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MEDICAL JOURNAL

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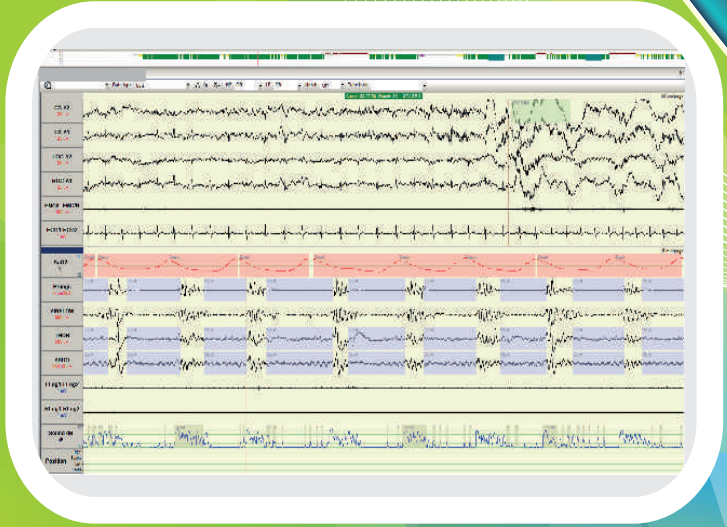

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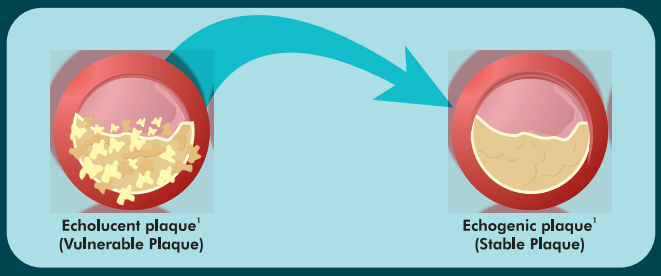

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Dialogue with the Stalwart

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Editorial

Vanakkam. This issue of the journal, besides the usual sections, carries a special section on "Obstructive sleep apnoea". "An interview with a stalwart "highlights the meeting with Prof. V. Shantha, gynaecologist and oncologist, Magsaysay awardee and a doyen among cancer specialists in India.

In assisted reproduction, at what size to trigger ovulation is often a debatable issue. An original article on "Follicular size and oocyte's maturity" outlines the author's observations in an Assisted Reproduction programme.

Obstructive sleep apnoea is a multi systemic disorder with impact on several bodily functions.

Several review articles bring out the patho physiology and management of obstructive sleep apnoea. This section was coordinated and edited by Prof. Mathangi Chandrasekhar.

Sleep is probably the most important voluntary body function which has an impact on almost every other system in the body. Lack of quality sleep is a universal phenomenon. Almost everyone is affected at some time or other. However, chronic lack of sleep is common among many of the upwardly mobile group of technocrats, bureaucrats, businessmen, professionals, politicians and their like. Many of these professionals have excessive day time sleepiness, lack of freshness, morning headaches, which affect their performance at the work place as well as personal life. All these put together with apnoea spells during sleep results in a disorder called obstructive sleep apnoea (OSA). Our current day erratic lifestyle, highly stressed work environment, sedentary life style leading to obesity, further compounds the occurrence of obstructive sleep apnoea. In addition, the craniofacial anatomy with narrow airway among Asians further increases the prevalence of sleep apnoea among Indians.

Though we have significant publication in this area from the west, there is dearth of information from our country. There is a lack of awareness of these disorders among physicians as well as public. Hence this issue concentrates on the various aspects of sleep apnoea.

The 1st article reviews the international guidelines and status on the diagnosis, pathophysiology and treatment of OSA as well as several of the co morbidities commonly associated with the disorder.

The 2nd article deals with the treatment aspects from an ENT perspective and the 3rd Dental perspective. The 4th article addresses this disorder in detail from an anaesthetic perspective. Untreated OSA can lead to high blood pressure, uncontrolled diabetes, heart attack, strokes, even heart failure. The cardiovascular morbidity and OSA is explained in the 5th article.

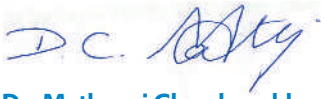
OSA gets compounded with other respiratory ailments and most interesting of it is the COPD, called the overlap syndrome described in the 6th article.

Adults with sleep apnoea have increased day time sleepiness; however children with sleep apnoea are hyperactive. OSA also affects cognition. Hence identification and treatment of this condition should start early. The 7th article details sleep apnoea from a peadiatricians perspective.

Sleep apnoea has also been identified in the west as one of the main causes for vehicular accidents and increased economic burden. We hope this issue of CHC Medical Journal, updates and enhances your knowledge on sleep apnoea.

Two case reports from the Dental College discuss the problem of Diastema and Dental Implants.

Vaccination has been one of the greatest advances in modern medicine which has helped save millions of lives. An article from the pages of history outlines the discovery of small pox vaccine. The usual column Medical Update suggests taking curry to avoid metastasis and has many more useful information from all over the world. Hope you enjoy going through the journal and give us your valuable feedback.



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Original Article

Size Of Follicle and Oocyte Maturation Status in an Assisted Reproductive Technology Programme

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Dr. Gayathiri Ganesan did her undergraduation and postgraduation (M.S (OBGY)) in Sri Ramachandra Medical College. Further she did fellowship in Andrology and Reproductive Medicine from Chettinad Hospital and Research Institute. She is currently a Junior Consultant in Department of Reproductive Medicine in Chettinad Super Speciality hospital.

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Abstract

Background : To asses the correlation between follicular size and oocyte maturation status in assisted reproductive technology programs.

Method : It was a prospective study done from September 2011 to May 2012 in the Department of Reproductive Medicine at a tertiary care hospital. Sixty patients undergoing assisted reproductive cycles either with agonist or antagonist protocol were included in this study. Follicles were subdivided into four arbitary groups according to their mean two dimension size, >21 mm, 16-20 mm, 12-15 mm and <12 mm. Microscopic examination of the follicular aspirates were performed by the embryologist.

Findings : If follicle size > 21 mm , there was 85% chance of retrieving an MII oocyte; when the size was between 16 – 20 mm,the chance of retrieval was 87%. In 12 – 16 mm group, it was 80% and in the follicles <12mm it was 55%. The level of significance was calculated between each group (with respect to MII oocytes). Between the first three groups, p value was not significant. When the larger sized follicles were compared with < 12 mm group, p = 0.000, which was statistically significant (p< 0.05).

Conclusion : It is better to trigger with HCG when the lead follicle is between 16 – 20 mm rather than waiting till > 21 mm, as this saves time and money for the patient. Small follicles of size < 12 mm also yielded MII oocytes, hence it is worthwhile aspirating small follicles also.

Funding : Nil

Key Words : Follicular size, Oocyte quality, Oocyte maturity, Controlled ovarian hyperstimulation

Chettinad Health City Medical Journal 2012; 1(3): 83 - 87

Introduction

Follicle size is associated with oocyte development in most species and this may indicate that a specific size is necessary to initiate the molecular cascade of normal nuclear and cytoplasmic maturation.[1,2]

The development and maturation of a follicle undergo a series of events in the natural menstrual cycle.

- Recruitment of group of follicles – The initial recruitment and growth of primodial follicles are not under the control of any hormone. After certain stage (2 – 5 mm in size) the growth and differentiation are under the control of FSH. Unless the follicles are rescued by FSH at this stage, they undergo atresia.

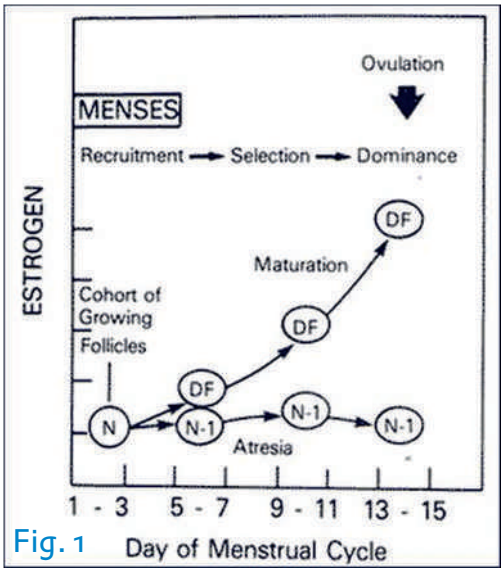

Fig. 1

- Selection of Dominant follicle and maturation – There is accelerated growth of all the components of the follicles. As early as day 5-7, one of the follicle out of so many in the cohort becomes dominant and undergoes further maturation. The one with maximum receptors for FSH, becomes the dominant follicle (Graafian follicle). The rest become atretic by day 8.

- Ovulation – The cumulus becomes detached from the wall so that the ovum with the surrounding cells float freely in the liquor folliculi. The oocyte completes first meiotic division with extrusion of the first polar body which is pushed to the perivitelline space. The follicular wall near the ovarian surface becomes thinner. The cumulus escapes out of the follicle by a slow oozing process along with varying amount of follicular fluid.

- Corpus Luteum formation – After ovulation, the ruptured Graafian follicle develops into corpus luteum. The colour is yellow due to the presence of lipids.

- Regression – On day 22-23 of cycle, retrogression occurs. The corpus luteum becomes corpus albicans.

Controlled ovarian hyperstimulation is not critical to assisted reproduction though soft and mild stimulation regimes have been advocated to closely mimic physiological events. Still many prefer the controlled ovarian hyperstimulation to augment the number of oocytes retrieved and embryos generated. Of these, only a small portion will be competent for fertilization and development into viable embryos. Understanding the process of selection, follicular growth and ovulation has guided the development of this important component of treatment. The medications, designed to override the selection of a single dominant follicle, drive multiple antral follicles into the growth phase. These follicles grow at different rates, and management is guided by their size rather than their competence. The administration of Human Chorionic Gonodotrophin, in mimicking the endogenous luteinizing hormone [LH] surge, is the final event that determines the follicular maturity and developmental competence. The timing of its administration is typically guided by the size of the lead follicle or lead follicular cohort [3].

The treatment is therefore based on an assumption that follicular size predicts the maturity of the oocyte. The assumption is based on limited studies using different models in animals. Yet the available data is conflicting, and although several human studies have suggested oocytes derived from larger follicles outperform [in terms of fertilization and embryo quality] oocytes originating from smaller follicles, the correlation of oocyte competence with follicular size, after controlled ovarian stimulation, has not been well characterized. For instance, while some have suggested the decreasing fertilization rate and embryo quality observed with oocytes originating from smaller follicles can be overcome with intracytoplasmic sperm injection [ICSI][4]. Others have suggested normal fertilization of an oocyte is independent of its follicular size origin[5] .

It should be noted that embryo competence is most likely due to the quality of the originating gametes . Therefore, the morphological appearance of the oocyte is likely to contribute to the development potential of the subsequent embryo.

Classification of oocyte maturity[6]

Normal oocyte

1. Metaphase II

A mature or a good metaphase II oocyte is defined as an oocyte with clear, moderately granular cytoplasm, small perivitelline space and clear to colourless zona pellicuda[7] . First polar body is round or ovoid with smooth surface[8,9,10]. Cumulous cells are fully radiating and easily stretchable.

2 .GV (Germinal Vesicle):

It is an immature oocyte where the cumulous cells are tightly packed. The nucleus is large. It is preincubated before insemination.

3.Metaphase – I

It is an immature oocyte which has tightly packed cumulus cells. There is no nucleus or polar body.

4.Very mature :

This oocyte is pale.It has little corona cell.

5.Luteinized:

This oocyte is very pale and difficult to find. Cumulus cell is broken down and becomes a gelatinous mass. There is low probability of fertilization. It is inseminated with little delay.

6.Atretic:

It is very dark oocyte with fragmented cumulus cells. It has a lace like appearance and is difficult to identify.

Materials and Methods

The present study is a prospective study conducted in the Department of Reproductive Medicine at a tertiary care hospital from September 2011 to May 2012. 60 patients undergoing assisted reproductive cycles either with agonist or antagonist protocol were included in this study. Individuals were serially monitored with transvaginal ultrasound from day 5 onwards of stimulation and all follicles were measured in two dimensions. The decision to administer HCG was based on the lead follicular cohort, usually with atleast 3 follicles measuring 20mm in diameter and also an endometrial thickness of 8 mm onwards. Follicular size measurements were made serially and on the day of HCG trigger. A transvaginal ultrasound guided follicular aspiration was conducted 35 hours after hCG administration.

Normal Oocytes

Metaphase II

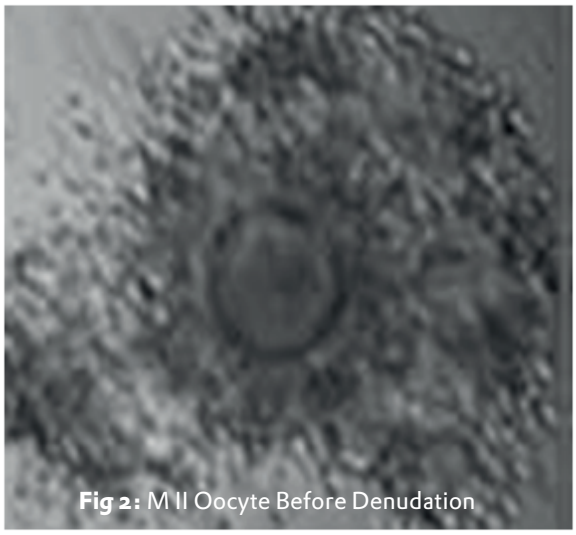

Fig 2: M II Oocyte Before Denudation

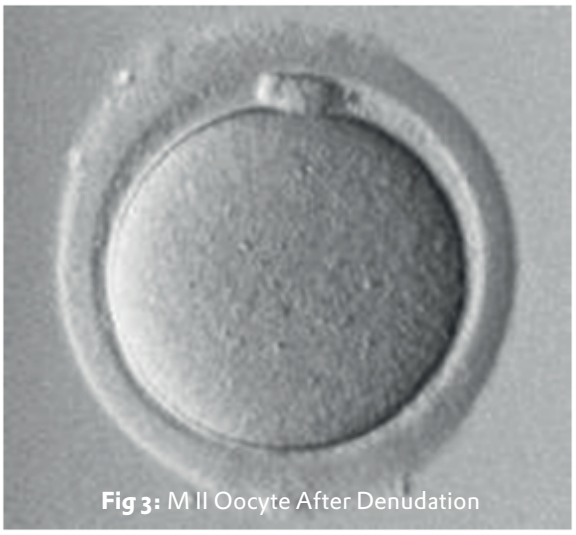

Fig 3: M II Oocyte After Denudation

Germinal vesicle

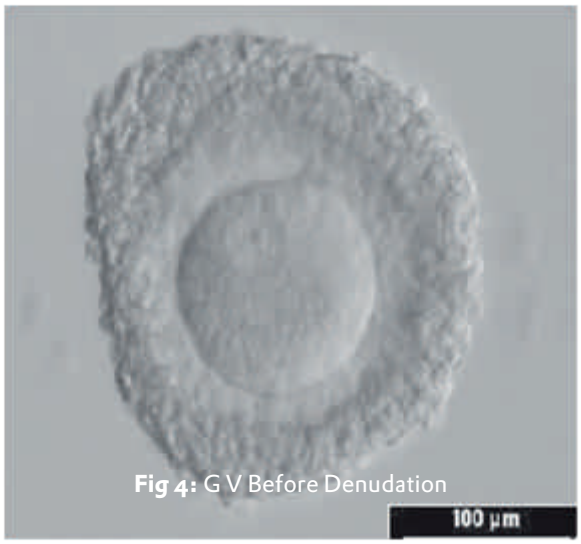

Fig 4: G V Before Denudation

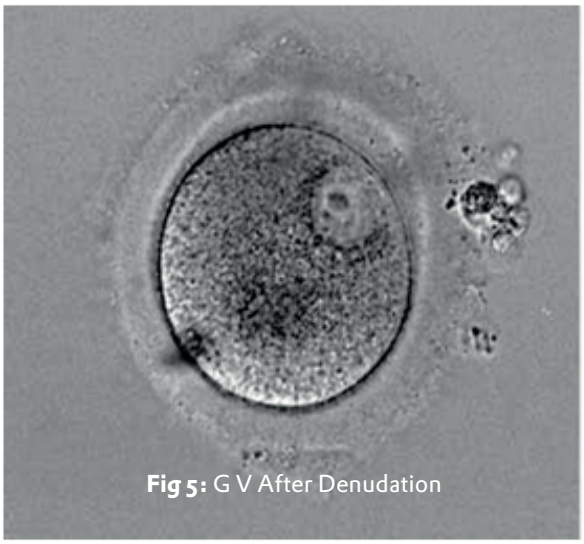

Fig 5: G V After Denudation

METAPHASE I

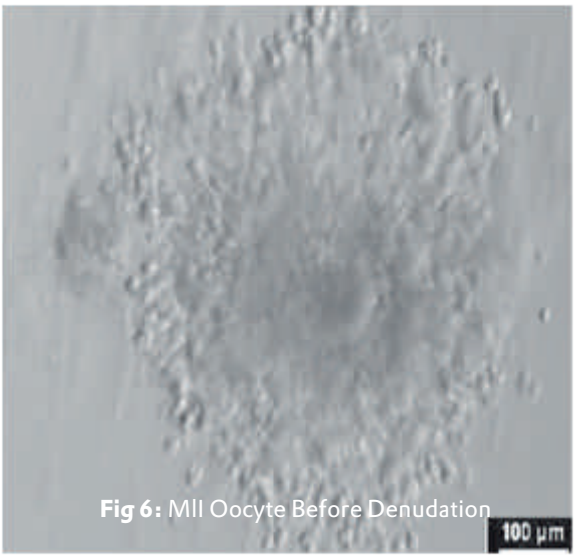

Fig 6: MII Oocyte Before Denudation

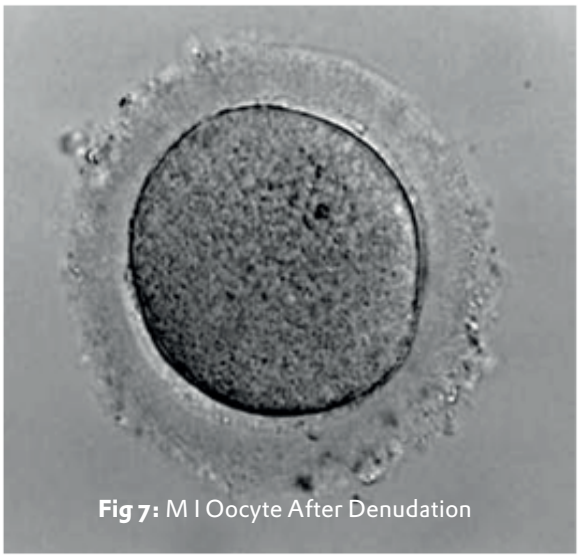

Fig 7: M I Oocyte After Denudation

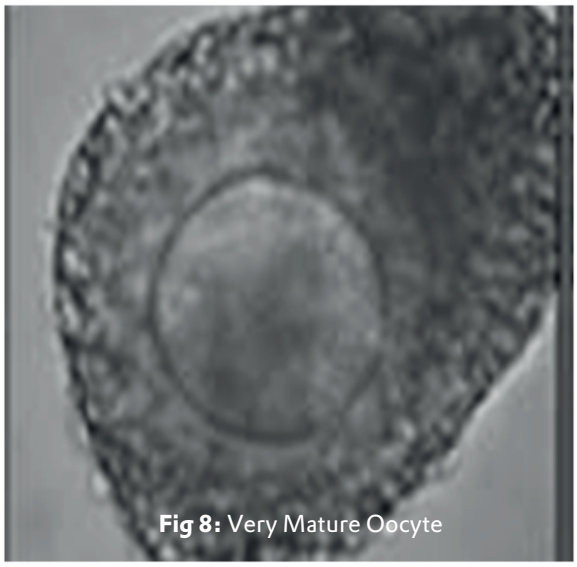

Fig 8: Very Mature Oocyte

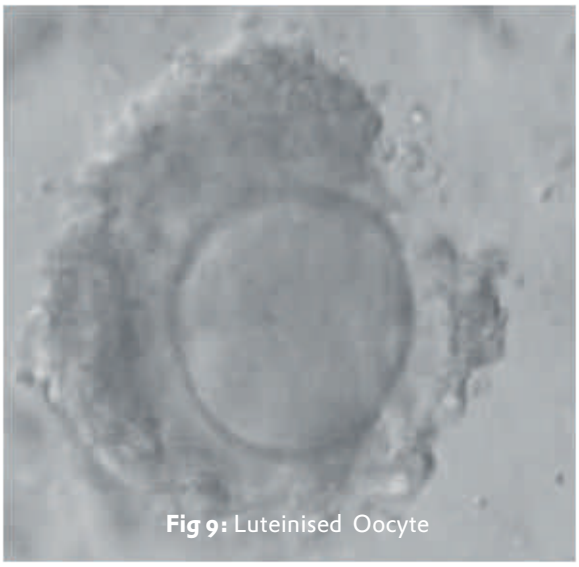

Fig 9: Luteinised Oocyte

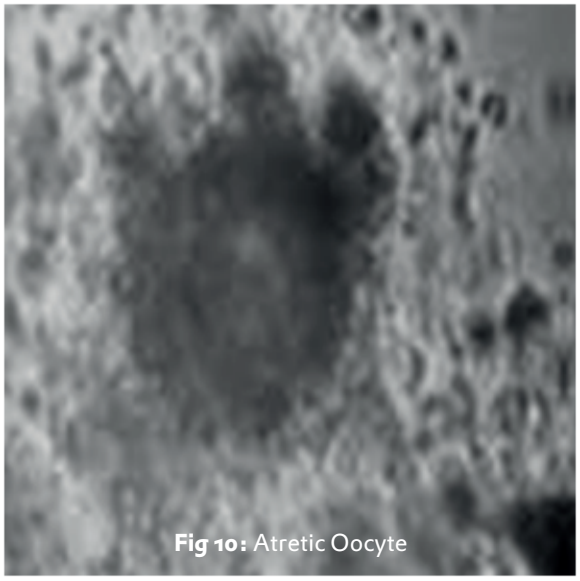

Fig 10: Atretic Oocyte

Follicles were subdivided into four groups according to their mean two dimension size, >21 mm, 16-20 mm, 12-15 mm and <12 mm. All follicles were aspirated under

transvaginal ultrasound guidance with a double lumen 17G oocyte pickup needle (Swemed) at 100 mmHg pressure. Flushing of aspirated follicles was performed with flushing medium phospate buffered saline (PBS-SAGE) once or twice if oocyte was not obtained in the initial aspirate. Volume of the aspirate was found to be >3 ml in larger follicles, around 2 ml in the intermediate follicles and < 1 ml in small follicles

Microscopic examination of the follicular aspirates were performed by the same embryologist. Once the oocytes were identified, they were collected and kept in the four well dishes with G-IVF media. Aspirates were screened individually and the maturity of oocytes were noted from each size of the follicle. Further study of the development of individual oocyte was not possible due to group culture.

Table 1 shows the association between the size of the follicles and maturity of the oocytes obtained in the

Results

Table 1 Oocyte Maturity and Size

SIZE(mm)	OOCYTE MATURITY				TOTAL (N=489)
	MII	M1	GV	ABNORMAL	
>21	110(85%)	5(3.8%)	9(6.9%)	6(4.3%)	130
16-20	179(87%)	8(3.9%)	6(2.9%)	13(6.2%)	206
12-15	71(80%)	10(11.2%)	6(6.7%)	2(2.1%)	89
<12	35(55%)	13(20%)	11(17.2%)	5(7.8%)	64

study. In follicle size > 21 mm , there was an 85% chance of retrieving MII oocyte. When the size was between 16 – 20 mm,the chance of retrieval was 87%. In 12 – 16 mm group, it was 80% and in the follicles < 12 mm it was 55%. The level of significance was calculated between each group (with respect to MII oocytes). Between the first 3 groups, p value was not significant. When the larger size follicles were compared with < 12 mm group, p = 0.000, which was statistically significant ($p < 0.05$).

Discussion

In the study by Mitchell et al3, they grouped the size of follicles into arbitrary five groups, > 18 mm, 16-18 mm,13-15 mm,10-12 mm and < 10 mm. The percentage of MII oocytes from each group were 90%, 79%, 73% ,53% and 47.6% respectively. The effect was a monotonic decrease in the odds of obtaining a mature oocyte with decrease in the follicle size group.

In a study done by Ectors et al[11] , they grouped the aspirated follicular fluid volume into three groups, < 2ml as small (size < 16 mm), 2-6 ml as medium (16 – 23 mm) and >6 ml as large (>23 mm). Higher percentage of oocytes were collected from the medium size follicles. 50.8% were MII oocytes, which were collected from medium sized follicles as compared to 24.7% and 24.5% from small and large follicles respectively.

They further concluded that good embryos were found in medium sized group. In the present study, a good yield of follicles were achieved from large follicles but small follicles also yielded mature oocytes.

In the present study. the chance of retrieving a MII oocyte from follicle size > 21 mm was 85%. When the size was between 16 – 20 mm,the chance of retrieval was 87%. In 12 – 16 mm group, it was 80% and in the follicle < 12mm it was 55%. The level of significance was calculated between each group (with respect to MII oocytes). Between the first 3 groups, p value was not significant. When the larger size follicles were compared with < 12 mm group, p = 0.000, which was statistically significant (p< 0.05).

In view of the above findings, it is impossible to lay down a treatment scheme. We conclude that it is advisable to aspirate all ultrasonically visible follicles (regardless of size) at the time of oocyte retrieval in order to achieve the maximum benefit from each cycle. Since each patient in every cycle responds differently to ovarian stimulation, it is impossible to lay down a uniform treatment scheme applicable to everyone. It is necessary to arrange the ovarian stimulation as individually as possible, according to patient's age, cause and the way they respond to stimulation protocol, aiming at a continuous multifollicular oocyte development. The degree of this maturation is indicated by follicular growth and development and is assessed most readily by transvaginal ultrasonography. Traditionally, oocyte retrieval is based on ultrasonographic measurement of the leading follicle, but if smaller follicles have oocytes of equal developmental potential, HCG could be administered earlier at a follicular size of about 16-18 mm to save time and expense for the patient.

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Review Article

Obstructive Sleep Apnoea: Prevalence, Consequences, Pathophysiology & Treatment

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Abstract

Obstructive sleep apnoea (OSA) is a common disorder characterized by repetitive narrowing or collapse of the pharyngeal airway during sleep. The disorder is associated with major comorbidities including excessive daytime sleepiness and increased risk of cardiovascular disease. The underlying pathophysiology is multifactorial and may vary considerably between individuals. The primary objective of this article is to review the diagnosis, pathophysiology and treatment of OSA as well as several of the comorbidities commonly associated with the disorder.

Key words: Obstructive sleep apnoea, Polysomnography, Continuous positive airway pressure, Sleep

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Introduction and Definition

Obstructive sleep apnoea (OSA) is characterized by repeated narrowing or collapse of the upper airway during sleep. Episodes of complete airway collapse or airway narrowing are often associated with oxygen desaturation and terminated by an arousal from sleep.[1] Individuals with OSA frequently have excessive daytime sleepiness (somnolence) due to sleep fragmentation from these repetitive arousals.

OSA is diagnosed using polysomnography (Figure 1), which provides objective measures of the stages of sleep as well as breathing pattern. Polysomnography incorporates measurements of electroencephalogram (brain activity), left and right electrooculograms (eye movement), submental electromyogram (chin muscle activity), tibial electromyogram (leg muscle activity), electrocardiogram (heart activity), abdominal and thoracic movement (respiratory effort), nasal and oral airflow, nasal pressure, oxygen saturation, body position and sound intensity. The time spent in each sleep stage can be defined, as well as the pattern of progression between stages to provide information on sleep architecture. The arousal index (number of arousals per hour of sleep) is used to quantify the degree of sleep fragmentation. Oximetry, nasal airflow (nasal pressure), oral airflow and abdominal and thoracic movement are used to identify disordered breathing events. Periods of apnoea (complete airway collapse) and hypopnoea (airway narrowing) are determined based on an abolition (in the case of an apnoea) or reduction (in the case of a hypopnoea) in airflow (Figure 1). The most current definitions describe an apnoea as ≥90% decrease in airflow lasting for more than 10s; a hypopnoea as a reduction in airflow of ≥30% or a reduction in airflow but accompanied by a ≥4% oxygen desaturation, also lasting more than 10s.[2] The severity of OSA is determined by the Apnoea-hypopnoea Index (AHI), which is defined as the number of apnoeas or hypopnoeas per hour of sleep. OSA is defined as 'mild' if the AHI is between 5 and 15; 'moderate' if the AHI is between 15 and 30; and 'severe' if the AHI is >30 events per hour. A clinical diagnosis of OSA syndrome (OSAS) is made if an individual has an AHI > 5 and they report excessive daytime somnolence

Prevalence of OSA

In a national sleep poll (questionnaire-based) in the United States of America [3], undertaken in 2005, 6% of individuals reported having apnoeas overnight, which had been witnessed by others with 26% of the overall population meeting the criteria for being a high risk of having OSA. Duran et al. [4], in a study investigating the prevalence of OSA in the general population, also found that 6% of individuals reported having witnessed apnoeas during sleep. In addition, approximately 30% of individuals report habitual snoring [4,5], a hallmark of OSA.

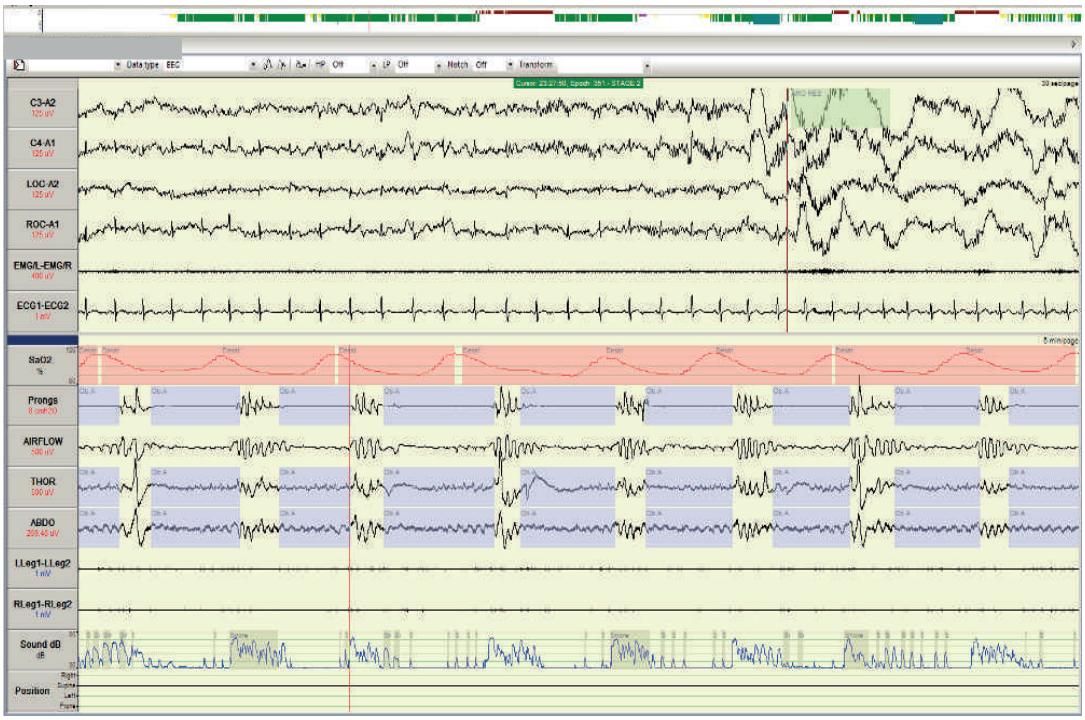

Figure 1. A section of recording taken during a polysomnographic study on an OSA patient. The top panel depicts 30s of monitoring (a 30 second epoch), the bottom panel, 5 minutes (a 5 minute epoch). The vertical red lines indicate coinciding timepoints between the two panes.

A summary of the whole night (sleep hypnogram) is shown at the top of the image (marked with an arrow): yellow periods = stage N1, green = stage N2; blue = stage N3; red = rapid eye movement (REM) sleep. The red line in the hypnogram also indicates the coinciding timepoints in the two panes below. The hypnogram shows a preponderance of stage N2 sleep ("light" sleep) and frequent awakenings throughout the night. This is characteristic of patients with OSA.

The recording channels depicted from top to bottom are as follows: C3-A2 = left central electroencephalogram (C3, brain activity) referenced to the right mastoid reference (A2); C4-A1 = right central electroencephalogram (C4, brain activity) referenced to the left mastoid reference (A1); ROC-A1 = right electrooculugram (ROC, eye movement) referenced to the left mastoid reference (A1); LOC-A2 = left electrooculugram (LOC, eye movement) referenced to the right mastoid reference (A2); L-EMG /R-EMG = left and right submental electromyogram (EMG, chin muscle activity); L-ECG/R-ECG = left and right electrocardiogram (ECG, heart activity); SaO2 = oxygen saturation measured with pulse oximetry; Prongs = nasal pressure signal; Airflow = nasal and oral airflow measured with a thermistor; Thorax = respiratory effort (thoracic chest wall motion); Abdo = respiratory effort (abdominal motion); LEG-L = left leg electromyogram; LEG-R = right leg electromyogram; Sound = snoring intenstity (decibels); and Position = body position.

The top panel shows that the individual is in stage N2 sleep. The bottom panel shows that the patient is having repeated disordered breathing events (obstructive apnoeas), each being accompanied by a transient arousal from sleep (top panel). Note the nasal pressure ("prongs") fluctuations, respiratory effort changes (in thorax and abdominal signals) and oxygen desaturations (red blocks) indicating apnoeas (purple blocks). Note also the respiratory arousal (green block) associated with an apnoea.

Large population based studies using polysomnography report the prevalence of OSA in men to be 4 to 5%.[4-6] The prevalence of OSA in females is lower than that in males and estimated to be 2 to 2.5%.[5,6] A review of the population-based epidemiology studies has estimated that the prevalence of OSAS, that is OSA with daytime impairment, in Western countries is approximately 5%.[7]

The prevalence of OSA reported by previous studies is likely to be underestimated as obesity is the most significant risk factor for OSA and the prevalence of obesity throughout developed countries has increased significantly in recent years [8,9], undoubtedly increasing the prevalence of OSA in the general population.

Consequences of OSA

Fragmented sleep

Increasing severity of OSA is associated with inefficient sleep with decreased sleep time, a reduced proportion of REM sleep [10, 11] and an increase in the number of arousals overnight coincident with obstructive respiratory events.[10] Sleep fragmentation is a hallmark of OSA due to an increased number and frequency of arousals from sleep in response to repetitive upper airway occlusion and is at least partly responsible for the other performance and health-related problems associated with OSA.

Daytime sleepiness and impaired quality of life

People with OSA are sleepier than those without, regardless of whether sleepiness is assessed objectively

by laboratory-based measures of sleep latency or subjectively by sleep symptom questionnaires. Excessive sleepiness is associated with increased morbidity including decreased productivity and increases in vehicular and work-related accidents.[12] Daytime sleepiness rapidly decreases after treatment for OSA with continuous positive airway pressure (CPAP).[13]

OSA patients have significantly lower general health and health-related quality of life than those without OSA.[14, 15] The level of impairment is directly related to the extent of sleep fragmentation indicating that poor sleep quality may be the most significant factor in determining quality of life in OSA patients.[16] Treatment for OSA with CPAP restores quality of life measures to levels similar to that reported in normal healthy individuals.[16]

Cognitive consequences

OSA has been associated with a wide range of cognitive impairments including deficits in vigilance, memory, psychomotor performance, attention and executive function.[17,18] The current belief is that these neurocognitive impairments are due to intermittent hypoxia [17, 19] and/or sleep fragmentation.[20]

Intermittent hypoxia has been reported to significantly affect sleepiness, memory, and executive function.[21, 22] In OSA, these changes have been attributed to decreases in grey matter and fiber integrity in brain regions that regulate memory and executive functions [23] such as the frontal lobe and hippocampus.[24, 25]

Sleep fragmentation may impact cognition via its effects on attention rather than executive function.[20, 26] There is a strong similarity between cognitive deficits seen in OSA and those seen in healthy individuals who have been experimentally deprived of sleep.[26] Such sleep-deprived individuals show increased daytime sleepiness and reduced activity in the prefrontal and posterior parietal cortices and in the thalamus.[27] These functional, central neural changes have been associated with reductions in attention and vigilance.[28] Sleep fragmentation might also mediate the cognitive deficits seen in OSA via dysfunction in neural networks, especially in the frontal lobes.[21] It is possible that these neurobehavioral sequele do not completely return to normal with therapy.[24]

Metabolic consequences

OSA is associated with alterations in metabolic function including decreased glucose tolerance and increased insulin resistance.[29, 30] Several studies have reported a relationship between insulin resistance, AHI and sleep-related hypoxemia.[29,30] These associations appear to be independent of obesity.[29, 30] Recently, increasing severity of OSA has been linked to poor glucose control in type II diabetics.[31]

Metabolic syndrome is a term used to describe the clustering of several proatherogenic factors including hypertension, dyslipidemia and impaired glucose tolerance.[32] OSA patients are reported to be 9 times more likely to have metabolic syndrome, independently of obesity, than those without it.[32] Recently, Sharma et al.[33] in a double-blind, placebo-controlled study showed that treatment of OSA with CPAP has significant benefits on the metabolic profile of individuals with OSA, decreasing the frequency of metabolic syndrome, decreasing total cholesterol, low density lipoprotein and plasma triglycerides as well as increasing high density lipoprotein levels.

The precise mechanism for metabolic dysfunction in individuals with OSA is unknown, however there are several possibilities. Firstly, untreated OSA patients have increased sympathetic nerve activity which is anti-insulin in its effects.[34] Secondly, sleep disruption and sleep deprivation and the associated sleep loss may be associated with detrimental changes in glucocorticoid regulation and abnormal glucose tolerance.[35] Finally, hypoxia may independently impair glucose metabolism.[36]

Cardiovascular consequences

Cardiovascular disease is reported to be the most common cause of death in OSA patients.[37] Individuals with OSA have up to an 11-fold increased risk of cardiovascular complications such as hypertension, ischaemic heart disease and cardiovascular disease.[38-40]

Severe OSA can cause significant sleep-related hypoxemia, pulmonary hypertension and right heart failure.[41-43] OSA increases left ventricular afterload, aggravating left ventricular failure.[42, 44] Treating OSA with CPAP in already treated heart failure patients results in further improvements in heart function.[44] While the exact mechanism for the association between OSA and cardiovascular disease remains undefined it is possible that increased generation of reactive oxygen species with exposure to chronic intermittent hypoxia and initiation and amplification of the inflammatory process in OSA may play an important role.[45] Support for this hypothesis comes from studies in healthy individuals showing that repeated exposure to intermittent hypoxia leads to increased sympathetic outflow, sustained daytime elevation in blood pressure, and decreased baroreflex function.[46]

All cause mortality

Several studies have reported a significantly increased risk of death from any cause in OSA patients compared to normal individuals, even when cardiovascular risk factors are accounted for.[47,48] Two studies, in Busselton (Australia) and Wisconsin (USA), using well-defined and long-standing general population cohorts have studied all-cause mortality in OSA patients compared to individuals without OSA.[49, 50] Both studies reported a significantly greater all-cause mortality in individuals with moderate-severe OSA than in individuals with no OSA. This increase appears to be at least partly reversible as treatment of OSA with CPAP results in reductions in mortality.[37, 47]

Mechanisms of pharyngeal collapse in OSA

The human upper airway (pharynx) can be thought of

as a collapsible tube. The presence of bony structures and soft tissues increase extra-luminal pressure on the tube and can predispose it to collapse. In contrast, the upper airway dilator muscles act to maintain patency via reflex pathways from the central nervous system and from receptors within the upper airway itself. The mechanisms underlying increased collapsibility of the upper airway in OSA are thought to be multifactorial in nature, but simplistically can be considered to be due to changes in the mechanical loads placed on the upper airway by surrounding structures (anatomical mechanisms) and/or to changes in dynamic neuromuscular responses (neurogenic mechanisms) to upper airway obstruction during sleep.

Anatomical mechanisms

Anatomical changes to the upper airway may be an important determinant of upper airway collapsibility during sleep.[51] Conditions such as tonsillar hypertrophy[52], acromegaly[53], retrognathia[54], and other changes in mandibular structure [55]have been associated with OSA, likely due to anatomy-related narrowing of the upper airway.

Ethnic differences in craniofacial structures are thought to underlie the different prevalence estimates of OSA among different ethnic groups for a given obesity level.[56] For example, Ip et al.[57] reported prevalence rates among Chinese men to be similar to white American males, however the mean BMI of the Chinese men was lower than that of the Americans, suggestive of a role for craniofacial structure in the pathogenesis of OSA.

Obesity, one of the major risk factors for development of OSA[6] is usually accompanied by increased neck circumference and fat deposition around pharyngeal structures.[58] These changes increase the load on the upper airway, reduce its cross sectional area and potentially contribute to the OSA pathogenesis. Fat deposition around the neck may be particularly important, with neck circumference being independently related to OSA severity, even when BMI is accounted for.[59, 60] OSA patients have increased pharyngeal fat deposits compared to age, BMI and neck circumference matched control subjects [61] and these have been associated with an increase in AHI.[62] A decrease in AHI has been reported with weight loss-related reductions in these fatty deposits.[62] It is likely that fat deposition around the neck and pharynx precipitates OSA by a direct compressive effect on the airway lumen.

Central obesity is also related to OSA, with studies reporting a relationship between AHI and waist circumference, an indirect measure of abdominal obesity[63], and intra-abdominal and subcutaneous abdominal fat.[64] Central obesity is likely to increase upper airway collapsibility through reductions in lung volume (functional residual capacity)[58] which is accentuated with sleep onset.[65] Such a decrease in lung volume may affect upper airway collapsibility via a decrease in caudal forces (traction) applied to the trachea and pharynx.[66, 67]

Neurogenic mechanisms

Skeletal muscle activity, including that of the upper airway dilator muscles, normally decreases with sleep onset. This decrease is particularly problematic in predisposed individuals as it can lead to sleep-related pharyngeal collapse. Increased baseline levels of upper airway dilator muscle during wakefulness in individuals with OSA is thought to represent a neuromuscular compensatory mechanism for a smaller or more collapsible airway.[68] This compensatory augmentation of activity is lost at sleep onset, permitting upper airway collapse to ensue.[68]

The mechanisms underlying the increase in wakeful muscle activity are thought to be central or reflex in origin and may include increases in wakeful drive to the dilator muscles and/or activation of the upper airway negative pressure reflex. This latter reflex is modulated by pharyngeal and laryngeal pressure sensors and causes an increase in upper airway dilator muscle activity when negative intrathoracic pressure is transmitted to the pharynx during inspiratory efforts.[69, 70]

It is also possible that neural pathways to and from the pharynx are impaired in OSA, predisposing to obstruction. There are several lines of evidence to support such a contention. Firstly, two-point discrimination and vibration sensation thresholds in the upper airway are impaired in OSA patients compared to normals[71], an impairment which is partially reversible with CPAP therapy for OSA. Secondly, OSA patients have histopathologic changes to upper airway muscles compared to normal individuals.[72,73] This may indicate a process of dennervation and degeneration of upper airway muscles in OSA patients. Such changes may result from trauma induced by repetitive collapse and re-opening of the upper airway during sleep. It is also possible that obesity-related hormones and cytokines such as leptin could impair neuroanatomical interactions necessary for stable breathing and increase the frequency of OSA.[58]

Treatment of OSA

The most common treatments for OSA include weight loss, CPAP therapy, mandibular advancement splint therapy and surgical therapy.

Weight loss

OSA is related to obesity.[3,7,74,75] Studies investigating the effect of surgical weight loss (i.e. bariatric surgery) on OSA report dramatic decreases in AHI [76,77] and arousal index and improvements in sleep architecture, daytime sleepiness and quality of life.[76] Likewise, studies investigating the effect of weight loss by diet modification report significant decreases in AHI[75, 78-80] the number of oxygen desaturations [79-81], arousal index [81], improvements in metabolic status [81] and daytime sleepiness.[79, 80] In addition, weight loss results in a decrease in upper airway collapsibility.[79, 82] With sufficient weight loss, the requirement for CPAP may be abolished and/or the therapeutic pressure requirement decreased.[76, 77]

The mechanism by which weight loss decreases the severity of OSA most likely relates to a decrease in neck and pharyngeal fat, decreasing the compressive forces on the upper airway. Central fat loss may also play an important role due to improved lung volumes and increased tension on the pharynx via caudal traction mechanisms. Indeed, the change in AHI after dietary weight loss has been shown to be strongly associated with waist circumference.[83]

Continuous positive airway pressure

CPAP involves administration of air under pressure to the upper airway via a nose or face mask. This provides a pneumatic splint for the upper airway preventing narrowing or collapse of the airway walls during sleep.[84] CPAP has been shown to reduce obstructive events, significantly improve both objective and subjective measures of daytime somnolence [85,86] and fatigue[87] and also improve sleep quality as it consolidates sleep and returns oxygen saturation and arousal indices to within normal limits.[88]

CPAP has been shown to reverse many of the complications associated with OSA: reducing risk of cardiovascular events (fatal and non fatal) or disease [38, 39]; reducing systolic and diastolic blood pressure[89]; reducing night time mean arterial pressure [89]; reducing signs of atherosclerosis[90]; improving metabolic function[33,91,92] and returning quality of life to that of individuals without OSA.[16] Its proven efficacy for reducing AHI and daytime symptoms makes CPAP the mainstay therapy for OSA.

An important determinant of therapy effectiveness is patient compliance, with hours of CPAP use related to the degree of improvements in Epworth Sleepiness Score, multiple sleep latency score, cognitive function and daytime functioning.[93] Treatment compliance with CPAP is reported to be between 31 and 80% [94,95], and is largely dependent on patient education and follow-up. Compliance in recent years has improved with the development of humidifiers, expiratory pressure relief, and improved nasal and oro-nasal interfaces. While it may be expected that patient compliance should improve with use of auto titrating positive pressure devices, a meta-analysis of 9 studies comparing the effectiveness of auto titrating positive airway pressure and traditional CPAP[96] showed that while mean pressure overnight was significantly lower with the auto titrating device, post-treatment AHI, subjective sleepiness and adherence were similar with both treatment modalities. This finding suggests that the mode of pressure delivery may not be a significant determinant of adherence to therapy.

Mandibular advancement splint

Mandibular advancement devices (MAD) are widely used as an alternative to CPAP therapy. They are designed to maintain upper airway patency by advancing the mandible and anteriorly displacing the tongue[97], increasing the size of the upper airway[98] thereby reducing its collapsibility during sleep.[99] Anterior displacement of the mandible and tongue may have neuromuscular, as well as anatomical, effects on the upper airway as MADshave been shown to increase the activity of upper airway dilator muscles which would stiffen the airway wall and decrease its propensity for collapse.[100]

In individuals with mild-moderate OSA, MAD therapy has been shown to decrease subjective daytime sleepiness[101,102] and objective daytime sleepiness.[102] Subjective and objective measures of snoring are also improved with MAD therapy[101,102], as are overnight oxygen saturation measures.[99,102] MAD therapy significantly decreases objective measures of OSA severity[99, 101, 102], with reported decreases in AHI of approximately 50%[101,102] and associated improvements in sleep architecture.[101-103]

Between 30 and 65% of patients achieve complete treatment success with MAD therapy.[99,101,102] Decreases in AHI of between 2 and 35 events per hour have been reported [86, 99, 101, 102] suggesting that issues such as design and degree of mandibular advancement, and patient selection are critical to its efficacy. The therapy appears most suited to those with mild to moderate OSA.

CPAP has a higher treatment success rate[104], decreases AHI by a greater amount[86,103,104] and normalises sleep architecture to a greater degree[86,103] than MAD therapy. When successful at decreasing AHI, both treatments are effective at improving daytime sleepiness.[86,103]

Surgery

The aim of surgical treatment of OSA is to increase upper airway size, make the airway less collapsible and prevent further obstruction. Surgical treatment has been separated into two phases, outlined below.

Phase I surgical therapy

Phase I surgery is the most conservative approach and addresses palatal and tongue base obstruction.

Uvulopalatopharyngoplasty (UPPP) is an example of phase I surgery and is the most common surgical procedure for the treatment of OSA. UPPP involves palate shortening with tonsillectomy and lateral pharyngoplasty and has been shown to improve quality of life[105] and daytime sleepiness, with a decrease in AHI of 33% [106] and up to 40% of patients being successfully treated (i.e. >50% fall in AHI and an AHI <20 events.hr-1).[107] However, the benefits of UPPP appear to deteriorate over time.[108]

Temperature controlled radio-frequency tissue ablation (TCRFTA) is used to induce a sub-mucosal thermocoagulation lesion in the tongue. Subsequent wound healing leads to fibrosis and tissue contraction. TCRFTA decreases AHI by 34%[106], however the therapy success rate is low, being approximately 20%. Further, the longevity of beneficial effects is unclear, as some individuals relapse and worsen after 2 years.[109]

Genioglossus advancement surgery involves a small window being made in the lower jaw. This bony window along with its attachment to the genioglossus muscle is pulled forward and down, then fastened to

the outside of the lower jaw.[110,111] The increased tension on the genioglossus may be sufficient to maintain airway patency at the level of the tongue base during sleep. Hyoid suspension surgery requires anterior movement of the hyoid complex and has been shown to increase upper airway cross sectional area.[110]

These surgical procedures can be performed in isolation or combined to increase treatment success. For example, combining UPPP with genioglossus advancement; hyoid suspension or radiofrequency treatment increases treatment success to 50 to 76% [112, 113] compared to 40% with UPPP alone.[107]

Recent developments in surgery for snoring and OSA include non-invasive procedures which can be performed under local anaesthesia such as soft palate implants which stiffen the palate. These implants have been shown to reduce snoring, daytime sleepiness and AHI in both habitual snorers and individuals with mild to moderate OSA.[114,115] However, the reported changes in AHI are relatively small. [106, 114, 115]

Phase II surgical treatment

Phase II surgery involves the surgical advancement of the mandible and/or maxilla and has been used to successfully treat OSA in individuals with and without craniofacial abnormalities.[116] Mandibular advancement advances the suprahyoid and tongue muscles [117] whereas maxillary advancement advances the velopharyngeal muscles.[118] Combined, these procedures significantly increase posterior air space and decrease airway collapsibility.[119] The procedure has been reported to decrease AHI, improve oxygen saturation, decrease stage N1 and stage N2 sleep and increase stage N3 sleep, decrease arousal index and improve fatigue and daytime sleepiness.[106,120,121] The magnitude of these changes is reported to be equivalent to that achieved with successful CPAP therapy.[120, 121]

Despite the high success rate, the pain and risk of complications associated with surgery and the proven efficacy of treatments such as CPAP therapy have meant that these relatively complex surgical procedures are not widely used in the treatment of individuals with OSA.

Hypoglossal Nerve Stimulation

Reduced upper airway muscle activity during sleep is fundamental to the pathogenesis of OSA. The hypoglossal nerve innervates multiple upper airway muscles, most importantly the genioglossus muscle which is considered to be the major upper airway dilator. Stimulation of the hypoglossal nerve results in contraction of the genioglossus muscle, moving the tongue in an anterior direction, thereby opening the airway and preventing collapse. Building on early work by Eisele et al.[122] and Schwartz et al.[123], several recent studies have investigated the efficacy of hypoglossal nerve stimulation as a treatment for OSA. These studies have reported significant increases in airflow [124], decreases in AHI and OSA symptoms and have shown this to be a safe and effective treatment for OSA.[125,126]

Summary

OSA is a highly prevalent sleep disorder, the pathophysiology of which is not yet fully understood. It is associated with significant health and safety risks as well as markedly decreased quality of life. Therapy, particularly CPAP is extremely effective in improving symptoms and other adverse health effects.

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Review Article

Obstructive Sleep Apnoea in Adults - The ENT Perspective

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Introduction

Obstructive sleep apnoea (OSA) is the most common type of Sleep Disordered Breathing seen in general population. It is characterized by 3 S- Snoring, Sleepiness, Significant other report of sleep apnoea episodes. In recent times it is gaining more attention from both clinician and patients because of its strong association with hypertension, cardiovascular diseases, coronary artery diseases, insulin resistance diabetes and depression.

Charles Dickens in The posthumous Papers of the Pickwick Club, published in 1837 suggested a correlation between obesity and snoring. Drs. A. G. Bicklemann and C. S. Burwell in their paper "Extreme Obesity Associated with Alveolar Hypoventilation: a Pickwickian Syndrome"[1], further supported the concept but the complete description of OSA syndrome with its adverse cardiovascular effects was given for the first time by Elio Lugaresi et al in 1970s.

Treatment of OSA has progressed from tracheostomy and weight loss to surgeries like Uvulopalatopharyngoplasty (UPPP), described by Fujita et al[2] and Simmons et al[3] but all these modalities have their own limitations with benefits at the most being only partial in most of the cases. Colin Sullivan suggested a non surgical treatment modality in the form of Continuous positive airway pressure (CPAP), which is currently the first line of treatment for this condition.

Classification

Sleep related breathing disorders range from partial airway collapse and increased airway resistance to episodes of hypopnoea and complete airway collapse with sleep apnoea.

The various sleep events are described as follows:

Apnoea is complete cessation of airflow for 10 seconds

Hypopnoea is defined as reduction in airflow (≥30%) for at least 10 seconds with a oxyhemoglobin desaturation of >=4% OR a reduction in airflow of 50% for 10 seconds with oxyhemoglobin desaturation of >=3%

Respiratory effort related arousals (RERA) refer to sleep events associated with arousals due to increased breathing efforts lasting for at least 10 seconds

Central sleep apnoea is characterized by lack of thoracoabdonimal effort associated with partial or complete cessation of airflow

Obstructive sleep apnoea is characterized by continuous thoracoabdonimal effort associated with partial or complete cessation of airflow.

Mixed type has features of both.

Snoring

Vibration of the pharyngeal soft tissues leads to snoring. It affects at least 40% of men and 20% of women and often accompanies sleep-disordered breathing (SDB)[5]. Not all patients with snoring are diagnosed to have OSA. Snoring in absence of OSA is diagnosed when habitual audible snoring occurs with an apnoea hypopnoea index (AHI) of less than five events per hour without daytime symptoms.

Upper airway resistance syndrome

Guilleminault et al first described upper resistance airway syndrome (UARS) for those patients who did not meet the criteria for OSA syndrome but had excessive daytime somnolence and other debilitating somatic complaints[6]. Some authorities don't treat UARS as a separate entity and club it with OSA because of similar pathophysiology.

Obstructive sleep apnoea syndrome

Obstructive sleep apnoea is defined by five or more respiratory events including apnoea, hypopnoea and

RERA in association with excessive daytime somnolence, waking with gasping, choking, or breath holding, or witnessed episodes apnoeas, loud snoring or both. More often than not it is the bed partner who brings the problem to notice.

Pathophysiology

Soft tissue collapse due to decreased transmural pressure at the level of nasopharynx, tongue (oropharynx) has been proposed as one of the factors for OSA. Anatomical factors like enlarged tonsils, volume of tongue, soft tissue length of soft palate, abnormal position of maxilla and mandible have also been implicated. Reduced ventilatory motor output to upper airway pharyngeal dilator muscles has been proposed to be another important factor.

Fujita et al classified[7] classified the patterns of obstruction into following types:

Type 1: collapse in retropalatal region only

Type 2: collapse in both retropalatal and retrolingual region

Type 3: collapse in retrolingual region only

Nasal obstruction though touted as a cause of OSA is rarely the sole cause, though it may contribute in worsening the symptoms. Baisch et al demonstrated in their study that surgical correction of nasal breathing led to subjective improvement in symptoms of OSA[8].

Obesity contributes in a multidirectional way to development of OSA by causing narrowing and compression of upper airway, reducing lung volume and causing a mismatch between alveolar ventilation and perfusion.

Adenotonsillar hypertrophy is a major cause of OSA affecting mainly the children. In adults it is mainly multiple structural characteristics are associated with OSA like increased distance of hyoid from mandible, decreased mandibular and maxillary projection, downward and posterior rotation of mandibular and maxillary growth, increased vertical facial length, increased vertical length of posterior airway and increased cervical angulation[9].

Diagnosis

OSA symptoms generally begin insidiously and are often present for years before the patient is referred for evaluation. It progresses through various stages of what is known as Sleep Disordered Breathing Continuum. The initial manifestation is just snoring. Untreated, it gradually progresses to upper airway resistance syndrome, which may subsequently progress to OSA[10].

Nocturnal symptoms may include the following:

- Snoring, usually loud, habitual, and bothersome to others
- Witnessed apnoeas, which often interrupt the snoring and end with a snort
- Gasping and choking sensations that arouse the patient from sleep
- Nocturia
- Insomnia
- Restless sleep, with patients often experiencing frequent arousals and tossing or turning during the night

Daytime symptoms may include the following:

- Nonrestorative sleep (i.e., "waking up as tired as when they went to bed")
- Morning headache, dry or sore throat
- Excessive daytime sleepiness (EDS) that usually begins during quiet activities (e.g., reading, watching television); as the severity worsens, patients begin to feel sleepy during activities that generally require alertness (e.g., school, work, driving).
- Daytime fatigue/tiredness
- Cognitive deficits; memory and intellectual impairment (short-term memory, concentration)
- Decreased vigilance
- Morning confusion
- Personality and mood changes, including depression and anxiety
- Sexual dysfunction, including impotence and decreased libido
- Gastroesophageal reflux
- Hypertension
- Depression

Excessive Daytime Somnolence is most frequently assessed with Epworth Sleepiness Scale (ESS). An ESS score greater than 10 is generally considered sleepy.

All patients must undergo a detailed examination including calculation of Body mass index, blood pressure measurement and neck circumference measurement along with assessment of body habitus and craniofacial proportions. This can been supplemented with fiberoptic nasopharyngoscopy in multiple positions to get an idea of the extent of airway compromise and the level of obstruction- nasal, retropalatal, or retrolingual.

The site of obstruction can be better identified in patients with OSA, if the above examinations are supplemented with drug induced sleep videoendoscopy.

Imaging modalities haven't shown much promise in delineating OSA patients from non OSA patients though cephalometric X rays, Ct scans and MRI are used frequently to assess the skeletal and soft tissue components of the airway[11, 12].

Nocturnal Polysomnography is currently the gold standard for diagnosing OSA.

Other pathologies like sinonasal polyposis, asthma, central sleep apnoea, chronic obstructive pulmonary disease, depression, gastroesophageal reflux disease,

0 = would never doze
1 = slight chance of dozing
2 = moderate chance of dozing
3 = high chance of dozing

Situation Chance of Dozing (0–3)

Situation	Chance of dosing (0-3)
Sitting and reading	
Watching television	
Sitting inactive in a public place (e.g. a theater or meeting)	
As a passenger in a car for an hour without a break	
Lying down to rest in the afternoon when circumstances permit	
Sitting and talking to someone	
Sitting quietly after a lunch without alcohol	
In a car, while stopped for a few minutes in the traffic	
TOTAL SCORE	

Total Score - Score Results:

1-6 Congratulations, you are getting enough sleep!
7-9 your score is average
10 and up Very sleepy and should seek medical advice

hypothyroidism, narcolepsy and periodic limb movement should be ruled out before embarking on the treatment for OSA.

Treatment

The approach to treatment of an OSA patient is in a step wise manner with medical management first and surgical management reserved for later.

Medical

- Weight loss should be recommended for all overweight patients with OSA.
- Bariatric surgery can be considered when treating patients who are morbidly obese. Surgically induced weight loss significantly improves obesity-related OSA and parameters of sleep quality[13], and this improvement can occur as early as 1 month after surgery[14].
- Continuous positive airway pressure (CPAP) is considered the gold standard treatment for moderate to severe OSA. However, patient adherence remains a significant obstacle.
- Bi-level positive airway pressure (BiPAP) and autoadjusting positive airway pressure (APAP) may be used to treat patients with neuromuscular disorders and ventilatory disease.
- Oral appliances may also be used in some patients with mild, moderate, and some severe OSA
- Modafinil is a central stimulant of postsynaptic alpha1-adrenergic receptors, which acts by promoting alertness. It is used for treatment of narcolepsy and idiopathic hypersomnia. Some studies have shown it to be effective in OSA[15].
- Nasal dilator strips and topical decongestants may be used in patients who have OSA and severe nasal obstruction.

Surgical

Surgical modality to be used for treatment of OSA should always be decided after taking patient's wishes and expectations into consideration and all the patients should be counseled for the need of tracheostomy. Some of the criterias used by surgeons to decide upon the surgical modalities are failure of medical therapy, significant cardiac arrhythmias, AHI>15and oxyhemoglobin desaturation <90%.

Steinhart and colleagues evaluated 117 OSA patients and found that 100% had retropalatal obstruction and 77% had retroglossal obstruction, thus illustrating that a majority of patients have a combination of the two[16]. In 2005, den Herder and colleagues evaluated 127 patients and found that 88% of patients had retropalatal obstruction while 49% had retroglossal obstruction. In this study, 51% exclusively had palatal obstruction whereas only 12% solely had obstruction at the base of tongue[17]. These studies demonstrate that most of these patients have a multilevel problem which should be identified diligently with endoscopies and other diagnostic modalities and treatment should be planned accordingly.

Nasal surgeries like septoplasty, turbinate reduction and sinus surgeries may improve the symptoms of OSA though they rarely are curative by themselves. The one definitive advantage they do offer is a more physiological breathing after the nasal obstruction has been relieved and also improve the adherence to CPAP.

UPPP aiming to eliminate palatal obstruction by resecting redundant palatal and pharyngeal tissue was described by Fujita et al[2]. Though one of the most commonly performed surgical procedure for OSA, it

has shown a success rate of not more than 50% due to its misuse as the first line surgical therapy for OSA regardless of coexistent patient factors such as obesity, retrognathia, and the existence of other sites of obstruction[18]. Friedman et al demonstrated the value of staging OSA patients for the prediction of success for UPPP[19]. They used palate position (based on the modified Mallampati staging), tonsil size, and BMI to stratify patients.

Modified Mallampati palate position divides the view into 4 positions:

1. The entire uvula can be seen with the tongue at rest.
2. A partial view of the uvula is seen.
3. Only the soft and hard palate can be seen.
4. Only the hard palate can be seen.

Stage I patients have an 80% success rate, stage II patients have a 40% success rate, and stage III patients have only an 8% success rate.

Complications associated with UPPP include temporary nasal reflux, postoperative bleeding, infection, and rarely altered speech.

Various modifications like Woodson's transpalatal advancement pharyngoplasty[20] and Friedman's Z-palatoplasty[21] have also been described especially for patients with persistent symptoms after UPPP.

Other lesser invasive procedures like palatal implants have also been advocated by various authors to reduce the morbidity and cost of treatment of OSA[22].

The management of retrolingual narrowing requires some specific surgical procedures like partial midline glossectomy, lingualplasty, and radiofrequency tongue base ablation. Most of these procedures aim at reducing the volume of tissue at the base of tongue or producing scar formation in the area thereby resulting in effective widening of retrolingual space.

Hypopharyngeal airway narrowing is addressed by procedures like Genioglossal advancement, Hyoid myotomy. The aim of these procedures is to prevent tongue collapse in the airway.

The hyoid bone is mobilized by inferior myotomy and is fixed anteriorly and inferiorly to the thyroid cartilage. The patients who are refractory to the above mentioned procedures may be considered for maxillo-mandibular advancement.

Despite of all the advancements in the management of OSA, tracheotomy still is the gold standard treatment because it bypasses the portion of airway where the obstructive symptoms arise. But the stigma associated with tracheostomy rarely makes it a surgical option of choice, although it must be considered in patients in the severity of symptoms warrants it like morbidly obese patients or on temporary basis in patients undergoing base of tongue surgery.

Conclusion

OSA if left untreated can cause cardiovascular problems like hypertension, coronary heart disease, congestive heart failure, arrhythmias, sudden death, pulmonary hypertension and stroke. It is also known to be an independent risk factor for insulin resistance23. Further it is associated with significantly higher incidence of Gastroesophageal reflux disease (GERD)[24].

Apart from this the patients suffer from daytime somnolence, decreased attention and executive functions which may lead to serious consequences in the form of automobile and workplace accidents. Impaired mood and neurocognitive deficits have also been noted. Bed partner dissatisfaction is also a common complaint among this patient group.

Treatment of OSA with CPAP and other surgical modalities has been shown to improve quality of life both for the patient and the bed partners25. Considering all the above facts and that the treatment has a well documented positive impact on the quality of life, utmost effort should be made to diagnose, evaluate the problem and offer the appropriate treatment to such patients.

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Eat Curry to Curb Mets!
12 Oct 2012

Turmeric (Curcuma Longa; "Indian Saffron") is an important spice of curry and many other dishes of Indian and other Asian cuisine. Its medicinal value has long been recognised in Ayurveda. The beneficial effects are considered to be due to one of its active ingredients, Curcumin. Several recent studies have highlighted its anti-inflammatory property and also a possible benefit when used in Parkinsonism. Now, in a study conducted in Ludwig-Maximilians-Universität (LMU) in Munich, Germany,Dr. Beatrice Bachmeier and team showed that curcumin averts the development of metastasis in patients with prostate cancer. Curcumin is safe and upto 8 gram may be consumed daily. In mice, it appears to inhibit the expression of chemokines CXCL1 and CXCL2, powerful pro-inflammatory mediators that promote metastasis. So, its action is mainly anti-inflammatory. It may also be useful in breast cancer. However, it is not a replacement for conventional therapy. The study has been published in Carcinogenesis.

- Dr. K. Ramesh Rao

Review Article

Surgical Management of Sleep Apnoea

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Abstract

Obstructive sleep apnea syndrome (OSAS) is a common sleep related breathing disorder with high morbidity secondary to day time somnolence. The level of obstruction of airway classified by Fujita determines the intervention of the specialist. Both medical and surgical management have been in practice for OSAS. Medical management includes weight loss and CPAP. Surgical management pre dominantly includes oral and maxillofacial procedures. Combination of both yields good results.

Key words: Obstructive sleep apnoea, Maxillo mandibular advancement, Uvulopalato pharyngoplasty

Chettinad Health City Medical Journal 2012; 1(3): 104 - 107

Introduction

Obstructive sleep apnoea (OSA) also called Pickwickian disease is a common sleep related breathing disorder of the present generation with an incidence of 1% -3% and up to 10- 24% in industrial workers[1,2]. It is the obstruction of the upper airway that will lead to apnoea episodes during Sleep. The airway obstruction can be at naso-pharyngeal or at the oro-pharyngeal level which can be due to central or peripheral causes. The central causes mainly involve the suppression of the respiratory centers of the brain that leads to a decrease in the muscle tonicity of the oro-pharyngeal muscles that will lead to the collapse of the airway. This is generally seen in patients on narcotics. The peripheral causes of obstructive sleep apnoea include obesity, enlarged adenoids, mandibular hypoplasia, macroglossia. Up to 18% of the obstructive apnoea episodes are secondary to the pathologies of the naso-pharynx and 50% of the obstructive apnoea cases could be secondary to the retroglossal airway obstruction.[3,4] This disease is characterized by presence of repetitive cycles of apnoea and hypoapnea during sleep. This not only disturbs the sleep pattern, but also leads to deleterious cardio respiratory problems. The patient presents with the main complaint of day time somnolence with snoring, headaches, decreased cognitive function. Clinical presentation of the patient with an average of 5 episodes of apnoea - hypoapnoea in a duration of one hour can be labeled as OSAS.

OSA can lead to potential cardiovascular complications like development of pulmonary hypertension which can potentially lead to right heart failure, tachy- brady syndrome, sinus bradycardia, ventricular ectopy etc. Pulmonary hypertension is due to increased amount of negative intra thoracic inspiratory pressures(less than 60 cm of Hg) which will increase the amount of venous return to the right side of the heart.[5,6,7] These side effects can be augmented by the ventilation – perfusion mismatch that occur due to the obstructive episodes. In these patients reduced oxygen tension will lead to polycythemia.

Clinical Diagnosis

The first step to the management of this disorder involves the identification of the level of obstruction. Clinical examination of the nasal cavity, tongue, mandible and the thyro - mental distance along with an endoscopic evaluation can give a fair idea to the level of obstruction. Mullers maneuver is also helpful to determine the same[3]. Obesity is an important factor that needs to be addressed for the successful management of the OSAS. Increase in the neck circumference due to obesity leads to deposition of the adipose tissue in the para pharyngeal areas causing floppiness of these walls resulting in upper airway obstruction. A neck circumference of greater than 17 inches has been proved to have a higher incidence of OSA[8]. (Table -1) Fujita had classified OSA based on the anatomic level of obstruction into

Type A: Associated with obstruction of the upper oro pharynx, Tonsils and adenoids,

Type B: A combination of upper and lower oro pharyngeal airway obstruction

Type C: obstruction at the level of the lower oro pharyngeal airway, epiglottis, hypopharynx and tongue base.

Radiographic evaluation of OSA includes lateral cephalograms, Mc. Namara's analysis, volumetric evaluation of the airway volume using computed tomograms. Polysomnography is considerd as a gold standard procedure in the evaluation of patients with OSA[6] which evaluates the type of obstruction (central/ peripheral/ mixed) and determines the pattern of the apnoea and hypoapnoea, facilitating the treatment plan.

Respiratory distress Index/ Apnoea – Hypoapnoea Index is calculated based on the number of the Apnoea – Hypoapnoea episodes in one hour's duration. An apnoea episode is defined as a cessation of airflow for greater than 10 seconds with persistent inspiratory effort. A Respiratory Distress Index (RDI) greater than 20 is associated with high mortality rates.

Management

Medical and surgical management modalities have been in practice for the management of OSA. The medical management involves weight loss, change in the sleeping position, use of continuous positive airway pressure (CPAP) and Bi level Positive airway pressure (Bi- PAP). CPAP is a standard successful medical management modality that has success rates of 80%. Application of continuous positive pressure to the pharynx acts as a pneumatic splint that will prevent the collapse of the airway. This procedure is not patient compliant. Bi- PAP application has shown better compliance compared to the CPAP. Surgical treatment modalities are reserved for patients with Respiratory Distress Index (RDI) greater than 20. The type of surgical intervention is determined based on the level of obstruction and the RDI. The Stanford protocol based on the above indices is in practice for the management of these cases (Table I). A uvulopalatopharyngoplasty is indicated in patients with an RDI less than 5 with Fujita's Type A obstruction.[3] This involves the correction of the uvular and the soft palatal length with correction of the redundant tonsillar tissue. The Type B obstruction pattern with RDI between 5- 20 are treated by maxillo-mandibular advancement. An RDI after 6 months post operatively would be a determining factor to assess the indication of a uvulopalatopharyngoplasty. Cases with Type C pattern of obstruction are treated by definite maxillo-mandibular advancement. Advancement of the maxilla pulls the soft tissues of the palate forward leading to increased space in the upper oro-pharynx. mandibular advancement along with pulling the tongue forward relieves retroglossal airway obstruction. The impact of the mandibular advancement can be augmented by advancement genioplasty (fig.4). Isolated procedures to decrease the tongue volume in cases of macroglossia involves the removal of excessive tongue tissue with an elliptical/ rhomboid shaped incision from the midline of the tongue. Direct hyoid suspension with fascia lata slings to the mandible have shown variable results.A combination of the surgical and medical interventions have shown good results. The surgical interventions for OSAS are

1. Uvulopalatopharyngoplasty (Fig .1)
2. Single jaw surgery maxilla (or) mandible (Fig. 2)
3. Bimaxillary Surgery – Lefort 1 for maxilla, sagittal split for mandible (Fig. 3)
4. Genioplasty and its modifications (Fig.4)

Conclusion

OSA is a common sleep related disorder with high morbidity secondary to the day time somnolence that needs attention. A combination of Medical and surgical management have shown good results. The condition has to be seen as a wholesome problem and a multi speciality treatment protocol has to be evolved. Change in the sleeping position, use of continuous positive airway pressure (CPAP), Bi level Positive airway pressure (Bi- PAP) and appropriate surgical procedures may give immediate relief.

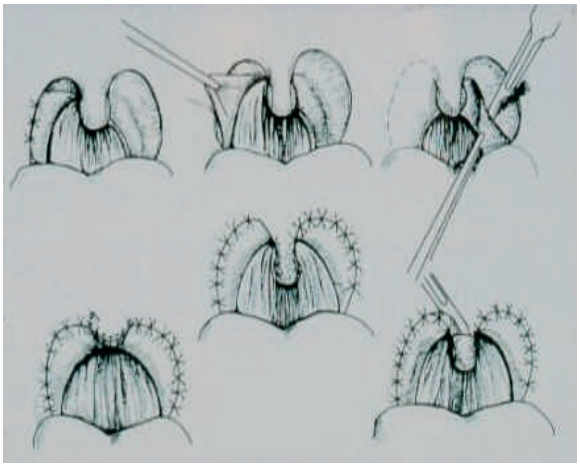

Fig. 1 Fujita type A - Uvulopalatopharyngoplasty

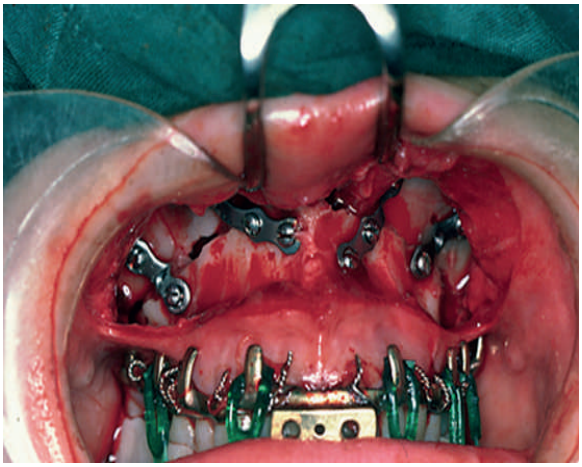

Fig. 2 Lefort 1 for maxilla for maxillary advancement

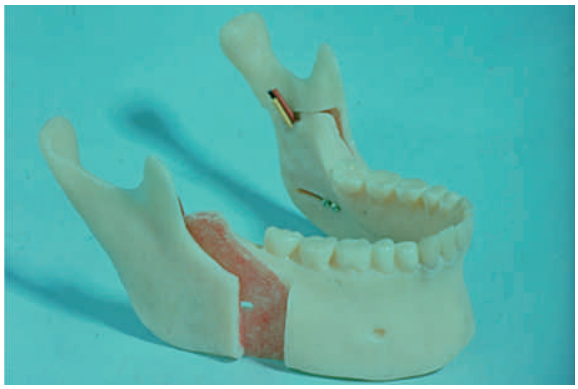

Fig. 3 Sagittal split for mandible for mandibular advance ment

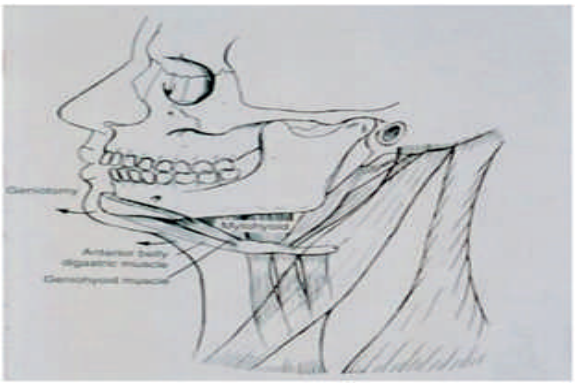

Fig.4 Genioplasty and its modifications for enhancing mandibular advancement

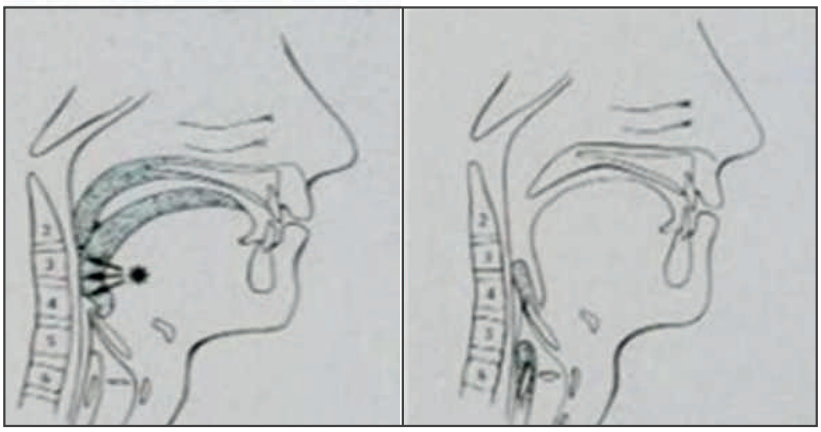

Fig .6, 7 Fujita's Anatomic type B & C patterns of obstruction are treated by definite Maxillo-Mandibular advancement. Advancement of the maxilla pulls the soft tissues of the palate forwards that will increase the space in the upper oro-pharynx. This accompanied by Mandibular advancement pull the tongue forward and relieves the retroglossal airway obstruction.

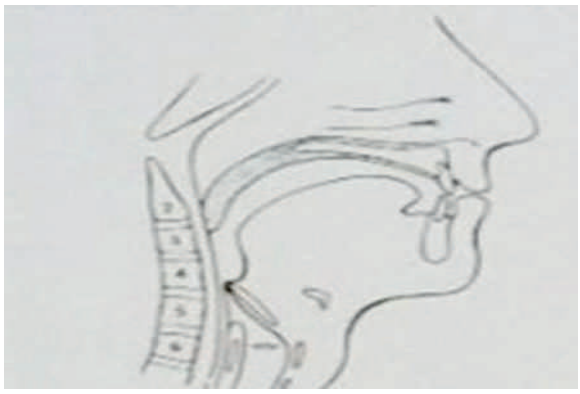

Fig.5 Fujita's Anatomic type A obstruction. This involves the correction of the uvular and the soft palatal length with correction of the redundant Tonsillar tissue.

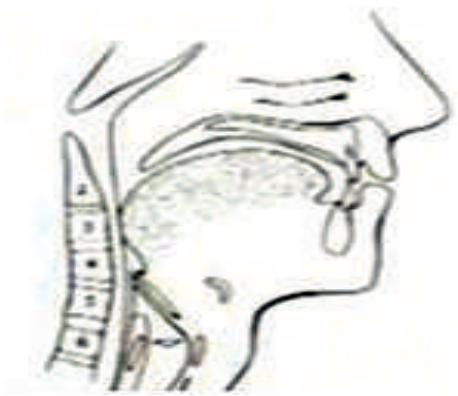

Fig. 8 This is fujita type C requiring only mandibular advancement.

Table I: Stanford Protocol

Fujita's Anatomic type	RDI Index	Treatment
Type A (fig.5)	5-20	Uvulopalatopharyngoplasty(fig. 1)
Type B (fig.6)	20-40	Maxillo Mandibular Advancement +/- (fig.2)Uvulopalatopharyngoplasty
Type C(fig.6,7,8)	>40	Maxillo mandibular advancement (fig.3)

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Magic Seven for Mental Health!
10 Oct 2012

Is there a simple way for humans to find happiness and sound mental health? When confronted with this profound question, economists and researchers from the University of Warwick knew exactly where to look for the answer; what the people ate. In a study done in collaboration with Dartmouth College, USA, they analysed the eating habits of 80,000 people in Britain. They found that the mental well-being was the highest in those consuming 7 portions (each portion is equal to 80 g) of fruits and vegetables every day. This is higher than what the western governments currently recommend (5-a-day) as a protection against cancer and cardiovascular disease risk. The authors do not specify which type of fruits and vegetables are to be consumed. The study is due to be published in Social Indicators Research. (www2.warwick.ac.uk/newsandevents/pressreleases/7-a-day_for_happiness/)

- Dr. K. Ramesh Rao

Cancer & Coloured Spots
12 Oct 2012

According to evolutionary biologists, the last common ancestor of humans and fruit flies (Drosophilidae) existed some 600 million years ago. Actually we share most of the body-building genes with lowly fruit fly. That is a disturbing thought for all those who believe that we are unique, hand-crated creations of a sky-daddy. Actually sharing genes with fruit fly helps us to study some human diseases in them. It also helps us to understand how genes behave in different environments and genetic pathways. Thomas Werner and Komal Kumar Bollepogu Raja of Michigan Technological University found that three proto-oncogenes that produce cancer in humans produce clearly identifiable coloured spots on the belly fruit fly. It is as if the old genes learn new tricks when they are placed in a new environment and genetic pathway. Authors feel that this discovery might help us in understanding the genetic pathways that cause cancer and in developing targeted gene therapies. (http://www.sciencedaily.com /releases/2012/10/121012143746)

- Dr. K. Ramesh Rao

Review Article

Anaesthetic Considerations in an Obese Patient with Obstructive Sleep Apnoea

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Abstract

Obstructive sleep apnoea (OSA) is a sleep disorder which is increasing in prevalence in India[1]. Obesity is the most common cause for OSA. Obesity is associated with a host of other comorbid illness due to the associated pathophysiologic abnormalities. The main victims of OSA and obesity are body metabolism, cardiovascular system (CVS), respiratory system (RS) and airway anatomy. Involvement of CVS and RS along with host of metabolic derangements and airway changes, and logistic of dealing with big patient makes anaesthetic management of morbidly obese patients different and difficult from non obese patients. As the association of OSA with obesity is common, it is difficult to dissociate the peri operative management of OSA and Morbidly obese (MO).

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Obesity and OSA

Definition and classification:

The imbalance in the calorie intake and expense leads to increase in fat deposits. This excess fat deposit leads to obvious increase in the total body weight which is measured to diagnose and quantify obesity. The direct measurement of body fat deposition can be done by imaging studies like CT scan.[2,3] But they are expensive and not useful for routine clinical or epidemiological measurement of obesity. Body Mass Index (BMI) is simple and robust measure used to define and classify obesity (Table 1).[4] (BMI is Weight /Height in kg /m2). The distribution of the excess fat is either truncal (android or central) or peripheral which is not identified by BMI measurement.[5] Waist – Hip ratio or waist circumference is a better predictor of this abnormality which is used for measuring central obesity. The central or abdominal fat is associated with many of pathological changes and illness associated with obesity.[6,7]

Obstructive Sleep Apnoea is a sleep disorder associated with frequent dynamic obstruction of airflow into lung due to partial or complete obstruction of upper airway. The salient feature that differentiates OSA from central cause of apnoea is the continued presence of respiratory effort against the obstructed airway. Deposition of fat in the upper airway along with nocturnal loss of pharyngeal dilator muscle tone makes obesity a leading cause of OSA.[8] The etiology, mechanism and patho physiologic changes associated with OSA has been described elsewhere in this issue. The medical management of OSA including role of nasal CPAP has been dealt separately. Hence subsequent part of this article deal with the anesthesia management of these patients when they present for surgeries.

Table 1: Obesity classification

BMI (kg /m^2)	Class
18.5-24.99	Normal weight
≥ 25	Overweight
25-29.99	Pre obese
≥ 30	Obese
30-34.99	Class I
35-39.99	Class II
≥ 40	Class III

Source: World health Organisation. Media centre obesity and overweight fact sheet.Updated March 2011. Available at http:// www.who.int/mediacentre/fact-sheet /fs311/en/index/html

Table 2: Obesity and OSA associated illness

System	Co morbidity
CVS	Hypertension, Arrythmias, Coronary artery disease, Congestive Cardiac failure, Pulmonary hypertension, Cor pulmonale
RS	Obesity Hypoventilation sysndrome
Metabolic disorders	Metabolic syndrome

Anaesthesia management

Pre operative evaluation

History: Pre operative clinical history taking should be focussed to identify the obesity related co morbid illness. (Table 2) History suggestive of Gastro Esophageal reflex Disorder (GERD) will influence the airway management technique. Obese patients have restricted physical activity and might be asymptomatic despite underlying cardio respiratory illness. Presence of shortness of breath and pedal edema if demonstrated can be a sign of right heart failure. The clinical predictors of OSA which suggests increased risk of perioperative complications has been identified by ASA task force.[9] This should be elicited to rule out any OSA in obese individuals even if there is no polysomnography (PSG). History to elicit or rule out diabetes and hypertension should be a routine in all OSA patients who are obese. The pre operative visit should be done well before surgery to optimise OSA as they might need Continuous positive airway pressure (CPAP) therapy. Uncontrolled diabetes and hypertension should be adequately controlled prior to surgery.

Investigation

Haemogram, RFT, LFT should be done prior to surgery. ECG signs of RBBB, LVH are common and need no further evaluation.[10] Further cardiac evaluation is based on associated co morbid illness and type of surgery and not based on increasing BMI and presence or absence of OSA. In patients suspected to have OHS echocardiogram to detect PHT and right heart failure is warranted.[11] Other investigations include PSG, lipid profile, stress testing, to confirm or refute clinically suspected OSA, metabolic syndrome, coronary artery disease. The array of investigations should be based on the clinical history and the type of the proposed surgery. Morbid obesity or OSA alone is not an indication for extensive cardiac or pulmonary evaluation. The cardiac workup can be done based on ACC/ AHA guidelines for non cardiac surgeries.

Airway assessment

Obesity and OSA is suggested as difficult airway predictor.[12] The increase in posterior cervical fat deposit will limit neck mobility. While this might be true, the fact is not all obese patients have difficulty in Back Mask Ventilation and/or intubation. Increasing BMI, OSA, GERD do not correlate with difficult airway.[13,14] The airway assessment tools like Mallampatti (MMP) score, Patil's test (Thyromental distance) do not identify all difficult airways. But MMP ≥3, abnormal thyromental distance and restricted jaw mobility have commonly lead to difficult airway in obese patients. [13] Neck circumference (NC) measured at the level of superior border of cricoid cartilage is useful in identifying difficult airway in obese patients. Increasing NC and mallampatti score ≥ 3 suggests possible difficult intubation.[14,15] Ultrasound detection of pretracheal soft tissue at the level of vocal cord along with neck circumference correlated with difficulty in laryngoscopy.[16] Neck circumference should be measured in addition to other airway assessment parameters to increase the chance of predicting difficult airway in obese patients. The airway management in obese patients should be tailored to the individual. The choice of technique can be anything ranging from RSI to awake intubation depending on the presence or absence of difficult airway predictor.

Premedications

Anti hypertensives, statins and anti diabetic medications should continued as in non obese patient. Antiplatelet therapy should be followed as per America Society Regional of Anaesthesia guidelines if regional analgesia is considered to be strongly beneficial. Any discontinuation or modification of cardiac medication should be done after discussion with operating surgeon and cardiologist. Patients using CPAP machine can be advised to bring their machine to hospital and continue their use in perioperative period.

Prevalence of obese patients with residual gastric volume of more than 25 ml and pH< 2.5 is higher than non obese patients. Even though incidence of clinically significant aspiration is not high, it is prudent to give proton pump inhibitors (PPI) night before and morning of surgery. If these patients have symptomatic GERD then consider H2 blockers like ranitidine along with PPI. Anxiolysis with benzodiazepines are better avoided due to common occurrence of OSA in morbidly obese.

Intra operative management

Specially designed operation tables or two tables joined together may be needed in extremely obese patients. Adequate padding around the pressure poins are important as obese patients are prone to pressure sores and neural injuries.[17] Standards of monitoting should be adhered to. The addition of invasive monitoring depends on associated co morbid illness and type of surgery. Invasive arterial blood pressure is indicated if blood pressure(BP) cuff of appropriate size is not available. Central venous line is placed in case of difficulty in intravenous (IV) access even if there is no need for Central Venous Pressure (CVP) monitoring.

Pre oxygenation: Absolute increase in metabolic rate seen in obese patients demands increased oxygen consumption.[18] Assuming supine position and induction of anaesthesia reduces arterial oxygen saturation due to reduction in FRC which is exaggerated in obese patients.[19,20] Hence preoxygenation is vital before airway intervention in obese individuals. 25 degree head up, Non invasive positive pressure ventilation(NIPPV) and CPAP/Positive End, Expiratory Pressure (PEEP) Present during preoxygenation increases the apnoea interval during laryngoscopy attemps.[21-23] 25 degree head up, and CPAP/PEEP during preoxygenation improves arterial oxygen tension by altering the cephalad position of diaphragm leading to reduction in basal atelectasis and intrapulmonary shunts. Nasopharyngeal insufflations of oxygen following preoxygenation further prolongs the time to desaturate during period of apnoea .[24]

Airway management

History of GERD and presence of predictors of difficult airway are two that will influence choice of airway technique. Considering the possibility of relatively high incidence of difficult airway in obese and/or OSA patients, it is prudent to keep difficult airway cart and help of a trained assistant available during airway management.

Not all obese patients have GERD and difficult airway. Some studies suggest the incidence of GERD is no different in obese individuals compared to non obese. The clinical relevance of increased gastric residual volume with low pH is questionable as the incidence of pulmonary aspiration is not higher than in non obese patients. Hence

1. RSI is not indicated in all obese patients
2. RSI is not contraindicated if the patient is obese and has history of GERD
3. Obese patient with H/O GERD itself is not an indication for awake intubation technique.

If there are no predictors of difficult intubation conventional laryngoscopy can be used as primary technique of airway management. Guedels airway is better used during Bag and Mask Ventilation (BMV) as better opening of airway minimises chance of gastric insufflations and improves ventilation. If still BMV is difficult to achieve adequate ventilation, then Laryngeal mask Airway (LMA), Proseal LMA (PLMA) and laryngeal tube(LT) can be temporarily used to ventilate before attempting intubation if general anaesthesia with paralysis is used as airway management technique.[25,26] Probably other supraglottic device may be used in this scenario. LMA can be used for minor surgeries as primary airway device.[27] RAMP/Head Elevated Laryngoscopy Position (HELP) position was initially described for intubation using laryngoscopy in morbidly obese patients.28 Recent study has reaffirmed, RAMP position instead of sniffing position will improve the chance of successful intubation by conventional laryngoscopy .[29] RAMP position is achieved by head and shoulder elevation to bring sternum in horizontal plane with the external auditory meatus. This can be done by either adjusting the operating table, using blankets or commercial devices.[30-33] RAMP position helps align the laryngoscopic axes in line aiding laryngoscopy guided intubation. The head up reverse trendelenberg position used for preoxygenation can be maintained during laryngoscopy.

The success rate using video laryngoscopes is better than conventional laryngoscopy in obese patients.[34,35] Different kind of video laryngoscope has been successfully used in morbid obese patients.[36] RAMP position can be used even with video laryngoscope if conventional laryngoscopy is the initial choice and proved unsuccessful. Morbidly obese patients have good success rate of intubation using intubating LMA (ILMA) and Ctrach LMA.[37,38] ILMA has been used even in emergency awake intubation in trauma setting.[39] Hence the choice of technique using alternate methods of securing airway depends on the availability of equipment and expertise of the individual practitioner.

Awake intubation using LMA CTrach can accomplished after adequate airway anaesthesia with lidocaine spray.[40] For facilitating awake fiberoptic technique in adult morbidly obese patients 40ml of atomised 2% lidocaine spray can be used.[41,42] Nerve blocks like translaryngeal nerve block with or without ultrasound guidance and dexmedetomidine infusion can be used along with lignocaine spray to facilitate awake fiberoptic bronchoscopy.[43,44]

Pharmacokinetics

The implications of drug dosing in OSA but non obese patient are minimal whereas considerable in obese patients. Induction of General anaesthesia causes decrease in the upper airway muscle tone. The implication in OSA patient is they are possibly more prone to airway obstruction following sedative and anaesthetic drug administration. The residual effects of the anaesthetic drugs might lead to more adverse respiratory events in post operative period. Pharmacokinetic studies for drug dosing are generally based on body weight in non obese patients.[45] The total blood volume, volume of distribution and cardiac output in obese patients is increased.[46] This will affect the peak plasma concentration following a bolus dose. This implies the induction dose of lipophilic drugs like propofol might be based on total body weight.[47] In obese person the volume of distribution is varied considerably due to change in body composition and along with possible co morbidities like steatohepatitis of organs of elimination makes this issue more complex.[48]

The minimal lipid solubility of sevoflurane and desflurane suggests faster onset and emergence from anaesthesia.[49,50] Onset time is not different between sevoflurane or desflurane based induction of anesthesia in obese patients.[51] The MAC of sevoflurane or isoflurane in obese is not different from non obese individuals based on a rodent model of metabolic syndrome.[52] Recovery profile in neurosurgical patients is better with desflurane compared to sevoflurane.[53] While in obese patients undergoing laparascopic surgery the difference was not seen between these two agents in their recovery profile.[54,55] But the recovery from sevoflurane is faster compared to Isoflurane in laparoscopic surgeries[56] Dexmedetomidine at dose of 0.2 to 0.8mcg/kg reduces the requirement of intraoperative inhalational agent and fentanyl. The recovery profile is positively influenced while minimising cardiovascular side effects.[57] Whether this reduction in drug requirement leads to reduced post operative respiratory complications in OSA patients needs to be studied.

Different 'body weight' used for drug dose calculation are: 1. Total body weight (TBW, Actual measured body weight) 2. Ideal body weight (IBW) 3. Lean body mass (LBM). In non obese subjects all these weights corresponds with each other hence dose calculation based on any of these weight is acceptable (In fact they will be same for all calculation). In morbidly obese, drug dose calculation based on TBW is higher than IBW whereas dose based on LBM (Best correlates with cardiac output in non cardiac patients) lies in between. Different body weight scalar has been suggested for

different drug. Some authors have suggested the initial dose based on LBM and titrate based on the individuals response[58] Table 3 below gives a guidance for dosing intravenous drug use in obese patients.

IBW	LBM	TBW
Non depolariser	Fentanyl, remifentanil and induction dose of propofol and thiopentone	Succinylcholine and maintenance dose of propofol

Source:Ingrande J and Lemmenens HJM. Dose adjustment of anaesthetics in the morbidly obese. Br J Anaesth 2010;105(S1)

In theory rapid recovery from remifentanil has advantage over other opioids in obese patients especially when associated with OSA. In morbid obese patients Target Control Infusion (TCI) sufentanil (0.3ng/ml) compared to TCI remifentanil(3 ng/ml) had delay in the immediate awakening but compensated with good quality of recovery and no difference in the duration of PACU stay.[59] Intraoperative TCI remifentanil usage needs higher morphine dose for postoperative pain management.[60] Intraoperatively fentanyl has been administered as bolus of 0.5mcg followed by 1mcg/kg/hr along with desflurane anaesthesia.[61]

The pharmacokinetic and clinical studies of anaesthetic drugs in morbidly obese patients and OSA are sparse. Even in this fewer studies the dosing and results are conflicting to suggest one drug over another in any class of anaesthesia drugs. The various choice of drug described and their dosing can at the best be considered expert opinion rather than based on consensus of evidence based medicine.

Hence pharmacodynamic end points can be used to titrate the drug dose. While neuro muscular (NM) monitoring is a good end point for titrating muscle relaxant dose, consider anaesthetic depth monitors when available.[62] Intraoperative opioids can be titrated based on haemodynamic response. Drugs with rapid onset and short acting are easy to titrate. Hence drugs like remifentanil, propofol, desflurane are considered choice by some of the authors. Opioid antagonist like naloxane and benzodiazepine antagonist flumazenil should be readily available to treat any respiratory depression that might occur with use of this group of drugs.

Regional anaesthesia and analgesia

Regional analgesia provides good pain relief and reduces parenteral opioid use in postoperative period. The advantage of catheter based technique is it provides continuous pain relief in the post operative period. Good pain relief is essential in upper abdominal and thoracic surgeries to minimise postoperative atelectasis. The concerns with regional anaesthesia technique in obese patients are identification of landmark, variation in drug dosing in central neuraxial block, positioning for block and appropriate equipment availability.

Obesity reduces the success rate and possibly increases incidence of vascular puncture in upper limb blocks using nerve stimulator.[63,64] Nerve stimulator guided paravertebral block has successfully been used as sole anaesthetic technique for breast surgeries in morbidly obese patients with a success rate of 76.9%.[65]

To improve the success rate ultrasound gram (USG) and fluoroscopy has been used in obese patients. Intraoperative fluoroscopy has been used for spinal needle placement.[66] USG use in obese patient has been described for various blocks including epidural[67]. The success rate of interscalene block using USG is high and is as good as in non obese patients.[68] The insertion of perineural catheter using ultrasound is more successful and the time for insertion is not different from non obese patients.[69]

Limitations of regional analgesia and USG in obese patients need to be considered while contemplating this technique. In general increasing BMI is a predictor of incomplete analgesia requiring frequent intra operative opioid supplementation. This occurs whether landmark based or USG guided technique is used.[70-71] Ultrasound guided technique has its limitation while using in obese patients as sound wave has to travel deep through fat tissue. [72] Another issue is complications specific to obese patients. Phrenic nerve paralysis is a common side effect of interscalene block which might become symptomatic in obese patients due to the pre existing pulmonary pathophysiologic alterations.[73]

The spinal CSF volume is reduced in obese patients. [74] The dose requirement of local anaesthetic in central neuraxial block is reduced in obese parturient.[75] The same can be true for non parturient obese patients too. But recent evidence suggests otherwise. The spinal dose needed to produce adequate block is not different in obese and non obese parturient as low dose produces inadequate sensory block with possibility of conversion to general anaesthesia.[76] The intrathecal bupivacine less than 10mg is not effective for caesarean section.[77] Similarly in non parturients the local anaesthetic dose is unaltered.[78] Considering the technical difficulties in surgery and possibility of prolonged duration of surgery, some authors suggests possibility of increase in need for combined spinal epidural (CSE) in caesarean section. [79]

Intra operative ventilation and extubation

Inadequate intraoperative ventilation might affect respiratory mechanics in obese patients undergoing surgery. Neither changing head up or down position or changing repiratory rate/tidal volume has any effect on oxygenation in patients undergoing laparoscopic surgery.[80] Intraoperatively mechanical ventilation using pressure controlled ventilation improves oxygenation by improving ventilation perfusion mismatch.[81] Pressure support ventilation improves intraoperative oxygenation which is maintained in moderately overweight patients undergoing minor procedures.[82] Morbidly obese patient are sensitive to the respiratory depressant effects of sedatives. The pulmonary mechanics suggests any decrease in neuro muscular function will lead to adverse respiratory

event. Hence extubation should be done after complete recovery when the patient is awake. NM monitoring can be used to ensure adequate reversal of residual muscle block.

Post operative period

Reduction in FRC during supine anaesthetised obese patients makes them prone to pulmonary complications. Postoperatively sleep pattern is disturbed in the initial 24-48 hours and OSA aggravates respiratory events in this period. Magnitude of pulmonary atelectasis with loss of lung volume is significantly higher and persists for longer period in morbidly obese patients.[83] Prophylactic early breathing exercise, incentive spirometry and coughing improves postoperative recovery of lung functions[84] Obesity is a risk factors for postoperative desaturaion following upper abdominal surgery in the first 48 hours.`[85] Episodes of postoperative hypoxaemia occurs in MO patients even in absence of OSA despite supplemental oxygen.[86] Association of OSA probably will increase such events. Prophylactic CPAP (10cmH2O) immediately after extubation maintains lung function better in patients undergoing bariatric surgery.[87] Vigilant monitoring of saturation by pulse oximetry in high dependency unit or ICU is warranted in the 24-48 hours of post operative period.

Adequate postoperative analgesia is another important aspect in preventing postoperative pulmonary complications. Regional analgesia should be used when ever feasible. PCA with morphine (1-2 mg bolus with 8 min lock out) can provide satisfactory analgesia similar to epidural analgesia.[88] Multi modal analgesia with ketorolac (30mg 6th hourly) along with PCA morphine provides better pain relief when used with surgical wound infiltration.[89] Continuous spinal anaesthesia using bupivaciane and fentanyl and intraperitoneal continuous infusion of bupivacaine (7.5mg/hr) has been described to be effective for postoperative bariatric surgery and allowed early ambulation. [90,91] Preemptive analgesia with ketamine and clonidine has reduced postoperative opioid use in morbidly obese patients.[92] Thus there are various effective options for postoperative pain management of obese patients. The technique and choice of drug depends on availability, type of surgery and individual patient. Whatever method is used the end point should be adequate analgesia.

Deep vein thrombosis (DVT)

Obesity is considered to be one of high risk factor for postoperative DVT.[93] Hence various preventive strategies have been described to decrease the incidence of DVT and fatal pulmonary embolism (PE). LMWH at dose of 30-60 mg sc is safe and effective in reducing the incidence of DVT.[94] Rather than considering obesity alone combination of venous stasis disease, BMI >/= 60, truncal obesity, OHS/Sleep apnea syndrome represents a high risk for DVT and fatal PE. In such group consider prophylactic IVC filter placement.[95] Obesity alone do not constitute high risk for DVT or PE and the incidence is found to be too low until associated with other coagulation abnormality.[96] Hence routine use of prophylaxis in all obese patient or bariatric surgery patient is questionable when no other risk factor for DVT is present.

The rising incidence along with the associated surgical problems in OSA and MO population suggest the practising Anaesthetist in India is going to face these patients more frequently in their practise. Careful preoperative assessment along with meticulous planning reduces perioperative complication and improves outcome in this group of patients. At present, there are only limited studies to rely while decision making in this group of patients. In future more randomised control trials are needed to build an evidence based consensus.

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Guilt Prone OR Scandal Prone?
13 Oct 2012

Not a day passes without eruption of some ethics-related scandal. The competition and the pressures of the modern world might force some to achieve their goals in an unethical manner. But many still appear to be bound by ethics. So, what actually predisposes individuals to ethical or non-ethical behavior? According to researchers, Taya Cohen and Nazli Turan of Carnegie Mellon University and A.T. Panter of the University of North Carolina, the answer could be the presence or absence of guilt-proneness. The persons who are guilt-prone anticipate a bad feeling even before they commit an unethical act (not the same thing as feeling guilty after the act) and their wide awake conscience acts as a deterrent. Guilt-proneness can be measured by Guilt and Shame Proneness Scale (GSPS). But, 30-40% of adults are likely to have a very low guilt-proneness. The latter are the ones likely to be involved in unethical business decisions, lying for monetary gain, or cheating during negotiations etc. The results of the study have been published in the latest edition of Current Directions in Psychological Science.

- Dr. K. Ramesh Rao

Review Article

Obstructive Sleep Apnoea and Cardiovascular Disease

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Abstract

Obstructive sleep apnea (OSA) is a common disorder associated with an increased risk of cardiovascular disease and stroke. As it is strongly associated with known cardiovascular risk factors, including obesity, insulin resistance, and dyslipidemia, OSA is an independent risk factor for hypertension and has also been implicated in the pathogenesis of congestive cardiac failure, pulmonary hypertension, arrhythmias, and atherosclerosis. Inflammation and oxidative stress has been recently proposed in the pathophysiology of cardiovascular disease related to sleep apnea.The current standard treatment for OSA-nasal continuous positive airway pressure (CPAP)-eliminates apnea and the ensuing acute hemodynamic changes during sleep. Long-term CPAP treatment studies have shown a reduction in nocturnal cardiac ischemic episodes and improvements in daytime blood pressure levels and left ventricular function. Despite the availability of effective therapy, OSA remains an under diagnosed and undertreated condition. A lack of physician awareness is one of the primary reasons for this deficit in diagnosis and treatment.

Key words: Sleep apnea, Inflammation, CPAP.

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Cardiovascular Diseases and OSA

Hypertension

Moderate to severe OSA presenting with an apnoea-hypopnoea index (AHI >15/hr) (apnoeas and hypopnoeas per hour of sleep) affects 4% of women and 9% of men in their middle age[1]. The prevalence of hypertension in OSA patients may be as high as 50% and in hypertensive patients, OSA can be diagnosed in up to 30%. With moderate to severe OSA, hypertension was 2.89 times more likely to occur in a 5-years period. Treatment of OSA may help decrease daytime blood pressure (BP), especially in patients with resistant hypertension (defined as a clinic BP of >140/90 mmHg while taking a combination of three or more antihypertensive drugs, titrated to maximally recommended doses) and in patients with relatively mild hypertension.

Heart failure

There is a high likelihood of OSA in patients with systolic heart failure and diastolic dysfunction. About 10 per cent of systolic heart failure patients are thought to have OSA. The association between these two conditions is reinforced by the observation that both systolic and diastolic functions improve with adequate treatment of the sleep disorder of breathing. While CPAP therapy seems to improve ejection fraction, there is as yet no evidence that treating OSA can reduce mortality in heart failure patients. Obstructive events, which may occur hundreds of times over the course of the night, and induce abrupt increases in left ventricle transmural pressure, could play an important role in the development of myocardial ischemia, contractile dysfunction, and ventricular dilation (see fig.1). The sympathetic surges and blood pressure increases may also be expected to worsen heart failure in patients with co-existent OSA. Heart failure may directly exacerbate OSA by edema formation in the soft tissues of the neck. Reduction in the intravascular volume and attenuated venous congestion resulting from heart failure treatment could potentially reduce OSA severity.

Pulmonary hypertension

The prevalence of pulmonary hypertension (PH) in OSA patients ranges from 17 to 53 per cent. The reason for this wide range may be due to methodological problems, such as selection bias[2]. Even though OSA patients experience frequent episodes of increased pulmonary artery pressure during sleep, the pulmonary hypertension is generally milder than in primary PH[3]. Patients with OSA in conjunction with PH tend to have higher BMI, left heart disease, parenchymal lung disease, and greater nocturnal oxygen desaturations. Hypoxic vasoconstriction with consequent vascular remodeling is thought to be the likely primary mechanism for any OSA-related pulmonary arterial hypertension. Pulmonary arterial pressure and pulmonary vascular reactivity to hypoxia is reduced with continuous positive airway pressure (CPAP) therapy[4].

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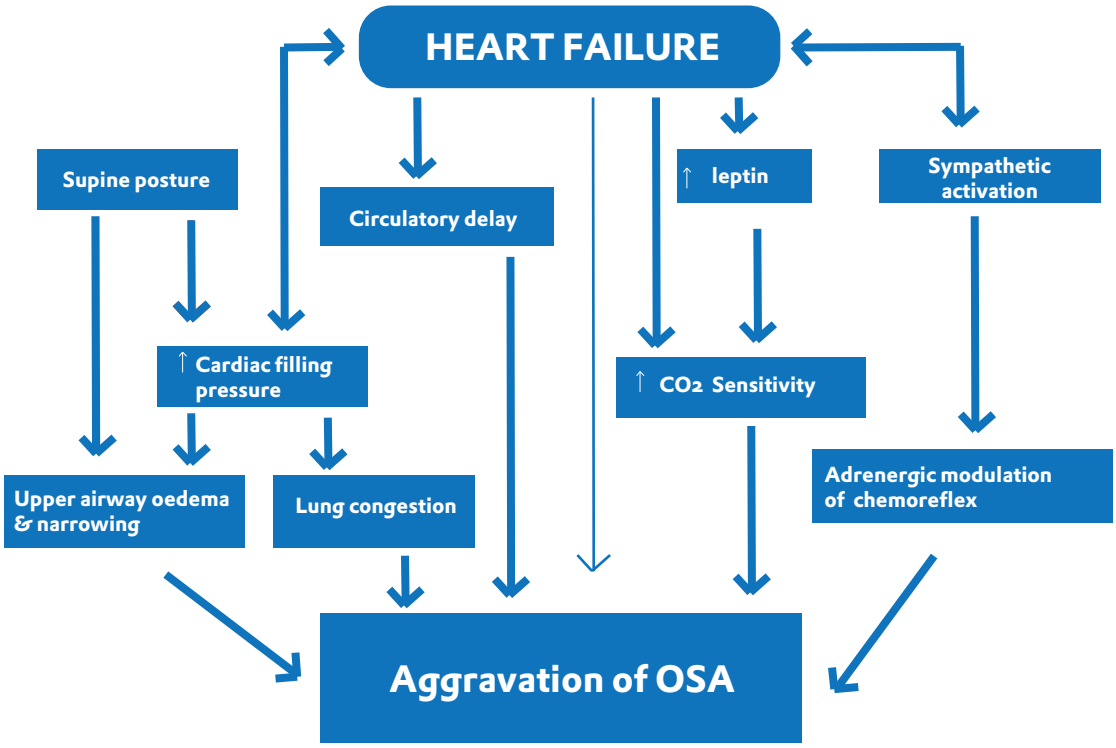

Fig 2. Schematic outlining possible mechanisms underlying development of OSA and the possible feedback from OSA resulting in exacerbation of heart failure.

Stroke

Stroke has been linked to OSA in both cross sectional and case-controlled studies, and sleep apnoea is highly prevalent in patients with stroke. Patients at risk for OSA and at risk for stroke share common demographic features. The potential for rehabilitation post-stroke may be improved with positive airway pressure treatment among stroke patients. CPAP treatment in acute stroke can be started in about 50 per cent of patients with sleep-disordered breathing but can be chronically maintained in only a minority of patients. On the other hand, the percentage of continued CPAP usage among stroke patients with OSA was higher in another study. It is still unclear whether OSA by itself, independent of other factors, is a significant cause of stroke.

Arrhythmias

OSA is associated with different types of cardiac arrhythmias. Their prevalence and complexity increase with the severity of the OSA and the associated hypoxemia. Brady arrhythmias are sometimes seen in OSA, in conjunction with obstructive apnoeas. Vagally mediated sinus bradycardia occurs as a physiological response to apnoea and hypoxemia. Various forms of nodal heart block are common and may occur even in the absence of any disease of the cardiac conduction system. Treatment of underlying OSA usually eliminates these arrhythmias. Atrial fibrillation is also common in people with OSA. CPAP ventilation has been shown to reduce the incidence of atrial fibrillation. Ventricular arrhythmias varying from benign premature ventricular contractions (seen in up to two-thirds of patients with OSA) to fatal ventricular tachycardia have been reported in patients with OSA. Nocturnal arrhythmias in OSA patients are often attenuated by effective treatment of the disordered breathing.

Molecular Basis

More recently[5], oxidative stress and consequently vascular inflammation resulting from the nocturnal hypoxia/reoxygenation cycles have been proposed to mediate the effects of sleep apnoea on the cardiovascular system.

Sleep apnoea patients have increased production of oxygen reactive species in granulocytes and monocytes. This leads to increased expression of adhesion molecules and proinflammatory cytokines, which results in increased avidity of monocytes and lymphocytes and increased cytotoxicity of lymphocytes against endothelial cells[5-6]. Circulating levels of several markers of inflammation like tumor necrosis factor alpha (TNF-alpha) and interleukin 6 (IL-6), chemokines such as IL-8, and C-reactive protein (CRP) have been implemented in the pathophysiology of sleep apnoea. The increased adhesion and cytotoxicity of sleep apnoea patients' monocytes and lymphocytes to endothelial cells in culture could be blocked by employing antibodies against selectins and tumor necrosis factor-, suggesting the active involvement of adhesion molecules and inflammatory cytokines in endothelial cell injury and dysfunction. Reports on increased plasma lipid peroxidation, C-reactive protein and serum amyloid-A, and decreased levels of plasma nitric oxide[7-10] in sleep apnoea, confirmed the existence of increased oxidative stress, vascular inflammation, and endothelial cell injury, all implicated in atherogenic sequelae. These observations are complemented by the demonstration that

cardiovascular disease-free sleep apnea patients display endothelial dysfunction as determined by assessment of endothelium-dependent vasodilation[11]. Endothelial dysfunction is considered to be the earliest manifestation of atherosclerosis and to predict cardiovascular events[12]. Finally, sleep apnea has been shown to be associated with classical markers of atherosclerosis such as increased carotid wall thickness[13] and the prevalence of calcified carotid artery atheromas[14].

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Review Article

Overlap Syndrome – the Coexistence of Sleep Disordered Breathing (SDB) and Chronic Obstructive Pulmonary Disease (COPD)

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Abstract

COPD is amongst the most common pulmonary disease and with the increasing diagnosis of SDB; it is prudent to give attention to their co-existence which is denominated as "Overlap Syndrome". Recent epidemiological data suggest prevalence of Sleep Apnea Hypopnea Syndrome (SAHS) is not higher in COPD than in general population, and that the coexistence of the two conditions is due to chance and not via any genetic-patho-physiologic linkage. This combination has important implications for diagnosis, treatment and outcome. Patients with overlap have more profound sleep related oxygen desaturation events; have an increased risk of developing hypercapnic respiratory insufficiency and pulmonary arterial hypertension as compared to COPD patients alone. Therapy of overlap syndrome consists of Positive Airway Pressure ventilation (PAP) or Non Invasive Ventilation (NIV), with or without associated nocturnal oxygen. Patients who are markedly hypoxemic during daytime (PaO_2 < 55 -60 mmHg) benefit with long term oxygen therapy (LTOT) in addition to NIV.

Key Words: Overlap syndrome, Chronic obstructive pulmonary disease, Sleep apnea hypopnea syndrome, Sleep related oxygen desaturation, Non invasive ventilation.

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Definitions and Epidemiology

Chronic Obstructive Pulmonary Disease (COPD), a common preventable and treatable disease, is characterized by persistent airflow obstruction that is usually progressive and associated with enhanced chronic inflammatory response in the airways and lungs to noxious particles and gases. Exacerbations and co morbidities contribute to the overall severity in individual patients.

COPD is a leading cause of morbidity and mortality worldwide and results in an economic and social burden that is both substantial and increasing[1,2]. COPD prevalence, morbidity and mortality vary across countries and across different groups within the countries. The Global Burden of Disease Study projected that COPD which ranked as the 6th leading cause of death in 1990 will become the 3rd leading cause by 2020; a newer projection estimated COPD will be the 4th leading cause in 2030[2].

Sleep Apnea Hypopnea Syndrome (SAHS):

There is no standardized definition of SAHS. Obstructive Sleep Apnea (OSA) is characterized by repetitive episodes of complete (apnea) or partial (Hypopnea) upper airway obstruction occurring during sleep. These events often result in reductions in blood oxygen saturation and are usually terminated by brief arousals from sleep. By definition apneic and hypopneic events last a minimum of 10 seconds.

OSA can occur in any age group. When OSA is defined as an AHI greater than 5 with a complaint of excessive daytime sleepiness, the prevalence was estimated to be 4% in men and 2% in women. The ratio of OSA in men compared to women is approximately two to one.

Overlap Syndrome:

The combination of COPD and SAHS has been denominated "Overlap Syndrome" by the late David Flenley [3]. In his opinion the term "overlap syndrome" could apply as well to the coexistence of SAHS and any chronic respiratory disease[3], but the use of this term is generally limited to the association of SAHS and COPD.

Prevalence data are not available for the overlap syndrome, probably as a consequence if the lack of a standardized definition along with the lack of a unique diagnostic code.

The earliest reports from Guilleminault and co-workers found 22 out of 26 patients in a case series suffered from sleep apneas. This might have been due to methodological bias as they had been referred to the

sleep clinic because they complained of excessive daytime sleepiness.[4] Conversely in studies by Bradley and colleagues[6,7] and by Chaouat and coworkers5 in which consecutive patients with SAHS were investigated the prevalence of an associated COPD was respectively 14% [7] and 11%[5].

Data was analyzed from the Sleep Heart Health Study, a prospective multicenter cohort study[8]. In this study no increased association was found between (generally mild) obstructive airways disease and OSA. Furthermore, the presence of airway obstruction did not seem to affect the respiratory disturbance index.

It is worth emphasizing that, although there may be no causative association between COPD and OSA, but because of the rising prevalence of these diseases, a patient with one of the disorders has a high chance of coexistence of the other. Thus when evaluating a patient with either OSA or COPD, it is reasonable to screen for the other, based on history, review of symptoms and questionnaires whenever possible.

Clinical consequences of overlap

Quality of Sleep

Many patients with COPD complain of poor quality sleep with more difficulty both initiating and maintaining sleep than controls, and also complain of excessive daytime sleepiness[9]. Objective evidence of disturbed sleep in COPD has been demonstrated by adequate EEG studies[10-14]; sleep efficiency is reduced, sleep onset is delayed, total sleep time is reduced and period of wakefulness are frequent and sometimes prolonged. The cause of this poor quality sleep is probably multifactorial, and includes nocturnal cough, nocturnal dyspnea, and use of drugs and effects of ageing on sleep. Sanders and colleagues[15] observed that after stratification for BMI quartile, RDI values were similar in participants with or without OAD. On comparing sleep variables and sleepiness they found subjects with overlap had lower sleep efficiency and % Total Sleep Time(TST) in Stage 1 as compared to subjects with SAHS alone & subjects with overlap as compared to those with OAD alone had lower sleep efficiency, lower TST, lower %TST in Stage Rapid Eye Movement Sleep, Stage 3/ 4 sleep, higher %TST Stage 2 sleep, higher sleepiness on Epworth Sleepiness Score, and higher arousal index.[15] Thus the quality of sleep in COPD is influenced by the presence of SAHS but not by the severity of airway obstruction.

Nocturnal desaturation

The most significant sleep abnormality associated with COPD is nocturnal oxygen desaturation [27, 28] Chaouat and coworkers[5] have found that nocturnal hypoxemia was more important in patients with overlap than in patients with SAHS alone. Sanders et al have reported that after adjusting for age, sex, height, race, smoking status and awake SpO2 the Odds Ratio for oxyhemoglobin saturation below levels of 85% for more than 5% of total sleep time was 20 fold greater in participants with SAHS alone compared with those who had neither disorder and 30 fold greater in participants with both disorders (subjects with overlap) 15

Perhaps most clinically relevant as observed by Flethcer et al, nocturnal oxygen desaturation in a patient of COPD with daytime SpO2 > 60 mmHg is associated with decreased survival.[16] Acutely, nocturnal oxygen desaturation causes surges in both systemic and pulmonary blood pressure[17]. It now seems likely that repetitive, transient oxygen desaturation can cause pulmonary hypertension[18]. Various arrhythmias are also reported during episodes of nocturnal desaturation[19]

Pulmonary functions and Arterial Blood Gases

Chaouat A et al, in a series of 30 patients compared the spirometric and arterial blood gases results of patients with overlap to those of patients with SAHS alone and also to a series of patients with obesity hypoventilation.[5,20]. Patients with overlap have lower pulmonary volumes and lower FEV1/FVC ratio than do subjects with SAHS alone. The coexistence of COPD and SAHS favors the presence of hypoxemia, which is rarely observed in patients with SAHS alone. Hypoxemia and hypercapnia are more severe in patients with obesity-hypoventilation than in patients with overlap.

Pulmonary Hypertension

Patients with overlap are at risk of developing pulmonary hypertension (PAH) even though their obstructive defect is not severe. Chaouat and colleagues[5] have observed that among the 26 patients with overlap who underwent right heart catheterization 11 patients had PAH defined by a mean pulmonary artery pressure (Ppa) greater than 20 mm Hg. The prevalence of PAH was 36% in patients with overlap, much higher than in usual SAHS (9%), but somewhat lower than in the obesity-hypoventilation syndrome[20]. In patients with COPD, PAH is generally observed when daytime PaO2 is less than 55 to 60 mm Hg[21], Chaouat et al have demonstrated that the average daytime PaO2 in patients with overlap is higher (66 ± 10 mmHg) and only 8/30 evaluated cases had PaO2 less than 60 mm Hg. In SAHS/overlap, the mean PaO2 during sleep in certainly lower because of the repetition of apneas and hypopneas. Patients with overlap can develop PAH even if they do not exhibit a marked degree of bronchial obstruction Thus the combination of marked nocturnal hypoxemia with a mild to moderate diurnal hypoxemia could explain the occurrence of pulmonary hypertension.[22]

Treatment

The goal of treatment is to maintain adequate oxygenation at all times and to prevent sleep disordered breathing events.

Weight Loss

Weight loss can clearly be of benefit to those with OSA and Obesity[23]. Conversely in COPD since cachexia sets in with increasing disease severity, weight loss is generally associated with increased mortality. Thus, there is no data to recommend weight loss as a therapeutic option in overlap syndrome; however it seems reasonable to deduce that those with less severe

COPD would benefit from a diet and exercise program.

Bronchodilators and Corticosteroids

Data suggests that the treatment of the underlying obstructive airway diseases in COPD with anticholinergics, β2 agonists and systemic steroids will prevent or ameliorate nocturnal oxygen desaturation,. Whether treatment of COPD in the overlap syndrome also improves OSA is not known.

Oxygen

Supplemental oxygen is the mainstay of treatment for those with daytime and nocturnal hypoxemia, and has been shown to improve overall mortality if used for more than 18 hours per day, including during sleep[24, 25] Alford and colleagues administered 4l/min supplemental oxygen to 20 men with both OSA and COPD. While nocturnal oxygenation improved, the duration of obstructive events increased from 25.7 seconds to 31.4 seconds, resulting in an end-apneic pCO_2 increase from 52.9 mm Hg to 62.3 mm Hg, with corresponding decrease in pH[26]. Thus oxygen alone should not be used for treatment of the Overlap Syndrome.[27]

Continuous Positive Airway Pressure

Continuous positive airway pressure (CPAP) is the first line of treatment of SAHS[28]. This treatment is efficient in suppressing apneas and hypopneas and sleep-related hypoxemia in patients with SAHS. CPAP may be inefficient for correcting nighttime hypoxemia in patients with associated COPD[29, 30]. In these patients some degree of sleep related hypoxemia may persist, particularly during REM sleep. Consequently, it is necessary to add supplementary O_2 to CPAP when the mean nocturnal SaO_2 under CPAP alone is < 90%. It is also possible in these cases to shift to bilevel positive airway pressure (BiPAP). The effect of therapy by CPAP or BiPAP in terms of reducing or preventing episodes of apnea, hypopnea and nocturnal oxygen desaturation events should periodically be assessed by nocturnal oximetry and whenever possible by polysomnography.

Finally in the most severe overlap patients, a marked daytime hypoxemia may persist in spite of the efficient treatment of nocturnal apneas – hypopneas. These patients require conventional long term oxygen therapy (LTOT) in addition to CPAP or NIV, when the standard criteria for oxygen therapy are fulfilled[31] – namely a daytime PaO_2 regularly less than 55 -60 mm Hg. These patients are the most likely to develop PAH[32] and LTOT may help to decrease or at least stabilize PAP[33]

Conclusion

Overlap Syndrome is not a rare condition due to high prevalence of both COPD and SAHS. A recent epidemiologic study has clearly shown that the presence of COPD does not increase the concurrence of SAHS and vice versa. The morbidity and mortality of overlap syndrome is greater than that of either COPD & SAHS alone. Many unanswered questions remain pertaining to the mechanical interaction between COPD and SAHS, like levels of SAHS and COPD that are clinically relevant, the degree of suspicion to be maintained in regards to the other disease in the presence of one and finally needed is assessment of NIV in the patients of Overlap Syndrome.

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Review Article

Obstructive Sleep Apnoea in Children

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Key words: Obstructive sleep apnoea & OSA syndrome, Polysomnography, CPAP, Apnoea-hypoapnoea index

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Introduction

The chronic debilitating Obstructive Sleep Apnoea (OSA or OSAS) syndrome in adults is now increasingly recognized in children.OSA was described nearly a century ago but sleep apnoea in infants was first described in 1975 in relation to sudden infant death syndrome and OSA in school children was described in 1976. It is a disorder of breathing during sleep characterized by "prolonged partial upper airway obstruction and or intermittent complete obstruction that disrupts normal ventilation during sleep and normal sleep patterns"[1]. OSA is the most common type of sleep-disordered breathing (SDB). OSA is part of the spectrum of sleep disordered breathing and includes Primary Snoring [PS], Upper airway resistance syndrome [UARS], Obstructive hypoventilation [hypo-apnoea], sleep apnoea[2]. If unrecognized and untreated OSA can lead to impaired day time functioning as well as more serious complications such as heart failure, developmental delay, poor growth and death. The long term neurocognitive metabolic and cardiovascular complications and the fact that with early treatment, these morbidities can be prevented warrant early diagnosis[3]. Elio Lugaresi described that Sleep Related Breathing Disorder Continuum has its least severe condition i.e. primary snoring in lower end and severe OSA in the other end with upper airway resistance syndrome (UARS) occupying between them and overlapping severity. Validity of this observation in children is to be studied.

Prevalence

Obstructive sleep-disordered breathing is common in children. Though there are not real epidemiological studies for OSA, the few published reports indicate that PS occurs in 3 to 12 percent of children[4-6].OSA affects 2 percent of children diagnosed by usual adult polysomnography values. There is no difference in sex till adolescence when males tend to have more OSA.

Definition

The consensus is evolving for definition and many researches are based on their centers' own definition for OSA. Apnoea is defined by the American Academy of Sleep Medicine, as cessation of airflow for at least 10 seconds and may last for 30 seconds or even longer[7]. But the time limitation in definition cannot be applied for all age groups as breath rates differ in different age groups from 60 per minute to 12 per minute. To address this, International Classification of Sleep Disorders 2nd edition defined apnoea as a cessation of airflow over two or more respiratory cycles. Again this cannot be applied to neonates, whose two cycles takes only two seconds which is considered as normal in periodic breathing[8-11]. Hypo-apnoea is defined as a recognizable transient reduction of breathing for 10 seconds or longer, a decrease of greater than 50% in the amplitude of breathing, or a reduction in amplitude of less than 50% associated with oxygen desaturation of 4% or more. Arousal is not taken in to account. With above background definitions, when the apnoea - hypopnoea index greater than 1 in a child it is abnormal. The Apnoea Hypo-apnoea Index (AHI) helps grading and is defined as the total number of apnoeas and hypo-apnoeas that occur divided by the total duration of sleep in hour[s1]2

Pathophysiology

The transition from wake to sleep involves muscle relaxation and this includes the pharyngeal dilator, intrinsic and extrinsic tongue muscles, which usually stiffen and maintain the upper airway. This relaxation in healthy individuals results in collapsibility of the airway, leading to increased resistance to air flow resulting in increase of PCO_2 of 3-5mmHg.[13-16] In children with Sleep Disordered Breathing (SDB), there is compensatory increased tone of the muscle in stage 2 sleep, and compensation also occurs by increasing respiratory effort and results in an arousal.[16-18] But children with SDB also show poor ventilator responses to hypercapnia and higher end-tidal CO_2. In severe OSA, apnoea may occur frequently, sometimes 1-2 times per minute. Such apnoeas are accompanied by varying heart rate, desaturations, EEG arousal simultaneously with stertorous breathing sounds as air is exhaled when the critical pressure exceeds and airway reopens.

There are three elements which appear to contribute to the pathophysiology of Sleep Disordered Breathing (SDB) which are anatomy, neuromotor tone and inflammation.

In children, adenotonsillar hypertrophy is an important factor, and it is known that relative large adenotonsillar tissue is at its largest in the first few years of life and then involutes by adolescence[19-21]. In infants and young children who are obligate nasal breathers, nasal obstruction is a factor. Difficult nasal breathing, commonly due to large adenoids in children, leads to chronic mouth breathing and this can lead to anatomical changes in facial growth. Tongue is unable to mould the palate in mouth breathing and results in a narrow, high arched palate and poor maxillary growth, which can also result in narrow nasal passages, narrow sdental arches and an anterior cross-bite. Children who sleep supine tend to have a smaller maxillary width, possibly because lying supine causes the tongue to maintain a more posterior position[22]. Other changes are increased anterior face height and a retro-gnathia, shorter maxilla and mandibular, longer and thicker soft palate and a more inferiorly placed hyoid bone. Macroglossia, glossoptosis, hypopharyngeal collapse, tracheal stenosis, laryngomalacia and recurrent enlarged adenoids are the reasons for Down syndrome developing SDB. Muscular relaxation occurs and genioglossus tone has been shown to decrease more so in patients with SDB compared to controls, when transitioning from wake to sleep[23]. Local inflammation can result in increased resistance, particularly at the adenotonsillar level[24]

Etiology

Anatomical obstruction

Obesity because of the fatty infiltration reducing the airway and hypertrophy of tonsils and or adenoids are common causes in children for obstructive sleep apnoea [25]. But any anomaly of the upper airway may produce intermittent obstructive symptoms during sleep. Facial, oral, and throat anatomical and physiological variations occur in many congenital syndromes. Hypothyroidism, Down syndrome and Storage diseases, result in upper airway crowding due to a relative larger tongue mass compared to mouth size.

Inflammation

It is well known that allergy and chronic inflammation is known to cause obstructive sleep apnoea. Gastroesophageal reflux predisposes to development of SDB[23]

Neuromuscular dysfunction

Chiari malformations and Neuromuscular diseases contribute to obstructive sleep apnoea due to abnormal muscle dysfunction and tone in the pharyngeal constrictors, which are responsible for maintaining airway patency[26-28].

Diagnosis

As in many illnesses the paediatric presentations are different from adults. The symptoms are varied and a single symptom leads us to wrong diagnostic algorithms, but group of such symptoms suggests us Sleep Disordered Breathing. Children also do not exhibit day time sleepiness but are often hyperactive. Only snoring, sleep arousals and witnessed apnoeas are present in all ages.

Snoring, apnoeas noted by parents, frequent arousals, mouth breathing, nocturnal sweating, failure to thrive, nasal congestion, hyper extended neck , recurrent otitis media and upper Respiratory infection are common symptoms seen in infants, toddlers, preschool and school children. In infants the poor suckling, poor day and night cycle, breath-holding spells and noisy breathing are subtle symptoms which may indicate SDB. Day time sleepiness, confusional arousal and restless sleep are symptoms occurring in toddlers, preschool and school children should alert the possibility of SDB. School children exhibit night terror, sleep talking, day time inattention, and hyperactivity.

History, physical examination, abbreviated polysomnography, and full polysomnography are the tools to help in diagnosis, identify candidates for further investigations, identify the candidates who are at risk and identify the management required[12,29-31]. The tools also help in avoiding unwanted interventions.

A sleep history screening for snoring should be part of routine health care visits. In children, OSAS is very unlikely in the absence of habitual snoring. If a history of nightly snoring is elicited, a more detailed history regarding labored breathing during sleep, observed apnoea, restless sleep, diaphoresis, enuresis, cyanosis, excessive daytime sleepiness, and behavior or learning problem, attention-deficit hyperactivity disorder should be obtained. Findings on physical examination during wakefulness are often normal.Evidence of complications of OSAS like systemic hypertension, accentuated second heart sound indicating pulmonary hypertension, and poor growth or obesity may be present.

Children with OSAS experience obstruction primarily during rapid eye movement (REM) sleep, which occurs predominantly in the early morning hours when their parents are not observing. Some children have a pattern of persistent partial upper airway obstruction associated with gas exchange abnormalities, rather than discrete, cyclic apnoeas and do not show pauses and gasps in their snoring, and therefore, the condition may be misdiagnosed as PS[32].

Nocturnal polysomnography or sleep study is the gold standard diagnostic technique and quantifies ventilatory and sleep abnormalities in sleep-disordered breathing and can objectively determine the severity of OSAS and related gas exchange and sleep disturbances. Polysomnography can be performed satisfactorily in children of any age. Studies in children should be scored and interpreted using age-appropriate criteria as outlined in the American Thoracic Society consensus

statement on pediatric polysomnography which can distinguish PS from OSAS 12,[29-31].

Treatment

An AHI of 1-5 is very mildly increased, 5-10 is mildly increased, 10-20 is moderately increased, and greater than 20 severely abnormal[8-11]. Weight control i.e. weight maintenance for a growing child in obese child helps in managing SDB. First line treatment in children is tonsillectomy and adenoidectomy when SDB is diagnosed. Even children with relatively small tonsils or those at risk for SDB for other reasons, such as obesity or Down syndrome may benefit from tonsillectomy and adenoidectomy[33-37]. Treatment of enlarged turbinate is also important in increasing airway diameter by radiofrequency ablation or treatment of allergies with intranasal steroids and or immunotherapy. Continuous positive airway pressure (CPAP) is useful for children who are unable to have T&A or who have residual SDB post operatively[38]. Further long term studies are required for further insight on OSA in children.

OSA	-obstructive sleep apnoea
OSAS	-obstructive sleep apnoea syndrome
SDB	-Sleep disordered breathing
PS	-Primary snoring
UARS	-upper airway resistance syndrome
AHI	-apnoea-hypoapnoea index.

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Smoking Again!
12 Oct 2012

There is not a single redeeming feature to smoking. Every new study throws up a new evidence to damn it further. The latest is from Institute of Ophthalmology, Zhejiang University in China.Juan Ye and team did an extensive meta-analysis of 16 cohort and 8 case controlled studies done all over the world. They found that the risk of developing age related cataract increased in current and past smokers compared to non-smokers. The types of cataract associated with smoking were found to be nuclear cataract and subcapsular cataract. But, no association was found between cortical cataract and smoking. The results are reported in the latest issue of Investigative Ophthalmology & Visual Science.(J. Ye, J. He, C. Wang, H. Wu, X. Shi, H. Zhang, J. Xie, S. Y. Lee. Smoking and Risk of Age-Related Cataract: A Meta-Analysis. Investigative Ophthalmology & Visual Science, 2012; 53 (7): 3885 DOI:10.1167/iovs.12-9820)

- Dr. K. Ramesh Rao

Case Report

Dental Implants with Simultaneous Guided Bone Regeneration

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Abstract

Bone defects at mandibular alveolar crest level complicate the placement of dental implants in the ideal location. Surgical reconstruction using bone grafts allows implant fixation in an aesthetic and functional manner. We describe a patient with presence of Seibert class B ridge in relation to maxillary anteriors secondary to periodontal inflammatory processes. Reconstruction of the mandibular alveolar process was carried out using allograft (Bio-oss) simultaneously with placement of dental implants. One year post operatively considerable increase in the volume of bone was evident on CT scan in the augmented area. Good implant stability was achieved at 6 months and one year postoperatively following placement of the crown with no gingival deformation around the implants.

Key words: Dental Implants, Guided bone regeneration, Alveolar bone defects.

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Introduction

Dental implants have become a predictable and successful long term treatment modality in periodontally compromised alveolar ridge. The placement of implants in a prosthetically driven position is clinically challenging. The certainty of implants depends on the quantity and quality of available bone. When the alveolar ridges lack sufficient bone volume, additional surgical procedures are required to augment the deficiencies[1]. Advanced procedures such as Guided bone regeneration have provided a conducive environment for successful placement of implants. In Guided bone regeneration non osseous cells are inhibited and osteoblast derived from the periosteum and the bones are induced to form new bone. There are two approaches in Guided bone regeneration (GBR) - simultaneous and staged approach[2]. In simultaneous approach fixture placement and GBR are performed simultaneously and is indicated only in narrow ridge defects. In staged approach GBR is used to increase the alveolar ridge before fixture placement. This article presents a case report of simultaneous approach of guided bone regeneration and implant placement in maxillary anteriors[3]

Case history

A female patient aged 26 years reported to the Department of Periodontology, Chettinad Dental College and Research Institute with a chief complaint of missing anterior teeth and need for replacement. The patient gives the history of extraction due to mobility of upper and lower anterior teeth one year back .On transgingival probing the presence of Seibert class B ridge in relation to maxillary anteriors 12 was evident. The three dimensional software analysis and Computed Tomography revealed the presence of deficient bone volume in 12 regions. The treatment plan included the placement of two stage implants in upper anterior along with simultaneous guided bone regeneration in relation to 12.

The surgical procedure included placement of crestal incision extending from 13-23, followed by elevation of full thickness mucoperiosteal flap (Fig-1,2).The dimensions of the ridge was deficient measuring 13.5 mm in length and 4.1 mm in width in 12 region and in other maxillary incisor region measuring around 12 mm x 0.5 mm.(Fig-3,4). Three maxillary implants with the dimension of 11mm x3.3 mm was placed in 11, 21, 22 region and 10 mm x 3.3 mm dimension of implant placed in 12 region. The primary stability was good in relation to all implants but in the midlabial surface of 12 regions two threads were exposed due to deficient ridge. This defect was treated with simultaneous guided bone regeneration using alloplast (Bio-oss) in relation to 12 regions (Fig-5). Flaps were sutured with No 3-0 black silk and primary closure was achieved. Antibiotics and analgesics were prescribed. Patient was advised to clean the surgical area with cotton dipped in 0.2% chlorhexidine mouth wash twice a day. Patient was called after one week and suture removal was performed. Two weeks following suture removal maxillary removable partial denture was given. Six months post operatively the maxillary second stage surgery was performed. The implant head was exposed using a crestal incision and the healing cap was placed in the maxillary implants (Fig-6). 2 weeks post

operatively a well formed gingival cuff was evident. The implant analog was placed and the impression was taken with rubber base impression material. The implant analog was transferred to the impression and the working model was made and ceramic crown was prepared. The abutment was placed followed by cementation of ceramic crowns in the patient's mouth (Fig-7). The patient was given proper supportive periodontal therapy and recalled every three months for one year to evaluate the periodontal status.

Post operatively a well formed gingival cuff was evident. The implant analog was placed and the impression was taken with rubber base impression material. The implant analog was transferred to the impression and the working model was made and ceramic crown was prepared. The abutment was placed followed by cementation of ceramic crowns in the patient's mouth (Fig-7).

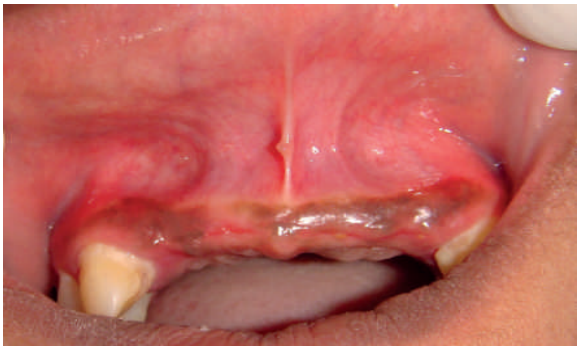

Fig 1: Preoperative view

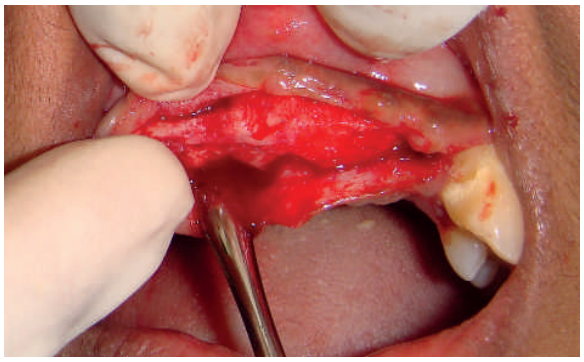

Fig 2: Elevation of Full thickness mucoperiosteal flap

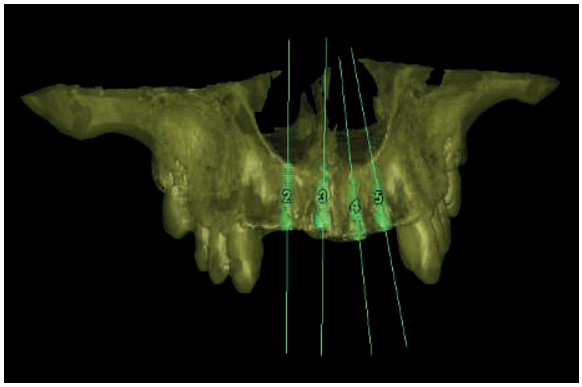

Fig 3: 3D facial view of maxilla

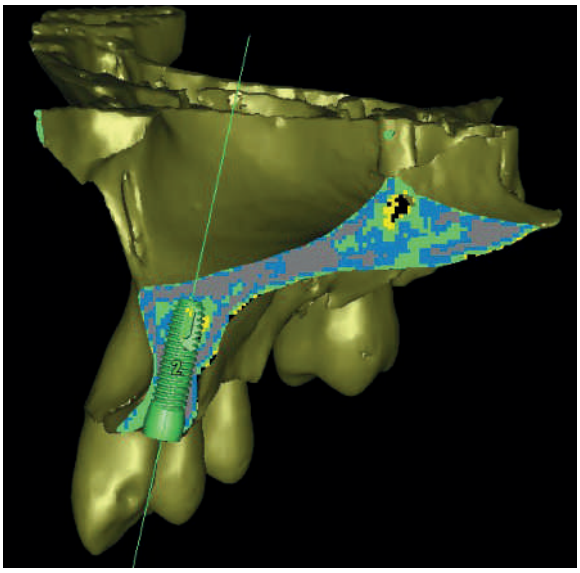

Fig 4: 3D lateral view of maxilla

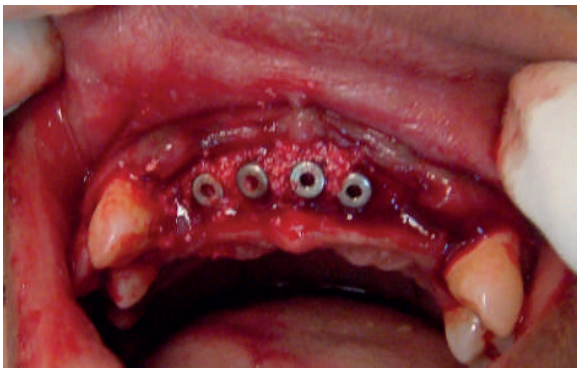

Fig 5: Dental implant placement with bone grafting (Bio-Oss)

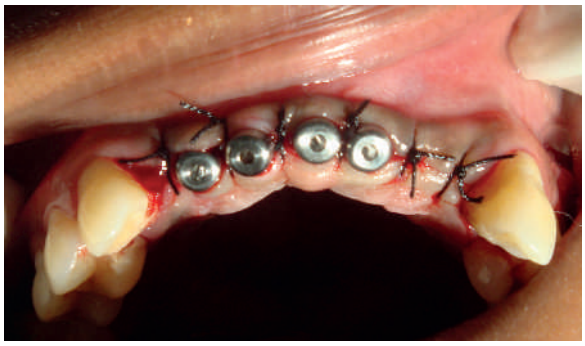

Fig 6: Placement of healing cap

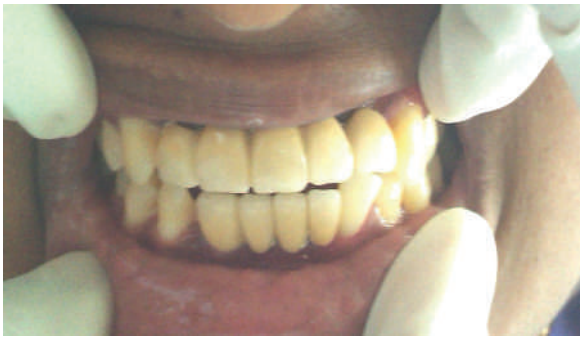

Fig 7: Postoperative with fixed prosthesis

The patient was given proper supportive periodontal therapy and reviewed every three months for one year to evaluate the periodontal status.

Discussion

Guided Bone Regeneration is a surgical procedure that utilizes barrier membranes to direct the growth of new bone and gingival tissue at sites having insufficient volumes or dimensions of bone. The present scenario focuses on the application of guided bone regeneration to defective alveolar ridges facilitating the placement of implants[4, 5].

Alveolar bone defects can be surgically corrected before or at the time of implant placement. The advantage of performing the combined graft implant procedure in a single step is reduction in the number of surgical intervention and graft stabilization procured by the implant. The disadvantages of the combined graft implant procedure are graft failure leading to implant failure and deficiency of Osseointegration in the coronal portion of the implant[6].

In this present case report simultaneous GBR was performed in the maxillary right lateral region during implant placement achieving good primary implant fixation and graft stability[7,8]. One year post operatively considerable increase in the volume of bone was evident on CT scan in the augmented area. Good implant stability was achieved at 6 months and one year postoperatively following placement of the crown with no gingival deformation around the implants. This is facilitated by maintenance of good oral hygiene.

The characteristics of regenerated bone are more dependent upon the bone quality of the receptor bed than on quality of the grafted bone, and in the case of simultaneous implant positioning; the achievement of increased percentage of bone-implant contact is dependent upon this same factor.

The outcome was implant survival described as presence of implant, implant success (according to the criteria in the respective study), absence of clinical implant mobility, absence of implant fracture, absence of progressive peri-implant crestal bone loss as assessed on radiographs without clinical signs of peri-implant infection, absence of peri-implant infection with suppuration. The survival rate of implants placed into sites with regenerated/augmented bone using barrier membranes varied between 79% and 100% with the majority of studies indicating more than 90% after at least one year of function.

The biological principle of GBR is highly predictable for ridge enlargement or defect regeneration under the prerequisite of a complication-free healing. The harmony of soft and hard tissue was achieved by implant placement with bone augmentation in aesthetically challenging situation[9,10]. Immediate placement of implants with simultaneous ridge augmentation may be a treatment option with higher patient satisfaction compared with conventional delayed approach. Further evaluation is needed to monitor hard and soft tissue changes on a long-term basis.

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Case Report

Prosthodontic Correction Of Midline Diastema

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Dr.Sridharan finished his BDS from Balaji Dental College in the Year 1997 & MDS in the year 2002. Presently heading the Dept.Of Prosthodontics & Implantology in CDCRI . He has academic experience of 9 years. Has attended many national & international conferences. He has Presented many scientific papers. He is presently member of Indian Prosthodontic Society.

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Abstract

Today's patients are more concerned about their physical appearance in which smile plays an integral role. Midline diastema is one of the common problem seen in either mixed, primary or permanent condition. Patient with these condition visit their dentist with high expectations to improve the appearance of the smile which elevates their self esteem in the society. So restorative dentist should diagnose and plan the treatment such that patient is satisfied with both functional and esthetic result of the restoration.

Key words: Midline diastema, porcelain fused to metal bridge.

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Introduction

A diastema is defined as a space greater than 0.5 millimeter between the proximal surfaces of adjacent teeth.[1] Maxillary midline diastema is common in primary mixed dentitions. It is termed as "developmental ", reflecting the spontaneous partial or complete closure that occurs with eruption of permanent lateral incisor and canine. In adult dentition reported incidence ranges from 5% to 20%.[2] Suggested causes include missing or undersized lateral incisors; mesiodens; Para functional habits such as thumb sucking, mouth breathing and tongue thrusting, flared or rotated incisors, anodontia; macroglossia; dentoalveolar disproportion; localized spacing; closed bite; ethnic and familial characteristic and midline pathology.[3]

Many forms of therapy can be employed for diastema closure. A carefully developed diagnosis and advanced planning allows the most appropriate treatment to be determined for each individual case to address the patient's needs.[4] Hence in this article history, diagnosis and treatment plan of a case of midline diastema is discussed.

Case report

A female patient aged 34yrs was refered to Department of Prosthodontics for replacement of missing tooth. Patient also complained about "gap between her front teeth" and the desire to correct the same (Fig 1). Her medical history was non contributory. Maxillary left retained deciduous canine tooth was extracted which made way for developing midline diastema (Fig 2).

Midline diastema of around 5-6mm was present between 11 and 21. Etiology of midline diastema was retained undersized left maxillary deciduous canine. No other associated conditions were observed. Patient's periodontal status was satisfactory with no caries. There were no signs of temperomandibular disorder and the occlusion was in class 1 molar relation. Radiographic findings of the teeth were also normal.

Alginate impressions (zelgan plus, dentsply) were made to prepare diagnostic wax up. Diagnostic wax up was evaluated and treatment plan was discussed with the patient. It was decided to fabricate 6 unit porcelain fused to metal bridge to correct midline diastema and also to replace missing 23 region. A putty index (Aquasil, dentsply) was made on the diagnostic wax up for the preparation of temporary crowns.

Shade selection was done before tooth preparation. Teeth to be prepared were anesthesized and 13, 12, 11, 21, 22 were prepared to receive porcelain fused to metal bridge to close midline diastema and to replace missing 23 region. Preparation was carried out using diamond points (Fig 3). After adequate preparation of the teeth, final impression was made using dual phase single step putty reline technique. Putty index was used to prepare temporary bridge (DPI) which exactly simulated the final restoration.

Metal try in was done to check the adaptation of framework followed by porcelain try in on which any occlusal interference were checked. Final cementation was done using glass ionomer cement (GC gold) and post cementation instructions were given to the patient (Fig 4).

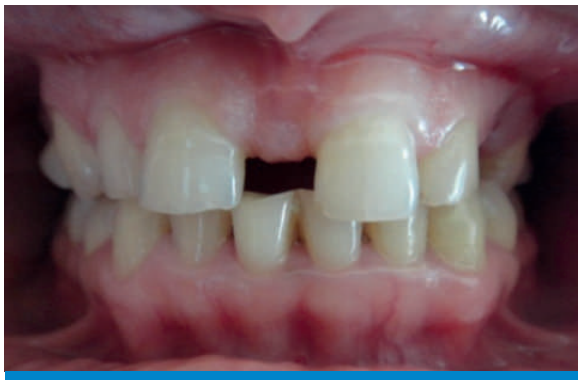

Fig 1 : midline diastema around 5-6mm between 11 and 21

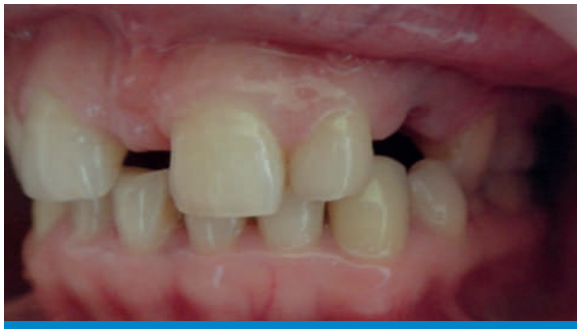

Fig 2: after extraction of maxillary left retained deciduous canine tooth

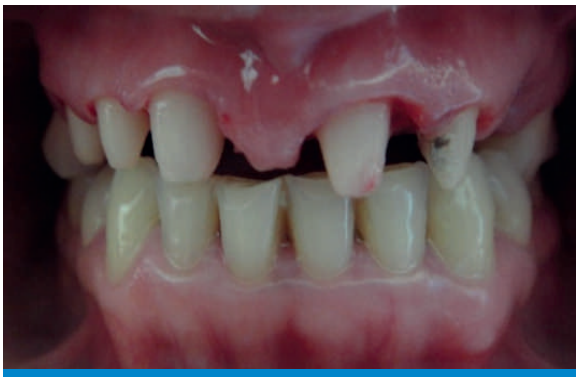

Fig 3: after tooth preparation of 13,12,11,21,22

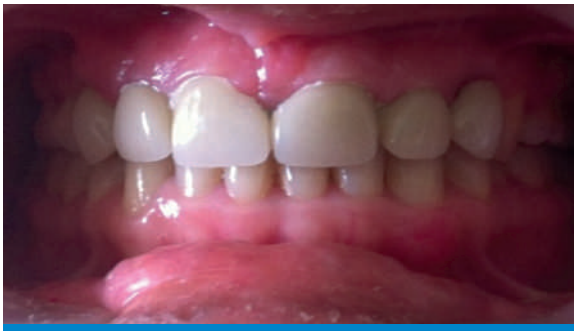

Fig 4: post restoration of midline diastema and missing 23 region

Discussion

Maxillary midline diastemas are a common esthetic problem that dentists must treat. Many innovative therapies have been used, varying from restorative procedures to surgery (frenectomies) and orthodontics.[5] Midline diastema can also be corrected by orthodontic intervention, flowable composites, laminates or bridges.

Patient was not willing for orthodontic correction as it was time consuming procedure. Laminates and flowable composite were not an ideal treatment option for this case as diastema was 5-6mm wide and would hamper the retention and would decrease the strength of these materials. And also there was an missing tooth 23 in the same arch. Patient didn't want to undergo surgical procedure to place implant for missing 23. So it was decided to fabricate 6 unit PFM bridge to close the midline diastema and also to replace missing 23.

Recently all ceramic restorations are prefered in anterior region compared to porcelain fused to metal ones. When analyzing the survival rates according to the position in the mouth, it was evident that all types of all-ceramic crowns performed better in the anterior.[6] No significant difference was seen for anterior or posterior-placed seated metal–ceramic crowns.[6] Patient was given an option of 6 unit all ceramic (zirconia) bridge, but she preferred metal ceramic bridge due to economical reasons.

Conclusion

Midline diastema is one of the common aesthetic problem faced in all age groups. The key to best results are the identification of the problem, assignment to the appropriate dentists, proper evaluation and diagnosis, and accurate communication between the treating dentists and the patient. Treating dentist should spend adequate time to properly evaluate, diagnose, and communicate with the patient to achieve the desired cosmetic change. This case report demonstrated the examination, diagnosis and execution of proper treatment plan for the patient.

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Nobel prize in Medicine 2012

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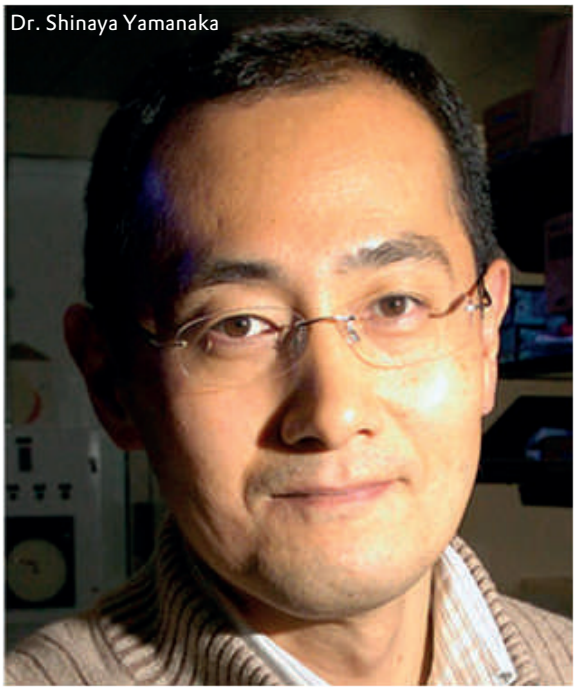
Chettinad Health City Medical Journal 2012; 1(3): 133 - 133

An average human body is made up of about 50 trillion cells. All of them are derived from the multiplication and progressive differentiation of a single fertilized ovum. The ovum and its immediate descendants (up to the stage of 8 cell embryo) are pluripotent, capable of differentiating into every cell in the body. Their descendants, however, mature and differentiate into more and more specialized cells performing unique but limited functions that help in the survival of the organism. This progressive specialisation is acquired at a price; the loss of ability to differentiate into other cells; actually, a programmed loss for common good. This loss is particularly noticeable in highly specialized cells like cardiac myocyte and neurons, which cannot even multiply. This loss seriously hinders the repair in these tissues. At first, this limitation was believed to be an irrevocable, unidirectional event following the arrow of time. But it was soon realized that these specialized cells have the same genetic constitution as the pluripotent cells; but some of the genes that confer pluripotentiality have been selectively silenced. Is it possible to make them sing again?

Two scientists, John B. Gurdon and Shinya Yamanaka, investigating the same question half a century apart in their separate ways, proved that it is possible to reprogram mature cells to become pluripotent. The Nobel Committee has honoured their groundbreaking discovery by awarding 2012 Nobel Prize for Physiology and Medicine to these two remarkable scientists.

Prof. John. B. Gurdon

Sir John B. Gurdon was born in 1933 in Dippenhall, UK. Having received his Doctorate from the University of Oxford in 1960,he did postdoctoral fellowship at California Institute of Technology. In 1962, in a series of seminal experiments, he replaced the nucleus of frog's egg cell with the nucleus from the mature specialized cell from the intestine of a tadpole. He managed to obtain cloned tadpole and in a later experiment, frog (Gurdon, JB - 1962. The developmental capacity of nuclei taken from intestinal epithelium cells of feeding tadpoles. Journal of Embryology and Experimental Morphology 10:622- 640).Though his work was initially received with skepticism, it was soon confirmed by other researchers. His work laid the foundation for cloning of mammals. Dr. Gurdon joined Cambridge University, UK, in 1972 and has served as Professor of Cell Biology and Master of Magdalene College. Gurdon is currently at the Gurdon Institute in Cambridge.



Dr. Shinaya Yamanaka

Prof. Gurdon's solution though elegant, required removal of the nucleus. The question that came up was "Is it possible to reprogram an intact cell?"In 2006, Dr. Shinya Yamanaka and his team answered this question first by isolating the genes that conferred pluripotency to pluripotential stem cell. In the next step, they introduced these genes in various combinations into mature cells in order to find the combination that worked. Finally they zeroed in on a group of four genes that reprogrammed mature fibroblast into a pluripotential stem cell (Takahashi, K, Yamanaka, S. (2006). Induction of pluripotent stem cells from mouse embryonic and adult fibroblast cultures by defined factors. Cell 126:663-676).

Shinya Yamanaka was born in Osaka, Japan in 1962 (The year Dr. Gurdon did his work). He obtained his MD in 1987 at Kobe University and trained as an orthopaedic surgeon before switching to basic research. Yamanaka received his PhD at Osaka University in 1993, after which he worked at the Gladstone Institute in San Francisco and Nara Institute of Science and Technology in Japan. Yamanaka is currently Professor at Kyoto University and also affiliated with the Gladstone Institute.

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From the Pages of History

Edward Jenner (1749–1823) - The Father of Vaccination

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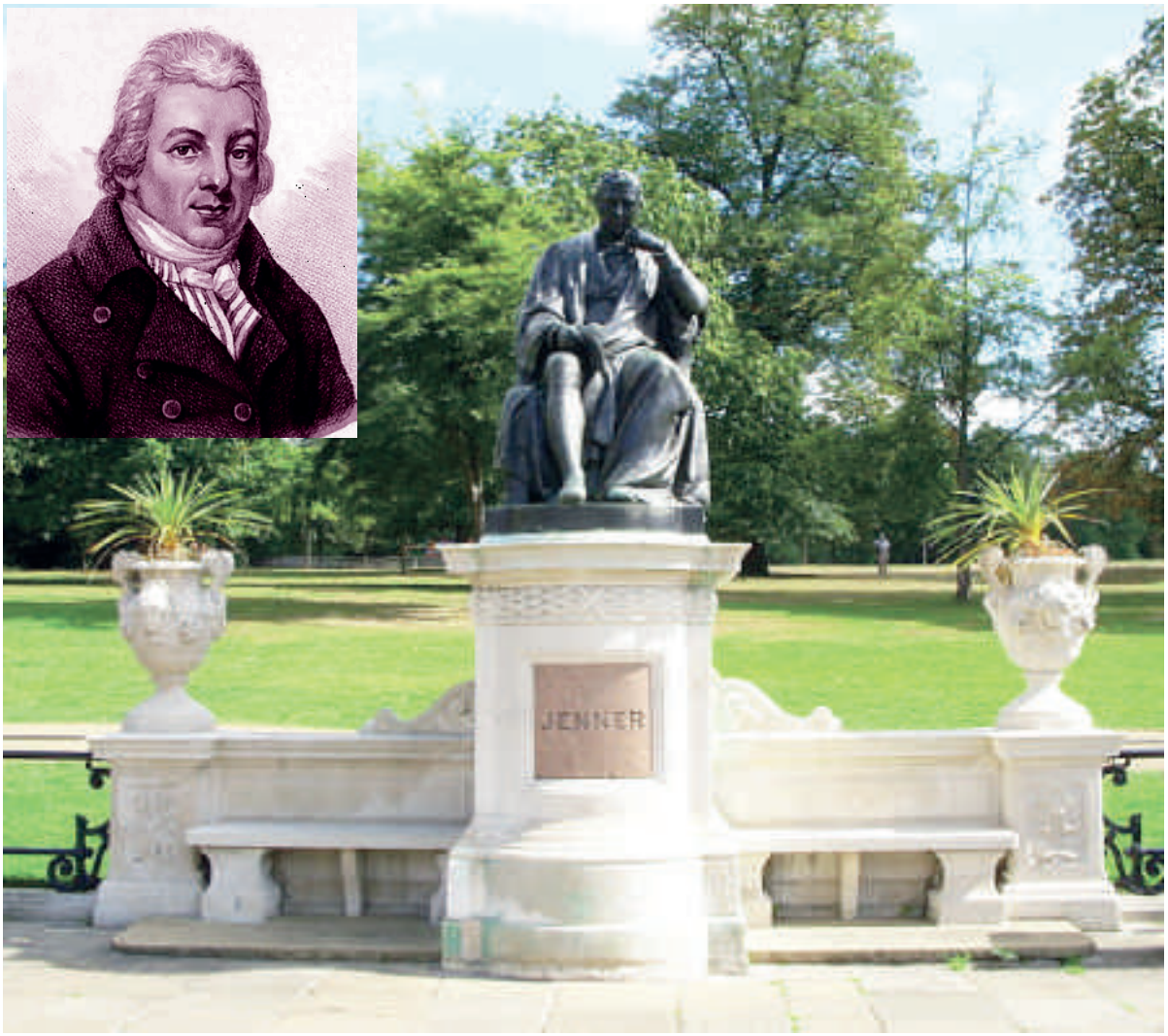
Chettinad Health City Medical Journal 2012; 1(3): 134 - 134



Edward Jenner was born on May 17, 1749, in Berkeley, Gloucestershire, England. He was the son of the Rev. Stephen Jenner, Vicar of Berkeley. Edward was orphaned at age 5 and went to live with his older brother. Edward developed a strong interest in science and nature in his early school days itself and this continued throughout his life. He apprenticed to a country surgeon and apothecary in Sodbury, near Bristol by the age of 13. On one occasion he heard a dairymaid saying that she will never get smallpox since she has had cowpox, and hence need not worry of ugly pockmark face. Jenner believed that dairymaids were in some way protected from smallpox , he did not know of immunology. Most of the early discoveries were such cause - effect correlation.

In May 1796, Jenner found a young dairymaid, Sarah Nelms, who had fresh cowpox lesions on her arms. On May 14, 1796, he collected the fluid from Nelms' pox lesions and inoculated an 8-year-old boy, James Phipps. Subsequently, the boy developed mild fever and discomfort in the axillae. Nine days after the procedure he felt cold and had lost his appetite, but on the next day he was much better. In July 1796, Jenner inoculated the boy again, this time with matter from a fresh smallpox lesion. No disease developed, and Jenner concluded that protection was complete – the 'Vaccination' was born (vacca = cow) – Thus in his honour (unwittingly) any procedure of immunization is called Vaccination, till today – a misnomer though.

A statue was planned to be erected for this greatest benefactor of Mankind, in the West Minster Garden. But the house of Lords rejected saying 'a commoner does not have a place amidst Lords'. The statue was thus placed in the mid western side fountain of Kensington Garden, in the heart of London – few visitors however realize the significance of Jenners statue. Don't forget to see this statue if you go to London and recall with nostalgia of your student days and of learning vaccines.

- RM. Pitchappan

Dialogue with the Stalwart

Interview with Dr. Shanta V

Interviewed by Dr.Thilaka Muthiah, Assistant Professor, Chettinad Hospital & Research Institute, Kelambakkam, Tamilnadu, India.

Chettinad Health City Medical Journal 2012; 1(3): 135 - 136

When one enters a hospital dedicated to the cure and care of cancer patients, one expects to see patients who are depressed, dejected and frustrated and staff and workers equally strained from witnessing continuous suffering. On the contrary, what one sees on visiting Cancer Institute is entirely different. Most of the patients were aware of what they were going through; still they were very confident about the treatment given and more importantly they radiated a positive attitude towards life. The OPD is flooded with patients; still the staff take time to enquire what without getting irritated. Dr. V. Shanta is the Chairman of the Cancer Institute and has played a pivotal role in its development since its inception. She hails from a distinguished scientific family; her grandfather and uncle Sir C.V.Raman and Dr. S. Chandrasekhar are Nobel Laureates. Dr. Shanta is the recipient of the Magsaysay award in 2005, Padma Shri, Padma Bhushan and many other awards for her undeterred and selfless service to humanity. The Magsaysay award citation is worth quoting to describe aptly Dr. Shanta's service. It reads in part:

"In an era when specialised medical care in India has become highly commercialised, Dr. Shanta strives to ensure that the Institute remains true to its ethos, `Service to all.' Its services are free or subsidised for some 60 per cent of its 100,000 annual patients [...] Seventy-eight-year-old Shanta still sees patients, still performs surgery, and is still on call twenty-four hours a day."

What prompted you to take up medicine as a profession, considering the fact that in those days medicine was not a usual option for women?

Wanting to become a doctor was my first and last choice. The decision was made during the time of schooling, in the 4th form (these days 9th standard) where we had to choose an optional.

What inspired you to join Cancer Institute and take up Oncology?

After completing MD in Obstetrics and Gynecology, I had a few options open. But it is mainly destiny and opportunity that made me join here. I really have no idea. I think it is God send and I have no regrets ever since. My first posting during House Surgeoncy was to the Cancer Unit under Dr.S.Krishnamurthi.

Can you share a few words about Dr. Muthulakshmi Reddy?

Amma (that is how she refers to Dr. Muthulakshmi Reddy) is one of the greatest ladies India has ever had. Though the time I spent with amma was brief as she was old by the time I joined, I had the unique opportunity and honour to work in close association with her. In fact I've worked with her son Dr. Krishnamurthy for almost five and a half decades. Dr. Krishnamurthi is the architect of what the Cancer Institute (WIA) is today. I am what I am because of him.

When the 1st national flag was hoisted on our Independence Day, it had the names of 7 people who contributed a lot to the country. Amma's name was in that list. She was the 1st lady medical graduate from India and the first woman Vice President of the Legislative Council. She lost her sister due to cancer in 1923. That is when she found that there were no facilities in India to treat cancer patients. Cancer Institute is her dream come true. We owe a great deal to her thoughts, deeds, commitment and dedication. She was the President of the Women's Indian Association. She is the one who started the Cancer Relief Fund.

How do you see the development of the Institute?

We just started as a 12 bedded hospital with the idea of doing something for the poor. We had to grow to keep in pace with the rapidly growing technology and scientific knowledge. This growth is not without obstacles and difficulties because from the time of inception it has been difficult to make people understand the need for a dedicated cancer hospital.

As the hospital was accessible and patients got better, more and more patients started coming to get treated. We have a lot of firsts to our credit like installation of the first supervoltage radiation unit in Asia, first Linear Accelerator in India, first and only Intraoperative Radiotherapy (IORT) facility in India, first Peadiatric Oncology Centre in the country, introduction of DM and MCh superspeciality courses etc. and we still are pioneers in most of the fields in oncology. Our ethos is "Service to all without social or economic divide" and "Service above self". Till date whatever be the hindrance, we have not paid a single rupee 'under the table' to anyone. Our staffs are also trained in the same way. We have grown with difficulty, but we are very happy to be honest and clean. When I go to sleep I am very clear that I've done my best.

Can you recall a satisfying and memorable moment?

There are multiple. The best reward one can get is when a child you treat grows up, completes education, gets married and comes back to see you. We can measure success or failure using four variables- 1.Care 2.Cure 3.Control and 4.Research.

Today we can cure 1 out of 3 patients who come to us. If they come at an early stage, we can cure 2 out of 3 patients, which is a big thing. To make sure the balance 1 gets treated, we need to concentrate on research. We need to have on-going research for progress. As for the patients who cannot be cured, we need to give them care, make them happy, so that they can die in dignity instead of dying in suffering.

How did you feel when they announced the Magsaysay award?

It was fantastic (she laughs and recollects it just like it happened yesterday). It was a Tuesday evening at 6.30 p.m. Dr. Krishnamurthy and I were having a discussion after returning from the operation theatre. In fact he attended the phone call and handed it over to me saying it was from Philippines. I was so overwhelmed and had nothing to say except that I was honoured and privileged. Seeing my reaction, Dr. Krishnamurthy asked if it was the Magsaysay award when I put the phone down. He was happier than I was and rightly said that I am getting it on behalf of the Institute and the entire team. It is definitely an added feather to the Institute.

In one of your previous interviews you've mentioned that only with time will we know the impact of the Magsaysay award on the Institute. Has it made any positive impact?

Nothing. I am being treated with great respect. Most awards have no meaning for me. Public do not respond to the Institute. Honouring me doesn't help. People should honour the cause and mission for which we are struggling. We've not been able to make any extra money for the institution. It is becoming increasingly difficult to tackle the cost of drugs and research with the limited support we generate. The number of underprivileged that we can support is minimal compared to the overall needs of the community. People must come forward to help and donate to fight cancer, to provide education, to help patients get treatment.

Have you seen changes in cancer prognosis over time?

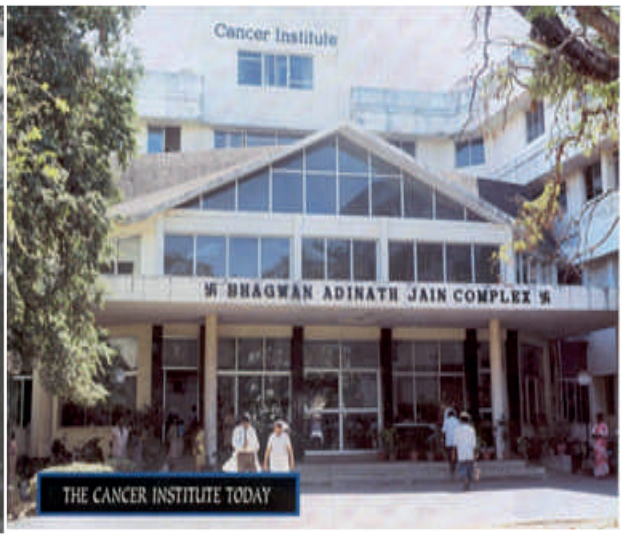
There is an enormous change. We have moved from an era of incurability to an era of curability. More importantly we also know ways to prevent cancer. Way back in 1955, we did not have a single child who survived 6 months after detecting cancer. Today almost 60% of the children go back normal and lead normal lives, which is an achievement. If you take osteosarcomas, amputation was the only available treatment years back. I still remember a patient Varnakula Surya from Colombo. He had a bone tumour refused amputation. I told him about Douglas Bade, the ace pilot of Britain battle who had only artificial limbs. He still refused amputation and we lost him. Today there is no need for amputation and we do limb salvage surgeries. Similarly for breast cancer, laryngeal tumours and a number of other cancers we do organ conserving surgeries.

What do you want to tell the young doctors?

Be proud of your Institute and do everything to make your Institute proud of you. How many Indians are proud about their country? That is where we fail. If you are not happy about something then try to do something to improve it. Try to work as a team and think of making a difference. It need not be for the entire nation. You can definitely make a change to a patient, to a group, to a community.

Take up something as a mission and motive in life. We had wonderful teachers. Teaching is not great these days and the students mind is not trained to think. Read about great people. The worst thing a young mind can get exposed to is a corrupt environment- about that, only God knows what we can do!

Cancer Institute- 1954



Congratulations!!!

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SIMSCON - 2012

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CERTIFICATE

This is to certify that Mr/Ms. NAGAMAHENDRAN participated in the SIMSCON - 2012 held at Sri Manakula Vinayagar Medical College and Hospital, Puducherry - 605 107 on 1st September 2012 and presented a paper/theme/case report titled APLA syndrome

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Campus interview was conducted in Chettinad College of Nursing

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