OROPHARYNGEAL EXERCISES AS ADJUNCT THERAPY TO THE MANAGEMENT OF OBSTRUCTIVE SLEEP APNEA

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LIST OF ABBREVIATIONS

AHI – Apnea-hypopnea index

BMI – Body mass index

CNS – Central nervous system

CPAP – Continuous positive airway pressure

ECG – Electrocardiogram

EEG – Electroencephalogram

EMG – Electromyogram

EOG – Electrooculogram

ESS – Epworth Sleepiness Scale

IBM – International Business Machines

ICU – Intensive care unit

IQR – Interquartile range

ORL-HNS – Otorhinolaryngology-Head and Neck Surgery

OSA – Obstructive sleep apnea

PSG – Polysomnography

REM – Rapid eye movement

SD – Standard deviation

SpO_2 – Peripheral capillary oxygen saturation

SPSS – Statistical package for the social sciences

TSS – Thornton Snoring Scale

UARS – Upper airway resistance syndrome

WHO – World Health Organization

ABSTRAK (Bahasa Malaysia)

Pengenalan

Obstructive sleep apnea (OSA) ataupun sindrom obstruksi apnea tidur ialah keadaan di mana saluran pernafasan tertutup semasa tidur. OSA boleh dirawat dengan penjagaan berat badan secara diet dan senaman, pengunaan alat ortodontik atau mesin alat bantuan pernafasan seperti 'continuous positive airway pressure' (CPAP). OSA boleh dirawat dengan pembedahan seperti adenotonsilektomi, tetapi keputusan pembedahan hanyalah 50% walaupun dengan pengunaan lebih daripada satu teknik bedah. Disebabkan oleh kesukaran untuk mendapatkan berat badan yang unggul, masalah kewangan untuk pembelian mesin CPAP dan risiko tinggi untuk pembedahan, pesakit boleh diberi pilihan untuk senaman tekak. Senaman tekak merangkumi 4 senaman lidah, 1 senaman lelangit dan 5 senaman untuk otot-otot muka selama 3 bulan. Senaman tekak ini akan menguatkan otot-otot rongga kerongkong yang tertutup semasa tidur.

Objektif

Untuk mengenal pasti keberkesanan senaman tekak sebagai rawatan alternatif atau tambahan kepada masalah OSA.

Metodologi

Ujikaji klinikal rambang terkawal akan dibuat ke atas pesakit OSA yang berumur 18 hingga 80 tahun yang menjalani rawatan di Hospital Sultan Abdul Halim, Sungai Petani, Kedah dari Mac 2016 sehingga Febuari 2017.

Lima puluh pesakit OSA yang bersetuju dan sesuai akan dibahagikan secara rambang kepada kumpulan terapi dan kumpulan kawalan. Kumpulan terapi akan diajar senaman tekak manakala kumpulan kawalan akan diajar senaman bernafas. Selepas 3 bulan melakukan senaman sebanyak 3 kali setiap hari, pesakit akan dikaji semula berdasarkan Epworth Sleepiness Scale, Thornton Snoring Scale, endoskopi fleksibel dengan Muller's maneuver dan ujian tidur.

Keputusan

Dalam kumpulan kawalan, tiada perbezaan ketara yang disaksikan selepas 3 bulan senaman pernafasan. Kumpulan terapi yang melakukan senaman tekak pulak menunjukkan penurunan yang mendadak dalam Epworth Sleepiness Scale dan Thornton Snoring Scale ($p = 0.001$ dan $p < 0.001$). Terdapat perubahan dalam gred Mallampti ($p = 0.030$). Endoskopi fleksibel dengan maneuver Muller menunjukkan pengurangan peratusan tutup semasa tidur di belakang lelangit ($p = 0.022$). Indeks apnea-hypopnea (AHI) turun secara ketara ($p < 0.001$).

Kesimpulan

Senaman tekak berjaya mengurangkan masalah berdengkur dan mengantuk berdasarkan pengurangan simptom melalui uji-selidik, keputusan ujian endoskopi fleksibel dan ujian tidur. Senaman tekak sesuai digunakan sebagai rawatan alternatif atau tambahan kepada penyakit OSA.

ABSTRACT (English)

Introduction

Obstructive sleep apnea (OSA) can be treated with weight reduction through diet and exercise, usage of intraoral lingual retainer and mandibular advancement device and continuous positive airway pressure (CPAP) machine. Most common operations such as adenotonsillectomy can reach only about 50% effectiveness. Due to the difficulty in losing substantial weight, financial factor in getting CPAP machine as well as high risk for operative procedures, there is a role for a more favorable alternative treatment such as oropharyngeal exercises. Oropharyngeal exercises consist of 4 tongue exercises, 1 soft palate exercise and 5 facial muscles exercises that will increase the tone of oropharyngeal and tongue muscles that collapse during sleep after 3 months of exercises.

Objectives

To determine the effectiveness of oropharyngeal exercises as an adjunct therapy in the management of OSA.

Methodology

A prospective randomized controlled trial study was carried out on age 18 to 80 years old patients with confirmed diagnosis of OSA through PSG in Hospital Sultan Abdul Halim, Sungai Petani, Kedah from March 2016 to February 2017.

Fifty consented OSA patients who fulfilled inclusion criteria were randomized into 2 groups, where therapy group of patients were taught oropharyngeal exercises while the control group were taught deep breathing exercises. After 3 months of 3 times daily exercises, patient will be

reassessed by repeat interview using Epworth Sleepiness Scale, Thornton Snoring scale, flexible scope with Muller's maneuver and subsequently repeat PSG with blinded sleep technician.

Result

There was no significant changes in control group of 25 patients. In the group that performed oropharyngeal exercises, there were significant reduction of Epworth Sleepiness Scale and Thornton Snoring Scale scored ($p = 0.001$ and $p < 0.001$) respectively. There was improvement in modified Mallampati grading ($p = 0.030$). Flexible endoscopy with Muller's maneuver also showed reduction of collapse over retropalatal level ($p = 0.022$). In PSG, the apnea-hypopnea index showed significant reduction ($p < 0.001$).

Conclusion

Oropharyngeal exercises significantly improve snoring, daytime somnolence and lifestyle based on subjective scoring from questionnaires and objective measurement through scope findings and PSG results. Oropharyngeal exercises can be used as an alternative or adjunct therapy in the management of OSA.

CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

1.1 Introduction

Obstructive sleep apnea (OSA) is a common sleep disorder that has high prevalence and wide spectrum of severity. This is especially true in the developed and developing countries. In Malaysia, OSA is affecting 8.8% male and 5.1% female population based on a study by Kamil et al. in 2007. OSA is characterized by repetitive upper airway obstruction leading to sleep fragmentation, cardiovascular stimulation and oxygen desaturation during sleep. These lead to symptoms such as snoring, unrefreshing sleep, excessive daytime sleepiness, increased risk of cardiovascular disease, hypertension and cerebrovascular disease (Banerjee, 2008). The objective method to diagnose OSA and to classify the severity of the symptoms is by polysomnography (PSG). Treatment can range from lifestyle modification to continuous positive airway pressure (CPAP) therapy, to surgical intervention or combination of these modalities.

1.2 Definitions of terms

According to Banerjee (2008), apnea is defined as cessation of airflow for more than 10 seconds while hypopnea is defined as at least 30% reduction in airflow for 10 seconds associated with a 4% decrease in saturation. Apnea usually indicates complete obstruction of the upper airway while hypopnea denotes a transient obstruction. OSA is defined by the presence of more than 5 episodes of apnea, hypopnea or both in 1 hour of sleep. OSA is classified based on the number of apneas and/or hypopneas per hour of sleep, known as the apnea-hypopnea index (AHI). Severity ranges from mild (AHI 5-15) to moderate (AHI 15-30) to severe (AHI>30).

1.3 Pathophysiology of OSA

Pathogenesis of airway obstruction in OSA patients is multifactorial. In a 2009, Guimaraes et al. proved that OSA is usually a combination of small/collapsible upper airway (anatomical factor) with reduction of upper airway muscle activity during sleep (neuromuscular factor). In a healthy awake person, the central nervous system (CNS) plays a role in keeping continuous neuromuscular activation of the pharyngeal muscles to maintain the patency of the upper airway. CNS activation is typically reduced during sleep hence compromising the patency. Pharyngeal narrowing can be periodic or non-periodic. Periodic obstruction causes apnea/hypopnea with interval of normal airflow while non-periodic obstruction produces sustained increase of airflow resistance with or without desaturation. Upper airway resistance syndrome (UARS) was first identified and described at Stanford University. The patients suffered from repetitive sleep disruption without real detection of desaturation by PSG. However, OSA symptoms such as unrefreshing sleep and daytime somnolence were still present in this group of patients.

The airway can be narrowed at multiple sites including nasal cavity, nasopharynx, velopharynx, oropharynx and hypopharynx. Based on Fujita classification, obstruction can take place at the level of soft palate (retropalatal), tongue (retrolingual) or both levels. In 2010, Valbuza et al. divided the pharyngeal muscles into 3 groups based on their role in maintaining airway patency. Group 1 muscles such as geniohyoid and sternohyoid will influence the hyoid bone position while genioglossus in Group 2 is synonymous with safety muscle of the tongue. Group 3 muscles include the tensor and levator palatini that elevate and tense up the soft palate.

Substantial narrowing of the upper airway will lead to poor ventilation. This in turn will promote hypoxia and hypercarbia. The presence of chemical stimuli due to imbalance in oxygen and carbon dioxide, will progressively trigger increase of respiratory efforts until arousal of the patient. This

vicious cycle repeat itself continuously throughout the night and if not discovered and intervened early, long term consequences will follow.

1.4 Clinical features of OSA

The symptoms for OSA can be classified into nocturnal symptoms, daytime symptoms and behavioral or personality changes (Table 1.1).

Table 1.1: Symptoms of OSA

Classification of symptoms	**Descriptions**
Common nocturnal symptoms	Snoring Witnessed apnea Nocturnal choking, snorting, gasping Restlessness Dry mouth, drooling Gastroesophageal reflux Diaphoresis Nocturia
Common daytime symptoms	Daytime sleepiness, fatigue Morning headache Impaired memory, concentration, dexterity
Personality changes	Irritability, aggressiveness Anxiety, depression Decrease libido, impotence

OSA is usually associated with high body mass index (BMI). However, OSA may also be found in normal body weight individuals due to less advantageous anatomical features such as retrognathia and narrow maxilla. Other risky anatomical OSA features (Table 1.2).

Table 1.2: Anatomical findings in OSA patients

Anatomy	**Findings**
General appearance	Obesity – especially central obesity Large neck circumference
Nasal cavity Nasopharynx	Nasal septal deviation Large turbinates Adenoid hypertrophy
Oral cavity Oropharynx	Narrow mandible or maxilla Retrognathia Dental malooclusion Macroglossia Elongated uvula Low hanging soft palate Tonsillar hypertrophy

1.5 Complications of OSA

1.5.1 Hypertension

About 30% of middle aged men with hypertension have OSA. It was demonstrated that blood pressure and AHI has a direct correlation (Young et al., 1993). In year 2000, Lavie et al. reported that the risk of developing hypertension can be increased by 1.5 to 3 folds in patients that were

diagnosed to have OSA. Therefore, successful treatment for OSA patients usually lead to reduction in blood pressure.

1.5.2 Cardiac disorders

1.5.2.1 Ischemic heart disease

The increase of adrenergic tone and nocturnal hypoxemia resulting from obstructive apnea or hypopnea increased the risk of cardiac ischemia. There were correlations between OSA and coronary artery disease. It was shown that 57% of patients that were inadequately treated for OSA will develop ischemic heart disease over the course of 7 years (Lavie et al., 2000). Myocardial infarction takes place in the event of hypoxemia and this risk is further increased when combined with elevated heart rate and blood pressure.

1.5.2.2 Congestive heart failure

OSA may lead to development of left ventricular dysfunction by increasing its afterload. This is from the combined effects of elevations in blood pressure, negative intrathoracic pressure and activation of sympathetic nervous system through the influence of hypoxia and arousals from sleep (Naughton and Bradley, 1998). In the event of undiagnosed OSA, this pathophysiology will be continuous in a vicious cycle. OSA heightens the sympathetic activity in patients with congestive heart failure thus accelerating the process of cardiac disease.

1.5.2.3 Arrhythmia

When the cardiac conduction system is exposed to repeated ischemic attacks, there may be abnormalities seen in the conduction pattern. Most common rhythm seen with OSA are

bradycardia during the apnea phase followed by tachycardia at the end of apnea. In severely affected heart, other types of arrhythmia may be seen, including heart block, atrial fibrillation, flutter and premature ventricular contraction (Hersi, 2010).

1.5.3 Pulmonary disorders

Cor pulmonale is a classical feature of Pickwickian syndrome. Pulmonary hypertension is rarely observed in the absence of daytime hypoxemia and the severity of nocturnal events measured in AHI does not appear to be the determining factor of pulmonary hypertension. Earlier studies have reported a high prevalence of pulmonary hypertension in OSA patients, but this has not been confirmed until recently where most studies agree on prevalence of 15-20% (Kessler et al., 1996). OSA syndrome and chronic obstructive pulmonary disease are two diseases that often coexist within an individual. This coexistence is known as overlap syndrome and is the result of chance rather than a pathophysiological link. Overlap patients present sleep-disordered breathing associated to upper and lower airway obstruction and a reduction in respiratory drive. Carlos et al. (2008) demonstrated that the coexistence is approximately 10%.

1.5.4 Cerebrovascular disease

Cerebral perfusion is directly correlated with good blood flow. However, during apnea episode, there may be reduction of blood flow causing the brain perfusion to be compromised. In patients with snoring, an odd ratio of 3.2 for the occurrence of stroke has been reported. This figure is even higher in patients with snoring, witnessed apnea, daytime somnolence and obesity, with odd ratio of 8.0 (Palomäki, 1991).

1.5.5 Social disability

In a large epidemiological study comparing overweight subjects with OSA symptoms and asymptomatic overweight subjects, it was shown that the former group had poorer health status, lower economic income, impaired work performance, divorces and also psychiatric issues (Grunstein et al., 1993). Another study in 1996 by Ulfberg et al. demonstrated that snoring patients had difficulties with concentration, learning new tasks and performing monotonous tasks when compared with non-snorers. A more recent study regarding the cognitive function of OSA subjects showed deficit in attention, concentration, verbal, visuospatial memory, constructional and psychomotor abilities (Aloia et al., 2004). Therefore, other than the obvious health related complications, OSA does affect activities of daily living in a significant way too.

1.5.6 Road traffic accident

Untreated sleep apnea is a significant contributor to motor vehicle accidents, thus increasing unnecessary mortality rate among young, productive population. The mean crash-rate ratio associated with OSA is within the range of 1.21 to 4.89. Characteristics that may predict crash in drivers with OSA include BMI, AHI, oxygen saturation and possibly daytime sleepiness (Tregear et al., 2009).

1.6 Diagnosis of OSA

OSA is suspected in individuals that present with nocturnal and daytime symptoms such as snoring, gasping or choking during sleep, witnessed apnea, morning headache, mood changes and

daytime sleepiness. Less advantageous body features such as obesity, short neck, small chin, nasal and oropharyngeal obstruction are likely to be present in OSA patients. However, a confirmed diagnosis can only be made using PSG. Further description on PSG in 1.6.4.

1.6.1 Body mass index

The BMI is defined as the body mass (in kilogram) divided by the square of the body height (in meter) and is universally expressed in units of kg/m^2. WHO classifies BMI as shown in Table 1.3.

Table 1.3: Classification of BMI (WHO 2004)

Classification	**BMI (kg/m^2)**
Underweight	BMI < 18.5 kg/m^2
Normal range	BMI 18.5-24.9 kg/m^2
Overweight	BMI > 25.0-29.9 kg/m^2
Obese Class I	BMI 30.0-34.9 kg/m^2
Obese Class II	BMI 35.0-39.9 kg/m^2
Obese Class III	BMI > 40.0 kg/m^2

1.6.2 Modified Mallampati score, Friedman tongue position and tonsils grading

The modified Mallampati score is assessed based on visualization of the oropharynx. This is done by instructing the patient to open his mouth widely and to protrude his tongue. Friedman tongue position is an evaluation of the oropharynx too but without the tongue protrusion. It is found that

Friedman's assessment is more accurate in predicting the severity of OSA (Friedman et al., 2013). Oropharyngeal crowding can be evaluated as described in Table 1.4.

Table 1.4: Grading of Friedman tongue position

Grades	**Descriptions**
Grade I	Tonsils, pillars and soft palate are clearly visible.
Grade II	Uvula, pillars and upper poles are visible.
Grade III	Only part of the soft palate is visible. Tonsils, pillars and base of uvula cannot be seen.
Grade IV	Only hard palate is visible.

The size of tonsils especially in pediatric age group, plays a vital role in contribution to OSA and its management (Friedman et al., 2015). Evaluation can be made using Brodsky and Friedman scale as shown in Table 1.5.

Table 1.5: Grading of tonsils size

Grades	**Descriptions**
Grade 0	Tonsils in the tonsillar fossa.
Grade I	Tonsils occupy less the 25% of the oropharynx.
Grade II	Tonsils occupy from 25 to 50% of the oropharynx.
Grade III	Tonsils occupy between 50-75% of the oropharynx.
Grade IV	Tonsils occupy more than 75% of the oropharynx. When the oropharynx is completely obstructed, it is also known as kissing tonsils.

1.6.3 Questionnaires

1.6.3.1 Epworth Sleepiness Scale

Epworth Sleepiness Scale (ESS) is the most widely used questionnaire to assess excessive daytime somnolence after its introduction in 1991 by Johns as shown in Table 1.6.

Table 1.6: Epworth Sleepiness Scale

Situation Chance of Dozing or Sleeping	**Score**
1) Sitting and reading :	0 / 1 / 2 / 3
2) Watching TV :	0 / 1 / 2 / 3
3) Sitting inactive in a public place :	0 / 1 / 2 / 3
4) Being a passenger in a motor vehicle for an hour or more :	0 / 1 / 2 / 3
5) Lying down in the afternoon :	0 / 1 / 2 / 3
6) Sitting and talking to someone :	0 / 1 / 2 / 3
7) Sitting quietly after lunch (no alcohol) :	0 / 1 / 2 / 3
8) Stopped for a few minutes in traffic while driving :	0 / 1 / 2 / 3
0-10: Normal 11-14: Mild sleepiness 15-17: Moderate sleepiness 18 and above: Severe sleepiness Total Score :	_____/24

ESS is a self-administered, 8 items questionnaire to describe or estimate how the subjects doze off inadvertently when engaged in relatively relaxed and immobile activities involving low level of stimulation. This test does not require any instruments and it is quick, flexible and reproducible.

The subject will answer the ESS questionnaire by giving a score of 0, 1, 2 and 3 for each of the 8 situations above, based on subject's chance of dozing off.

However, the accuracy is subjective because it depends on the subject's own estimation.

1.6.3.2 Thornton Snoring Scale

Thornton Snoring Scale (TSS) is used to assess the quality of lifestyle when the subject has complaint of snoring. This scale is subjective because it depends on subject and partner's interpretation and the chronicity of snoring. It may be difficult to get accurate scoring when the bed partner do not accompany the subject during consultation with the doctors. TSS is a self-administered, 5 items questionnaire to describe the frequency and loudness of snoring and its effect on subject's quality of life as shown in Table 1.7. Any score above 5 indicates significant effect of snoring on subject's lifestyle.

Table 1.7: Thornton Snoring Scale

Details of Snoring (Thornton Snoring Scale). Snoring : Yes / No
Scoring 0 = Never 1 = Infrequently (1 night per week) 2 = Frequently (2-3 nights per week) 3 = Most of time (4 or more nights per week)
1. My snoring affects my relationship with my partner : 2. My snoring causes my partner to be irritable or tired : 3. My snoring requires us to sleep in separate rooms : 4. My snoring is loud : 5. My snoring affects people when I am sleeping away from home (i.e. hotel, camping, etc.) :
Total Score :
Score of 5 or greater indicates your snoring may be significantly affecting your quality of life.

1.6.4 Polysomnography

According to a 2009 guideline by Adult Obstructive Sleep Apnea Task Force of the American Academy of Sleep Medicine, the gold standard as an objective diagnosis of OSA is sleep study or also known as polysomnography. Multiple physiologic parameters are measured when the subject is asleep. It includes electroencephalography (EEG) to determine arousal from sleep, electrooculography (EOG) to detect rapid eye movement, electromyography (EMG) to detect limb movement, oxygen saturation, oral and nasal airflow, chest wall monitoring to detect respiratory

effort and electrocardiography (ECG) to monitor heart activity. There are 4 levels of PSG used for diagnosis of OSA (Table 1.8).

Table 1.8: Level of polysomnography

Type	Descriptions
Level 1	Full in lab sleep study with level 1 equipment and attended by sleep technician.
Level 2	Level 1 equipment but unattended.
Level 3	No EEG. 4 channels including airflow, oximetry, respiratory effort and body position. Unattended.
Level 4	No EEG. 1-3 channels with minimum of oximetry only. Unattended.

1.7 Treatment of OSA

A multi-dimensional approach is necessary in treating subjects with OSA. The treatment of OSA can be divided into non-surgical and surgical methods. Non-surgical methods include lifestyle modification, orthodontic devices and CPAP therapy. Surgical interventions are planned depending on the level of obstructions.

1.7.1 Lifestyle modification

Other that focusing on alleviating the obstruction in OSA, the risk factors for OSA must also be addressed. This include encouraging subjects to lose weight through diet and exercises, refrain from tobacco, alcohol, drugs and also to get enough sleep. Weight reduction is a good therapeutic option because 10% loss of weight may lead to reduction of up to 26% of AHI (Peppard et al., 2000). However, long term success rate is discouraging because a study demonstrated that only 11% of 216 overweight patients with OSA showed resolution after weight loss alone and only 3%

were able to maintain the new weight and remain symptom free on 3rd year follow up (Guilleminault, 2005).

1.7.2 Orthodontic treatment

OSA can also be treated using orthodontic devices prescribed by oromaxillofacial surgeons. These devices displace the jaw and tongue forward hence increasing the retrolingual space. Orthodontic treatment like intraoral lingual retainer and mandibular advancement device is indicated only to selected group of patients. These patients possess retrognathic features, not overweight with mild-moderate OSA and without severe oxyhemoglobin desaturations. Study in 2010 by Hultcrantz et al. showed poor success rate which is 50% while acceptance rate is only 25%. Such devices are not recommended in patients with central sleep apnea, severe OSA with significant desaturation and patients with temporomandibular joint disease.

1.7.3 Continuous Positive Airway Pressure therapy

CPAP therapy for OSA was popularized in the 1980s. Since then, CPAP has been regarded as the gold standard for OSA treatment. In cases of severe OSA, CPAP is the most established and effective treatment in elimination of snoring, reduction of daytime sleepiness and improving quality of life. The principal of CPAP include delivery of positive pressure air through nasal or facial mask, creating pneumatic splint which prevents the collapse of airway. Despite widely accepted and available, some subjects reject CPAP due to intolerance, non-compliance or common side effects that include mouth dryness, mask discomfort and irritation, skin abrasion, claustrophobic feeling, limited mobility, noisy device and even intolerance from bed partner. Due to the cost and other listed factors, non-compliance rate is deemed high, at 46% (Wolkove, 2008).

1.7.4 Surgical interventions

Surgery is usually reserved for patients with specific obstruction or with craniofacial abnormalities which aim at different level of obstructions as shown below in Table 1.9. Septoplasty, inferior turbinates reduction surgery and adenotonsillectomy are routinely done for OSA because deviated nasal septum and adenotonsillar hypertrophy constitute as commonest causes of obstruction. It is between 40-50% efficiency and most of the times more than one technique must be combined at the same surgery or in two different occasions to obtain a satisfactory outcome (Sher et al., 1996).

Table 1.9: Levels of obstruction and the proposed surgeries

Level of obstruction	**Proposed surgery**
Nasal cavity and nasopharynx	Septoplasty with turbinate reduction surgery (submucosal diathermy, trimming of inferior turbinate, turbinoplasty) Adenoidectomy
Oropharynx	Tonsillectomy Uvulopalatopharyngoplasty Base of tongue reduction
Multilevel	Mandibular osteotomy with genioglossus advancement Hyoid myotomy suspension Maxillormandibular advancement Tracheostomy

General complications of surgery include bleeding, infection and upper airway obstruction caused by surgical edema or hematoma. Patients should be monitored postoperatively in the intensive care unit (ICU) especially after prolonged, elaborated surgeries. If all the treatment modalities fail,

especially in morbid obesity patients with severe OSA and comorbidities, a tracheostomy can be considered as the final option.

1.8 Oropharyngeal exercises

Oropharyngeal exercises for the treatment of OSA were created in response to the variety of disadvantages including cost, possible risk and complications as well as inefficiency in both non-surgical and surgical methods. Any exercise that focus on strengthening the pharyngeal, tongue or facial muscles are considered oropharyngeal exercises. These exercises were designed to be simple to follow so that they can be emulated at home by patients. It can be prescribed to all OSA patients, regardless of severity of OSA, age, comorbid nor social background. As of today, there are no side effects or complications ever reported in available literatures.

In year 2000, Ojay and Ernst compared semi-professional singers and non-singer subjects. It showed significant lower score in both severity of snoring and daytime somnolence in singers' group. This pilot study involved 20 chronic snorers that agreed on 20 minutes daily singing for 3 months duration.

Some investigators also found that snoring were less common in singers and musicians that play wind instruments like didgeridoo, pipe or trumpet (Puhan et al., 2006). This study involved 25 patients with didgeridoo lessons and daily practice at home for 4 months. The reduction of AHI and less disturbance to bed partners were observed in this study. Author concluded that this result is attributed to stronger pharyngeal muscles that prevent upper airway collapse. Most researchers conclude that snoring is less seen in musically inclined individuals (both singers and musicians

that play wind instruments) due to the increase in airway dilatation and pharyngeal tonicity over years of practicing (Pai et al., 2008).

In Brazil, Guimaraes et al. (2009) taught oropharyngeal exercises to 16 adult patients with moderate OSA. In this study, the patients were taught exercises that involve the tongue, soft palate and the facial muscles. There are a total of 10 exercises, 4 exercises for tongue including brushing, sliding, sucking and contraction, 1 for soft palate that include pronunciation of vowel and 5 for facial muscles that include blowing, sucking and elevation of the angle of mouth. The exercises were done 30 minutes daily for 3 months. Despite no changes in BMI, Guimaraes et al. (2009) noticed reduction of snoring complaint and severity of OSA (measured in AHI) by 39%.

In a recent 2015 study, Ieto et al. demonstrated that oropharyngeal exercises were indeed useful as treatment for mild to moderate OSA subjects. This study showed significant reduction of snoring intensity in 19 patients that was prescribed with daily oropharyngeal exercises for 3 months compared to the control group that received sleeping with nasal dilator strips. There was no improvement in control group while the positive result for treatment group may be due to increased tone of pharyngeal and tongue muscles after oropharyngeal exercises.

1.9 Rationale of the study

Oropharyngeal exercises can be used as an alternative or adjunct therapy in the treatment of OSA. Oropharyngeal exercises are free to learn and has possibly higher rate of acceptance due to convenience and lower level of commitment.

Statistic showed that number of OSA patients are growing in this country and most are in between mild-moderate in severity. OSA is on the rise in developing countries and Malaysia happens to be

most affected in Southeast Asia. In Malaysia, 15.1% of adult population has BMI>30 and 15.2% has daytime hypersomnolence based on ESS (Kamil et al., 2007). Another community study in Malaysia with PSG in 279 high risk clinically OSA patients with mean BMI of 29.4 showed that 44.3% had AHI of 5 and 6.6% had AHI of 30 (Yusoff et al., 2010).

This study has not been done in Asia yet. Previously oropharyngeal exercises were taught in Brazil of South America and Egypt which was located in Middle East, Africa.

Hypothetically, oropharyngeal exercises will be more beneficial to Asians due to the anatomical disadvantage in Asians pertaining to OSA (Genta et al., 2008). This is due to the differences in anthropometric characteristics between Caucasian and Asian. The facial and neck structures including less prominent mandible, lower cheek bone, crowded posterior oropharynx and steeper thyromental plane in Asians (Lam et al., 2005). OSA correlation with BMI is different in different ethnicity and Asians are more predisposed to OSA than Caucasians despite being thinner in BMI. Caucasians are also found to have higher muscle-to-fat ratio compared to Asians. Asians tend to have central obesity, more fat over the abdomen, thorax and neck region. Therefore, Asians tend to have larger neck circumference in relation to the body.

In regard to potential risk, at the current moment, there is no concrete evidence for potential risks and side effects of oropharyngeal exercises based on literature reviews.

However, the potential benefit outweigh the almost non-existent risks. Guimaraes et al. (2009) noticed that oropharyngeal exercises' patients had reduction of snoring intensity and apnea episode on average of 39% while avoiding invasive surgery and CPAP usage.

CHAPTER 2: OBJECTIVES OF THE STUDY

2.1 General objective

To determine the effectiveness of oropharyngeal exercises as an adjunct therapy in the management of OSA

2.2 Specific objectives

1. To compare the Epworth Sleepiness Scale scores before and after commencement of oropharyngeal exercise in therapy and control group
2. To compare the results of polysomnography taken before and after commencement of oropharyngeal exercises in therapy and control group

CHAPTER 3: METHODOLOGY

3.1 Study design

This was a prospective, randomized, double-blind, placebo-controlled, parallel group, single-center trial to assess the efficacy and safety of oropharyngeal exercises as an adjunct therapy in the management of OSA.

This study was assessor-blinded as the PSG was performed by a blinded sleep technician. Randomized-controlled trial because the patients were randomized into therapy group and control group. Placebo-controlled because there was a control group that performed deep breathing exercises alongside therapy group that performed oropharyngeal exercises. The study was carried out in a single center, only in Hospital Sultan Abdul Halim.

3.2 Population and sample

Adults in Malaysia between the age of 18-80 that reside in in Sungai Petani district in the state of Kedah and attended ORL-HNS clinic in Hospital Sultan Abdul Halim. These subjects had OSA symptoms and were confirmed by objective measurement, the PSG.

3.3 Sampling frame

The subjects were obtained through convenience sampling from a list of patients under the follow up of ORL-HNS clinic in Hospital Sultan Abdul Halim, Sungai Petani, Kedah. The subjects that participated in this study have consented and fulfilled the inclusion criteria.

3.4 Inclusion criteria

1. All patients between the ages of 18-80 with symptoms such as snoring, gasping/choking during sleep, witnessed apnea, morning headache, mood changes and daytime sleepiness.
2. Confirmed diagnosis of OSA with polysomnography.

   Mild OSA (AHI of 5-15), moderate (AHI of 15-30) and severe OSA (AHI more than 30).

3.5 Exclusion criteria

1. Untreated craniofacial malformation.
2. Unoperated anatomical structure that cause obstruction like grade 3 tonsils or severe deviated nasal septum.
3. Patients who are on intraoral device for treatment of OSA because these patients have retrognatic and micrognatic features that will not improve with oropharyngeal exercises.
4. Medical comorbidities such as uncontrolled hypothyroidism, neuromuscular disease, decompensated heart and lung disease, history of recent cerebrovascular accident.
5. Any usage of illegal, recreational drugs or alcohol abuse.

3.6 Sample size

For Objective 1, sample size is calculated from the independent t-test formula.

$$n = \frac{2\sigma^2}{\Delta^2} (Z_\alpha + Z_\beta)^2$$

n = sample size

σ = SD of 4.8, cited from Effects of Oropharyngeal exercises on patients with moderate OSA by Kátia C. Guimaraes et al, University of Sao Paulo Brazil.

Zα = 1.96 (95% of confidence interval)

Zβ = 0.84 (refer to 80% power of study)

Δ = 4.2 (anticipated difference)

Sample size = 21 subjects

Assuming 20% of drop out, so minimum sample size is 21 + 4 = 25.

n = 25 subjects

For the 2nd objective, sample size is calculated using two mean calculation based on software by Power and Sample Size Calculations (version 3.12) SD cited from Effects of Oropharyngeal exercises on patients with moderate OSA by Kátia C. Guimaraes et al., University of Sao Paulo Brazil.

Level of significant (α)	: 0.05
Power of study	: 0.8
SD (σ)	: 5
Anticipated difference (δ)	: 4.5
Sample size ration between 2 groups (m)	: 1.0

Sample size = 20 subjects

Assuming 20% of drop out, so minimum sample size is 20 + 4 = 24

n = 24 subjects

Therefore, the final sample size was 25 in therapy group and 25 in control group.

3.7 Study protocol and ethics

Study protocol was initially proposed and reviewed in the ORL-HNS department of Universiti Sains Malaysia. Subsequently it was reviewed and approved by USM Research Ethics Committee (Human) after meeting on 17th January 2016 with the code of USM/JEPeM/15100401 (Appendix A).

This study was also reviewed and approved by Medical Research & Ethics Committee (MERC), Ministry of Health Malaysia after meeting on 8th September 2016 with the protocol number NMRR 16-1182-31610 (IIR) (Appendix B).

3.8 Recruitment, consent and instrumentations

All patients with symptoms that were suggestive of OSA who attended ORL-HNS clinic Hospital Sultan Abdul Halim underwent history taking and routine clinic assessment for OSA and then PSG to determine the severity of OSA: mild OSA (AHI of 5-15) or moderate OSA (AHI 15-30) or severe OSA (AHI more than 30).

For history taking, patients were interviewed regarding demographic data, past medical and surgical history, medication history and OSA symptoms according to the proforma (Appendix C). Patients were asked on the severity of daytime somnolence using ESS questionnaire. Patients and the sleeping partner were also asked regarding the intensity of snoring that may affect the quality of lifestyle using TSS questionnaire.

Clinical assessment consist measurement of height, weight and BMI. Clinical examination of nose, oropharyngeal including modified Mallampati, Friedman tongue position and neck assessment were documented. Routine flexible endoscopy with Muller's maneuver were performed by the investigators involved in this study. Muller's maneuver is a routine examination for all OSA patients to determine the level of obstruction. It involves passing of a lubricated flexible scope (Appendix D) with a diameter of 3.8 mm and length of 300 mm through the nostril to assess the patency of airway over the retropalatal and retrolingual levels during a reverse Valsalva maneuver, where patient attempt to inhale while keeping the mouth and nose closed.

Then proceed with a single night laboratory level 2 PSG (using level 1 equipment but without the presence of a sleep technician) in sleep lab, Ward K4, Hospital Sultan Abdul Halim (Appendix E). PSG was performed by a blinded sleep technician using Alice 6 LDE PSG machine from Philips Respironics. Leads and sensors were attached to the patient. These include the EEG, ECG, anterior tibial EMG, snoring sensor, nasal pressure cannula, thoracic belt, abdominal belt and pulse oximetry. Parameters that were measured include the sleep architecture and sleep stages, nasal flow (pressure), body position (limb movement), oximetry (SpO_2), respiratory effort in apnea/hypopnea and snore.

Upon confirmation of OSA with PSG, patient was screened for inclusion and exclusion criteria. Consent (Appendix F for Bahasa Malaysia and Appendix G for English language) to participate in the study was taken after the patient has been thoroughly explained regarding the study including its purpose, importance, benefit and possible risk and complication from it.