Comparing fixed and auto adjusting continuous positive airway pressure (CPAP) amongst symptomatic Obstructive Sleep Apnoea patients - A randomised controlled trial

Gan Wee Leng, MD, Andrea Ban Yu-Lin, MD, Mohamed Faisal Abdul Hamid, MBBS

Respiratory Unit, Department of Medicine, Universiti Kebangsaan Malaysia Medical Centre, Malaysia

ABSTRACT

Introduction: Continuous Positive Airway Pressure (CPAP) is required for obstructive sleep apnoea (OSA). Thisstudy compares the efficacy between Fixed Pressure CPAP (Fixed CPAP) and Auto-adjusting Pressure (APAP) based on Apnoea Hypopnoea Index (AHI), Epworth Sleepiness Score (ESS) among patients with symptomatic OSA and to ascertain their CPAP preference.

Methods: This is a prospective, randomised, crossover, single-blinded study conducted from February 2018 to February 2019 among adult subjects attending respiratory clinic Universiti Kebangsaan Malaysia Medical Centre (UKMMC).

Results: Forty-six subjects were recruited with 27 males (58.7%). The mean age was 54 (+11) year old. The baseline median Body Mass Index (BMI) was 34.2 kg/m² (Interquartile Range IQR: 30.8 kg/m² -41.7 kg/m²); baseline median AHI 28.8 /hour (IQR 21.2/hour-54.0/hour); andbaseline median ESS 15 (IQR 13-16).

After intervention, the median AHI was 5.0 / hour (IQR 4.2/hour-6.0/hour) at fixed CPAP arm; APAP arm was 5.5/ hour (IQR 4.2/hour-6.3/hour); p<0.01. The median ESS at fixed CPAP arm was 2 (IQR 0-3); APAP arm was 2 (IQR 1-3); p < 0.01. Those who preferred APAP were 22 subjects (47.8%) and had median optimal CPAP pressure 13.0 cmH_2O (IQR 12.0 cmH_2O -13.5 cmH_2O); 24 subjects (52.2%) who preferred Fixed CPAP had median optimal CPAP pressure 8.0 cmH_2O (IQR 6.3 cmH_2O -8.7 cmH_2O); p<0.01. Median baseline BMI was 37.6 kg/m² (IQR 30.8 kg/m² -43.0 kg/m²) for those who preferred APAP and 32.3 kg/m² (IQR 30.8 kg/m² - 38.4 kg/m²) for subjects preferred Fixed CPAP; p=0.03.

Discussion: Fixed CPAP maybe considered as first line therapy for symptomatic moderate and severe OSA with titrated optimal CPAP pressure less than 8 cmH2O and BMI less than 32.3 kg/m²; based on subjects' preference. Baseline AHI and average daily CPAP usage was not statisticallysignificant in affecting patient preference between fixed and auto adjusting CPAP. This is the first study of its kind conducted in Malaysia.

KEYWORDS:
Sleep Apnoea, Obstructive, Continuous Positive Airway Pressure, Mode Efficiency

INTRODUCTION

Obstructive Sleep Apnoea (OSA) is a major health burden. In Malaysia, the prevalence of OSA was estimated at 8.8% for male and 5.1% for female population.[1] Moderate to severe sleep apnoea is independently associated with increased risk of all-cause mortality.[2-5] Continuous Positive Airway Pressure (CPAP) machine therapy is the mainstay of treatment for OSA.[6] There are two modes of CPAP namely Fixed Pressure CPAP (Fixed CPAP) and Auto-Adjusting Pressure CPAP (APAP). Fixed CPAP delivers relative constant positive airway pressure throughout the respiration cycle.[7] On the other hand, the APAP delivers positive airway pressure that is dependent on respiratory event during sleep.[7] CPAP therapy improves the quality of life of sufferers and reduced all-cause mortality in symptomatic moderate to severe OSA.[4,8]

The cost of OSA treatment is substantial in Malaysia. The APAP costs Ringgit Malaysia (RM)6500-RM7500. The Fixed CPAP is relatively cheaper, costing RM4000-RM5000. CPAP machine for OSA is not covered by private medical insurance in Malaysia. Expensive treatment cost may influence patients' decisions to accept CPAP therapy in OSA.

Studies outside Malaysia have shown no difference in the efficacy between fixed CPAP and APAP for OSA.[9-11] However, there are no published data in Malaysia on the efficacy of fixed CPAP and APAP. Therefore, the objectives of our study were to evaluate the efficacy of fixed CPAP and APAP among Malaysian symptomatic OSA subjects based on Apnoea Hypopnoea Index (AHI) and Epworth Sleepiness Score (ESS) and ascertain their CPAP preference. We also looked at the key determining factors for CPAP mode device preference among recruited subjects.

MATERIALS AND METHODS

Study design

This is a prospective, randomised, crossover, single-blinded study conducted from February 2018 to February 2019 among adult subjects attending respiratory clinic Universiti Kebangsaan Malaysia Medical Centre (UKMMC), Malaysia. This study was approved by the UKM Research Ethics Committee, Ethic code: FF-2018-207. A flow chart of the study design is shown in Figure 1.

Study subjects

We included newly diagnosed symptomatic OSA subjects aged 18 years old to 70 years old, with ESS of more than

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Corresponding Author: Mohamed Faisal Abdul Hamid
Email: faisal.hamid@ppukm.ukm.edu.my

10/hour and sleep study AHI more than 5/hour. Subjects had no previous CPAP usage and willing to initiate long term CPAP therapy. We excluded subjects with the following comorbidities: congestive cardiac failure (CCF), severe chronic obstructive pulmonary disease with Forced Expiratory Volume in 1 second (FEV1) less than 50%, ischemic or haemorrhagic stroke, parkinsonism, neuromuscular diseases, psychiatry disorder, central sleep apnoea, craniofacial abnormalities and Pickwickian syndrome.

Sample Size

Sample size was calculated using Power and Sample Size Program (PS) version 2.1.31. Based on the reference journal Vennelle et al. with adjusted power of 80% and alpha error of 5% (p=0.05) the sample size calculated was 31.[9] To cover for 25 % drop out rate, a total sample size of 40 subjects was decided during the ethics committee meeting at UKMMC.

Procedure

A total of 50 subjects provided written consent for CPAP trial and data collection prior to enrolment into the study. Subjects were required to self-administer the validated ESS questionnaire according to their preferred language. Permission to use the validated ESS questionnaire from Mapi Research Trust France was granted. Subjects with ESS of more than 10 proceeded with sleep study. Those with high pre-test probability of moderate to severe OSA; Body Mass Index (BMI) more than 25 kg/m^2 and ESS more than 10 underwent type 3 limited sleep study at respiratory ward UKMMC. However, subjects needed to exclude other sleep breathing disorders underwent type 1 polysomnography at sleep laboratory UKMMC. Only subjects with AHI more than 5/hour were recruited.

The basic function of CPAP machine operation was explained to subjects who met the inclusion criteria and appropriate mask interface selected. Helpline provided to all subjects. They were given 3 to 5 days trial of CPAP under A-Flex mode at home to obtain the appropriate CPAP setting. Optimal pressure was taken as 95 percentiles of average CPAP pressure under A-Flex mode derived from CPAP machine memory card. Subjects were then randomised by using computer generated block of 4 randomisation by first author to either APAP (Labelled as CPAP A) or Fixed CPAP (Label as CPAP B) for 2 weeks respectively. Both groups received similar CPAP machine (Philips Respironics). Subjects were blinded to the mode of CPAP, as the CPAP screens were concealed. This was followed by 1 week of washout period. They were then crossed over to the next mode of CPAP for another 2 weeks. APAP was kept at between 4 cmH20 to 20 cm$H_2$0. The optimal pressure for fixed CPAP was derived from the 95 percentile of CPAP pressure under A-Flex mode. Subjects were followed up again at the end of respective mode of CPAP trial. Home visit was done for subjects who sought assistance via the helpline provided.

AHI and ESS changes were assessed at the end of the respective CPAP mode study. Upon completion of the study, subjects were asked for their preference between APAP and fixed CPAP machine therapy.

Statistical analysis

Statistical analysis was performed by using IBM SPSS, version 25. Demographic and baseline characteristic variables were analysed using descriptive analysis. Upon performing Shapiro Wilk normality test, baseline AHI and ESS were not normally distributed. Thus, AHI and ESS changes from baseline were analysed using Wilcoxon signed rank test, p-value less than 0.05 was considered statistically significant. Mann-Whitney test was used to compare the AHI and ESS changes between Fixed CPAP and APAP, p-value less than 0.05 was considered statistically significant. The subjects' optimal CPAP pressure, average duration of CPAP usage, baseline BMI and baseline AHI were not normally distributed. Thus, Mann-Whitney test was performed for patient CPAP mode preference in comparison with optimal CPAP pressure, average duration of CPAP usage, baseline BMI and baseline AHI. A p-value of less than 0.05 was considered statistically significant.

RESULTS

Of the 50 subjects recruited, 46 successfully completed the study. There were no complications reported during the washout period. Four subjects withdrew from the study due to shift work and frequent traveling which contributed to 8% dropout rate. Finally,34 subjects with high pre study probability of OSA without major comorbidities underwent limited sleep study (Type 3 sleep study) at respiratory ward of UKMMC. The remaining 12 subjects who needed to exclude other sleep breathing disorders had full polysomnography (Type 1 sleep study) Among the 46 subjects who completed the study, 27 (58.7%) were males and 19 (41.3%) were females. The study population consisted of 36 (78.3%) Malays, seven (15.2%) Chinese, two (4.3%) Indians and one (2.2%) Punjabi. The mean age was 54 (+11) years, baseline median BMI 34.2 kg/m^2 (IQR: 30.8 kg/m^2 -41.7 kg/m^2), baseline median AHI of 28.8 /hour (IQR 21.2/hour-54.0/hour), baseline median ESS of 15 (IQR 13-16) (Table I).

Efficacy Between Fixed CPAP and APAP

Both fixed CPAP and APAP showed significant clinical improvement of AHI and ESS from baseline by Wilcoxon signed rank test (Table II). However, Mann-Whitney test demonstrated the efficacy between fixed CPAP and APAP were statistically not significant (Table III).

Determining factors for CPAP mode device preference

Of the 46 subjects in this study, 22 (47.8%) preferred APAP and 24 (52.2%) subjects preferred fixed CPAP. Mann-Whitney test shown that baseline BMI and optimal CPAP pressure were the determining factors for CPAP mode device preference among symptomatic OSA subjects in this study. However, baseline AHI and average CPAP usage per day were statistically not significant to affect the CPAP mode device preference among the subjects (Table IV).

DISCUSSION

The subjects in this study were mostly in their middle ages with grade 2 obesity and moderate excessive daytime sleepiness.[12,13] They had moderate to severe symptomatic OSA.[14] The ethnic composition in this study represented Malaysian demography ratio.[15]

Table I: Baseline descriptive characteristics of subjects

Characteristic	Data
Mean age + (Standard deviation)	54 (+11) year old
Gender	
Male	27 subjects (58.7%)
Female	19 subjects (41.3%)
Ethnicity	
Malay	36 subjects (78.3%)
Chinese	7 subjects (15.2%)
Indian	2 subjects (4.3%)
Punjabi	1 subject (2.2%)
Median BMI	34.2 kg/m^2 (IQR: 30.8 kg/m^2 - 41.7 kg/m^2)
Median AHI	28.8 /hour (IQR 21.2/hour-54.0/hour)
Median Epworth Sleepiness Score	15 (IQR 13-16)

*BMI: Body mass index.
*AHI: Apnoea hypopnoea index
*IQR: Interquartile range

Table II: AHI and ESS improvement from baseline between fixed CPAP and APAP

Main parameter	Baseline Median (IQR) n=46	Fixed CPAP Median (IQR) n=46	APAP Median (IQR) n=46	p value[§]
AHI [Events/hour]	28.8 (21.2-54.0)	5.0 (4.2-6.0)	5.5 (4.2-6.3)	<0.01
ESS	15 (13-16)	2 (0-3)	2 (1-3)	<0.01

*AHI: Apnoea hypopnoea index
*ESS: Epworth sleepiness score
*Fixed CPAP: Fixed pressure CPAP
*APAP: Auto-adjusting pressure CPAP
*IQR: Interquartile range
[§] Wilcoxon signed rank test

Table III: Efficacy between fixed CPAP and APAP among symptomatic obstructive sleep apnoea

Main parameter	Fixed CPAP Median (IQR) n=46	APAP Median (IQR) n=46	p value[§]
AHI [Events/hour]	5.0 (4.2-6.0)	5.5 (4.2-6.3)	0.62
ESS	2 (0-3)	2 (1-3)	0.78

*AHI: Apnoea hypopnoea index
*ESS: Epworth sleepiness score
*Fixed CPAP: Fixed pressure CPAP
*APAP: Auto-adjusting pressure CPAP
*IQR: Interquartile range
[§] Mann-Whitney test

Table IV: Confounding factors for CPAP device mode preference among study subjects

Parameter	Preferred Fixed CPAP Median (IQR) N 24	Preferred APAP Median (IQR) N 22	p value[§]
Baseline BMI [kg/m^2]	32.3 (30.8-38.4)	37.6 (30.8-43.0)	0.03
Optimal CPAP pressure [cmH^{2}0]	8.0 (6.3-8.7)	13.0 (12.0-13.5)	<0.01
Baseline AHI [event/Hour]	33.4 (21.6-59.0)	25.6 (20.7-53.1)	0.63
Average daily CPAP usage [Hours: Minutes: Seconds]	5:19:26 (5:10:15-5:38:32)	5:20:16 (4:52:51-5:37:56)	0.60

*BMI: Body mass index
*AHI: Apnoea hypopnoea index
*Fixed CPAP: Fixed pressure CPAP
*APAP: Auto-adjusting pressure CPAP
*IQR: Interquartile range
[§] Mann-Whitney test

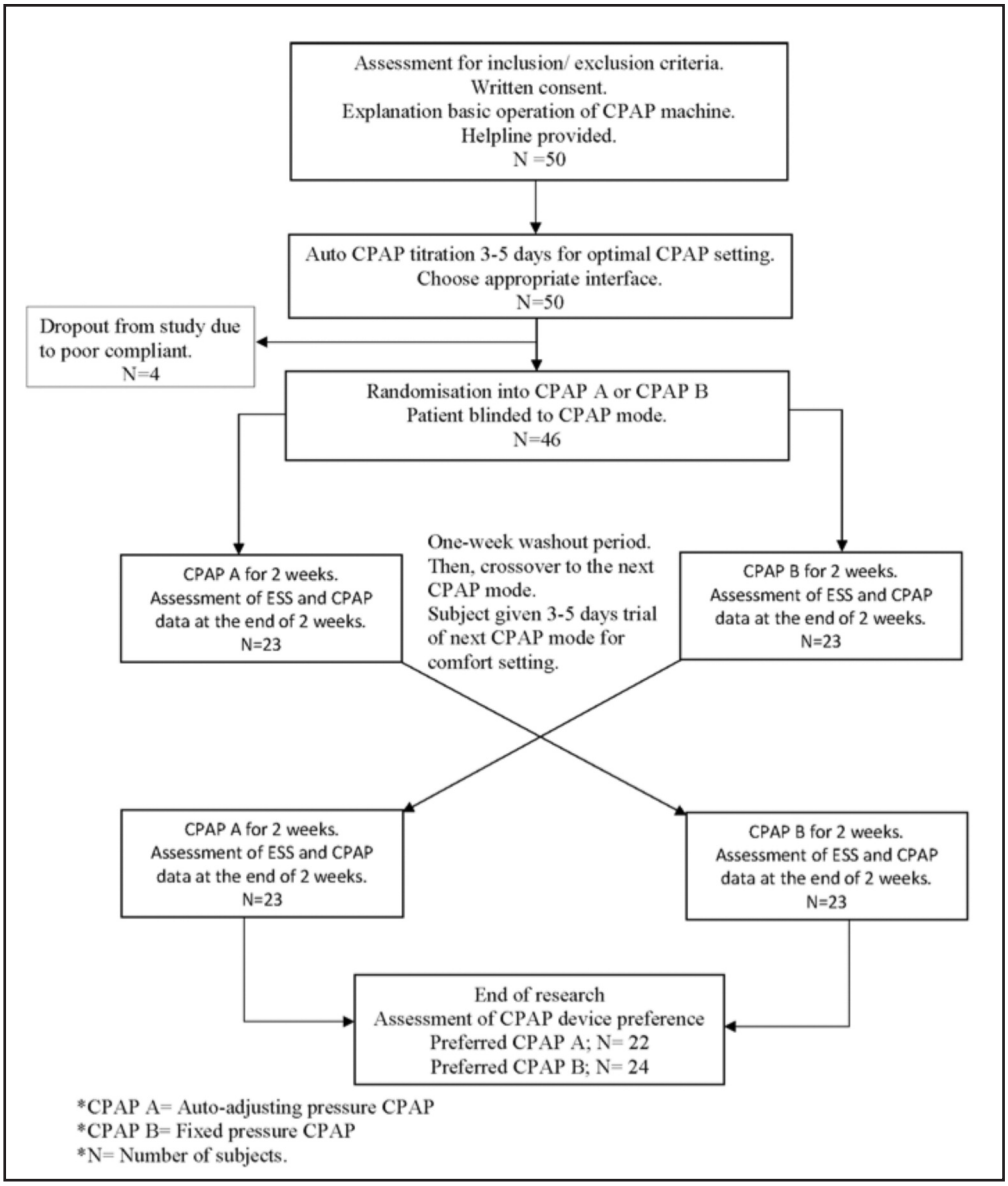

Fig. 1: Study flow chart.

In our study, 34 subjects with high pre study probability of OSA proceeded with limited sleep study (Level 3 study) at respiratory ward. However, 12 subjects who needed to exclude other sleep breathing disorders had full polysomnography at UKMMC sleep laboratory (Level 1 study). Following full polysomnography test, all these 12 subjects were diagnosed as OSA.

Our study has shown that both fixed CPAP and APAP had similar efficacy. In the fixed CPAP arm, the median AHI was 5.0 / hour (IQR 4.2/hour-6.0/hour) $p < 0.001$. In the APAP arm, the median AHI was 5.5/ hour (IQR 4.2/hour-6.3/hour) $p < 0.001$. The rate of AHI reduction between fixed CPAP and APAP (from baseline) were statistically not significant, p=0.616. Randerath et al. with almost similar study design and sample size support the outcome of our study where the AHI was obtained from polysomnography at the end of the respective mode of CPAP trial.[16] Due to our limited resources, the AHI was derived from the CPAP machine memory card at the end of the respective CPAP mode trial.

The ESS questionnaire is a simple and reliable method for measuring persistent daytime sleepiness in adults.[17] In this study, validated self-administered ESS questionnaire in English, Malay, Chinese and Tamil languages from France Mapi Research Trust were used. Both fixed CPAP and APAP demonstrated the same efficacy for improvement of ESS from baseline. The median ESS at fixed CPAP arm was 2 (IQR 0-3) and APAP arm was 2 (IQR 1-3) $p < 0.01$. Our findings show near similarity with a Hong Kong study by To et al.[11]

Contrary to our research, Noseda et al. reported that the mean ESS was significantly ($p < 0.01$) lower on APAP (5.1+ 2.8) than on fixed CPAP (6.1+ 2.8) with mean difference of 1.18 As no objective assessment of daytime vigilance was made with their small sample size, this small difference

should be interpreted with caution. Other studies, including Galetke et al. from German and Nussbaumer et al., which were double blinded studie,s have shown no statistical significance for the difference of ESS improvement among OSA patients between APAP and fixed CPAP.[19,20]

In our study, 22 subjects preferred APAP and 24 preferred fixed CPAP. Subjects who preferred APAP had higher median optimal CPAP pressure and baseline BMI compared with those patients who preferred fixed CPAP. Those preferring APAP had median optimal CPAP pressure was 13.0 cmH_2O (IQR 12.0 cmH_2O -13.5 cmH_2O) and subjects who preferred fixed CPAP had median optimal CPAP pressure of 8.0 cmH_2O (IQR 6.3 cmH_2O -8.7 cmH_2O) $p<0.01$. The median baseline BMI was 37.6 kg/m^2(IQR 30.8 kg/m^2 -43.0 kg/m^2) for those preferred APAP and 32.3 kg/m^2 (IQR 30.8 kg/m^2 -38.4 kg/m^2) for subjects preferred fixed CPAP, p 0.03. The association of optimal CPAP pressure with subjects' CPAP mode preference was similar toa study by Nolan et al. from Ireland.[10]

Contrary to our study, Nolan et al. stated that BMI was not the determining factor for CPAP mode preference among the OSA subjects.[10] However, the baseline BMI in Nolan et al. was 30.6 kg/m^2 (± 3.8 kg/m^2) for those who preferred APAP and 28.5 kg/m^2 (± 5.1 kg/m^2) for those who preferred fixed CPAP.10 The baseline BMI of subjects in Nolan et al. were relatively lower as compared to our study. The relative lower baseline BMI may have contributed to the insignificant of subjects' preference towards CPAP mode. The Randerath et al. study in 2001 found a correlation of body mass index and CPAP treatment pressures. Subjects' CPAP pressure requirement increased with higher BMI.[16] This may explain the subjects in our study with higher BMI preferred APAP. Those with higher pressure viability may do better with APAP. Further study needed in this field to define this variability.

In our study, subjects' CPAP modes preference was not affected by baseline AHI and average CPAP usage per day. We noted the compliance among those who preferred APAP and fixed CPAP were good. CPAP compliance is defined as using the therapy for an average of 4 hours a night for at least 70% of the nights.[21] In our research, those who preferred APAP had median average CPAP usage per day of 5 hours 20 minutes 16 seconds. (IQR: 4 hours 52 minutes 51 seconds- 5 hours 37 minutes 56 seconds) and 5 hours 19 minutes 26 seconds (IQR: 5 hours 10 minutes 15 seconds-5hours 38 minutes 32 seconds) for those preferred fixed CPAP. The good compliance may be due to more regular follow up by the researcher, with 24 hours helpline available for those recruited in this study. The variability of average duration of CPAP usage per day is small between those preferred APAP and fixed CPAP.

There are few limitations to our study. Firstly, our subjects were recruited from a single tertiary centre UKMMC. Besides, this is a single blinded study and manual CPAP titration was not done due to the limited resources.

CONCLUSION

In summary, APAP and fixed CPAP are equally effective in treating symptomatic OSA. If the optimal CPAP pressure is less than 8 cmH_2O and BMI less than 32.3 kg/m^2, fixed CPAP may be considered as first line modality of treatment for symptomatic OSA as it is cheaper compared with APAP.

CONFLICT OF INTEREST

None to declare.

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REFERENCES

1. Kamil MA, Teng CL, Hassan SA. Snoring and breathing pauses during sleep in the Malaysian population. Respirology 2007; 12(3): 375-80.
2. Marti S, Sampol G, Munoz X, Torres F, Roca A, Lloberes P, et al. Mortality in severe sleep apnoea/hypopnoea syndrome patients: impact of treatment. Eur Respir J 2002; 20(6): 1511-8.
3. Marshall NS, Wong KK, Liu PY, Cullen SR, Knuiman MW, Grunstein RR. Sleep apnea as an independent risk factor for all-cause mortality: the Busselton Health Study. Sleep 2008; 31(8): 1079-85.
4. Yuan X, Fang J, Wang L, Yao L, Li L, Zhan X, et al. Adequate continuous positive airway pressure therapy reduces mortality in Chinese patients with obstructive sleep apnea. Sleep Breath 2015; 19(3): 911-20.
5. Young T, Finn L, Peppard PE, Szklo-Coxe M, Austin D, Nieto FJ, et al. Sleep disordered breathing and mortality: eighteen-year follow-up of the Wisconsin sleep cohort. Sleep 2008; 31(8): 1071-8.
6. Jordan AS, McSharry DG, Malhotra A. Adult obstructive sleep apnoea. Lancet 2014; 383(9918): 736-47.
7. Ayas NT, Patel SR, Malhotra A, Schulzer M, Malhotra M, Jung D, et al. Auto-titrating versus standard continuous positive airway pressure for the treatment of obstructive sleep apnea: results of a meta-analysis. Sleep 2004; 27(2): 249-53.
8. Batool-Anwar S, Goodwin JL, Kushida CA, Walsh JA, Simon RD, Nichols DA, et al. Impact of continuous positive airway pressure (CPAP) on quality of life in patients with obstructive sleep apnea (OSA). J Sleep Res 2016; 25(6): 731-8.
9. Vennelle M, White S, Riha RL, Mackay TW, Engleman HM, Douglas NJ. Randomized controlled trial of variable-pressure versus fixed-pressure continuous positive airway pressure (CPAP) treatment for patients with obstructive sleep apnea/hypopnea syndrome (OSAHS). Sleep 2010; 33(2): 267-71.
10. Nolan GM, Doherty LS, Mc Nicholas WT. Auto-adjusting versus fixed positive pressure therapy in mild to moderate obstructive sleep apnoea. Sleep 2007; 30(2): 189-94.
11. To KW, Chan WC, Choo KL, Lam WK, Wong KK, Hui DS. A randomized cross-over study of auto-continuous positive airway pressure versus fixed-continuous positive airway pressure in patients with obstructive sleep apnoea. Respirology 2008; 13(1): 79-86.
12. Johns MW. A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 1991; 14(6): 540-5.
13. Lim TO, Ding LM, Zaki M, Suleiman AB, Fatimah S, Siti S, et al. Distribution of body weight, height and body mass index in a national sample of Malaysian adults. Med J Malaysia 2000; 55(1): 108-28.

14. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999; 22(5): 667-89.
15. Nagaraj S, Nai-Peng T, Chiu-Wan N, Kiong-Hock L, Pala J. Counting Ethnicity in Malaysia: The Complexity of Measuring Diversity. In: Simon P, Piché V, Gagnon AA, editors. Social Statistics and Ethnic Diversity: Cross-National Perspectives in Classifications and Identity Politics. Cham: Springer International Publishing 2015. p. 143-73.
16. Randerath WJ, Schraeder O, Galetke W, Feldmeyer F, Ruhle KH. Autoadjusting CPAP therapy based on impedance efficacy, compliance and acceptance. Am J Respir Crit Care Med 2001; 163(3 Pt 1): 652-7.
17. Johns MW. Reliability and factor analysis of the Epworth Sleepiness Scale. Sleep 1992; 15(4): 376-81.
18. Noseda A, Kempenaers C, Kerkhofs M, Braun S, Linkowski P, Jann E. Constant vs auto-continuous positive airway pressure in patients with sleep apnea hypopnea syndrome and a high variability in pressure requirement. Chest 2004; 126(1): 31-7.
19. Nussbaumer Y, Bloch KE, Genser T, Thurnheer R. Equivalence of autoadjusted and constant continuous positive airway pressure in home treatment of sleep apnea. Chest 2006; 129(3): 638-43.
20. Galetke W, Anduleit N, Richter K, Stieglitz S, Randerath WJ. Comparison of automatic and continuous positive airway pressure in a night-by-night analysis: a randomized, crossover study. Respiration 2008; 75(2): 163-9.
21. Kribbs NB, Pack AI, Kline LR, Smith PL, Schwartz AR, Schubert NM, et al. Objective measurement of patterns of nasal CPAP use by patients with obstructive sleep apnea. Am Rev Respir D 1993; 147(4): 887-95.