

**THE EFFECTIVENESS OF ORAL APPLIANCE IN COMPARISON WITH
CONTINUOUS POSITIVE AIRWAY PRESSURE IN THE TREATMENT OF
OBSTRUCTIVE SLEEP APNOEA: A RANDOMISED CLINICAL TRIAL**

MOMEN ZAKY ELSAYED ELSHERBINY

UNIVERSITI SAINS MALAYSIA

2016

**THE EFFECTIVENESS OF ORAL APPLIANCE IN COMPARISON WITH
CONTINUOUS POSITIVE AIRWAY PRESSURE IN THE TREATMENT OF
OBSTRUCTIVE SLEEP APNOEA: A RANDOMISED CLINICAL TRIAL**

By

MOMEN ZAKY ELSAYED ELSHERBINY

Thesis submitted in fulfilment of the requirement

for the degree of

Master of Science (Dentistry)

February 2016

ACKNOWLEDGEMENTS

First and foremost, I am very grateful to Allah swt for making this thesis possible.

I would also like to thank my family especially my beloved wife for the endless support and help throughout my study.

Finally, I would like to thank my supervisors for their continuous guidance and advice.

TABLE OF CONTENTS

	Page
Acknowledgements	ii
Table of contents	iii
List of Tables	ix
List of Figures	x
List of Abbreviations	xi
Abstrak	xiii
Abstract	xv
 CHAPTER 1 – INTRODUCTION	
1.1 Background	1
1.2 Objectives	4
1.2.1 General objectives	4
1.2.2 Specific objectives	4
1.3 Research null hypothesis	5

CHAPTER 2 – LITERATURE REVIEW

2.1	Epidemiology (Prevalence)	6
2.2	Pathogenesis	7
2.3	Aetiological factors	8
2.3.1	Gender	9
2.3.2	Age	9
2.3.3	Obesity	10
2.3.4	Snoring	11
2.3.5	Soft tissue abnormalities	11
2.3.6	Ethnicity	12
2.3.7	Hereditary factors	13
2.3.8	Smoking	13
2.3.9	Menopause	14
2.3.10	Medication and Alcohol	14
2.4	Symptoms	15
2.4.1	Symptoms during sleep & day time	15

2.5	Diagnosis	16
2.6	Treatment	18
2.6.1	Behavioural treatment	19
2.6.2	Positional therapy	19
2.6.3	Continuous Positive Airway Pressure (CPAP)	20
2.6.3(a)	Mechanism of CPAP action	20
2.6.3(b)	Indications for CPAP treatment	20
2.6.3(c)	Advantages of CPAP treatment	22
2.6.3(d)	Acceptance and adherence to CPAP	23
2.6.3(e)	Side effects of CPAP	24
2.6.4	Surgery	24
2.6.4(a)	Upper airway surgery	25
2.6.4(b)	Weight loss surgery	26
2.6.5	Oral appliances	27
2.6.5(a)	Types of oral appliances	28
2.6.5(b)	Mechanism of action of oral appliances	29

2.6.5(c) Appliance design	31
2.6.5(d) Appliance titration	34
2.6.5(e) Efficacy of oral appliance in OSA	35
2.6.5(f) Advantages of oral appliance treatment	37
2.6.5(g) Side effects of oral appliances	39
2.6.5(h) Comparison with CPAP	41
CHAPTER 3 – METHODS AND MATERIALS	45
3.1 Study design	45
3.2 Reference population	45
3.3 Source population	45
3.4 Inclusion criteria and exclusion criteria	46
3.5 Sample size determination	47
3.6 Research tools	52
3.6.1 Polysomnography machine	52
3.6.2 CPAP	55
3.6.3 OA	58

3.6.4	Epworth Sleepiness Scale	60
3.6.5	Calgary Sleep Apnoea Quality of Life Score	60
3.7	Data collection	62
3.8	Group (A) Oral appliance	63
3.9	Group (B) CPAP	66
3.10	Data analyses	67
3.11	Ethical consideration	67
CHAPTER 4 – RESULTS		69
4.1	Sample profile	69
4.2	Pre-treatment baseline sleep parameters for patients in CPAP and OA groups	71
4.3	Changes in sleep parameters after treatment with CPAP	72
4.4	Changes in sleep parameters after treatment with OA	73
4.5	Comparison of changes in sleep parameters after treatment between CPAP and OA	74
4.6	Comparison between Patient’s acceptance of OA and CPAP	75
CHAPTER 5 – DISCUSSION		76
5.1	Baseline parameter	76

5.2	Changes in AHI in the CPAP group	77
5.3	Changes in AHI in the OA group	78
5.4	Changes in MinO ₂ and MeanO ₂ in the CPAP group	80
5.5	Changes in MinO ₂ and MeanO ₂ in the OA group	80
5.6	Changes in SAQLI and ESS in the CPAP group	81
5.7	Changes in SAQLI and ESS in the OA group	82
5.8	Comparison of the changes in parameters between the two groups	84
5.9	Patient's acceptance of OA and CPAP	85
5.10	Study limitations	86
	CHAPTER 6 – CONCLUSION	87
	CHAPTER 7 – RECOMMENDATIONS	88
	References	89
	Appendices	107

LIST OF TABLE

		Page
Table 4.1	Sample profile of patients in group CPAP and OA	70
Table 4.2	Comparison of pre-treatment baseline sleep parameter for patients treated with CPAP and OA	71
Table 4.3	Changes in sleep parameters after treatment with CPAP	72
Table 4.4	Changes in sleep parameters after treatment with OA	73
Table 4.5	Comparison of changes in sleep parameters after treatment between CPAP and OA	74

LIST OF FIGURES

	Page
Figure 3.1 The PSG machine	53
Figure 3.2 PSG sensors attached to the patient	54
Figure 3.3 The CPAP machine	56
Figure 3.4 A patient using CPAP machine	57
Figure 3.5 Adams clasp	59
Figure 3.6 The oral appliance	59
Figure 3.7 Bite registration	64
Figure 3.7 OA in the patient's mouth	65
Figure 3.9 Trial flow chart	68
Figure 4.1 Figure 4.1 Patient's acceptance of OA and CPAP	75

LIST OF ABBREVIATIONS

OSA	Obstructive sleep apnoea
AI	Apnoea index
AHI	Apnoea/hypopnea index
OSAS	Obstructive sleep apnoea syndrome
CPAP	Continuous positive airway pressure
OA	Oral appliance
MAS	Mandibular advancement splint
MinO ₂	Minimum nocturnal arterial oxygen saturation
SDB	Sleep disorder breathing
BMI	Body mass index
EMG	Electromyogram
EEG	Electroencephalography
EOG	Electrooculography
ESS	Epworth Sleepiness Scale
SAQLI	Sleep Apnoea Quality of Life Index

ECG	Electrocardiography
ODI	Oxygen desaturation index
ARI	Arousal index
PSG	Polysomnography
EDS	Excessive daytime sleepiness
CBT	Cognitive behavioural therapy
APAP	Auto-titrating positive airway pressure
UPPP	Uvulopalatopharyngoplasty
LAUP	Uvulopalatoplasty
TRD	Tongue retaining device
MRI	Magnetic resonance imaging
TMJ	Temporomandibular joint
AMP	Anterior mandibular positioner
ENT	Ear, Nose and Throat
USM	Universiti Sains Malaysia
AMDI	Advanced Medical and Dental Institute

**KEBERKESANAN APLIAS ORAL BERBANDING TEKANAN UDARA
POSITIF BERTERUSAN DALAM RAWATAN APNEA TIDUR
OBSTRUCTIF: PENYELIDIKAN KLINIKAL RAWAK**

ABSTRAK

Satu kajian klinikal rawak berbentuk selari telah dijalankan di Institut Perubatan & Pergigian Termaju (IPPT) Universiti Sains Malaysia (USM) untuk menentukan keberkesanan aplians oral (OA) berbanding dengan tekanan udara positif berterusan (CPAP) dalam rawatan apnoea tidur obstruktif. Pesakit yang dirujuk dari Klinik Telinga, Hidung & Tekak telah disaring untuk kelayakan menyertai kajian. Selepas mengambilkira semua kriteria kemasukan dan pengecualian, seramai 40 orang pesakit telah diambil dan dibahagikan secara rawak kepada dua kumpulan rawatan; 19 orang pesakit dalam kumpulan CPAP dan 21 pesakit dalam kumpulan OA. Namun, seorang orang pesakit daripada setiap kumpulan tidak meneruskan kajian, menjadikan jumlah keseluruhan peserta kajian seramai hanya 38 orang, 18 orang pesakit dalam kumpulan CPAP dan 20 pesakit dalam kumpulan OA. Ujikaji telah mengambil masa selama sebulan yang mana Indeks Apnoea/Hypopnea, ketepuan oksigen nokturnal minima (MinO₂) dan ketepuan oksigen purata (MeanO₂) telah direkodkan sebelum dan selepas rawatan bagi kedua-dua kumpulan pesakit dengan menggunakan polisomnografi sepanjang malam. Skala Mengantuk Epworth (ESS) dan Indeks Kualiti Kehidupan Apnoea Tidur Calgary (SAQLI) versi Bahasa Melayu telah diberikan kepada pesakit sebelum dan selepas rawatan, masing-masing untuk menilai perubahan-perubahan dari segi

rasa mengantuk pesakit pada siang hari serta kualiti kehidupan yang berhubungkait dengan kesihatan. Selepas ujikaji, perubahan signifikan telah dapat dilihat pada skor purata ESS ($P=0.022$), AHI ($P<0.001$), MinO₂ ($P=0.008$) dan MeanO₂ ($P=0.003$) selesai rawatan menggunakan CPAP tetapi tiada perubahan signifikan didapati pada skor SAQLI. Selepas rawatan menggunakan OA, perubahan signifikan pada purata skor ESS ($P=0.002$), AHI ($P<0.001$), MinO₂ ($P=0.019$) dan skor SAQLI ($P=0.044$) telah didapati. Bagaimanapun, tiada perbezaan signifikan pada MeanO₂. Selepas kajian, tiada perbezaan signifikan dilihat pada semua parameter yang dinilai antara pesakit dirawat dengan OA dan pesakit dirawat dengan CPAP. Pesakit-pesakit di dalam kumpulan OA telah menunjukkan penerimaan dan toleransi yang lebih terhadap kesan sampingan yang berkait dengan penggunaan OA sebagai suatu kaedah rawatan berbanding dengan pesakit-pesakit di dalam kumpulan CPAP. Kesimpulannya, walaupun CPAP kekal sebagai piawaian emas dalam rawatan OSA namun OA merupakan satu kaedah rawatan yang berkesan untuk mengurangkan AHI dan rasa mengantuk pada siang hari serta menambahbaik MinO₂ dan kualiti kehidupan yang berkait dengan kesihatan bagi pesakit yang menderita OSA ringan sehingga peringkat teruk. Dalam kajian ini, keberkesanan OA didapati setara dengan CPAP dalam merawat OSA.

**THE EFFECTIVENESS OF ORAL APPLIANCE IN COMPARISON
WITH CONTINUOUS POSITIVE AIRWAY PRESSURE IN THE
TREATMENT OF OBSTRUCTIVE SLEEP APNOEA: A RANDOMISED
CLINICAL TRIAL**

ABSTRACT

A parallel design randomised controlled trial was conducted at the Advanced Medical and Dental Institute (AMDI) Universiti Sains Malaysia (USM) to determine the effectiveness of oral appliances (OA) in comparison to the continuous positive airway pressure (CPAP) in the treatment of obstructive sleep apnoea. Patients referred from the Ear, Nose and Throat clinic were screened for eligibility to participate in the trial. After considering all the inclusion and exclusion criteria, 40 patients were recruited and were randomised by an online randomization software available on (www.randomization.com) which was used to produce a randomization plan. This trial was blinded and patients were randomised into two groups by a nurse opening a sealed envelope that had been prepared earlier by the researcher which contained either the letter A or B. As a result 19 patients in the CPAP group and 21 patients in the OA group were recruited. However, 1 patient from each group did not continue the trial, leaving only 38 study participants in total, 18 patients in the CPAP group and 20 patients in the OA group. The trial period was one month. Apnoea/Hypopnea index (AHI), minimum nocturnal oxygen saturation (MinO₂) and mean oxygen saturation (MeanO₂) were recorded before and after treatment for patients in both groups by overnight polysomnography. Epworth Sleepiness Scale

(ESS) and the Malay version of Calgary Sleep Apnoea Quality of Life Index (SAQLI) were given to the patients before and after treatment to assess the changes in patient's daytime sleepiness and health-related quality of life respectively. After the trial significant changes were observed in mean ESS score ($P=0.022$), AHI ($P<0.001$), MinO₂ ($P=0.008$) and MeanO₂ ($P=0.003$) following treatment with CPAP but no significant changes in the SAQLI score. After the treatment with OA, significant changes in mean ESS score ($P=0.002$), AHI ($P<0.001$), MinO₂ ($P=0.019$) and the SAQLI score ($P=0.044$) were observed. However the MeanO₂ was not significantly different. After the trial, no significant differences were seen in all the parameters measured between patients treated with OA and patients treated with CPAP. Patients in the OA group had shown more acceptance and more tolerance to the side effects associated with the use of OA as a means of treatment compared to patient in the CPAP group. In conclusion, even though CPAP remains the gold standard for the treatment of OSA but OA is an effective means of treatment to reduce AHI and day time sleepiness as well as improving MinO₂ and health-related quality of life for patients who are suffering from mild to severe OSA. In this study, OA was found to be as effective as CPAP in treating OSA.

CHAPTER 1

INTRODUCTION

1.1 Background

The definition of obstructive sleep apnoea (OSA) is a cessation of air flow for 10 seconds or more. On the other hand the definition of obstructive hypopnea is the reduction of 50% in air flow. The number of apnoea events per hour during sleep (AI = apnoea index) as well as the number of apnoea/hypopnea events per hour during sleep (AHI = apnoea hypopnea index) are recorded in an overnight sleep study.

Obstructive sleep apnoea (OSA) is a widespread chronic condition affecting 3 to 7% of the population (Bixler et al., 2001; Bixler et al., 1998; Young et al., 1993; Bearpark et al., 1995). Patients with OSA suffer from continuous complete or partial collapse of the upper airway during sleep, which causes sleep fragmentation and oxygen desaturation (Cistulli and Sullivan, 1993). Previous study reported that OSA is significantly prevalent in many of the developing as well as industrialised countries (Punjabi, 2008). Studies done by Young et al. (1997) and Davey (2003) suggested that the majority of patients (about 80-90 %) suffering from OSA remain undiagnosed due to the lack of awareness among the patients and the doctors. Many studies had shown that OSA if untreated can cause several cardiovascular complications such as hypertension as reported by Peppard et al. (2000), stroke, congestive heart failure and arterial fibrillation as reported by Shahar et al. (2001) and Ng et al. (2005).

There are three kinds of sleep apnoea: obstructive, central, and mixed central apnoea which is defined as a lack of airflow accompanied by a cessation of respiratory effort. Obstructive sleep apnoea OSA is by far the most common kind of apnoea documented. OSA occurs at sleep with periods of cessation of breathing, despite the presence of the inspiratory effort. This results in clinically obvious symptoms, such as sleep fragmentation, poor quality of sleep and sleepiness. This clinical manifestation was termed obstructive sleep apnoea syndrome (OSAS). It is not a new condition, but the true health risks have been identified only recently. Mixed apnoea has both central and obstructive component of sleep apnoea.

Conservative treatment of OSA involves behaviour modification including weight loss, exercise, sleep posture and hygiene, alcohol avoidance and avoidance of certain medications. However specific treatment of OSA includes continuous positive airway pressure, oral appliances, and surgery. Nasal continuous positive airway pressure (CPAP) is the current gold standard treatment of choice. It is proven to be highly effective because it pneumatically splints the entire airway, regardless of regional pathophysiology (Montserrat et al., 2001). Unfortunately its hefty nature makes tolerance and compliance quite hard for many patients (Kribbs et al., 1993). This has led to research focusing on alternative treatment methods which are potentially as effective as CPAP, and well accepted. One example is oral appliance (OA) therapy, the most studied of which is the mandibular advancement splint (MAS). Some of the advantages of the OA as compared to CPAP are that it is portable, easier to be used, cheaper, do not need any power source and patients often prefer to use it. Recent practice parameters suggests that they are indicated for

patients with mild to moderate OSA, or for patients with severe OSA who are unable to accept CPAP or refuse treatment with CPAP (Kushida et al., 2006).

Most of the previous studies suggested that it is more advisable to use OA in long term treatment of OSA due to patient's preference (Ferguson et al., 1996). It has also shown improvements in various polysomnographic indices, blood pressure, snoring, and sleepiness, neurocognitive functioning and quality of life. However, despite the growing evidence base for OA therapy, a number of limitations still exist and include: not being as effective overall as CPAP therapy, uncertainty about the effect of appliance design on treatment outcome and side effects, adherence to treatment, and potential long-term complications of treatment (Fritsch et al., 2001).

Hence the overall aim of this study is to investigate the effectiveness of OA in the treatment of OSA and to compare it with the standard treatment of OSA the CPAP which will be of great clinical relevance and also will contribute to further understanding of the mechanisms of OA in the treatment of OSA. The OA used in this study was custom made to each patient and its' design and function was inspired from the Twin Block functional appliance. Patients suffering from all grades of OSA severity (mild, moderate and severe) were included in the trial which was lacking in the previous studies comparing between the two means of treatment.

1.2 Objectives

1.2.1 General objectives

To compare the effectiveness of oral appliance (OA) in comparison to continuous positive airway pressure (CPAP) in treatment of obstructive sleep apnoea (OSA).

1.2.2 Specific objectives

1. To compare changes in excessive daytime sleepiness in OSA patients following treatment with OA and CPAP.
2. To compare changes in apnoea hypopnea index (AHI) in OSA patients following treatment with OA and CPAP.
3. To compare changes in minimum nocturnal arterial oxygen saturation in OSA patients following treatment with OA and CPAP.
4. To compare changes in mean nocturnal arterial oxygen saturation in OSA patients following treatment with OA and CPAP.
5. To compare changes in quality of life scores in OSA patients following treatment with OA and CPAP.

1.3 Research null hypothesis

There is no difference between the effectiveness of OA and CPAP in terms of:

- 1- Reducing the excessive daytime sleepiness in OSA patients.
- 2- Reducing the AHI in OSA patients.
- 3- Improving the minimum nocturnal arterial oxygen saturation in OSA patients.
- 4- Improving the mean nocturnal arterial oxygen saturation in OSA patients.
- 5- Improving the quality of life scores in OSA patients.

CHAPTER 2

Literature Review

2.1 Epidemiology (Prevalence)

OSA is a common disease with a prevalence of 4% among males and 2% among females. The prevalence of sleep disordered breathing (SDB) (defined as AHI ≥ 5 and without daytime sleepiness) is 9–28% among women and 17–26% for men (Young et al., 1993). OSA well known daytime symptoms are excessive daytime sleepiness (EDS), but other symptoms, such as low quality sleep, poor concentration, and fatigue are frequently reported (Littner et al., 2001). Despite its high prevalence, OSA often goes undiagnosed. For example, in the general population, according to an American investigation, the Wisconsin Sleep Cohort Study, about 82% of males and 93% of females suffering from moderate to severe OSA had not been clinically diagnosed (Young et al., 1997).

The occurrence of OSA is most common in the age group between 40 and 65 years, and males have a higher prevalence of sleep apnoea than females in all age groups, with the highest prevalence between 40 and 49 years (Telakivi et al., 1987; Young et al., 1993). Females have the highest prevalence between 50 and 60 years of age. The severity of OSA increases with age in both males and females, but males have a consistently higher AHI for each age group. According to a recent epidemiologic study, there is a linear correlation between AHI and females age, in both obese and non-obese females. In males, the effect of age on AHI is different:

their BMI interacted in such a way that in obese men, the AHI increased from age 20–40 years but remained stable after that (Gabbay and Lavie, 2012).

The incidence of OSA has been much less studied than the prevalence. A longitudinal cohort study in the US communities assessed the incidence rate on two occasions, which were 5 years apart. Over the 5-year period, the overall incidence of moderate to severe OSA, defined by an AHI > 15, was 11% in males and 5 % in females (Newman et al., 2005).

2.2 Pathogenesis

Sleep apnoea is a slowly progressive disorder (Young et al., 2002). The dilator muscles play a very important role to prevent the collapse of the pharyngeal airway which is the cause of almost all apnoea. The upper airway dilator muscles contract during each inspiration to stop the closure of the airway by suction and to insure the pharyngeal clearness. These muscles include the palatal muscles (levator veli, palatoglossus, and tensor veli palatine), supra-hyoid muscles (genioglossus, geniohyoid), infra hyoid muscles (sternohyoid, sternothyroid) and laryngeal muscles (cricothyroid and posterior cricoarytenoid) (Lee-Chiong et al., 2002). The activity of the upper airway dilator muscles is decreased during sleep, as well as a decrease in electromyogram (EMG) activity of genioglossus and tensor palatine, therefore predisposing to collapse of the pharyngeal airway (Tangel et al., 1991; Tangel et al., 1992; Pack et al., 2006).

When an individual sleeps the muscles tone in the whole body tends to decrease that includes the upper airway dilation muscles which tend to be in a state of relaxation. This will contribute in the narrowing of the upper way which will cause turbulent air flow and snoring vibration. In some individuals the upper airway dilator muscles relaxation may progress to cause a clinically significant airway narrowing or total collapse which will cause OSA (Douglas and Polo, 1994). Other changes in the upper airway can also occur either because of the snoring or the large swing in intraluminal pressure during sleep (Pack et al., 2006). Among these changes are denervation of soft palatal tissue and an inflammatory cell infiltration in both the mucosal and muscle layers in the upper airway (Friberg et al., 1998; Boyd et al., 2004). These secondary changes have led to the belief that OSA can be caused by untreated chronic snoring (Friberg et al., 1998).

2.3 Aetiological factors

Previous studies had mentioned age, gender, snoring and obesity to be the main risk factors causing OSA (Young et al., 2002). Other secondary factors that might play a role in the development of OSA are medication and alcohol, menopause, hereditary factors, ethnicity, smoking and anatomical abnormalities (Strohl and Redline, 1996).

2.3.1 Gender

Several previous studies have shown that males had significantly higher chances of developing OSA compared with females (Young et al., 1993). Anatomical differences between males and females are the possible reason. These differences are represented in the fact that males have more volume of fat in the pharyngeal walls, less genioglossal muscle activity, longer airway and higher pharyngeal resistance than females (Malhotra et al., 2002). A study by Ware et al. (2000) reported that the significant difference in prevalence of OSA between the male and female is most obvious in the age group between 40-60 years and there were almost no differences in the elderly. This might be caused by the fact that the female hormones helps to improve the stability of the upper airway (Popovic and White, 1998). Studies done by Ambrogetti et al. (1991) and Redline et al. (1994) suggested that the significant difference in prevalence might as well be caused by the reason that females usually do not report that they are suffering from snoring

2.3.2 Age

The majority of the previous studies done have shown that the risk of OSA increases with age (Grunstein et al., 1993; Young et al., 2002). Results from OSA studies done on individuals with the age of 65 or more had reported that older patients have about 13-62 higher risk of developing OSA compared to younger individuals (Sandberg and Delirium, 2000). But other studies have found that even though the prevalence of OSA increases with age younger individuals tend to be more aware of the importance of reporting snoring which is one of the main OSA

symptoms (Bixler et al., 1998; Lindberg et al., 1998). Studies investigating the relation between the type of OSA and age found that older individuals tend to have central apnoea in which the neuromuscular component plays a bigger role compared to younger individuals (Bixler et al., 1998).

2.3.3 Obesity

Almost all of the previous studies concluded that obesity is one of the main risk factors of OSA (Young et al., 1993; Sandberg and Delirium, 2000). An obese individual has more fat depositions in the pharyngeal walls which contribute to the narrowing of the upper airway which is a direct cause of OSA (Katz et al., 1990; Mortimore et al., 1998). The results from this study had shown that there was a significant difference in the neck circumference between individuals suffering from OSA and healthy individuals. The mean neck circumference was (43.7 cm) and (39.6 cm) respectively.

Results from this study and other studies such as Davies and Stradling (1990) has shown the importance of neck circumference as predictor of association with OSA. However, another study had suggested BMI to be a better predictor of association between OSA and obesity than the neck circumference (Grunstein et al., 1993).

A study by Young et al. (2002) reported that according to several uncontrolled dietary and surgical weight loss trials there was a significant relationship between the individuals' weight loss and the reduction of their AHI. Results from other controlled

trials reported about 47-60% reduction in AHI as a result of a weight loss of about 9-17% (Smith et al., 1985; Schwartz et al., 1991).

2.3.4 Snoring

Snoring might increase the risk of developing OSA either directly or indirectly. Some studies reported that snoring might cause pharyngeal narrowing by reducing the activity of the pharyngeal dilator muscles (Deegan and McNicholas, 1995). Snoring can also cause pharyngeal narrowing by vibration injury to the upper airway mucosa and/or the surrounding structures (Friberg, 1999). Snoring can also indirectly cause OSA as a marker of nasopharyngeal allergy.

2.3.5 Soft tissue abnormalities

Several studies had reported different soft tissue and anatomical abnormalities that might contribute in the development of the narrowing of the upper airway and eventually causing OSA (Hudgel, 1992; Deegan and McNicholas, 1995; Bassiri and Guilleminault, 2000). Among these abnormalities are the increase in the fat depositions in the lateral pharyngeal walls (Katz et al., 1990; Mortimore et al., 1998), enlarged tonsils and macroglossia (Schwab et al., 1995; Nelson and Hans, 1997), low hyoid bone position (Partinen et al., 1988; Sforza et al., 2000) and reduction in the length of the mandibular body and cranial base (Battagel and L'estrangé, 1996; Battagel et al., 1998). Results from one trial conducted on 240 OSA patients reported that the most anatomical abnormality associated with OSA is narrowing of the

airway by the lateral pharyngeal walls followed by enlarged tonsils, enlarged uvula and macroglossia (Schellenberg et al., 2000).

2.3.6 Ethnicity

Several studies had been conducted before to investigate the relationship between ethnicity and OSA among them is a study done by Redline et al. (1997) which suggested that the prevalence of OSA is higher in African-American compared to Caucasians. Another study done by Kripke et al. (1997) conducted home questionnaire and sleep studies on 355 individuals living in San Diego reported a significantly higher risk factor for individuals from (Hispanic, Black and others) 16.3% compared to White individuals 4.9%.

The relationship between ethnicity and the prevalence of snoring and other OSA main symptoms was investigated by a study conducted by Ng et al. (1998) in Singapore to compare between the three main races in Singaporean community. The results showed that Indians have the highest prevalence (10.9%) followed by Malays (8.1%) and Chinese (6.2%). The results from another study conducted in Malaysia on Malay security officers showed that there was a range of prevalence of the main symptoms of OSA with 45 out of 661 patients categorized in the high risk group for OSA (Hashim and Samsudin, 2014).

Another study conducted in New Zealand compared the OSA in two races Polynesian and White (Coltman et al., 2000). The result showed that Polynesian males have higher OSA prevalence which might be due to the fact that they have

larger and more prognathic mandibles, wider neck circumference and larger craniofacial skeleton than White individuals.

2.3.7 Hereditary factors

Several previous studies had studied the possible relationship between the hereditary factor and the prevalence of the OSA (Mathur and Douglas, 1995; Redline et al., 1995). These two studies were conducted on first degree relatives and the results were independent from other risk factors like gender, age and obesity. Results from these studies have reported there were a significant relationship between the hereditary factor and the prevalence of OSA based on both OSA symptoms and sleep study. They also suggested that the overall relationship is not strong enough to justify screening of family members who are symptom free.

2.3.8 Smoking

Strong relationship between smoking and OSA was found by several studies among them are studies suggesting that smoking induce pharyngeal inflammation which causes narrowing of the upper airway (Wetter et al., 1994; Kashyap et al., 2001). In a study, which focused on smoking, Wetter et al. (1994) also found that smoking significantly increase the risk of snoring (odds ratio = 2.3) as well as the occurrence of moderate to severe OSA (odds ratio = 4.4) OSA. A 10 years follow-up study conducted by Lindberg et al. (1998) reported that smoking might cause the development of snoring.

2.3.9 Menopause

Studies have shown that the females have a low prevalence of OSA before menopause and one of the factors that might be involved is the preventive role of the female hormones that keep the tone of the pharyngeal dilator muscle and contribute to its activity (Popovic and White, 1998; Krystal et al., 1998). Studies that link the increase in OSA prevalence with the postmenopausal females are little but there is a widespread belief that menopause is among the risk factors of OSA. Results from two population based epidemiological studies support the claim reporting 0.6% OSA prevalence in premenopausal females compared to 2.7% in postmenopausal females (Bixler et al., 2001; Young et al., 2003).

2.3.10 Medication and alcohol

Previously conducted studies have shown that sedative medications are among the risk factors that might cause respiratory depression and apnoea by decreasing the tone of the pharyngeal dilator muscles. Examples of these medications are antihistamines, benzodiazepines and morphine (Dolly and Block, 1982; Bresnitz et al., 1994). Even though there are studies reported that alcohol can increase nasal and pharyngeal resistance in awake individuals (Robinson et al., 1985), other studies shown that alcohol consumption right before sleeping may cause respiratory disturbance during sleep (Tsutsumi et al., 2000; Scanlan et al., 2000). Another study conducted by Aldrich et al. (1999) investigated the long-time alcohol consumption effect on developing OSA by performing sleep study on 188 alcoholic individuals

undergoing alcoholism treatment. Results from this study reported a prevalence of 17% in the 40-59 age group and 50% in the over 60 age group.

2.4 Symptoms

The major symptoms of OSA are snoring, excessive daytime sleepiness (EDS) and deficits in neuropsychological function (Greenberg et al., 1987), which adversely impact on quality of life. Other symptoms that are associated with OSA are hypertension, myocardial infarction, stroke (Shahar et al., 2001; Weiss et al., 2007), heart failure (Leung and Bradley, 2001); Shahar et al. (2001), arrhythmias (Harbison et al., 2000), difficult anaesthesia (Loadsman and Hillman, 2001), insulin resistance (Brooks et al., 1994) and clotting problems (Chin et al., 1998). Symptoms in OSA are usually multiple and variable, occurring both at night (during sleep) and during the day.

2.4.1 Symptoms during sleep & day time

The main symptoms that OSA patients suffers during sleep are heavy snoring, gasping for breath, nocturnal panic, chest discomfort, palpitations, disrupted sleep, night sweat, dry mouth, sore throat, gastro-oesophageal reflux and nocturnal diuresis. On the other hand symptoms that OSA patients suffer during daytime are excessive daytime sleepiness, morning headaches, erectile dysfunction, reduced concentration, memory disturbance, depression and impaired mood.

Overall, not all symptoms can be seen in one patient and symptoms are generally non-specific and can be confused and mixed with symptoms from other disorders like depression or hypothyroidism. Nevertheless, sleeping symptoms are more specific for OSA than daytime symptoms which tend to be caused by insufficient sleep even though not caused by OSA (Bassiri and Guilleminault, 2000). Daytime fatigue or sleepiness is the most common symptom in patients with OSA and may occur in both passive and active situations. Lack of snoring does not definitively exclude the diagnosis of OSA but practically all patients snore. Apnoea episodes are reported by almost three quarters of bed partners (Hoffstein et al., 1995), around half of OSA patients report restlessness and excessive sweating and one quarter reports a choking sensation that interrupts sleep (Kales et al., 1985).

2.5 Diagnosis

Full medical examination is always the first step in the way to correctly diagnose an individual to be suffering from OSA. Perfect history taking should be undertaken using questionnaires about the patient's habits such as sleeping habits, smoking, OSA symptoms that the patient might have and cardiovascular diseases. Height, weight, neck circumference and blood pressure should be measured and recorded. All these preliminary examinations are important but previous studies had suggested that the diagnosis of OSA cannot be confirmed from the patient history (Crocker et al., 1990; Viner et al., 1991), clinical examination (Viner et al., 1991) or observation during sleep (Haponik et al., 1984).

In order to confirm the diagnosis of OSA an overnight sleep study must be performed for each individual. In the past this study could only be conducted in the laboratory polysomnography. Recently, with the development of portable equipment that allows the patient to perform sleep study at home therefore, the sleep study has become easier than ever.

Obstructive events cause either cessation or reduction of airflow despite the presence of respiratory efforts and an over compensatory response by the autonomic nervous system (Kushida et al., 2005; Dempsey et al., 2010). This condition results in significant arterial hypoxemia and arousals from sleep. The diagnoses of OSA should take into consideration both the clinical symptoms and the polysomnographic data obtained from the sleep study. During sleep symptoms of OSA which include heavy snoring and airflow interruptions are usually reported by the bed partner (Kushida et al., 2005). The severity of OSA which is determined by AHI correlates poorly with the severity of daytime symptoms as reported by Kushida et al. (2005).

There is standardisation of the techniques of polysomnographic recording during sleep study which is used in the diagnosis of OSA (Iber et al., 2007). These techniques include recording of electroencephalography (EEG), electro-oculography (EOG), nasal and oral airflow, abdominal and chest movements, pulse oximetry, body position, electrocardiography (ECG), arousals and leg movements. AHI is an index that shows the number of the full and partial obstructive events that occur per hour during sleep. OSA severity is usually described as follows: mild with AHI range from 5-15, moderate with AHI range from 15-30 and severe when the AHI is over 30. The oxygen desaturation index (ODI) on the other hand shows the number of at least 4% drops in blood oxygen levels per hour during sleep. The arousal index

(ARI) shows the number of arousals from sleep per hour and is an indicator of sleep fragmentation (Kushida et al., 2005).

Total sleep time is an important variable because the diagnosis of OSA is based on an index value. Sleep recordings which is made by a portable recording system have to be based on the patient's individual experience of sleep compared with a more accurate measurement of the sleep time using laboratory polysomnography. However, Franklin and Svanborg (2000) conducted a study on 100 patients to evaluate the accuracy of individual sleeping time with a polysomnographic registration. They found that the mean AHI based on the individual sleep time did not show any significant difference compared with the mean AHI based on EEG recorded total sleep time.

2.6 Treatment

The best treatment of OSA differs from one patient to another with many factors influencing the choice of the right treatment that is suitable for each individual. These factors include the sleep study findings, the severity of the symptoms and the patient's motivation for treatment. The treatment method must be discussed with the patient and the sleep specialist to insure treatment success which will lead to improved sleep, daytime function and quality of life and will help to reduce medical complications of OSA.

2.6.1 Behavioural treatment

Behavioural treatment basically means the reduction of all the risk factors that may cause the development of OSA for instance smoking which can cause upper airway inflammation, obesity which causes more fat deposition around the neck and alcohol consumption particularly near bedtime. Each patient should be advised to follow a weight loss programme, stop smoking and alcohol consumption.

2.6.2 Positional therapy

The way the patient sleep may contribute in the occurrence of OSA. For instance sleeping in the lateral position might reduce OSA by reducing pressure on the airway (Isono et al., 2002; Srijithesh et al., 2014). Sleeping in the lateral position might also prevent the tongue from falling back and block the airway causing OSA.

It might be beneficial to try positional therapy with patients who are newly diagnosed with OSA before the decision of using other methods of treatment is taken. Some devices have been used to support OSA patients to remain sleeping in the lateral position. Other studies like Epstein et al. (2009) also recommended sleep positional therapy as an effective secondary treatment for patients with OSA.

2.6.3 Continuous Positive Airway Pressure (CPAP)

CPAP applied to the upper airway through a mask attached to the patient's face during sleep remains the gold standard treatment of choice. The advantages of treatment are still being shown but current evidence suggests improvements in sleepiness, neuropsychological performance and cardiovascular disease. Unfortunately acceptance and adherence remain a problem despite significant research in this area, and has led to the search for alternative treatments.

2.6.3(a) Mechanisms of CPAP Action

The mechanism of CPAP action is thought to be by forming a diffuse 'pneumatic splint' of the upper airway. Lung volume effects are also likely to be important since CPAP induced lung expansion has been shown to stimulate reflexes which increase upper airway tone (Series et al., 1990). It also cause a 'tracheal tug' which stiffens and stabilises the airway (Begle et al., 1990).

2.6.3(b) Indications for CPAP Treatment

A study published in Chest recommended that CPAP should be the treatment method of choice to all OSA patients who are symptomatic and suffering from the following: EDS, impaired cognition, mood disorders, insomnia, cardiovascular disease, or stroke with an AHI > 5 events/hour (Loube et al., 1999). It was recommended that all patients with an AHI $\geq$ 30 events/hour be treated with CPAP

regardless of whether they are symptomatic or not because of the increased risk of hypertension (Young et al., 1997). The American Academy of Sleep Medicine guidelines, however, are slightly different recommending patients with an apnoea index (AI) > 20 events/hour or an AHI > 30 events/hour should receive CPAP regardless of symptoms (Chesson Jr et al., 1997). Patients with EDS and either an AHI > 10 events/hour, or a respiratory arousal index of > 10 events/hour also should receive CPAP.

More recent practice parameters suggested by Kushida et al. (2006) concluded that CPAP is indicated for the treatment of all severities of OSA mild to severe because of its ability to improve EDS, lowering blood pressure in hypertensive patients and improving quality of life. Despite these practice parameters, treatment with CPAP has sometimes been regarded as controversial (Yim et al., 2007). Until recently, comparison studies have evaluated CPAP against conservative management or tablet placebo with varying results.

With the invention of 'sham' CPAP some clinical trials showed interesting results. For example, a multi-centre, randomised, placebo-controlled trial of asymptomatic patients with $AHI \geq 30$ events/hour showed no benefit with CPAP treatment after 6 weeks when compared with placebo i.e. sham CPAP (Barbé et al., 2001). At the other hand, patients with an AHI from 5-15 events/hour who complained of EDS, had improved individual sleepiness, cognition, feelings of depression, and quality of life when treated with CPAP versus an oral control plate (Engleman et al., 1999). Patients, however, preferred the oral placebo and it is in this grade of OSA severity that treatment alternatives are likely to have their role.

2.6.3(c) Advantages of CPAP Treatment

1-Daytime Sleepiness

Sleep fragmentation caused by OSA affects sleepiness, memory, learning and performance. CPAP has been shown to improve daytime sleepiness both subjectively and objectively (Gay et al., 2006). Studies has also suggested that missing one night of CPAP reverses almost all of the previous improvements in alertness and sleepiness (Kribbs et al., 1993).

2-Quality of Life

Quality of life studies have compared the impact of CPAP relative to placebo (Barnes et al., 2002; Engleman et al., 2002; Profant et al., 2003), conservative treatment (Redline et al., 1998; Ballester et al., 1999; Monasterio et al., 2001) or positional therapy (Jokic et al., 1999). These studies have used generic and disease specific measures, with some demonstrating significant improvements and others not. One trial conducted on a 40 OSA patients suffering from heart failure randomised patients to either 3 months of CPAP treatment or a control placebo group. The patients treated with CPAP showed improvements in cardiovascular functions, quality of life and sympathetic activities (Mansfield et al., 2004).

2.6.3 (d) Acceptance and Adherence to CPAP

Although CPAP can be a very effective treatment in OSA, acceptance and adherence have been significant problems since the introduction of CPAP and remain a challenge to this day. Objective measurement studies of CPAP compliance show that only 46% of patients use CPAP for minimum of 4 hours/night for 70% of the week (Sanders et al., 1986), patients on average use CPAP for only 4.7 hours/night (Engleman et al., 1994) , and long-term studies show that 20% of patients stop CPAP all together (McArdle et al., 1999). Patients who are more likely to tolerate CPAP treatment including those with excessive daytime sleepiness (EDS) and severe hypoxaemia during sleep (Meurice et al., 1994), and those who underwent intensive educational/psychological intervention (Hoy et al., 1999; Hui et al., 2000). Patients who do not initiate the referral, those who live alone, those with a poor initial experience with CPAP, those with recent life events and those experiencing side effects (for example air leaks, nasal congestion) were found to adhere poorly to treatment (Sanders et al., 1986; Rolfe et al., 1991; Kribbs et al., 1993; Popescu et al., 2001).

A trial by Richards et al. (2007) randomised one hundred OSA patients into two 1 hour cognitive behavioural therapy (CBT) sessions or usual management. They found that CBT resulted in greater adherence of CPAP. Although the level of CPAP pressure does not seem to predict CPAP usage Douglas and Engleman (1998), many interventions have focused on delivering lower pressures. Auto-titrating (CPAP) machines deliver optimal pressures throughout the night recognizing that the amount of pressure needed can vary depending on sleep stage and body position. By

doing so, less pressure overall can be delivered, which may be more tolerable for the patient.

2.6.3(e) Side Effects of CPAP

As previously mentioned, adherence to CPAP relies upon the patient's initial experience with the device. Side effects such as rhinorrhoea, nasal congestion and dryness, poor mask fitting, air leaks and mouth leaks are common. Minimizing these side effects as early as possible is likely to improve adherence (Yim et al., 2007).

2.6.4 Surgery

Surgery for OSA started before the development of CPAP and oral appliances. Patients often prefer such procedures because they want a permanent 'cure' rather than temporary relief. Unfortunately treatment outcomes are mixed and often do not deliver the desired outcome. Common surgical procedures such as palatal surgery, uvulopalatopharyngoplasty (UPPP), adenotonsillectomy and mandibular advancement generally are about modification of the upper airway, although more recently, obesity surgery has been increasingly performed.