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ORIGINAL RESEARCH

Long-Term Adherence to Positive Airway Pressure Therapy in Saudi Ambulatory Patients with Obesity Hypoventilation Syndrome and Severe Obstructive Sleep Apnea: A One-Year Follow-Up Prospective Observational Study

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Purpose: Long-term studies assessing positive airway pressure (PAP) therapy adherence in patients with obesity hypoventilation (OHS) are limited. The aim of this study was to assess PAP therapy adherence in Arab (Saudi) patients with OHS and an apnea-hypopnea index (AHI) >30/h.

Methods: A prospective cohort study of consecutive adult patients diagnosed with OHS between March 2010 and September 2019 was conducted. During the therapeutic sleep study, all OHS patients were started on continuous PAP (CPAP). Patients who failed to maintain oxygen saturation ≥88% despite the elimination of obstructive respiratory events were shifted to bi-level PAP (BPAP). Objective assessment of adherence was performed at 1, 6, and 12 months after initiating PAP therapy. We adopted the American-Thoracic-Society criteria for PAP adherence.

Results: The study included 101 patients (women = 65 patients) with OHS, an AHI ≥30/h, and a mean age of 54.9 ± 12.7 years. Successful titration on CPAP was achieved in 64.4% of the patients and BPAP was required for 35.6% of the patients who failed CPAP titration. At the end of the study, 43.6% of the patients used PAP therapy in an acceptable manner. Adherence after 1 and 6 months was the only independent predictors of adherence at 12 months.

Conclusion: PAP adherence among Saudi patients with OHS and severe obstructive sleep apnea was relatively low. Almost two-thirds of patients tolerated CPAP titration with the elimination of respiratory events and desaturation. Early adherence to PAP therapy was the only predictor of PAP therapy adherence at the end of the study.

Keywords: CPAP, bi-level positive airway pressure, compliance, obstructive sleep apnea, desaturation, titration

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Introduction

Obesity hypoventilation syndrome (OHS) is characterized by chronic awake hypercapnia ($PaCO_2$>45 mmHg, at sea level) and obstructive sleep apnea (OSA) in obese individuals (BMI>30kg/m^2) in the absence of other causes of chronic hypercapnia.[1] Burwell et al[2] first described this condition as a "Pickwickian Syndrome" and limited treatment options were available, including weight loss, tracheostomy, and

short-term breathing stimulants. Over the last 10 years, obesity rates increased worldwide,[3] accompanied by increasing awareness of the high healthcare costs,[4] morbidity, and mortality associated with OHS.[4–6] Consequently, interest in the early diagnosis and treatment of OHS increased,[7,8] and investigation into the long-term adherence to PAP therapy in OHS patients is essential.

The development of awake hypercapnia in OHS is the culmination of a complex interplay of factors, which vary from individual to individual. Factors contributing to hypercapnia in OHS patients include decreased lung volumes, increased respiratory system elastance, increased upper airway narrowing during wakefulness and sleep, subnormal respiratory drive to compensate for obesity, weakened inspiratory muscle function, and impaired chemoreceptor sensitivity to hypercarbia and hypoxia.[9] Obstructive breathing during sleep is consistently present in most patients with OHS and is associated with periods of hypoventilation, particularly during rapid eye movement (REM) sleep.[10] OSA occurs in approximately 90% of the OHS patients. The pure hypoventilation phenotype occurs in 10–15% of the patients.[11]

The aim of positive airway pressure (PAP) therapy is to normalize breathing and gas exchange during sleep. In OHS, this involves maintaining upper airway patency, improving alveolar ventilation, reducing the work of breathing, and eliminating hypoxemia. Patients with OHS can be divided into those with comorbid OSA and those with pure OHS and different PAP modes can be successfully used depending on the clinical phenotype and setting. Several studies compared the short or medium-term (up to 3 months) physiological outcomes of continuous positive airway pressure (CPAP) versus non-invasive ventilation (NIV) in patients with OHS and reported no superiority of either modality.[12]

Limited long-term studies have assessed adherence to PAP therapy in patients with OHS in Western societies. However, race is a predictor of adherence to PAP therapy in OSA patients.[13–16] Thus, assessing PAP adherence in Arab (Saudi) patients with OHS is essential in understanding the impact on this patient population. To date, no study has reported adherence to PAP therapy in Arab patients with OHS. Due to the significant comorbidities and cognitive impairment associated with OHS,[17] adherence to PAP therapy may be lower than adherence among OSA patients. We hypothesized that adherence of OHS patients with concomitant severe OSA [apnea-hypopnea index (AHI)≥30/h] to PAP therapy is below the standard recommendations (at least 4 hours per night, 70% of the recorded period). Therefore, this study sought to assess the adherence to PAP therapy in Arab (Saudi) patients with OHS and AHI≥30/h accompanied by close follow-up and monitoring with easy access to medical and technical support.

Methods

Subjects

This study is a part of a larger project, with prospectively collected data, to assess OHS.[18–20] Consecutive patients (>18 years) who were diagnosed with OHS at the University Sleep Disorders Center (USDC) at King Saud University Medical City at King Saud University between March 2010 and September 2019 were approached to participate in the study (n=310). Exclusion criteria were chronic illnesses that may affect breathing, such as chronic neurological, muscular, or pulmonary disorders, deformity of the vertebral column or thoracic wall, decompensated congestive heart failure, and being on medications that suppress the respiratory drive such as hypnotics.

PAP adherence in OHS patients was compared with adherence in an age-, BMI-, and major comorbidity-matched group of OSA patients. In compliance with the USDC therapeutic policies, all patients had spirometric measurements based on the American Thoracic Society/European Respiratory Society (ATS/ERS) task force guidelines using a Master Screen (Jaeger, Germany).[21] As an OHS diagnosis criterion, arterial blood samples were obtained from all patients with suspected OHS after 15 minutes of rest while awake, seated, and breathing room air using a GEM® Premier™ 4000 analyzer (Instrumentation Laboratory, Lexington, MA). The Epworth sleepiness scale (ESS) was used to assess daytime sleepiness.[22] Incomplete data were completed by calling patients or relatives to obtain missing items. Comorbidities were obtained from patient histories and electronic medical records.

Polysomnography

As part of the clinical work-up, all patients with sleep-disordered breathing underwent a standard overnight sleep study (Type 1). The type 1 sleep study includes collection of neurological, cardiac, respiratory, and muscular data using EEG, chin and leg EMG, ECG, pulse oximeter, end-tidal CO_2, and respiratory monitoring. Alice® diagnostic equipment (Philips, Respironics Inc., Murrysville, PA,

USA) was used to acquire sleep study data. The scoring of raw data was performed manually and rechecked by certified staff according to the latest American Academy of Sleep Medicine (AASM) scoring criteria.[23] The severity of obstructive sleep-disordered breathing was assessed using the AHI, which quantifies the number of apneas and hypopneas (obstructive events) per hour of sleep.

OHS Diagnosis

The third edition of the International Classification of Sleep Disorders Manual (ICSD-3) criteria was used to diagnose OHS. Diagnostic criteria included: 1) daytime hypercarbia (arterial $PaCO_2$ >45 mm Hg), 2) obesity based on the World Health Organization (WHO) definition (BMI >30 kg/m2), and 3) exclusion of other causes of hypoventilation and daytime hypercarbia, such as chronic lung disease, chest wall deformity, respiratory suppressant medications, neuromuscular disorders, or idiopathic or congenital central alveolar hypoventilation syndrome.[24] Patients with OHS were divided into two groups: OHS with a major obstructive sleep disorder (AHI≥30/h) and OHS with AHI<30/hr. In this study, we only included patients with AHI≥30/h.

PAP Therapy Titration Protocol

As per the USDC recommendations, all ambulatory patients with OHS were initially started on CPAP. If oxygen saturation could not be maintained at ≥88% despite the elimination of obstructive respiratory events, the patient was shifted to bi-level PAP (BPAP). All PAP devices had a built-in heated humidifier.

Definition of PAP Acceptance and Good Adherence

We adopted the American Thoracic Society (ATS) criteria for PAP adherence.[25] The ATS criteria state that "good adherence" to PAP means "the use of PAP therapy regularly for more than 4 h/night for >70% of the recorded period" and "partial adherence" implies "the use of PAP therapy > 2 h/night that is accompanied by subjective improvement in OHS-related symptoms such as quality of life".[25] Patients who did not meet the above criteria were considered non-adherent.[25] Adherence to PAP therapy was documented via downloading "mask-on time tracking" data from PAP devices. This technique permitted the objective estimation of adherence to PAP therapy.[26]

Follow-Up Protocol and PAP Adherence Assessment

As per the protocol of the USDC, patients with OHS were provided with information about the sleep study and PAP therapy by a health educationalist before undergoing the sleep study. A session was dedicated to selecting the best interface (mask) for PAP therapy. After the sleep study, a clinic visit was arranged for the patient and a family member, where a physician member of the USDC met patients and discussed the sleep study findings, diagnosis, known short-term and long-term complications of OHS, and the OHS complications and beneficial results and potential adverse events of PAP therapy. Following the clinic visit, an educational session was arranged with a health educationalist to have hands-on training for patients on the operation and components of PAP devices. Additionally, written educational material about OHS and PAP therapy was provided for all patients. During each subsequent follow-up visit, all practical educational points were repeated to patients.

Figure 1 demonstrates the study protocol. Patients spent two nights in the sleep laboratory; a diagnostic night was followed by a therapeutic night, where PAP was applied. The therapeutic study was performed within 2–3 weeks of the diagnostic study. Patients underwent three hands-on educational (training) sessions during the first month after the therapeutic sleep study. During these sessions, hands-on training sessions on operating PAP devices, interface application and removal, handling the humidifier and filter, and cleaning of PAP devices were reviewed. The following hands-on sessions were provided:

Session 1: The day they receive the PAP device
Session 2: Two weeks after initiating PAP therapy
Session 3: Four weeks after initiating PAP therapy

Outpatient follow-up of patients with OHS on PAP therapy was performed at 1, 6, and 12 months after initiating PAP therapy. During each visit, training and education were conducted and data about adverse events were collected. A dedicated sleep technologist worked with patients during each visit to solve PAP-related adverse events. Adherence to PAP therapy was objectively obtained from the PAP device during each visit. Patients were encouraged to adhere to treatment and the required adjustments were made to PAP settings and masks. Between follow-up visits, patients with OHS had direct access to medical and technical support by the USDC team via a direct phone number during daytime working hours and an accessible visit to the PAP therapy clinic if required within 1–2 weeks.

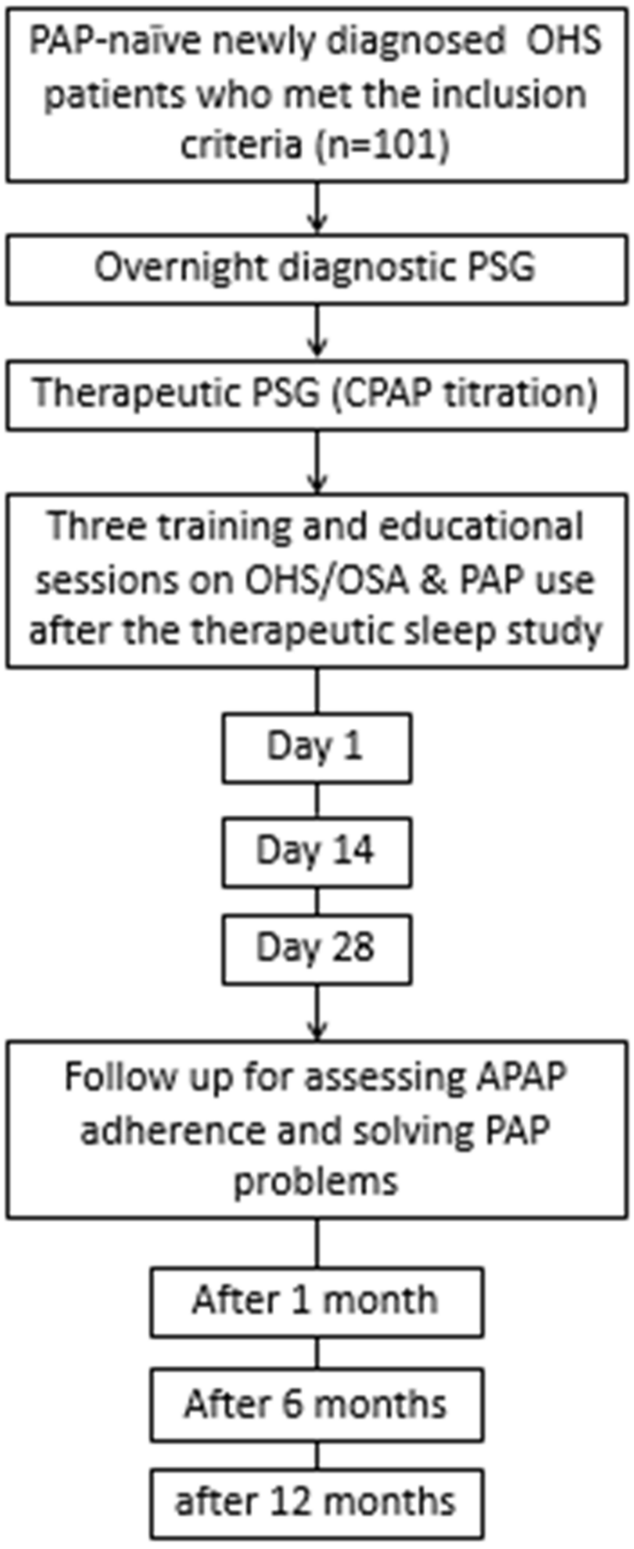

Figure 1 A flowchart of the recruited patients.

Statistical Analysis

Data are presented in the text and tables as mean ± standard deviation (SD) or number (%). Comparisons between groups were made using t-tests for continuous variables and Chi-square tests for dichotomous data. For three group comparisons, one-way analysis of variance (ANOVA) was used. To identify predictors of PAP adherence, we combined good adherence and partial adherence into a compliant group. A univariate logistic regression analysis was conducted whereby one independent variable was tested at a time in the model. Independent variables included demographics, clinical data, sleep study variables, and adverse events measured during each follow-up visit. Variables with significant p-values were included in the multivariable logistic regression analysis model. The correlation matrix assessed the multicollinearity between variables in the model, and no multicollinearity was detected. Moreover, the standard error in the model was used to reassess multicollinearity. A p-value < 0.05 was considered statistically significant. Data were analyzed using the SPSS statistical software (version 23; Chicago, IL, USA).

Results

During the study period, 129 patients were diagnosed with OHS with an AHI ≥30 and met the inclusion criteria; of whom 14 patients abandoned PAP therapy before the 12 months follow-up period, 13 did not show up for the final assessment, and one patient died during the follow-up period. These patients did not differ from those who completed the study regarding age, sex, BMI, comorbidities, AHI, mean nocturnal SpO2, baseline PaCO2, and PaO2, and type of PAP therapy prescribed. The remaining 101 patients (including 65 women) completed the study. All included patients were Arabs. The mean age of the study group was 54.9 ± 12.7 years, and the mean BMI of 43.4 ± 9.8 kg/m^2. Patient characteristics at baseline are summarized in Table 1. Successful titration on CPAP was achieved in 64.4% of the patients; 35.6% failed CPAP titration and required BPAP. The mean CPAP and BPAP pressures were 12.6 ± 3.8 cmH_2O and 18.5 ± 2.3/13.9 ± 3.1 cmH_2O, respectively.

Figure 2 shows patient adherence at 1, 6, and 12 months of follow-up. At the end of the study, 43.6% of the patients were still using PAP therapy in an acceptable manner. Adherence in men and women is shown in Figures 3 and 4, respectively. At the end of the study, 49.3% of the women (Figure 3) and 33.3% of the men were still using PAP therapy in an acceptable way (good adherence + partial adherence). As patients were recruited from 2010 to 2019, improvements in PAP devices technology might have affected adherence. Therefore, we

Table 1 Baseline Characteristics of the Study Group According to PAP Adherence at 12 Months

Variables	Total (n=101)	Mean ± SD			P-value
		Good Adherence	Partial Adherence	Non-Adherent	
Age (years)	54.9 ± 12.7	51.4 ± 10.7	58.1 ± 14.7	54.4 ± 12.1	0.2
Body Mass Index (kg/m^2)	43.4 ± 9.8	40.6 ± 9.9	44.6 ± 7.5	43.7 ± 10.8	0.2
Sex (Female)	65 (64.4)	12 (70.6)	20 (74.1)	33 (57.9)	0.3
Postmenopausal (of total women)	53 (81.5)	7 (58.3)	18 (90)	28 (84.8)	0.1
Epworth Sleepiness Scale	11.4 ± 5.6	9.1 ± 4.5	12.7 ± 5.2	11.4 ± 6	0.1
Smoking status					
Smoker	6 (5.9)	2 (11.8)	0 (0)	4 (7.3)	0.4
Ex- Smoker	7 (6.9)	1 (5.9)	3 (12)	3 (5.5)	
PH	7.4 ± 0.04	7.4 ± 0.1	7.4 ± 0.04	7.4 ± 0.04	0.09
$PaCO_2$ (mmHg)	52.6 ± 8.7	53.3 ± 12.3	54.1 ± 9.8	51.6 ± 6.8	0.7
PaO_2 (mmHg)	66.1 ± 16.5	72.9 ± 16.2	64.3 ± 17.7	65 ± 15.7	0.2
HCO_3 (mmol/L)	30.3 ± 4.7	30.8 ± 4.3	30.1 ± 5	30.2 ± 4.8	0.7
FEV1/FVC (%)	85.9 ± 8.5	83.9 ± 9.7	86.9 ± 8.3	85.9 ± 8.2	0.8
FVC (% predicted)	67.9 ± 18.4	72.8 ± 19	66.3 ± 19.6	67.2 ± 17.7	0.5
FEV1 (% predicted)	70.4 ± 21.1	74.2 ± 21.7	70.4 ± 18.7	69.3 ± 22.4	0.7
Comorbidities					
Hypertension	68 (67.3)	9 (56.3)	21 (80.8)	38 (66.7)	0.2
Ischemic heart disease	12 (11.9)	2 (12.5)	5 (19.2)	5 (8.8)	0.4
Diabetes mellitus	53 (52.5)	8 (50)	16 (61.5)	29 (50.9)	0.6
Renal Failure	6 (5.9)	1 (6.3)	2 (7.7)	3 (5.3)	0.4
Compensated heart failure	7 (6.9)	0 (0)	3 (11.5)	4 (7)	0.4
Stroke	0 (0)	0 (0)	0 (0)	0 (0)	-
Bronchial Asthma	31 (30.7)	3 (18.8)	9 (33.3)	19 (33.3)	0.5
Allergic rhinitis	6 (5.9)	1 (16.7)	3 (18.8)	2 (5.6)	0.3
Hypothyroidism	17 (16.8)	6 (37.5)	5 (19.2)	6 (10.5)	0.04
Hypercholesterolemia	40 (39.6)	6 (40)	9 (39.1)	25 (46.3)	0.8
Polysomnographic findings					
Sleep Efficiency (%)	68 ± 21.3	72.4 ± 13.4	63.2 ± 20.4	68.9 ± 23.4	0.2
Stage N1 (%)	16.3 ± 17.5	10.2 ± 7	17.1 ± 19	17.7 ± 18.8	0.7
Stage N2 (%)	67.3 ± 20.6	72.8 ± 15.5	60.5 ± 23.9	68.9 ± 19.7	0.2
Stage N3 (%)	7 ± 14.3	8.2 ± 10.7	7.7 ± 16.6	6.2 ± 14.3	0.2
Stage REM (%)	9.8 ± 12.2	9.3 ± 11.5	13.9 ± 17.8	8 ± 8.2	0.4
Apnea Hypopnea Index (AHI) (events/h)	81.3 ± 34.2	63.5 ± 32	82.8 ± 34.4	85.9 ± 35.2	0.2
Desaturation Index (desaturations/h)	60.8 ± 47.2	51.3 ± 42.4	70.3 ± 51.1	59.2 ± 46.7	0.5
Time with SpO2 <90% (mins)	45.6 ± 38.2	50.3 ± 41.4	49.6 ± 33.4	42.3 ± 39.6	0.7
Lowest Recorded SpO2 (%)	68.9 ± 16.9	74.9 ± 11.1	67.5 ± 18.9	67.7 ± 17.3	0.3
Mean Nocturnal SpO2 (%)	87.8 ± 8.3	89.5 ± 6.8	87.8 ± 6.9	87.2 ± 9.3	0.5
Arousal Index (arousals/h)	78.9 ± 43.2	68 ± 35.9	75.8 ± 44.7	83.5 ± 44.4	0.4
PAP side effects	27 (26.7)	4 (40)	5 (25)	18 (64.3)	0.04
PAP device pressure					
Residual AHI (events/h) after titration	5 ± 6.4	3.1 ± 2.6	4.8 ± 6.1	5.5 ± 8.5	0.2
CPAP Recommended Pressure	13.4 ± 4.8	13.1 ± 6.4	10.1 ± 5.1	14.3 ± 5.3	0.4
Recommended Pressure IPAP	19.1 ± 3.3	19.9 ± 2.6	17.8 ± 3.5	18.2 ± 4.4	0.8
Recommended Pressure EPAP	14.2 ± 3.1	13.3 ± 7.2	14.8 ± 4.1	14.9 ± 3.1	0.9

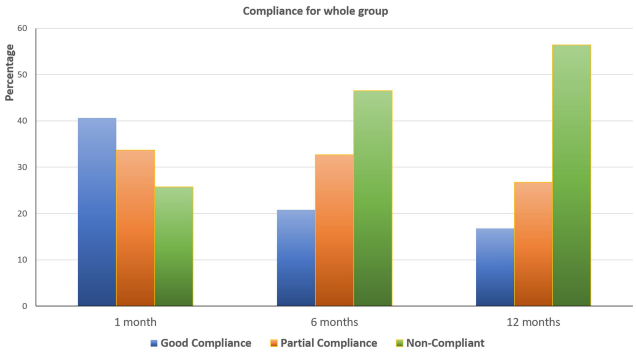

Figure 2 PAP therapy adherence at 1, 6, and 12 months in the whole group.

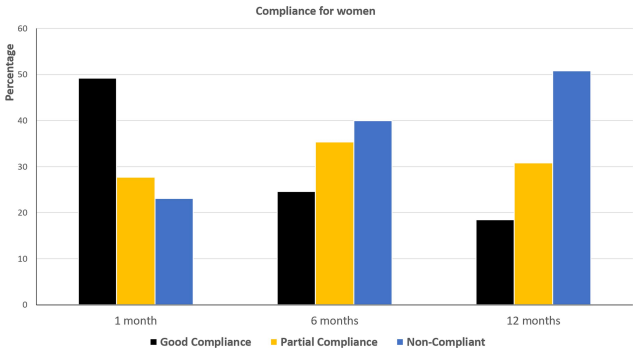

Figure 3 PAP therapy adherence at 1, 6, and 12 months in women.

Figure 4 PAP therapy adherence at 1, 6, and 12 months in men.

compared adherence across the 10 study years; no difference in adherence was detected between years from 2010 to 2019.

No differences in the general characteristics, blood gases, spirometric parameters, PSG findings, comorbidities, the level of PAP used were observed in patient groups with good adherence, partial adherence, and non-adherence at the 12-month follow-up (Table 1). A comparison of adherence parameters in CPAP and BPAP users is shown in Table 2. No differences in adherence parameters were observed between the two groups.

Table 3 shows the univariate and multivariate regression analyses for the predictors of good adherence at 1, 6, and 12 months of follow up. At 1 month, no independent predictor could be identified. At 6 months, time with SpO2 <90% (mins), absence of side effects, and adherence (after 1 month) were the independent predictors of PAP adherence. Adherence after 1 month and adherence after 6 months were the only independent predictors of adherence at 12 months.

Table 4 shows a comparison of PAP adherence at 1, 6, and 12 months between patients with OHS and an age-, BMI-, and comorbidity-matched group of OSA patients. OHS patients had higher AHI and more desaturations compared to OSA patients. No differences in adherence between the two groups were detected.

Discussion

This prospective observational study demonstrated that even with intensive education, support, and close monitoring, only 43.6% of the patients with OHS adhered to PAP therapy after 12 months of initiating therapy. This is much lower than the PAP adherence that our team has previously reported in Saudi patients with OSA (80%) after applying the same educational and follow-up program.[27] However, the previously reported OSA patients were younger and had lower BMI and fewer comorbidities. Therefore, we compared OHS patients in this study with an OSA group matched for age, BMI, and major comorbidities. No difference in adherence was detected between the two groups.

Almost two-thirds of the patients in this study attained successful CPAP titration, indicating that CPAP can be successfully titrated in a majority of stable ambulatory OHS patients with AHI ≥ 30 events/h. However, age and comorbidities may influence PAP adherence in patients with sleep-disordered breathing. Studies have shown that patients with OHS have progressive disease paths, higher healthcare consumption, poorer prognoses, and increased likelihood of hospitalization and death compared with obese subjects without OHS and pure OSA patients.[28,29]

In a recent multicenter randomized controlled trial (RCT) of patients with OHS and an AHI >30 events/h, patients were followed for more than 5 years. This study reported a median treatment adherence for CPAP and NIV of 6 h per day, and among CPAP and NIV users, the percentage of those who used the device >4 h per day was 76% and 63%, respectively.[30] In general, previous RCTs and observational studies in Western societies

Table 2 Comparison of Adherence Between CPAP and BPAP Users

Variable Total (n=101)	Mean ± SD/n (%)		P-value
	CPAP n=65 (64.4)	BPAP n=36 (35.6)	
Adherence after 1 month			
Good adherence	27 (41.5)	14 (38.9)	0.9
Partial adherence	21 (32.3)	13 (36.1)	
Adherent (good + partial)	48 (73.8)	27 (75)	0.9
Non-adherent	17 (26.2)	9 (25)	
Residual AHI (events/h) after titration	3.4 ± 3.5	6.5 ± 12	0.8
Residual AHI <5 events/h (%)	43 (78.2)	27 (77.1)	0.06
Percent Days with PAP Usage	68 ± 33.5	71 ± 31	0.6
Average CPAP Usage (h/day)	3.3 ± 2	3.7 ± 2.4	0.6
Average CPAP Usage (h/day) (non-adherent)	1.7 ± 1.2	1.8 ± 1.1	0.8
Average CPAP Usage (h/day) (adherent)	4.9 ± 1.2	5 ± 2.1	0.8
Adherence after 6 months			
Good adherence	14 (21.5)	7 (19.4)	0.9
Partial adherence	21 (32.3)	12 (33.3)	
Adherent (good + partial)	35 (53.8)	19 (52.8)	0.9
Non-adherent	30 (46.2)	17 (47.2)	
Residual AHI (events/h)	3.4 ± 2.9	5.4 ± 8.4	0.9
Residual AHI <5 events/h (%)	41 (74.5)	29 (80.6)	0.008
Percent Days with CPAP Usage	52.8 ± 34.6	54.1 ± 34.8	0.8
Average CPAP Usage (h/day)	2.8 ± 2.5	3 ± 3	0.9
Average CPAP Usage (h/day) (non-adherent)	1.5 ± 1.2	1.6 ± 1.3	0.8
Average CPAP Usage (h/day) (adherent)	6.2 ± 1.7	7.1 ± 2.8	0.4
Adherence after 12 months			
Good adherence	13 (20)	4 (11.1)	0.1
Partial adherence	13 (20)	14 (38.9)	
Adherent (good + partial)	26 (40)	18 (50)	0.3
Non-Compliant	39 (60)	18 (50)	
Residual AHI (events/h)	3.9 ± 5.8	6.8 ± 11.9	0.9
Residual AHI <5 events/h (%)	42 (75)	27 (75)	0.2
Percent Days with CPAP Usage	45.3 ± 34.4	48.7 ± 32.4	0.6
Average CPAP Usage (h/day)	2.3 ± 2.4	2.7 ± 2.9	0.5
Average CPAP Usage (h/day) (non-adherent)	1.1 ± 1.1	1.5 ± 1.3	0.3
Average CPAP Usage (h/day) (adherent)	6.1 ± 1.5	6.9 ± 3.2	0.8
PAP device pressure at the end of the study			
CPAP Recommended Pressure	12.6 ± 3.8	-	-
Recommended Pressure IPAP	-	18.5 ± 2.3	-
Recommended Pressure EPAP	-	13.9 ± 3.1	-

reported daily PAP use (among OHS patients) ranging from 4 to 6 h per day.[31–33] Adherence to PAP among Saudi patients with OHS is lower than that reported in the West. This lower adherence is not related to access to medical care or the availability of the PAP devices. All Saudis and all government employees have free access to government-funded healthcare services and PAP devices.[34] Additionally, studies in Western countries that showed high adherence to PAP therapy were RCTs. A prospective observational study in the US that used a study design comparable to our study reported objective adherence less than that reported in RCTs of 56%, which is closer to our study's adherence rate.[35] In the current study, PAP-related side effects were significantly

Table 3 Independent Predictors of Good CPAP Adherence Using Univariate and Multivariate Logistic Regression at 1, 6, and 12 Months

		Predictors	P-value	OR	[95% CI]
Month 1	Univariate model	Sex (Female) Hypothyroidism	0.020 0.030	2.9 3.4	[1.2–7.1] [1.1–9.9]
	Multivariate model*	No Predictors			
Month 6	Univariate model	Time with SpO2 <90% (mins) No Side Effects Adherence (after 1 month) (Compliant)	0.013 0.039 < 0.001	1.01 3.09 7.9	[1.003–1.02] [1.06–9.04] [2.7–23.4]
	Multivariate model*	Time with SpO2 <90% (mins) No Side Effects Adherence (after 1 month) (Compliant)	0.012 0.012 0.003	1.02 5.7 10.8	[1.005–1.04] [1.5–22.3] [2.2–52.3]
*Multicollinearity: No, Overall Accuracy: 72.4%, Sensitivity: 76.7%, Specificity: 67.9%, Area under the Curve (ROC): 81%, Omnibus Tests of Model: p < 0.001, Hosmer-Lemeshow goodness of fit: p =0.229, Nagelkerke R Square: 41.5%					
Month 12	Univariate model	Nasal mask (vs face mask) Hypothyroidism Adherence (after 1 month) (Compliant) Adherence (after 6 months) (Compliant)	0.034 0.047 0.001 < 0.001	3 3.02 9.2 78.8	[1.08–8.3] [1.01–8.97] [2.6–33.5] [16.6 −372.8]
	Multivariate model*	Adherence (after 1 month) (Compliant) Adherence (after 6 months) (Compliant)	0.046 <0.001	12.5 87.9	[1.04–150.6] [12.3–627.9]
*Multicollinearity: No, Overall Accuracy: 89%, Sensitivity: 95.1%, Specificity: 84%, Area under the Curve (ROC): 94.9%, Omnibus Tests of Model: p < 0.001, Hosmer-Lemeshow goodness of fit: p =0.808, Nagelkerke R Square: 75.4%					

Abbreviations: CI, confidence interval; N2, stage N2 sleep, REM, rapid eye movement sleep; TST, total sleep time.

high among non-adherents. Therefore, educational and support programs in local sleep disorders centers are needed to improve PAP therapy adherence among OHS patients. Additionally, close follow-up of patients on PAP therapy, particularly in the first few weeks of PAP use, is essential to resolve PAP-related side effects and enhance PAP adherence; poor adherence to PAP treatment has been linked to increased mortality.[36] Moreover, good adherence to PAP therapy at 1 and 6 months was a predictor of adherence to PAP at 12 months, which further stresses the importance of early and close follow-up.

Telemedicine is a potentially powerful tool in improving adherence to PAP therapy, where actual adherence can be distantly measured.[37,38] This technology may be beneficial in patients with OHS who usually have several comorbidities and have difficulties attending sleep disorders clinics.

In the current study, we found that two-thirds of OHS patients with AHI ≥30 events/h accepted and tolerated CPAP during titration, and there was no difference between adherence in the CPAP and BPAP groups. Several studies comparing the effectiveness of CPAP and NIV in OHS reported no superiority of one modality over the other on physiological outcomes and respiratory failure resolution in OHS patients with severe OSA.[12] CPAP provides static pressure during both inspiration and expiration and does not directly augment minute ventilation. However, CPAP helps patients with OHS by eliminating upper airway repetitive obstructions during sleep and, hence, decreasing the mechanical load.[1] By maintaining upper airway patency and removing the recurrent obstructive events, CPAP minimizes the cycle of low ventilation during upper airway obstructive periods and, subsequently, the resulting hypoxemic burden, CO_2 accumulation, and longer-term bicarbonate preservation.[39] Moreover, increased lung volume reduces airway resistance and flow limitations, leading to reduced work of breathing, particularly when in the recumbent position.[40] In general, 50–80% of ambulatory stable OHS patients with comorbid OSA respond to CPAP.[5,33,41,42] Additionally, CPAP is more cost-effective than BPAP and other modes of NIV.[43] Therefore, CPAP should be the initial treatment

Table 4 Comparison of Demographics, Comorbidities, and PAP Adherence Between Patients with OHS and Age- and Body Mass Index-Matched OSA

Variable Total (n=272)	Mean ± SD/n (%)		P-value
	OHS (101)	OSA (171)	
Age (years)	54.9 ± 12.7	54 ± 12	0.6
Body Mass Index (kg/m2)	43.4 ± 9.8	41.1 ± 7.9	0.06
Apnea Hypopnea Index (AHI) (events/h)	81.3 ± 44.2	60.4 ± 36.8	< 0.001
AHI-NREM (events/h)	80.9 ± 46.3	58.9 ± 38.7	< 0.001
AHI-REM (events/h)	72.6 ± 40.5	58.9 ± 33.3	0.046
Desaturation Index (desaturations/h)	60.8 ± 47.2	39.1 ± 33.9	< 0.001
Time with SpO2 <90% (mins)	45.6 ± 38.2	18.2 ± 29	< 0.001
Obstructive Sleep Apnea Severity			
Normal OSA	0 (0)	10 (6)	0.04
Mild OSA	0 (0)	5 (3)	
Moderate OSA	0 (0)	24 (14.4)	
Severe OSA	101 (100)	128 (76.6)	
Comorbidities			
Hypertension	68 (68.7)	97 (59.1)	0.1
Ischemic heart disease	12 (12.1)	13 (7.9)	0.3
Diabetes mellitus	53 (53.5)	75 (45.7)	0.2
Renal Failure	6 (6.1)	4 (2.4)	0.2
Bronchial Asthma	31 (31)	44 (26.8)	0.5
Hypercholesterolemia	40 (43.5)	79 (52)	0.2
Hypothyroidism	17 (17.2)	31 (18.7)	0.8
Adherence after 1 month			
Good adherence	41 (40.6)	61 (35.7)	0.4
Partial adherence	34 (33.7)	47 (27.5)	0.3
Adherent (good + partial)	75 (74.3)	108 (63.2)	0.06
Non-adherent	26 (25.7)	63 (36.8)	0.06
Residual AHI (events/h)	4.6 ± 7.9	4.3 ± 6.5	0.8
Residual AHI <5 events/h (%)	70 (77.8)	117 (78.5)	0.9
Percent Days with PAP Usage	69.1 ± 32.5	71 ± 31.2	0.7
Average CPAP Usage (h/day) (adherent)	4.9 ± 1.6	6.1 ± 1.4	< 0.001
Adherence after 6 months			
Good adherence	21 (20.8)	49 (28.7)	0.2
Partial adherence	33 (32.7)	39 (22.8)	0.08
Adherent (good + partial)	54 (53.5)	88 (51.5)	0.8
Non-adherent	47 (46.5)	83 (48.5)	0.8
Residual AHI (events/h)	4.1 ± 5.7	4.3 ± 5.8	0.8
Residual AHI <5 events/h (%)	70 (76.9)	111 (75)	0.7
Percent Days with CPAP Usage	53.2 ± 34.5	54.9 ± 37.4	0.8
Average CPAP Usage (h/day) (adherent)	6.5 ± 2.1	6.1 ± 1.3	0.4
Adherence after 12 months			
Good adherence	17 (16.8)	43 (25.3)	0.1
Partial adherence	27 (26.7)	42 (24.7)	0.7
Adherent (good + partial)	44 (43.6)	85 (50)	0.3
Non-Compliant	57 (56.4)	85 (50)	0.3
Residual AHI (events/h)	5 ± 8.7	4.1 ± 5.5	0.9
Residual AHI <5 events/h (%)	69 (75)	113 (76.9)	0.7
Percent Days with CPAP Usage	46.5 ± 33.6	47.3 ± 36.6	0.9
Average CPAP Usage (h/day) (adherent)	6.4 ± 2.2	5.9 ± 1.5	0.4

for stable ambulatory patients with OHS associated with severe OSA due to its relatively simple application, low cost, and efficacy. If alveolar hypoventilation persists despite the elimination of obstructive events, patients should be switched to BPAP treatment.

The current study demonstrated no difference in adherence between patients on CPAP or BPAP. Our results concur with Howard et al, who reported no difference in adherence to CPAP and BPAP therapy among 60 OHS patients over three months.[31] On the other hand, in a long-term prospective observational study, Bouloukaki et al reported that patients using BPAP adhered better to therapy than patients using CPAP [40].[35] However, this study included OHS patients with mild, moderate, and severe OSA. In the current study, we only included patients with severe OSA. Our results also concur with a previous paper that assessed adherence to PAP among Saudi patients with moderate to severe OSA and reported no difference in adherence between CPAP and BPAP.[27]

Several studies have reported associations and predictors of PAP adherence among patients with OSA.[15] However, limited data are available on the adherence to PAP therapy among patients with stable OHS. Age, BMI, daytime sleepiness (measured by the ESS), PAP pressure, and AHI did not predict subsequent PAP use in the current study. At month 6, the presence of side effects was an independent predictor of PAP adherence. Despite the progress in the design of PAP devices and interfaces, about 60% of the patients experience PAP-related side effects, which could affect long-term adherence.[26] Therefore, patients should understand and report the side effects of PAP therapy so the treatment team can solve these problems to enhance treatment adherence.

The time spent with SPO2 less than 90% was a predictor of PAP adherence at 6 months. Several studies have demonstrated that increased OSA severity, measured by the AHI or oxygen desaturation index, may also affect adherence.[15] An interesting finding is that adherence at 1 and 6 months were the only predictors of adherence at 12 months. Our findings concur with previous studies showing that early adherence to PAP in OSA patients could predict long-term adherence.[44,45] Therefore, early support and interventions to troubleshoot problems are likely to improve adherence.[46]

A limitation of the current study is that the findings are from a single tertiary center. Hence, the data cannot be extrapolated to other sleep disorders centers in Saudi Arabia. Moreover, no data about the outcomes of physiological parameters were collected. Additionally, it would be interesting to show carbon dioxide levels during PSG monitoring in CPAP versus BPAP patients to detect differences in carbon dioxide levels during sleep in both groups and data on carbon dioxide levels or oxygen saturation among CPAP and BPAP users at the end of the study. Unfortunately, carbon dioxide levels are not available for all patients during PSG, nor arterial blood gases result at the end of the study. Future studies should monitor and report these parameters.

In summary, this is the first study to assess the acceptance and long-term adherence to PAP in Arab patients with OHS. The current long-term prospective study demonstrates that PAP adherence among Saudi patients with OHS and concomitant severe OSA is lower than the adherence reported in Western patients. The adherence reported in this study is also lower than adherence in Saudi patients with moderate to severe OSA. During this therapeutic study, almost two-thirds of OHS patients tolerated CPAP titration with the elimination of respiratory events and desaturation. Adherence to PAP therapy in the first and sixth month was the only predictor of PAP therapy adherence at the end of the study, indicating the importance of close follow-up of OHS patients on PAP therapy. In particular, close monitoring in the first few weeks of PAP therapy is important to resolve PAP therapy-related side effects and enhance adherence to PAP therapy. Future studies should assess the impact of PAP adherence on physiological parameters among Arab patients with OHS.

Data Sharing Statement

Data are available upon request. However, releasing data needs IRB approval.

Ethics Statement

Ethical approval of the study protocol was obtained from the Institutional Review Board (IRB) of the College of Medicine, King Saud University, and Medical City. All participants gave written informed consent. This study was conducted in accordance with the Declaration of Helsinki.

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Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

The authors report no conflicts of interest for this work.

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