UNIVERSITI KEBANGSAAN MALAYSIA
The National University of Malaysia

Comparing A Conventional CPAP Airsense 10 VS Portable Air-Mini CPAP For Obstructive Sleep Apnea From Users' Perspective; A Cross – Over Study (CASPAM)

Research Identification No : FF-2024-303
Date of Document : Version 1st August 2024

Dr Fatin Syahirah Nahrowi

Principle Supervisor : Assoc Prof Dr Mohamed Faisal Abdul Hamid
Respiratory Unit, Faculty of Medicine UKM.

TABLE OF CONTENTS

LIST OF ABBREVIATION

1. **OBSTRUCTIVE SLEEP APNEA (OSA)**
2. **APNEA-HYPOPNEA INDEX (AHI)**
3. **POLYSOMNOGRAPHY (PSG)**
4. **CONTINOUS POSITIVE AIRWAY PRESSURE MACHINE (CPAP)**
5. **EPWORTH SLEEPINESS SCALE (ESS)**
6. **STOP QUESTIONNAIRE (SQ)**
7. **STOPBANG QUESTIONNAIRE (SBQ)**
8. **BERLIN QUESTIONNAIRE (BQ)**

CHAPTER 1

INTRODUCTION

1.1 INTRODUCTION / BACKGROUND RESEARCH.

Obstructive sleep apnea (OSA) has been one of the topmost global health problems. It is an underdiagnosed disease which have a huge burden on healthcare if left untreated. Almost 80-90% of adults are underdiagnosed of OSA [(1)].

Obesity primarily is one of the supreme risk factors for developing OSA. Globally, obesity cases have risen affecting almost two billion people. According to National Health and Morbidity Survey (NHMS) 2019, 1 in 2 adults in Malaysia were overweight or obese. Statistics showed, 54.7% are females, 63.9% are of Indian ethnicity and 60.9 % falls in the age group of 55-59 years old [(2)]. Report from World Obesity Atlas 2023 predicts that adult obesity will rise 4.7% annually from 2020 – 2035, while child obesity will increase by 5.3% per year over similar timeline [(3)]. Overweight individuals will have a significant economic impact on Malaysia's Gross Domestic Product (GDP) by 2035 by 2.8% which is estimated to be about RM 3.2 trillion [(3)].

Sequalae of OSA is divided into two (cardiovascular-metabolic effect and neurocognitive effect). This group of patients are at high risk of developing hypertension, insulin resistance, dyslipidemia which then leads to pulmonary hypertension and heart failure. More importantly, from the neurocognitive point of view, persistent sleep deprivation will lead to poor concentration, impaired memory, personality changes affecting overall self-performance which can lead to depression and compromising safety as they have higher risk of work-related accidents.

Therefore, in our study, we would like to educate our group of patients regarding risk factor and early diagnosis of OSA hence to offer the appropriate treatment. In this study, our patients will compare the difference in the usage of 2 types of continuous positive airway pressure machine (CPAP) as the mainstay treatment of OSA [(4)]. They will then determine the most accessible and preferred machine to ensure compliancy thus preventing the unwanted consequences of the disease.

CHAPTER 2

LITERATURE REVIEW

OSA is defined as a sleeping disorder in which the upper airway collapse which results in partial (hypopnea) or complete (apnea) breathing cessation [(5)]. An apneic episode may last at least 10 seconds during sleep. Most pauses last between 10 to 30 seconds but may persist a minute or longer [(5)]. This will lead to sudden desaturation with oxygen falling as much as 40 percent or more in severe cases [(5)]. In response to that, the body will try to compensate by partially being awakened to restore normal breathing. This cycle continues hundreds of times overnight resulting in poor quality of sleep and increases daytime sleepiness. People with OSA snores loudly and have period of silence when the airflow is reduced or blocked. They also make snoring or choking or gasping sounds when their airway reopens.

OSA occur in all age, but has its prevalence in between middle and older age group of male, and postmenopausal female. The risk prevalence of OSA in Asian population ranges between

4.98 % to 27.3% [5]. Multiple risk factors are known. These includes obese patients with BMI > 30kg/m^2, patients with large neck size, Down syndrome patients, patients with abnormalities of the bony and soft tissue structure of the head and neck, children with large tonsils or adenoid, and patients with acromegaly and hypothyroidism [5].

Symptoms of OSA are fatigue, daytime sleepiness, snoring, and drooling. They also complain of headache and tendency to fall asleep while driving or watching television. They are more likely to be involved in motor-vehicle accident [6]. The American Academy of Sleep Medicine reported that 46% of the people having at least mild sleep apnea, 34% have frequent snoring, 30% have insomnia symptoms and 25% reported to have excessive daytime sleepiness [7].

OSA leads to multiple major contributors of respiratory and heart diseases. Theoretically, OSA induces a chronic inflammatory state. It has been shown to stimulate white adipose tissue (WAT) leading to production of inflammatory mediators such as TNF- alpha, IL-6 and IL-8. Due to intermittent hypoxemia and recurrent hypercapnia, it stimulates the sympathetic activity, increases systemic inflammation and increases oxidative stress. It results in endothelial and metabolic dysfunction and increases the prevalence of hypertension and cardiovascular disease risk [8].

Shah et al assessed whether OSA increase risk of CV events. They found that despite controlling other CV risk such as diabetes, hypertension, alcohol and tobacco usage, OSA has increase the CV outcome risk [9].

The prospective sleep heart study (SHHS) was done to establish the association between OSA and incident coronary artery disease and heart failure. For the purpose of data collection and analysis regarding incident coronary disease, the first occurrence of myocardial infarction, coronary heart disease, death or revascularization were recorded. The rate of CHD was 20.1% per 1000 person – years of follow-up in men and 8.7% events per 1000 person-years of follow up in women. Event rates increased with severity of OSA in men [10].

OSA is a contributing factor for heart failure as well. Paulina et al. demonstrated of sleep breathing disorder was 81% in 316 patients, 30% of whom classified as Central sleep apnea and 70% as OSA [10]. Sympathetic activation is the triggering factor for heart failure to occur. Also, the high negative intrathoracic pressure exerted during inspiration through a narrow or occluded upper airway may increase pulmonary capillary fluid efflux contributing to interstitial edema. Increased sympathetic activity leads to increase angiotensin II release promoting aldosterone production. Aldosterone increases water and salt resorption and leads to increase intravascular volume. In return, worsening hypertension and heart failure.

Atrial fibrillation is the most common arrythmia linked with OSA. The prevalence is about 5% [10]. OSA trigger its onset and contributes to its persistence. The known effect of hypoxemia and hypercapnia leads to tachycardia and hypertension. It increases the myocardial demand despite the restricted supply during these episodes. It leads to myocardial injury, conduction abnormalities, prolonged sinus node recovery time and later on fibrosis which will promote the development of AF.

As of today, we have 4 tools to stratify the risk of developing OSA. Stop questionnaire (SQ), STOP-BANG questionnaire (SBQ), Epworth Sleepiness Scale (ESS) and Berlin Questionnaire (BQ) are the current questionnaires available in literature [11]. STOP questionnaire consist of four yes/no answer questions assessing snoring, tiredness, observed apneas and high blood pressure. While the BANG portion assess the clinically observed quantities, with yes/ no answer. These includes BMI > 35kg/m2, age > 50 years, neck circumference 40cm and male gender. Positive answer three out of eight indicates high risk for sleep apnea.

ESS assess the severity of daytime sleepiness in common daily situations based on eight administered questions with answer scoring from zero to three. A score of 11 or higher indicates excessive daytime sleepiness.

Berlin questionnaire is a set of questions consist of 11 questions focusing on three categories of apnea sign and symptoms: snoring, daytime sleepiness and obesity/ high blood pressure. 2 or more positive categories indicates high likelihood of OSA.

A meta-analysis found that the sensitivity and diagnostic odds ratio (DOR) of the SB were higher than BQ, SQ and ESS in detecting mild, moderate and severe OSA. However, the specificity of SBQ was lower compared to ESS. Hence the study concluded that SBQ was superior in detection of various severity of OSA in adults compared to others [(11)].

The diagnosis is established only after an overnight sleep study called polysomnogram (PSG) is conducted. It is a consented procedure with a minimum of 6 hours study.

OSA can be divided into 3 types which are mild, moderate and severe based on the PSG report. Mild is defined as Apnea-hypopnea index (AHI) 5-15. Moderate is diagnosed when AHI is 15 – 30, and severe OSA is known when AHI > 30 [(11)].

Treatment options includes non-surgical based or surgical based. Non-surgical based treatment advises for lifestyle modifications namely good dietary intake and weight reduction. Another lifestyle modification is targeting towards education of good sleeping hygiene such as avoiding daytime nap, fixed bedtime routine, avoiding alcohol, caffeine or heavy or spicy food prior bedtime and eliminating noises and lights [(12)]. Positional therapy is also recommended for mild OSA. Patients are advised to stay off the back and raise the head of the bed to reduce symptoms [(12)].

Most common management of moderate to severe OSA is the use of Positive airway pressure (PAP) device [(12)]. Its function is to hold the airway open by using air pressure that is introduce through the nasal mask or similar device [(12)]. The needed amount of pressure set on the device is determined by PSG result or automated technique setting within the device itself [(12)]. Most commonly used PAP device for moderate to severe OSA is the CPAP machine. This machine is proven to improve sleepiness, thus giving a better quality of life and most importantly is able to prevent the daunting consequences of persistent hypoxemia such as myocardial ischemia, stroke, arrythmias and heart failure.

In European Respiratory Journal publish in 1998, survey of 3225 patients treated with CPAP for at least 6 months of treatment in which > 80% have reported symptoms improvement. [(13)]

Meanwhile, according to British Cardiac Society by a study in October 2023, they reported impact of 12 weeks of CPAP usage and the clinical improvements in echocardiographic parameters of right ventricle. Improvement of Isovolumetric acceleration (IVA) by 0.5ms2 and tricuspid annular plane systolic excursion (TAPSE) value significantly improve after twelve weeks of CPAP by 2.05mm. [(14)]

Currently in Malaysia we have different companies offering different types of machines. The manufacturers are constantly improvising new technology in order to make the device more user friendly. Available options include conventional PAP machine with the newer smaller and portable machine such as AirMini.

According to research study by Brian W. Rotenberg, Claudio Vicini, Edward B Pang, and Kenny P Pang, adherence to CPAP has been a problem. In their review of 83 CPAP trials, the average patient in bed for 7 Hours across 83 closely supervised clinical trials was not using the machine in average of 32.9% of the night. This is a problematic percentage as multiple different RCTs have documented that a minimum level of 4H use of CPAP per night is required to gain benefit from it (14). Even though CPAP is the main gold standard treatment proposed,

however the real-world effectiveness of CPAP is low, with large number of patients abandoning the machine within one year of prescription (15)

Surgical therapy played an important role in surgically correctable obstructive lesion in upper airway among OSA patients. The type of surgical intervention is depending on the site and level of obstruction which may include nasal, palatal, oro-hypopharyngeal, maxillofacial, tracheostomy or hypoglossal nerve stimulation [12]. Surgical options are currently vast and may change from time to time according to the latest surgical advances and technology.

CHAPTER 3

RESEARCH OBJECTIVES

3.1 Objectives

3.1.1 Primary

1. To compare the overall satisfaction using Visual Analogue Score 100mm among moderate to severe OSA patients between two types CPAP machine – conventional Airsence 10and AirMini CPAP.

3.1.2 Secondary

1. To evaluate the efficacy between two CPAP machine (conventional Airsence 10and AirMini CPAP) in terms of AHI reduction.
2. To compare the average 95th centile pressure required using conventional Airsence 10and AirMini CPAP
3. To determine the correlation between the satisfaction score and reduction of AHI using Airsence 10and AirMini CPAP machine.
4. To compare the difference between conventional Airsence 10and AirMini CPAP in terms of:
   a) Air leak
   b) Comfort
   c) Compactness & portability
   d) Maintenance & configuration

Hypothesis

1) Patient's overall satisfaction is better using AirMini CPAP compared to AirSense CPAP machine.
2) There is no difference in terms of AHI reduction and average 95th centile pressure required between AirMini CPAP compared to AirSense CPAP machine.

3) There will be positive correlation between overall satisfaction and AHI reduction for AirMini CPAP compared to AirSense CPAP machine.
4) There is improvement in air leak, comfort, compactness and maintenance in AirMini CPAP machine compared to AirSense CPAP.

3.1 Significance of Research

Consequences of OSA is detrimental in multiple level. It reduces work performance and quality of life individually. It causes healthcare burden later as it significantly increases the CV, stroke and other metabolic risk. Globally the government is bound to spend more to treat the affected group of people.

This research will give a comparison in overall satisfaction among the OSA patients using both conventional AirSense CPAP machine and AirMini CPAP machine and hence will enhance the compliancy among user and minimise unwanted complications following OSA.

CHAPTER 4

RESEARCH METHODOLOGY

4.1 Type of Study

This is a prospective cross over trial study of group of patients with moderate to severe OSA based on the severity of the AHI.

4.2 Study Design

4.2.1 Period of Study

September 2024 until December 2026.

4.2.2 Study Setting

This study will be conducted for all moderate to severe OSA patients in Hospital Canselor Tuanku Muhriz (medical and non-medical department).

4.2.3 Sampling Population

This study will be conducted either to inpatient setting or outpatient setting clinic. Selection of patients will include patients with BMI > 30, Neck circumference > 17cm. Age group of patients will include those who are 20-65 years old. Both female or male patients may be selected.

4.2.4. Type of Sampling

Type of sampling method in this study is convenient type of sampling.

4.2.5 Inclusion criteria

- Aged ≥ 18 years.
- Patients diagnosed with moderate to severe OSA (based on AHI classification from sleep study performed).
- Patients who are able to understand and answer the questionnaire given.

4.2.6 Exclusion Criteria

- Patients who are unable to give consent to the study.
- Patients who have been diagnosed with OSA and already on CPAP machine.
- Patients who had underlying Obesity Hypoventilation Syndrome (OHS).
- Patients who had underlying co-morbidities that worsen apnea symptoms, such as congestive cardiac failure, active malignancy, narcolepsy, active alcohol or drug abuse, treatment-refractory dementia, psychotic illness and active use of drugs that disturb the sleep architecture (i.e hypnotics or stimulants of central nervous system).

4.2 Study Protocol and Data Acquisition

This is a cross over trial that includes patients with medium to high risk of OSA according to STOPBANG score. Once these group of patients are selected, consent will be taken from them to go through a scheduled sleep study. Diagnosis is established after AHI score is concluded from the polysomnographic study. Those who are diagnosed with moderate to high AHI score will be recruited in this study. All subjects will be given a CPAP trial using both AirSense and AirMini model for 7 days each device. Upon recruitment, the subject will be randomised using 1:1 block randomisation either to receive AIrsense CPAP machine or Airmini CPAP machine.

Those subjects that use AirSense CPAP machine first for 7 days will be given a set

of Questionnaire at the end of 7th day of the trial. Subsequently, they will be switch to use AirMini CPAP machine for another 7 days and the same set Questionnaire will be given on the 7th day of the trial. The type of the interface used will be based on subject's preferences, i.e., full face mask / nasal masak / nasal pillow, during the initial 1 – 2 days of CPAP trial. The same interface as per subject's preferences will be used throughout the CPAP trials for both AirSense as well as Airmini CPAP machine.

The Questionnaire given comprises of a 100mm Visual Analogue Score (VAS) for: 1) Overall satisfaction, 2) Air Leak, 3) Comfort, 4) Compactness & Portability, 5) Maintenance & Configuration. The data collected will be analyzed using SPSS Version 27.

4.3 Operational Term Definition

a) Air Leak

- For the purpose of this study, air leak is defined as the degree of the air that was noticed by the patients to be leak out via the interface (full face mask / nasal mask / nasal pillow) that was used during the CPAP trial for both types of CPAP machine.

b) Comfort

- For the purpose of this study, Comfort is defined as the ability of the patients to be able to fall asleep satisfactorily without interruptions while on the CPAP machine, and waking up in the morning feeling more refresh and energetic.

c) Compactness & Portability

- For the purpose of this study, Compactness & Portability is defined as the degree of assembling and operating the CPAP machine without any difficulties as well as the mobility of the machine in users' perspective.

d) Maintenance & Configuration

- For the purpose of this study, Maintenance & Configuration is defined as the feasibility to maintain the optimum state of the CPAP machine to serve its function accordingly. This includes cleaning the parts of the CPAP machine,

maintaining the humidifier and changing the filters.

4.4 Sample Size

This is a cross-sectional prospective study; hence the sample size calculation will be based on Machin et al. (2018) - *Machin, D., Campbell, M. J., Tan, S. B., & Tan, S. H. (2018). Sample Sizes for Clinical, Laboratory and Epidemiology Studies. doi:10.1002/9781118874905*

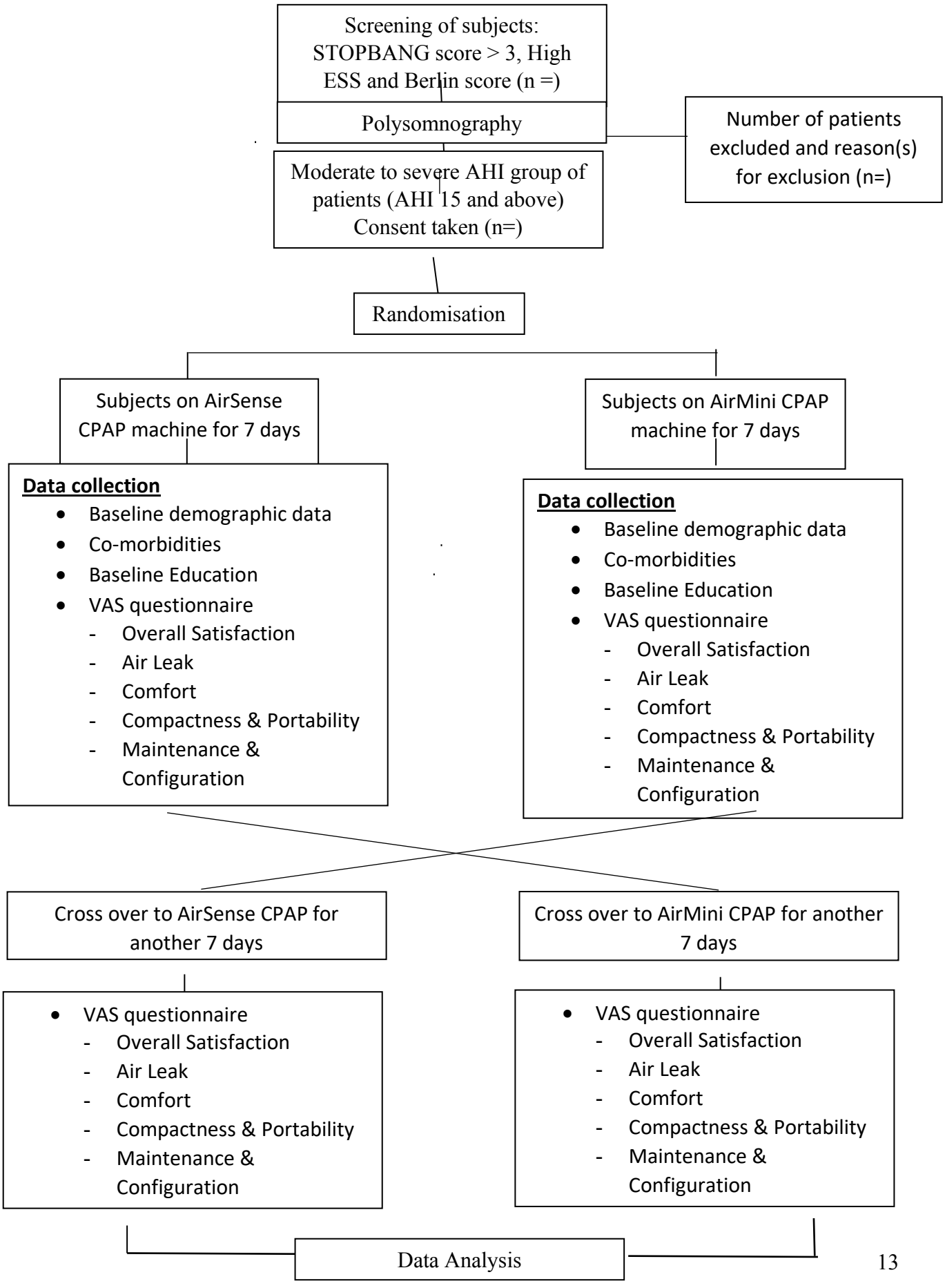
Table 16.2 Flat rule-of-thumb for the total sample size of a two equal-group comparative External-Pilot trial (partly based on Whitehead, Julious, Cooper and Campbell, 2015, Table 4).

Reference	N_{Pilot}
Birkett and Day (1994)	20
Julious (2005)	24
Kieser and Wassmer (1996)	20 to 40
Sim and Lewis (2011)	≥55
Browne (1995)	60*
Teare, Dimairo, Shephard, *et al* (2014)	≥ 70

*Actually recommended 30 for a single-arm study

The sample size decided for this study was 40 subjects. Considering and taking into account of about 10% dropout / missing data, hence the total sample size that will be recruited for this study are 50 subjects.

Data Collection Pathway



CHAPTER 5

RESEARCH ETHICS

Approval from the Research and Ethics Committee of Universiti Kebangsaan Malaysia Medical Centre (UKMMC) was done. All the collected information will be strictly confidential and only accessible by the research team members. All patients will be kept anonymous and coded into the data collection sheet.

Participants will only be recruited in this study once informed consent given, and will be allowed to withdraw from the study at any point. The research will be conducted according to the standard of good clinical practice and the rights and safety of the participants are guaranteed throughout the study.

CHAPTER 7

RESEARCH INFORMATION

INFORMATION SHEET FOR PATIENTS (ENGLISH VERSION)

Research title: Comparing Conventional CPAP vs Mini Portable CPAP for OSA treatment compliancy from users' perspective.

Researcher's name:

Dr Fatin Syahirah Nahrowi/ Associate Professor Dr Mohamed Faisal Abdul Hamid /
Dr Mas Fazlin binti Mohamad Jailaini / Dr Azat Azrai Dato' Azmel

Place of Conduct:

Hospital Canselor Tuanku Muhriz

Introduction:

Obstructive sleep apnoea (OSA) is an underdiagnosed disease that has fatal implication if left untreated. Risk of cardiovascular disease, stroke, heart failure and metabolic disease such as dyslipidaemia and diabetes has been connected to OSA. Concurrently it poses negative implication to patients' quality of life due to daytime sleepiness leading, easy fatiguability. depression and higher risk of accidents. Thereby this study will help to identify groups of patients with risk of OSA and offer comparison between two different machines as treatment of OSA. Our group of patients will be able to choose themselves the preferred type of machine. Thus, ensuring compliancy and prevent the listed unwanted side effects of the disease.

Purpose of study:

The main purpose of this study is to identify the group of patients with moderate to high risk of OSA. They will be educated regarding the disease. Each individual will then be investigated through sleep study to identify their AHI (Apnoea-hypopnea Index) level. Those who has AHI

level moderate to severe will have their self-test with two different CPAP machine. After the usage of these CPAP machine, you will be given a score sheet to compare their differences and your personal preference. In which after the study, we will then apply the needed appliance to necessary committee to help the patient purchase the machine for their own self use in the future.

Study conduct:

You will be given written consent to take part in this study. The data needed for this study will be documented and provided by ward staff and monitored directly under supervision of the doctor in charge.

Benefit:

Your participation in this study may assist physicians in future, to determine which CPAP machine has a higher preference. In the clinic, we will be able to help future patients to decide on the type of machine to be purchased.

Risk:

There is no additional risk to your health, and you do not have to pay any extra treatment cost while participating in this study.

Participation in this study is entirely voluntary. It is your choice to participate (or allow patients to participate). Regardless of your choice, the standard quality of care and treatment remain the same. All data obtained will be recorded and will be used for analysis.

Confidentiality:

Information collected during this study will be kept confidential. Access to the data is only by the research team and Research Ethic Committee of Hospital Canselor Tuanku Muhriz. No specific reference to any individuals will be reported in this study. Participants have the right to know the outcome of this study.

Reimbursements:

Participants do not have to pay additional cost in hospital bills. Participants will not be paid for participating in this study.

Right to Refuse or Withdraw:

This study is a voluntary basis, patients or his/her next of kin have the right to withdraw from this study. The choice is yours and all your rights will be respected.

Who to contact:

Dr Fatin Syahirah Nahrowi (+60192401448)

Respiratory Unit, Department of Internal Medicine, Universiti Kebangsaan Malaysia Medical Centre, UKMMC.

CHAPTER 8

INFORMED CONSENT FORM

I …… I/C NO: ……..

I have read and understood the 'Patient Information Sheet' attached to this 'Patient Consent Form'. Information regarding the reasons for the study, how it will be carried out and the inconveniences that are expected has been explained to me. I have been allowed to ask questions about this study and these questions have been answered to my satisfaction.

I understand that my participation in this study is voluntary and I can withdraw myself from this study at any point of time during the test. My treatment will be continued and will not be affected by my decision to not participate in this study.

I hereby allow the collected information to be analyzed in the computer and the information to be forwarded to the medical authorities, if necessary. I hereby consent to participate in this study

……
Signature / Thumbprint of patient
Name: …….
IC No: …….
Date: ……

……	……...
Signature / Thumbprint of witness	Signature of Doctor
Name: ……...	Name: …….
IC No: ……...	IC No: …….
Date: ……	Date: ……

GANTT CHART

Progression/Timeline	January 2023-March 2023	March 2023-July 2023	July 2023-August 2023	September 2023-September 2025	September 2025-November 2026
Literature review and proposal write up					
Proposal submission and correction					
Presentation to ethics committee and approval					
Patient recruitment and conduction of study					
Statistical analysis and preparation of result					
Manuscript writing and submission					

REFERENCES

References

1) *American academy of sleep clinical practice guideline (https://aasm.org/resources/factsheets/sleepapnea.pdf)*
2) *National health and morbidity survey (https://iptk.moh.gov.my/images_Booklet_NHMS_2019)*
3) *(http: // codeblue.galencentre.org/2023)*
4) *Malayisa e-cpg management of OSA (https: // www.moh.gov.my)*

5) *American academy of sleep clinical practice guideline (https://aasm.org/ resources/factsheets/sleepapnea.pdf)*
6) Abbasi A, Gupta SS, Sabharwal N, Meghrajani V, Sharma S, Kamholz S, Kupfer Y. A comprehensive review of obstructive sleep apnea. Sleep Science. 2021 Apr;14(2):142.*7) Otorhinolaryngology sleep service guidelines Ministry of Health Malaysia*
7) Ryan S, Taylor CT, McNicholas WT. Systemic inflammation: a key factor in the pathogenesis of cardiovascular complications in obstructive sleep apnoea syndrome?. Postgraduate medical journal. 2009 Dec;85(1010):693-8.
8) *Shah NA, Yaggi HK, Concato J, Mohsenin V. Obstructive sleep apnea as a risk factor for coronary events or cardiovascular death. Sleep and Breathing. 2010 Jun;14:131-6.*
9) Abbasi A, Gupta SS, Sabharwal N, Meghrajani V, Sharma S, Kamholz S, Kupfer Y. A comprehensive review of obstructive sleep apnea. Sleep Science. 2021 Apr;14(2):142.*7) Otorhinolaryngology sleep service guidelines Ministry of Health Malaysia*
10) *Malaysia e-cpg management of OSA (https: // www.moh.gov.my)*
11) *American academy of sleep clinical practice guideline (https://aasm.org/ resources/factsheets/sleepapnea.pdf)*
12) *Meslier N, Lebrun T, Grillier-Lanoir V, Rolland N, Henderick C, Sailly JC, Racineux JL. A French survey of 3,225 patients treated with CPAP for obstructive sleep apnoea: benefits, tolerance, compliance and quality of life. European Respiratory Journal. 1998 Jul 1;12(1):185-92.*
13) *Murphy G, King G, Coss P, Coyle M, McLaughlin AM, Murphy R. 56 Improvements of right ventricular function after intervention with CPAP in patients with obstructive sleep apnoea.*
14) *Rotenberg BW, Vicini C, Pang EB, Pang KP. Reconsidering first-line treatment for obstructive sleep apnea: a systematic review of the literature. Journal of Otolaryngology-Head & Neck Surgery. 2016 Jan;45(1):23.16)*
15) *Malayisa e-cpg management of OSA (https: // www.moh.gov.my)*