate data [23]. There is no verified study on the usefulness of transportable monitors for complicated patients with serious

comorbid settings, such as chronic lung issues, cardiomyopathies, or brain disorders. Data is also lacking on head-to-head comparison on one monitor with the other [30].

OSA treatment

The guideline by the American College of Physicians (ACP) is intended to provide clinicians with evidence-based recommendations that will have positive, long-term effects on patients' cardiovascular risk, as well overall health and quality of life [20]. Three recommendations have been suggested by the guidelines which can be used to tailor our OSA management.

First recommendation is to encourage weight loss in all overweight and obese patients diagnosed with OSA. There is strong evidence showing how weight loss interventions can reduce the apnoea/hypopnoea index (AHI) and improve symptoms. OSA severity can be categorized as mild, moderate and severe. In which, mild means having 5-14 events per hr, moderate means 15-30 events per hr, and severe means having more than 30 events per hr. In patients with mild OSA, weight loss alone can be sufficient to normalize the apnoea/hypopnoea index, thereby reducing the need for continuous positive airway pressure (CPAP). In those with persistent OSA, weight loss may reduce the amount of positive airway pressure required, which can increase tolerance of and adherence to CPAP. However, weight loss alone may not be sufficient to reduce OSA in all patients. In obese patients, weight loss must be encouraged with another primary treatment. In a meta-analysis of 12 published trials, weight loss produced substantial reductions in apnoea/hypopnoea index, however, almost all of the patients continued to have persistent OSA after significant weight reduction. So, while weight loss must always be urged in OSA patients, it should not be assumed that this intervention alone will be sufficient; patients need to be reassessed to determine whether OSA persists and if so, CPAP should be continued.

Second recommendation is to prescribe CPAP as the first-line treatment for OSA patients. CPAP is as critical as it is effective not only in reducing the AHI but also in improving sleep continuity and architecture and decreasing the sleep hypoxia that is associated with OSA. Because of the lack of adherence to CPAP, many new features have been added including heated humidification, broad pressure adjustments, and expiratory pressure relief. Again, it is critical that each patient's needs be taken into consideration. Some patients, particularly those with mild forms of OSA, may not need CPAP and may benefit from positional therapy or weight loss. Other therapy such as surgery or mandibular advancement devices (MADs) may be better suited for some patients despite their lesser effectiveness when compared with CPAP [33].

Third recommendation suggests that for OSA patients who favour MAD or for those with side effects due to CPAP, MAD can be considered as an alternate therapy to CPAP. MADs can be considered for patients with moderate to severe OSA, those with apnoea/hypopnoea index values between 18-40 events/hour, and for individuals who experienced adverse events on CPAP or who can't tolerate using it. While CPAP is still considered to be primary therapy, for those who must use a mandibular advancement device, it can often be very effective. Patients may find it easier to be compliant with MAD than with CPAP. One group of researchers observed that MADs were able to provide appropriate decrease in obstructive events in 70% of patients with mild OSA, 48% of those with moderate OSA, and 42% of those with severe OSA [21]. The ACP concluded that, without sufficient evidence, it is unclear which patients will benefit from MADs. Data from several studies show that patients who are younger and thinner, with less severe OSA, may benefit more from the use of MADs. Although the ACP does not recommend surgery or pharmaceutical therapy for OSA, the ACP does acknowledge that it may work for certain patients. However, the documented efficacy rate ranges from 20%-100%, thereby making it challenging to determine its true effect [29].

OSA in hypertensive patients

There is a rising trend in the incidence of OSA in patients with hypertension. 20%–40% of OSA patients have been detected amongst drug resistant hypertensives patients [25-28]. Since the earliest description of PSG, acute changes in cardiovascular parameters are known to accompany OSA events at

night. Wide fluctuations of blood pressure (BP) and heart rate, are well known acute effects which have been contributed by alternating obstructive apnoea and hyperventilation episodes during sleep [5].

Few mechanisms have been associated with increased cardiovascular risk among OSA patients, which include autonomic alterations, reformed mechanics of ventilation leading to serious physiologic changes of negative intrathoracic pressure, alteration of renin–angiotensin–aldosterone system causing resistant hypertension, endothelial dysfunction, inflammation, metabolic factors and genetic predisposition [17-23].

Possible influence of OSA to the progression of resistant hypertension have been looked into by several studies. In OSA patients, refractory hypertension is primarily systolic and relatively more prominent at night [7-9]. Nocturnal raises in systolic BP due to OSA may have particular adverse influences in patients with refractory hypertension, since night-time systolic BP forecasts cardiovascular morbidity and mortality more precisely than daytime systolic BP.

In patients with resistant hypertension, OSA evaluation should emphasize on recognizing causative factors and excluding other causes of secondary (resistant) hypertension [24-27]. In patients with significant signs of catecholamine excess in whom a catecholamine-producing tumour cannot be recognized, a diagnosis of OSA should be considered. A tailored and personalized diagnostic evaluation for other identifiable causes for each individual should be steered by their respective signs and symptoms [30].

A seemingly resistant hypertension, usually due to a "white coat hypertension" or "isolated office hypertension'' state (blood pressure raised in the office environment but normalized out of the office) must be differentiated from exact resistant hypertension. Serious overestimation of blood pressure might be caused by inability to use proper and correct cuffs on OSA patients with large arms [32].

OSA in diabetic patients

Among OSA patients, type 2 diabetes mellitus (T2DM) have been postulated to be one of the main driver that increased risk of cardiovascular morbidity. A cross-sectional correlation between OSA severity and T2DM prevalence have been identified from community and sleep laboratory-based populations data [12,13]. A recent cross-sectional study assessing the correlations between OSA severity and T2DM prevalence in a vast multinational population involving 6,616 patients in the European Sleep Apnoea Cohort (ESADA) analysis have shown that T2DM prevalence increased with OSA severity [11, 33].

This study also found out that Diabetic patients with severe OSA had poorer glycaemic control, with adjusted mean HbA1c levels 0.72% higher compared to those without sleep-disordered breathing (P <0 .001). They also concluded that worsening OSA severity is directly correlated with increased likelihood of having concomitant T2DM and worse diabetic control in subjects with T2DM [11].

Another study done amongst 544 participants without any pre-existing diabetes assessed in a Yale sleep clinic by Botros et al suggested a possible contributory role for OSA in propagating the development of T2DM. This population-level data showed that a OSA diagnosis conversed a significantly increased risk of emerging T2DM over a mean follow-up period of 2.7 years, despite modification for confounding demographic and clinical factors (HR 1.43 per quartile of OSA severity) [14].

OSA amongst obese patients

The prevalence of OSA is noted to be rising among obese patients, given that obesity is the most common risk factor in OSA. OSA is closely linked with the metabolic syndrome, and it is proposed that OSA propagate cardiometabolic dysfunction, and ultimately vasculopathy as suggested by recent data. Well-known pathophysiological triggers in OSA include alternating hypoxia and sleep disturbances. Few possible ways of OSA–obesity–metabolic syndrome correlations have been proposed, which include activation of sympathetic nervous system, presence of oxidative stress, inflammatory changes and neurohumoral activation involving adiponectin and leptin [32, 33].

The data from human and animal/cell studies of intermittent hypoxia to describe these pathways are accumulating [28-31]. A balanced and healthy food intake accompanied by proper lifestyle adjustments play important roles in managing metabolic syndrome

and are equally important as CPAP usage in OSA management as a whole [10, 30].

OSA in Asian patients

Despite being reported as a common disease in Western population, surprisingly, the data on OSA prevalence in Asian population are still lacking. A systematic review on OSA prevalence in Asian population by Mirrakhimov et al [6] which included 24 articles, covering 47, 957 patients have shown that OSA prevalence were observed to range from 3.7% to 97.3%. Several risk factors have been associated with OSA among Asian patients, which include male sex, elderly patient, high BMI and waist to hip ratio, larger neck circumference, presence of arterial hypertension, smoking habits, snoring events and daytime drowsiness. Differences in prevalence rates among previous Asian studies can be explained by different sample size, different study populations and different inclusion criteria (some studies included subjects with a high pre-test probability of OSA). The prevalence of snoring, witnessed apnoea, EDS and insomnia, rather than OSA diagnosis have been reported by few other studies. Thailand has been reported to have the lowest snoring prevalence of 4.6% [18] while Taiwan has been reported to have the highest prevalence of 59.1% [17]. A much higher number of women have been included in the study from Thailand[18] and the younger subjects were included in the study from Taiwan and China [17]. Taiwan was reported to have the lowest 2.6% [17], and Malaysia was reported to have the highest prevalence of witnessed apenas of 15.2%[19]., In Turkish studies, EDS symptoms ranged from 3.85% [16] to 24% [15]. Different sample sizes and populations studied explained the difference in EDS prevalence findings

The results of many published studies on Asian population evaluated subjects with high pre-test probability of OSA; hence their findings may overemphasize the exact load of the disease. More researches with larger samples are required in order to expand our understanding on OSA amongst Asian population.

CONCLUSION

Obstructive sleep apnoea (OSA) is a progressively evolving health threat in both developed and developing nations. Major recommendations have been suggested for OSA diagnosis and treatment. Early identification and management of OSA is paramount in reducing cardio metabolic risks in global population. Some aspects of pathophysiology and correlations of OSA remain unexplored. Future research with larger study population are needed to establish the OSA correlations and its long-term effect especially in specific population.

Conflict of Interest

Author declare none.

Acknowledgements

Author would like to express gratitude to supervisors, consultants, fellow associates and all clinicians, who have helped in various ways for the preparation of this manuscript.

REFERENCES

1. Masood A, Phillips B. Sleep apnea. Curr Opin Pulm Med. 2000; 6: 479-84.
2. Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med. 1999; 131: 485-91.
3. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep. 1991; 14: 540-5.
4. Eastwood PR, Malhotra A, Palmer LJ, Kezirian EJ, Horner RL, Ip MS, Thurnheer R, Antic NA, Hillman DR. Obstructive sleep apnoea: from pathogenesis to treatment: current controversies and future directions. Respirology. 2010; 15: 587-95.
5. Coccagna G, Mantovani M, Brignani F, Parchi C, Lugaresi E. Continuous recording of the pulmonary and systemic arterial pressure during sleep in syndromes of hypersomnia with periodic breathing. Bull Physiopathol Respir (Nancy) 1972; 8: 1159-72.
6. Mirrakhimov AE, Sooronbaev T, Mirrakhimov EM. Prevalence of obstructive sleep apnea in Asian adults: a systematic review of the literature. BMC Pulmonary Medicine. 2013; 13: 10.

7. Lavie P, Hoffstein V. Sleep apnea syndrome: a possible contributing factor to resistant. Sleep 2001; 24: 721-5.
8. Logan AG, Perlikowski SM, Mente A, Tisler A, Tkacova R, Niroumand M, Leung RS, Bradley TD. High prevalence of unrecognized sleep apnoea in drug-resistant hypertension. J Hypertens 2001; 19: 2271-7.
9. Logan AG, Tkacova R, Perlikowski SM, Leung RS, Tisler A, Floras JS, Bradley TD. Refractory hypertension and sleep apnoea: effect of CPAP on blood pressure and baroreflex. Eur Respir J 2003; 21: 241-7.
10. Lam JMC, Mak JCW, Ip MSM. Obesity, obstructive sleep apnoea and metabolic syndrome. Respirology 2012; 17; 223-36.
11. Kent BD, Grote L, Ryan S, Pépin JL, Bonsignore MR, Tkacova R, Saaresranta T, Verbraecken J, Lévy P, Hedner J, McNicholas WT. Diabetes mellitus prevalence and control in sleep-disordered breathing: the European sleep apnea cohort (ESADA) study. CHEST 2014; 146(4): 980-90.
12. 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 (12): 1590-5.
13. Ronksley PE, Hemmelgarn BR, Heitman SJ, Hanly PJ, Faris PD, Quan H, Tsai WH. Obstructive sleep apnoea is associated with diabetes in sleepy subjects. Thorax. 2009; 64 (10): 834-9.
14. Botros N, Concato J, Mohsenin V, Selim B, Doctor K, Yaggi HK. Obstructive sleep apnea as a risk factor for type 2 diabetes. Am J Med. 2009; 122 (12): 1122-7.
15. Ozdemir L, Akkurt I, Sümer H, Cetinkaya S, Gönlügür U, Ozşahin SL, Nur N, Doğan O. The prevalence of sleep related disorders in Sivas. Turkey. Tuberk Toraks. 2005; 53: 20-7.
16. Kart L, Dutkun Y, Altın R, Ornek T, Kıran S. Prevalence of major obstructive sleep apnea syndrome symptoms in coal miners and healthy adults. Tuberk Toraks. 2010; 58: 261-7.
17. Chuang LP, Hsu SC, Lin SW, Ko WS, Chen NH, Tsai YH. Prevalence of snoring and witnessed apnea in Taiwanese adults. Chang Gung Med J. 2008; 31: 175-81.
18. Suwanprathes P, Won C, Komoltri C, Nana A, Kotchabhakdi N, Guilleminault C. Epidemiology of sleep-related complaints associated with sleep-disordered breathing in Bangkok. Thailand. Sleep Med. 2010; 11: 1025-30.
19. Kamil MA, Teng CL, Hassan SA. Snoring and breathing pauses during sleep in the Malaysian population. Respirology. 2007; 12: 375-80.
20. Qaseem A, Owens DK, Starkey M, Holty JE, Shekelle P. Diagnosis of obstructive sleep apnea in adults: a clinical practice guideline from the American College of Physicians. Ann. Intern. Med. 2014; 161: 210-20.
21. Mostafiz W, Dalci O, Sutherland K, Malhotra A, Srinivasan V, Darendeliler MA, Cistulli PA. Influence of oral and craniofacial dimensions on mandibular advancement splint treatment outcome in patients with obstructive sleep apnea. Chest. 2011; 139: 1331-9.
22. Mitler MM, Gujavarty KS, Browman CP, Maintenance of wakefulness test: a polysomnographic technique for evaluation treatment efficacy in patients with excessive somnolence. Electroencephalogr Clin Neurophysiol.1982; 53: 658-61.
23. Kapur VK, Auckley DH, Chowdhuri S, Kuhlmann DC, Mehra R, Ramar K, Harrod CG. Clinical practice guideline for diagnostic testing for adult obstructive sleep apnea: an American Academy of Sleep Medicine clinical practice guideline. Journal of Clinical Sleep Medicine. 2017; 13(3):479-504.
24. Fletcher EC, DeBehnke RD, Lovoi MS, Gorin AB. Undiagnosed sleep apnea in patients with essential hypertension. Ann Intern Med. 1985; 103(2): 190-5.
25. Lavie P, Ben-Yosef R, Rubin AE. Prevalence of sleep apnea syndrome among patients with essential hypertension. Am Heart J. 1984; 108(2): 373-6.

26. Worsnop CJ, Naughton MT, Barter CE, Morgan TO, Anderson AI, Pierce RJ. The prevalence of obstructive sleep apnea in hypertensives. Am J Respir Crit Care Med. 1998; 157(1): 111-5.
27. Gonçalves SC, Martinez D, Gus M, de Abreu-Silva EO, Bertoluci C, Dutra I, Branchi T, Moreira LB, Fuchs SC, de Oliveira AC, Fuchs FD. Obstructive sleep apnea and resistant hypertension: a case-control study. Chest. 2007; 132(6): 1858-62.
28. Culadeeban R, Jameel M, Joerg S. Clinical update sleep: year in review 2015-2016. J Thorac Dis. 2016; 8(2): 207-12.
29. Karadeniz Y, Onat A, Akbaş T, Şimşek B, Yüksel H, Can G. Determinants of obstructive sleep apnea syndrome: pro-inflammatory state and dysfunction of high-density lipoprotein. Nutrition. 2017; 43: 54-60.
30. Kim J, Mohler ER, Keenan BT, Maislin D, Arnardottir ES, Gislason T, Benediktsdottir B, Gudmundsdottir S, Sifferman A, Staley B, Pack FM. Carotid artery wall thickness in obese and nonobese adults with obstructive sleep apnea before and following positive airway pressure treatment. Sleep. 2017; 1; 40(9).
31. Turino C, Bertran S, Gavaldá R, Teixidó I, Woehrle H, Rué M, Solsona F, Escarrabill J, Colls C, García-Altés A, de Batlle J. Characterization of the CPAP-treated patient population in Catalonia. PLoS One. 2017; 12(9).
32. Yetkin O, Aydoagn D. Effect of CPAP on sleep spindles in patients with OSA. Respir Physiol Neurobiol. 2017; 17: 30278-1.
33. Godoroja DD, Cioc DA. Identification of significant obstructive sleep apnoea in the obese patient: development of the novel DX-OSA score. Rom J Anaesth Intensive Care. 2016; 23(2): 111-21.