REVIEW ARTICLE

Obstructive Sleep Apnea: An Overview

Ashish Goel[1], Anju Loomba[1], Poonam Goel[2], Prachi Goel[1], Rajat Mathur[3] and Ragni Tandon[1]

ABSTRACT

Aim: To overview the basic principles in understanding pathophysiology and diagnosing obstructive sleep apnea (OSA).

Summary: Normal sleep is a complex and critical physiological activity. It is characterized by discrete neurological patterns that represent different stages of sleep. In each phase of sleep: non-rapid eye movement (NREM) and rapid eye movement (REM) must be completed. Sleep is associated with specific neurological events that can be quantified in the sleep laboratory with the polysomnogram (PSM). Obstructive sleep apnea (OSA) refers to the temporary cessation of airflow during sleep for 10 seconds or more despite continuing ventilatory effort. Airflow obstruction results in a reduction of blood oxygen saturation known as hypoxemia. In adolescents obesity and mandibular retrognathism are major risk factors.

Keywords: Apnea, Asphyxia, Polysomnogram

INTRODUCTION

Obstructive sleep apnea (OSA) is a multifactorial sleep disorder that is gaining greater recognition among both physicians and the lay public. A history of "heroic" snoring in conjunction with daytime somnolence may alert the physician to the possible presence of this syndrome.[1] However, the majoriry of snoring individuals do not have an OSA disorder.[2]

OSA is a spectrum ranging from hypopnea to apnoea. Obstructive apnea refers to the temporary cessation of airflow during sleep for 10 seconds or more despite continuing ventilatory effort, whereas hypopnea means reduction of 30% to 50% in airflow for 10 secs or more.[3] Inspiratory excitation of upper airway muscles maintains patency when awake.[4] Excessive relaxation or loss of compensatory excitation of upper airway muscles explains the propensity to collapse during sleep.[5] Among school-aged children, 8% to 10% snore, and the incidence of obstructive sleep apnea syndrome is estimated to be 2% prevalence.[6-8] OSA the most widely known disorder in the category of middle aged adults and affects 2% to 4%.[3,9] OSA is more common among women than previously suspected [10] and not all patients with OSA are obese.[11]

The hallmark of OSA is airway obstruction during sleep due to increased upper airway resistance,[12,13] and the site of the obstruction may be at any of three general levels within the upper airway. Careful evaluation of potential obstruction at all three levels must be made to identify the individual patient's problem and accurately address it; nasopharynx, oropharynx, and hypopharynx.[1]

OSA syndrome is characterized by disruption of normal sleep architecture by complete or partial obstruction of respiratory airflow resulting in hypoxemia. The apnea leads to progressive asphyxia until there is a brief arousal from sleep, where upon airway patency is restored and airflow resumes. The patient then returns to sleep, and the sequence of events are repeated, often up to 400 to 500 times per night, resulting in marked fragmentation of sleep;[14] due to which the quality of sleep diminishes. This cycle results in excessive daytime somnolence, which is one of the hallmark features of this disease condition. Excessive daytime somnolence greatly diminishes the quality of life in affected individuals and impacts their state of health unfavorably. Affected individuals have greatly diminished productivity, impaired cognition, greater accident rates, and multiple medical-dental disorders that impact every aspect of their lives. Depression is also more prevalent in patients with OSA.

In adolescents, obesity and mandibular retrognathism figure as major risk factors. Altogether, this evidence indicates that

Dr Ashish Goel completed his graduation (BDS) from College of Dental Sciences, Manglore in year 2002 and postgraduation (MDS) in Orthodontics & Dentofacial Orthopedics from Saraswati Dental College & Hospital, Lucknow (UP), India in 2008. Currently he is working as Senior Lecturer in Saraswati Dental College & Hospital, Lucknow (UP), India.

[1]Department of Orthodontics & Dentofacial Orthopedics, [2]Oral & Maxillofacial Surgery, [3]Prosthodontics, Saraswati Dental College & Hospital, Lucknow (UP), India.

Address for Correspondence:
Dr Ashish Goel, Department of Orthodontics & Dentofacial Orthopedics, Saraswati Dental College & Hospital, 233, Tiwari Ganj Faizabad Road, Chinhat, Lucknow (UP), India. Contact: +919935098425, E-mail: dr.ashishgoel@gmail.com

Date of Submission : 04-08-2011
Reviews Completed : 20-12-2011
Date of Acceptance : 31-12-2011

the exact mechanism of OSA is not fully understood. Craniofacial abnormalities commonly occur in OSA patients and may predispose them to apnea through an adverse effect on upper airway dimensions. The relationship of the mandible to the cranial base was retrognathic in children and adolescents with a history of upper airway obstruction. Furthermore, skeletal Class II pattern with a reduction in mandible length, an increased overbite, and a hyoid bone in a more superior position was also reported in children with OSA. Nevertheless, maxillary constriction may also play a role in the pathophysiology of OSA and is often associated with other craniofacial abnormalities, such as sagittal mandibular deficiency.[4,15,16]

NORMAL SLEEP ARCHITECTURE

Normal sleep is a complex and critical physiological activity. It is characterized by discrete neurological patterns that represent different stages of sleep. To have restful sleep, each phase of sleep must be completed; otherwise sleep disruption will result.[17] Normal sleep architecture is characterized by two forms. These forms are referred to as non-rapid eye movement (NREM) and rapid eye movement (REM). These sleep states alternate throughout the sleep cycle. Each of the sleep states is associated with a specific electroencephalogram (EEG) pattern, altered skeletal muscle tone, altered psychological activity and respiratory pattern.

Sleep is initiated in stage one NREM and progressively moves through deeper stages 2, 3, and 4 before reaching REM sleep and NREM sleep cycles alternate approximately every 90 minutes. REM sleep is associated with vivid dreaming and diminished tone of the skeletal muscles of the airway and limbs.

As humans age, there are changes in sleep architecture and patterns. However, after puberty REM sleep occupies 20% to 25% of total sleep throughout life and continues alternating with NREM except in dementia.[18]

Most adults in the absence of disease conditions or other abnormal environmental intrusions sleep between 7.5 and 8.5 hours per sleep cycle. This amount is highly variable and defies easy attempts to quantify what is normal. There exist age-related changes in sleep architecture.[19] Nonetheless, the amount of REM sleep remains constant in the absence of pathology for all ages after puberty.[20-22] Arousal from sleep increases with age. These arousals can be the result of many factors, including respiratory disturbances.

Ingestion of drugs or alcohol has an effect on sleep architecture. Alcohol consumption before sleep increases the deep sleep period; NREM stages 3 and 4, but suppresses REM sleep early in the sleep cycle. Later as the alcohol is metabolized there can be REM sleep rebound. Sleep is a critical physiological activity that affects all aspects of an individual's existence. Sleep is associated with specific neurological events that can be quantified in the sleep laboratory with the polysomnogram. Incomplete or fragmented sleep can negatively impact the quality of life and result in systemic disease.[17]

BREATHING PATTERN DURING SLEEP

During NREM sleep, breathing frequency and respiratory flow rate are reduced and minute ventilation falls. In part this reflects the reduced physical activity during sleep, but because there is a small (about 3 mm Hg) rise in $PaCO_2$, there must also be a change in either the sensitivity or the set point of the carbon dioxide controller.[23] In the deepest stage of NREM sleep (stage IV breathing is slow, deep, and very regular. However, in stages I and II the depth of breathing sometimes varies periodically. The explanation is that in light sleep, removal of the wakefulness stimulus varies over time in a periodic fashion: when removed, sleep is deepened and breathing is depressed; when returned, breathing is excited not only by the wakefulness stimulus but also by the carbon dioxide retained during the interval of sleep. This periodic pattern of breathing is known as Cheyne-Stokes breathing.[24]

In REM sleep, breathing frequency varies erratically while tidal volume varies little. The net effect on alveolar ventilation is probably a slight reduction, but this is achieved by averaging intervals of frank tachypnea (excessively rapid breathing) with intervals of apnea. Unlike NREM sleep, the variations during REM sleep do not reflect a changing wakefulness stimulus but instead represent responses to increased central nervous system activity of behavioral, rather than autonomic or metabolic, central systems.

Both NREM and REM sleep cause an important change in responses to airway irritation. Specifically, a stimulus that causes cough, tachypnea and airway constriction during wakefulness will cause apnea and airway dilation during sleep unless the stimulus is sufficiently intense to cause arousal. The limited information available suggests that the lung stretch reflex is unchanged or somewhat enhanced during arousal from sleep, but the effect of stretch on upper airways during sleep may be important.[24]

Several stimuli cause arousal from sleep of less intensity, shift to a lighter sleep stage without frank arousal. In general, arousal from REM sleep is more difficult than from NREM sleep. In humans, hypercapnia is a more potent arousal stimulus than is hypoxia, the former requiring a $PaCO_2$ of about 55 mm Hg and the latter requiring $PaCO_2$ less than 40 mm Hg. Airway irritation and airway occlusion induce arousal readily in NREM sleep but much less readily during REM sleep. All of these arousal mechanisms probably are effective through activation of a reticular arousal mechanism similar to the wakefulness stimulus. They serve a very important role in protecting the sleeper from airway obstruction, alveolar hypoventilation of any cause, and entrance into the airways of irritating substances. Recall that cough depends on the aroused state and without arousal airway irritation leads to apnea. It should be obvious that wakefulness altered by other than natural

sleep, such as during drug-induced sleep, brain injury, or anesthesia, leaves the individual exposed to risk because arousal from those states is impaired or blocked. Indeed it has been said that from a teleological point of view the most important role of sensors of the respiratory system may be to cause arousal from sleep.[25]

There is a general reduction in skeletal muscle tone during sleep that is particularly prominent during REM sleep. Muscles of the larynx, pharynx and tongue share in this relaxation, with the result that the upper airway is variably obstructed. Furthermore, airway muscle relaxation may be enhanced somewhat by the increased effectiveness of the lung inflation reflex. A common consequence of this airway narrowing is snoring, but in many individuals, most often men, the degree of obstruction may at times be sufficient to cause essentially complete occlusion. In such individuals an intact arousal mechanism prevents disaster, and this sequence is not in itself unusual or abnormal. In some subjects, however, obstruction is more often complete and more frequent and the arousal threshold may be raised. Repeated obstruction leads to significant hypercapnia and hypoxemia, and repeated arousals cause sleep deprivation that lead to excessive daytime sleepiness, often interfering with daily activity.

RISK FACTORS AND CLINICAL FEATURES OF OSA

Body mass index (BMI) and neck circumference as indications of obesity have been shown in more than one study to have good predictive power for OSA.[25-30] The immediate factor leading to collapse of the upper airway in OSA is the generation of a critical sub-atmospheric pressure during inspiration that exceeds the ability of the airway dilator and abductor muscles to maintain airway stability. Sleep plays permissive but crucial role by reducing the activity of the muscles to sub-atmospheric airway pressures. Alcohol is frequently an important cofactor because of its selective depressant influence on the upper airway muscles and on the arousal response that terminates each apnea. In most patients the patency of the airway is also compromised structurally and therefore predisposed to occlusion. In a minority of patients the structural compromise is due to obvious anatomic disturbances, such as adenotonsillar hypertrophy, retrognathia, macroglossia.[31] However, in the majority of patients the structural defect is simply a subtle reduction in airway size that can often be appreciated clinically as "pharyngeal crowding" and that can usually be demonstrated by imaging and acoustic reflection techniques. Obesity frequently contributes to the reduction in size of upper airways, either by increasing fat deposition in the soft tissues of the pharynx or by compressing the pharynx by superficial fat masses in the neck. Snoring, a high frequency vibration of the palatal and pharyngeal soft tissues that results from the decrease in size of the upper airway lumen may aggravate the narrowing by producing edema of the soft tissues. More sophisticated studies demonstrate a high airway compliance i.e. the airway is "floppy" and therefore prone to collapse. In some patients, a high upstream (i.e. nasal) resistance predisposes to collapse of the upper airway by increasing the sub-atmospheric pressure generated in the pharynx during inspiration as the strength of diaphragmatic contraction is increased to overcome airflow resistance in the nose.[32-39]

The narrowing of the upper airways during sleep, which predisposes to OSA, inevitably results in snoring.[51] In general, men with a neck circumference of 17 inches or greater and women with a neck circumference of 16 inches or greater are at a risk for OSA. In most patients, snoring antedates the development of obstructive events by many years. However, the majority of snoring individuals do not have an OSA disorder. Although a few recent studies suggest that snoring per se may be associated with long-term health risks, definitive evidence in this regard is lacking. Hence, in the absence of other symptoms, snoring alone does not warrant an investigation for OSA but does call for preventive counseling, particularly with regard to weight gain and alcohol consumption.[39]

Initially, daytime sleepiness manifests under passive conditions, such as reading or watching television; but as the disorder progresses, sleepiness encroaches into all daily activities and can become disabling and dangerous. Several studies have demonstrated two to three times more motor vehicle accidents in patients with OSA compared with other drivers.[40] Other related symptoms include intellectual impairment, memory loss, and personality disturbances. In men with OSA, impotence is a relatively frequent complaint.

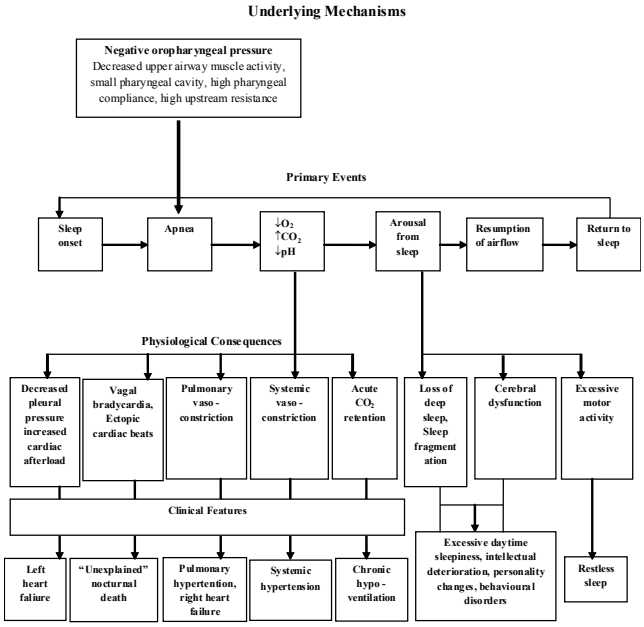
The other major manifestations of OSA are cardio-respiratory in nature and are thought to arise from the recurrent episodes of nocturnal asphyxia.[41] Many patients demonstrate a cyclical slowing of the heart during the apneas to 30 to 50 beats per minute, followed by a tachycardia of 90 to 120 beats per minute during the ventilatory phase. A small number of patients develop severe bradycardia with asystoles of 8 to l2 second duration or dangerous tachyarrhythmias, including unsustained ventricular tachycardia. Unlike in healthy subjects, in patients with OSA systemic blood pressure fails to decrease, during sleep. In fact, blood pressure typically rises abruptly at the termination of each obstructive event.

OSA AS A SYSTEMIC RISK FACTOR

Several epidemiologic studies have implicated OSA as a risk factor for the development of systemic hypertension, myocardial ischemia and infarction, stroke, and premature death. However, because these studies were cross-sectional or retrospective in design, the natural history of OSA remains largely undefined. OSA also markedly aggravates left ventricular failure in patients with underlying heart disease. This complication is probably due to the combined effects of increased left ventricular afterload during each obstructive event, secondary to increased negative intrathoracic pressure, recurrent nocturnal hypoxemia, and chronically elevated sympathoadrenal activity. Treatment of OSA in such

patients often results in dramatic improvement in left ventricular function. Finally, a small proportion of patients with OSA (<10 percent) develop pulmonary hypertension, right ventricular failure, polycythemia, and chronic hypercapnia and hypoxemia. All such patients have evidence of sustained daytime hypoxemia in addition to the nocturnal ventilatory disturbance, usually as a result of reduced ventilatory drive and/or diffuse airways obstruction. Most of these patients are obese and sleepy and are therefore said to have the Pickwickian syndrome[39] (Table 1).

Table 1: The primary sequence of events, underlying mechanisms, physiologic responses, and clinical features of obstructive sleep apnea



LABORATORY INVESTIGATION

Polysomnogram (PSG) is considered the gold standard for the diagnosis of sleep apnea and other sleep disorders.[3] It involves an overnight sleep in the laboratory with multichannel monitoring of multiple physiologic variables with the presence of a technician throughout the study. During the study, sleep stages and sleep continuity, respiratory effort, airflow, oxygen saturation, body position, electrocardiogram, and movements are recorded. In the analysis of the study, the number of apneas per hour is expressed as AI, which determines the severity of the OSA.

MANAGEMENT PROTOCOL FOR OSA

Dentists have recently become one of the team players in the field of sleep medicine. Oral appliances for the treatment of snoring and OSA fall into two main categories – those that hold the tongue forward and those that reposition the mandible (and the attached tongue) forward during sleep. Having concluded that treatment with an oral appliance is indicated, the physician provides the dentist who has the skill and the experience in oral appliance therapy with a written referral or prescription and a copy of the diagnostic report.[42]

Oral appliances have been considered as treatment option for upper airway obstruction caused by mandibular deficiency since the early part of this century. In the 1980's dentists and orthodontics teamed up with pulmonologists to explore the use of oral appliances to treat patients with OSA. Conservative therapies include weight loss, changes in sleep posture, placement of intraoral devices, nasal continuous positive airway pressure (CPAP), and drug therapy. Surgical methods include tracheostomy, uvulopalatopharyngoplasty (UPPP), nasal septoplasty and surgical mandibular advancement.[43-51]

CONCLUSION

OSA syndrome is characterized by disruption of normal sleep architecture by complete or partial obstruction of respiratory airflow resulting in hypoxemia. The apnea leads to progressive asphyxia until there is a brief arousal from sleep, where upon airway patency is restored and airflow resumes. Corrective management protocol of such patients require a team approach, in which dentist has a significant role to play.

REFERENCES

1. Haponik EF, Smith PL, Bohlman ME, Allen RP, Goldman SM, Blecker ER. Computerized tomography in obstructive sleep apnea. Correlation of airway size with physiology during sleep and wakefulness. Am Rev Respir Dis 1983; 127: 221-6.
2. Kryger M, Roth T, Dement W. Principles and Practice of Sleep Medicine. 4th ed, 2005.
3. Bahammam A, Kryger M. Decision making in obstructive sleep-disordered breathing. Putting it all together. Clin Chest Med 1988; 19: 87-97.
4. Deatherage JR, Roden RD, Zouhary K. Normal sleep architecture. Semin Orthod 2009; 15: 86-7.
5. Strobel RJ, Rosen RC. Obesity and weight loss in obstructive sleep apnea: A critical review. Sleep 1996; 19: 104-15.
6. Schütz TC, Dominguez GC, Hallinan MP, Cunha TC, Tufik S. Class II correction improves breathing. Angle Orthod 2011; 81: 222–8.
7. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993; 328: 1230-5.
8. Young T, Skatrud J, Peppard PE. Risk factors for obstructive sleep apnea in adults. JAMA 2004: 291; 2013-16.
9. Young T, Peppard PE, Gottlieb DJ. Epidemiology of obstructive sleep apnea: a population health perspective. Am J Respir Crit Care Med 2002; 165: 1217-39.
10. Scharf SM, Garshick E, Brown R, Tishler PV, Tosteson T, McCarley R. Screening for subclinical sleep-disordered breathing. Sleep 1990; 13: 344-53.
11. Ancoli-Israel A. Epidemiology of sleep disorders. Clin Geriatr Med 1989; 5: 347-62.
12. Remmers JE, deGroot WJ, Sauerland EK, Anch AM. Pathogenesis of upper airway occlusion during sleep. J Appl Physiol 1978; 44: 931-8.

13. Brown IG, Bradley TD, Phillipson EA, Zamel N, Hoffstein V. Pharyngeal compliance in snoring subjects with and without obstructive sleep apnea. Am Rev Respir Dis 1985; 132: 211-5.
14. Redline S, Kump K, Tishler PV. Gender differences in sleep disordered breathing in a community based sample. Am J Respir Crit Care Med 1994; 149: 149-54.
15. Tourne LP. The long face syndrome and impairment of the nasopharyngeal airway. Angle Orthod 1990; 60: 167-76.
16. Solow B, Ovesen J, Nielsen PW, Wildschiødtz G, Tallgren A. Head posture in Obstructive sleep apnea. Eur J Orthod 1993; 15: 107-14.
17. Bonora M, Shields GI, Knuth SL, Bartlett D Jr, St John WM. Selective depression by ethanol of upper airway motor activity in cats. Am Rev Resp Dis 1984; 130: 156-61.
18. Linder-Aronson S. Adenoid obstruction of the nasopharynx. Nasorespiratory function and craniofacial growth. Monograph 9, Craniofacial series. Ann Arbor, MI, University of Michigan, 1979, 121-47.
19. Guilleminault C, Pelayo R, Leger D, Clerk A, Bocian RC. Recognition of sleep disordered breathing in children. Pediatrics 1996; 98: 871-82.
20. Chan J, Edman JC, Koltai PJ. Obstructive sleep apnea in children. Am Fam Phys 2004; 69: 1147- 54.
21. Marcus CL. Sleep-disordered breathing in children. Am J Respir Crit Care Med 2001; 164: 16-30.
22. Isono S, Shimada A, Utsugi M, Konno A, Nishino T. Comparison of static mechanical properties of the passive pharynx between normal children and children with sleep-disordered breathing. Am J Respir Crit Care Med 1998; 157: 1204-12.
23. Schweitzer PK, Chambers GW, Birkermeier N. Nasal continuous positive airway pressure (CPAP) compliance at six, twelve and eighteen months. J Sleep Res 1987: 16; 186.
24. Guilleminault C, Stoohs R, Kim YD, Chervin R, Black J, Clerk A. Upper airway sleep-disordered breathing in women. Ann Intern Med 1995; 122: 493-501.
25. Kump K, Whalen C, Tishler PV, Browner I, Ferrette V, Strohl KP, *et al*. Assessment of the utility and validity of a sleep symptom questionnaire in a community sample. Am J Respir Crit Care Med 1994; 150: 735-41.
26. Olson LG, King MT, Hensley MJ, Saunders NA. A community study of snoring and sleep-disordered breathing. Am J Respir Crit Care Med 1995; 152: 711-6.
27. Stradling JR, Crosby JH. Predictors and prevalence of obstructive sleep apnea and snoring in 1001 middle aged men. Thorax 1991; 46: 85-90.
28. National Heart, Lung and Blood Institute Working Group on Sleep Apnea. National Institute of Health, Bethesda, Maryland. Sleep apnea: Is your patient at risk? Am Fam Physician 1996; 53: 247-53.
29. Pouliot Z, Peters M, Neufeld H, Kryger MH. Using self-reported questionnaire data to prioritize OSA patients for polysomnography. Sleep 1997; 20: 232-6.
30. Heimer D, Scharf SM, Lieberman A, Lavie P. Sleep apnea syndrome treated by repair of deviated nasal septum. Chest 1983; 84: 184-5.
31. Robin P. Glossoptosis due to atresia and hypertrophy of the mandible. Am J Dis Child 1934; 48: 541-47.
32. Faber CE, Grymer L. Available techniques for objective assessment of upper airway narrowing in snoring and sleep apnea. Sleep Breath 2003: 7; 77-86.
33. Strollo PJ Jr, Rogers RM. Obstructive sleep apnea. N Engl J Med 1996; 334: 99-104.
34. Schwab RJ, Goldberg AN. Upper airway assessment: Radiographic and other imaging techniques. Otolaryngol Clin North Am 1998; 31: 931-68.
35. Shepard JW Jr, Gefter WB, Guilleminault C, Hoffman EA, Hoffstein V, Hudgel DW, *et al*. Evaluation of the upper airway in patients with obstructive sleep apnea. Sleep 1991; 14; 361-71.
36. Adams GL, Gansky SA, Miller AJ, Harrell WE Jr, Hatcher DC. Comparison between traditional 2-dimensional cephalometry and a three dimensional approach on human dry skulls. Am J Orthod Dentofac Orthop 2004; 126: 397-409.
37. Joseph AA, Elbaum J, Cisneros GJ, Eisig SB. A cephalometric comparative study of the soft tissue airway comparative dimensions in persons with hyperdivergent and normodivergent facial patterns. J Oral Maxillofac Surg 1998; 56: 135-9.
38. Lowe AA, Gionhaku N, Takeuchi K, Fleetham JA. Three-dimensional CT reconstructions of tongue and airway in adult subjects with obstructive sleep apnea. Am J Orthod Dentofac Orthop 1986; 90: 364-74.
39. Carlson JT, Hedner JA, Ejnell H, Peterson LE. High prevalence of hypertension in sleep apnea patients independent of obesity. Am J Respir Crit Care Med 1994; 150: 72-7.
40. Shintani T, Asakura K, Kataura A. The effect of adeno-tonsillectomy in children with OSA. Int J Pediatr Oto Rhinolaryngol 1998; 44: 51-8.
41. Fauci AS, Braunwald E, Kasper DL, Hauser SL, Longo DL, Jameson JL, *et al*. Harrison's Principles of Internal Medicine. 16th ed, Mc Graw-Hill, 1811 -2.
42. Krieger J, McNicholas WT, Levy P, De Backer W, Douglas N, Marrone O, *et al*. Public health and medicolegal implications of sleep apnea. Eur Respir J 2002; 20: 1594-609.
43. Riley RW, Powell NB. Maxillofacial surgery and obstructive sleep apnea syndrome. Otolaryngol Clin North Am 1990: 23; 809-26.
44. Turnbull NR, Battagel JM. The effects of orthognathic surgery on the pharyngeal airway dimensions and quality of sleep. J Orthod 2000: 27; 235-47.
45. Waite PD. Obstructive sleep apnea. A review of the pathophysiology and surgical management. Oral Surg Oral Med Oral Pathol Oral Radiol Endod 1998: 85; 352-61.
46. Louis PJ, Austin RB, Waite PD, Mathews CS. Soft tissue changes of the upper lip associated with the maxillary advancement in obstructive sleep apnea patients. J Oral Maxillofac Surg 2001: 59; 151-6.
47. Waite PD, Wooten V. Maxillomandibular advancement surgery for obstructive sleep apnea. J Oral Maxillofac Surg 1990: 48; 770-1.
48. Li KK, Powell NB, Riley RW, Troell R, Guilleminault C. Overview of phase I surgery for obstructive sleep apnea syndrome. Ear Nose Throat J 1999: 78: 836-7.
49. Li KK, Powell NB, Riley RW, Guilleminault C. Distraction osteogenesis in adult obstructive sleep apnea surgery: A preliminary report. J Oral Maxillofac Surg 2002: 60; 6-10.
50. Li KK, Powell NB, Riley RW, Troell RJ, Guilleminault C. Long term results of maxillomandibular advancement surgery. Sleep Breath 2000: 4: 137-40.
51. Nooreyazdan M, Trotman CA, Faraway JJ. Modeling facial movement II. A dynamic analysis of differences caused by orthognathic surgery. J Oral Maxillofac Surg 2004: 62; 1380-6.