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Published in:
Respirology

DOI:
10.1111/resp.13704

Official Journal of the Asian Pacific Society of Respirology
Respirology

ORIGINAL ARTICLE

Obesity hypoventilation syndrome treated with non-invasive ventilation: Is a switch to CPAP therapy feasible?

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ABSTRACT

Background and objective: **Obesity hypoventilation syndrome (OHS) can be treated with either continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV) therapy; the device choice has important economic and operational implications.**

Methods: **This multicentre interventional trial investigated the safety and short-term efficacy of switching stable OHS patients who were on successful NIV therapy for ≥3 months to CPAP therapy. Patients underwent an auto-titrating CPAP night under polysomnography (PSG); if the ensuing parameters were acceptable, they were sent home on a fixed CPAP for a 4–6-week period. It was hypothesized that blood gas analysis, PSG parameters and lung function tests would remain unchanged.**

Results: **A total of 42 OHS patients were recruited, of whom 37 patients were switched to CPAP therapy. All patients had a history of severe obstructive sleep apnoea syndrome; chronic obstructive pulmonary disease (COPD) (Global Initiative for Obstructive Lung Disease (GOLD) I/II) was present in 52%. Regarding the primary outcome, 30 of 42 patients (71%, 95% CI: 55–84%) maintained daytime partial pressure of carbon dioxide ($PaCO_2$) levels ≤45 mm Hg after the home CPAP period. There was no further impairment in quality of life, sleep parameters or lung function. Interestingly, 24 patients (65%) preferred CPAP as their long-term therapy, despite the high pressure levels used (mean: 13.8 ± 1.8 mbar). After the CPAP period, 7 of 37 patients were categorized as CPAP failure, albeit only due to mild hypercapnia (mean: 47.9 ± 2.7 mm Hg).**

Conclusion: **It is feasible to switch most stable OHS patients from NIV to CPAP therapy, a step that could significantly reduce health-related costs. The auto-adjusted CPAP device, used in combination with the analysis of the PSG and capnometry, is a valid titration method in OHS patients.**

SUMMARY AT A GLANCE

A total of 42 obesity hypoventilation syndrome (OHS) patients undergoing home non-invasive ventilation (NIV) therapy were switched to a 4–6-week period of continuous positive airway pressure (CPAP) therapy. This protocol proved to be safe and well-tolerated by patients. There was no impairment in quality of life, sleep parameters or lung function. These data could significantly reduce costs for the health system.

Clinical trial registration: DRKS00008943 at www.drks.de/drks_web/ (German Clinical Trials Register)

Key words: continuous positive airway pressure, hypoventilation, non-invasive ventilation, obesity hypoventilation syndrome, polysomnography.

INTRODUCTION

During the last few decades, the western world has witnessed an alarming and persistent increase in the incidence of obesity.[1] One of the most serious consequences is 'obesity hypoventilation syndrome' (OHS), characterized by obesity (body mass index (BMI) of ≥30 kg/m^2) and diurnal hypercapnia (partial pressure of carbon dioxide ($PaCO_2$) ≥ 45 mm Hg), the latter of which cannot be explained by other causes of hypoventilation.[2,3] Moreover, almost 90% of OHS patients suffer concomitant obstructive sleep apnoea syndrome.[4] OHS is associated with an increase in mortality rate, mostly due to cardiovascular

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Received 22 March 2019; invited to revise 21 May and 18 August 2019; revised 26 July and 20 August 2019; accepted 3 September 2019 (Associate Editor: Amanda Piper; Senior Editor: Chris Grainge)

disease; it also leads to the use of more healthcare resources and lowers the health-related quality of life (HRQL) of affected individuals.[5,6] Currently considered a major public health problem, streamlining diagnosis, recognizing phenotypical characteristics and optimizing treatment remain a clinical challenge.[7–9]

Positive airway pressure is the gold standard therapy for OHS. It can be administered as either continuous positive airway pressure (CPAP) or non-invasive ventilation (NIV), with both therapies aiming to restore upper airway patency and reverse alveolar hypoventilation.[10,11] Importantly, selection of the therapy mode is a matter that must be carefully addressed, given its relevant economic implications; indeed, the price of a CPAP device is approximately one-third of that of an NIV device (Appendix S1 in Supplementary Information).[12] Moreover, a CPAP device is easier to use, smaller and less noisy.

Three randomized controlled trials comparing the efficacy of CPAP and NIV in patients with mild to moderate OHS have showed that both therapy modes yielded similar improvements in gas exchange, diurnal symptoms and sleep architecture.[12–14]

On the basis of these findings and the discussed considerations, CPAP presents as a more preferable mode of therapy in these patients. Nevertheless, OHS continues to be one of the most frequent indications for home NIV therapy worldwide, with an increasing trend.[15,16] This probably relates to the fact that up to 50% of OHS patients are diagnosed and initiated on NIV during an acute episode, and subsequently discharged on NIV.[14] It is also worth noting that some physicians underestimate the potential effectiveness of CPAP therapy in OHS, which subsequently favours NIV initiation.

It has been suggested that following therapy initiation, OHS patients become stable after a certain amount of time. This is due to a resetting of the respiratory drive centre, which, in turn, allows an improved response to hypercapnia.[17–19] Accordingly, a CPAP device might be sufficient to effectively treat hypoventilation in this cohort of patients.[20] The aim of the present study was to probe the safety and short-term efficacy of switching stable OHS patients from NIV (≥3 months) to CPAP therapy, irrespective of the reasons that led to NIV initiation. It was hypothesized that gas exchange, sleep quality, patient satisfaction and lung function would remain unchanged. Furthermore, this is the first trial to use an auto-adjusted CPAP (APAP) device under polysomnography (PSG) as a titration method in OHS patients.

METHODS

Study design

This was a prospective multicentre interventional open-label study registered in a publically accessible database (ID: DRKS00008943). Patients were recruited from August 2015 to August 2016 in the sleep units of the following hospitals: Cologne Merheim Hospital, Cologne;

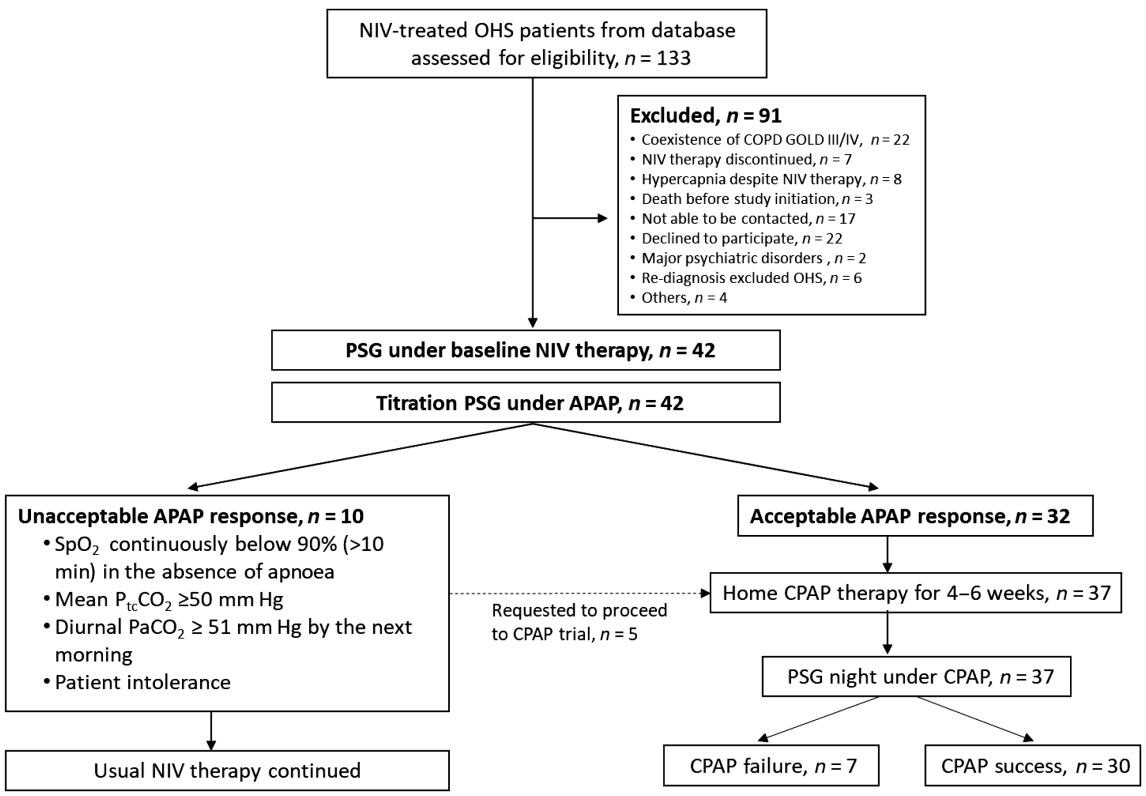

Figure 1 Study's flow diagram. Please note that five patients who met the APAP failure criteria were allowed to switch to CPAP therapy after presenting an informed request to do so. APAP, auto-adjusted CPAP; COPD, chronic obstructive pulmonary disease; CPAP, continuous positive airway pressure; GOLD, Global Initiative for Obstructive Lung Disease; NIV, non-invasive ventilation; OHS, obesity hypoventilation syndrome; $PaCO_2$, partial pressure of carbon dioxide; PSG, polysomnography; $P_{tc}CO_2$, transcutaneous capnography; SpO_2, oxygen saturation measured with pulse oximetry. CPAP success criteria: maintaining daytime $PaCO_2$ levels of ≤45 mm Hg after the home CPAP period.

Augustinerinnen Hospital, Cologne; and St. Remigius Hospital, Leverkusen, Germany. The ethics committee at the Witten/Herdecke University approved the study design (Nr.: 65/2015).

The inclusion criteria were: (i) Initial OHS diagnosis before NIV implementation that fulfilled the conventional diagnostic criteria[2,3]; (ii) Successful NIV therapy for at least 3 months, specifically diurnal $PaCO_2$ of ≤45 mm Hg (on spontaneous breathing) and <20% of total sleep time with oxygen saturation levels <90%; (iii) Adherence to NIV therapy for ≥4 h in at least 50% of nights over the last 3 months; and (iv) Age ≥ 18 years. The exclusion criteria were: (i) forced expiratory volume in 1 s/forced vital capacity (FEV_1/FVC) % ratio < 70% plus a FEV_1 < 50% of the predicted value; (ii) ≥2 hospital admissions for acute respiratory failure in the preceding year; (iii) acute decompensated comorbidity; (iv) coexistence of another condition that could lead to hypoventilation; and (v) psychophysical incapability to participate.

After providing written informed consent, a blood gas analysis was performed. If $PaCO_2$ was ≤45 mm Hg, patients could participate in the study and were hospitalized for two nights. Patient's medical record and baseline NIV information were reviewed. During the first night, sleep was monitored by PSG and transcutaneous capnography ($P_{tc}CO_2$) under usual NIV therapy.

After this baseline evaluation, only patients meeting ideal NIV treatment criteria were eligible to be switched to CPAP therapy.[21] Otherwise, patients were allowed to be re-evaluated to enter the study after undergoing at least 1 month of optimized ventilation.

On the second night, CPAP titration took place using an APAP device under PSG (Appendix S1 in Supplementary Information). In the case of an unacceptable APAP titration response, the patient remained on standard NIV therapy and was evaluated as a 'CPAP failure'. The APAP failure criteria were pre-defined as: mean $P_{tc}CO_2$ ≥ 50 mm Hg; oxygen saturation continuously below 90% (>10 min)

Table 1 Baseline characteristics

	n = 42
Age, years, mean (SD)	60 (11)
Gender (female/male)	19/23
BMI, kg/m^2, mean (SD)	45 (8)
Weight reduction ≥10 kg, *n* (%)[†]	8 (20)
Waist circumference, cm, mean (SD)	137 (14)
Neck circumference, cm, mean (SD)	47 (4)
Never smoker, *n* (%)	7 (17)
Active/former smoker, *n* (%)	35 (83)
Pack-years index, mean (SD)	43.5 (25)
Karnofsky index, %, mean (SD)	71.4 (12)
Use of supplemental oxygen, *n* (%)	16 (38)
Obstructive sleep apnoea syndrome, *n* (%)	42 (100)
AHI at diagnosis (events/h), median (IQR)	80 (42–98)
COPD with FEV_1 > 50%, *n* (%)	22 (52)
Arterial hypertension, *n* (%)	36 (86)
Ischaemic heart disease, *n* (%)	2 (5)
Chronic heart failure, *n* (%)	14 (33)
Diabetes mellitus, *n* (%)	20 (48)
Pulmonary hypertension, *n* (%)	3 (7)
Atrial fibrillation, *n* (%)	9 (21)
Stroke, *n* (%)	3 (7)
Baseline blood gas analysis on room air	
PaO_2, mm Hg, mean (SD)	64.7 (6.9)
$PaCO_2$, mm Hg, mean (SD)	39.0 (3.8)
HCO_3, mmol/L, mean (SD)	25.4 (1.8)
pH, mean (SD)	7.42 (0.02)
SaO_2, %, mean (SD)	93.5 (2)

Data are expressed as mean (SD) or median (IQR), according to their distribution.

[†]From diagnosis to study participation.

AHI, apnoea–hypopnoea index; BMI, body mass index; COPD, chronic obstructive pulmonary disease; FEV_1, forced expiratory volume in 1 s; HCO_3, arterial concentration of bicarbonate; IQR, interquartile range; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, partial arterial pressure of oxygen; pH, potential of hydrogen; SaO2, oxygen saturation of arterial blood

Table 2 Baseline characteristics of home NIV therapy

Reason for initial NIV therapy *n* = 42	*n* (%)
Initial CPAP failure under PG/PSG[†]	15 (36)
Severe initial daytime hypercapnia ($PaCO_2$ ≥ 62 mm Hg)[‡]	8 (19)
Acute hypercapnic respiratory failure (pH ≤ 7.35)	5 (12)
CPAP intolerance[†]	1 (2)
Severe obesity BMI ≥50 kg/m^2	2 (5)
Clinician's preference	9 (21)
Unknown	2 (5)
Baseline ventilator settings	
Time under NIV, months, median (IQR)	34 (13–57)
IPAP, cm H_2O, mean (SD)	23.1 (6)
EPAP, cm H_2O, mean (SD)	9.6 (2)
Ventilatory mode, *n* (%)	
aPCV	7 (17)
ST	35 (83)
Use of VAPS mode, *n* (%)	2 (5)
Back-up respiratory rate, mean (SD)	16 (3)
Mask, *n* (%)	
Nasal	16 (38)
Full face	24 (57)
Nasal pillows	2 (5)
Need for NIV therapy adjustment, *n* (%)	7 (17)
Time under adjusted NIV therapy, days, median (IQR)	56 (30–90)
Number of different NIV device brands	10

Data are expressed as mean (SD) or median (IQR), according to their distribution.

[†]Reference 21.

[‡]Reference 14.

aPCV, assisted pressure-control ventilation; BMI, body mass index; CPAP, continuous positive airway pressure; EPAP, expiratory positive airway pressure; IPAP, inspiratory positive airway pressure; IQR, interquartile range; NIV, non-invasive ventilation; $PaCO_2$, partial pressure of carbon dioxide; PG, polygraphy; pH, potential of hydrogen; PSG, polysomnography; ST, spontaneous timed; VAPS, volume-assured pressure support ventilation.

in the absence of apnoea; and $PaCO_2 \geq 51$ mm Hg 4 h after APAP removal the next morning.

Patients who were categorized as acceptable APAP responders were discharged under a fixed CPAP level for 4–6 weeks. Finally, patients were hospitalized for one night to undergo the same measurements as initially performed.

Patients filled out specific questionnaires at baseline and after the CPAP trial to explore the following factors: diurnal sleepiness,[22] subjective sleep quality[23] and HRQL specific to respiratory failure.[24] In addition, a simple questionnaire assessed patients' perspectives.

Statistical analysis

Sample size calculation was based on the primary endpoint 'successful switch to CPAP', defined as maintaining daytime $PaCO_2 \leq 45$ mm Hg after the home CPAP period. Calculations were performed using exact binomial distribution and based on the following assumptions: The study should have a power of 90% to show at a one-sided significance level of 2.5% that the probability of a successful switch to CPAP is larger than 0.5, if this probability is 0.75 or higher in reality. The required sample size was 42 patients.

For primary endpoint analysis, the rate of patients successfully switched to CPAP was calculated with a two-sided 95% CI. The primary analysis was based on the intention-to-treat population including all patients who underwent the nocturnal APAP titration trial and fulfilled the inclusion and exclusion criteria. Also, an analysis of the primary endpoint was performed in the sub-population with acceptable APAP response.

Linear regression models of repeated measurements were used for intra-patient comparison of secondary endpoints according to the different ventilator modes for patients who switched to CPAP. No adjustments for multiple testing were made. All *P*-values should be interpreted in a descriptive sense. All analyses were performed with Statistical Analysis System (SAS 9.4) software (SAS Institute, Inc., Cary, NC, USA).

Table 3 Pulmonary function tests: Baseline NIV versus switch to CPAP

n = 37	NIV	CPAP	*P*-value
PaO_2 (mm Hg)	66.9 (8.8)	64.7 (9.0)	0.14
$PaCO_2$ (mm Hg)	39.4 (3.9)	41.5 (4.9)	0.004
HCO_3 (mmol/L)	25.2 (1.6)	26.0 (1.8)	0.02
pH	7.42 (0.029)	7.42 (0.028)	0.69
FEV_1 (%)	70.4 (12.6)	67.4 (13.4)	0.019
FVC (%)	76.1 (11.5)	73.7 (13.9)	0.12
FEV_1/FVC (%)	74.8 (10.5)	74.6 (11.8)	0.89
6MWD (m)	342 (120)	351 (140)	0.43
Borg after 6MWD	3.0 (2.6)	3.3 (2.5)	0.47
% of use >4 h/day	81.7 (5.1)	80.8 (6.0)	0.21

Data are expressed as mean ± SD.

6MWD, 6-min walk distance; CPAP, continuous positive airway pressure; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; HCO_3, arterial concentration of bicarbonate; NIV, non-invasive ventilation; $PaCO_2$, partial pressure of carbon dioxide; PaO_2, arterial partial pressure of oxygen; pH, potential of hydrogen.

Table 4 Sleep polysomnography and transcutaneous capnography: Baseline NIV versus switch to CPAP (*n* = 37)

	NIV	CPAP	*P*-value
TST (min)	294.4 (82)	298.8 (81)	0.78
Sleep efficiency (%)	77 (14)	80.5 (13)	0.12
N2 sleep (%)	50 (15)	50.8 (13)	0.74
Deep sleep (%)	19.3 (14)	23.6 (15)	0.067
REM sleep (%)	17 (9)	16.5 (8)	0.79
Arousal index (events/h)	18.5 (10)	20.3 (13)	0.37
RDI (events/h)	1.7 (3)	2.4 (3)	0.31
Desaturation index (events/h)	4.3 (7)	3.6 (4)	0.56
Mean SpO_2 (%)	93.2 (2)	93.6 (2)	0.24
% TST < 90 (%)	10.5 (16)	6.7 (15)	0.31
Mean $P_{tc}CO_2$ (mm Hg)	42.2 (5)	46.3 (5)	<0.001

Data are expressed as mean ± SD.

CPAP, continuous positive airway pressure; N2, sleep stage 2; NIV, non-invasive ventilation; $P_{tc}CO_2$, transcutaneous capnography; RDI, respiratory disturbance index; REM, rapid eye movement; SpO_2, oxygen saturation measured with pulse oxymetry; % TST < 90, percentage of TST below 90% of oxygen saturation; TST, total sleep time.

RESULTS

Of the 133 patients eligible for the study, 91 were excluded and 42 were recruited (Fig. 1). There were no dropouts. Table 1 summarizes the baseline anthropometric characteristics of the recruited cohort. The mean age was 60 ± 11 years, with a mean BMI of 45 ± 8 kg/m^2.

All patients suffered from severe obstructive sleep apnoea syndrome. Eighty-three percent of study participants were either active or former smokers, while 52% had chronic obstructive pulmonary disease (COPD) (Global Initiative for Obstructive Lung Disease (GOLD) I/II) as a comorbidity.

Baseline characteristics of home NIV therapy are described in Table 2. Patients were experienced NIV

Table 5 HRQL and sleep questionnaires: Baseline versus switch to CPAP (*n* = 37)

SRI	NIV	CPAP	*P*-value
SRI-SS (/100)	61.2 (16)	65.3 (14)	0.10
SRI-RC (/100)	63.2 (19)	65.7 (18)	0.40
SRI-PF (/100)	51.8 (20)	54.8 (21)	0.20
SRI-AS (/100)	57.4 (20)	59.3 (20)	0.56
SRI-SR (/100)	72 (20)	77.9 (17)	0.086
SRI-AX (/100)	58.5 (25)	69.6 (22)	0.006
SRI-WB (/100)	62.4 (19)	64.2 (20)	0.58
SRI-SF (/100)	63.1 (19)	65.6 (18)	0.47
Sleep questionnaires			
ESS (/24)	8.1 (4)	7.6 (4)	0.49
Pittsburgh Quality Sleep Questionnaire (/21)	7.14 (3)	7.5 (3)	0.46

Data are expressed as mean ± SD.

AS, attendant symptoms and sleep; AX, anxieties; CPAP, continuous positive airway pressure; ESS, Epworth Sleep Scale; HRQL, health-related quality of life; NIV, non-invasive ventilation; PF, physical functioning; RC, respiratory complaints; SF, social functioning; SR, social relationships; SRI, Severe Respiratory Insufficiency; SS, summary scale; WB, well-being.

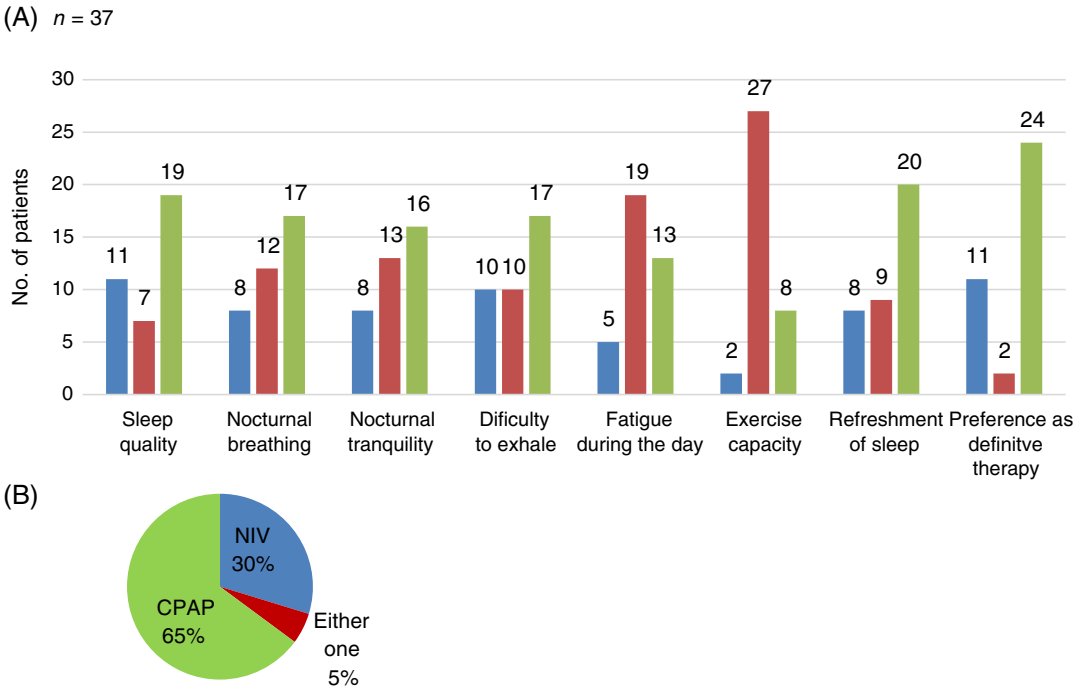

Figure 2 Results of the Patient Questionnaire. (A) Graph representing the type of therapy preferred by patients for seven different items listed in the questionnaire (■, non-invasive ventilation; ■, no difference; ■, continuous positive airway pressure). (B) Mode of ventilation preferred by patients for long-term therapy.

users. While the predictive factors of CPAP failure in OHS patients remain unknown, the initial choice of NIV over CPAP was deemed justified by the authors in 67% of patients: 36% were due to initial CPAP failure under polygraphy (PG)/PSG according to consensus criteria,[21] 19% due to severe initial hypercapnia[14] and 12% due to acute hypercapnic respiratory failure. The remaining 33% of cases corresponded to rather subjective reasons. In 17% of patients, an NIV optimization period was required before switching to CPAP, which was mainly related to increasing pressure support in order to overcome hypercapnia.

The results of the APAP titration night are presented in Appendix S1 (Supplementary Information). Only one patient presented with APAP intolerance. Interestingly, 5 of 10 patients who met the APAP failure criteria requested to try the home CPAP trial, based on their satisfactory experience during the APAP night. Their request was accepted, as they only showed mild differences to the arbitrarily defined acceptable APAP response (four patients were normocapnic but met the other two APAP failure criteria, while one patient presented with a $PaCO_2$ of 51.6 mm Hg). After the CPAP period, three of these patients met the CPAP success criteria (to maintain daytime $PaCO_2 \leq 45$ mm Hg).

Regarding the primary endpoint, 30 of the 42 patients for whom the CPAP switch was intended (71%, 95% CI: 55–84%) maintained daytime $PaCO_2$ levels of ≤45 mm Hg after the home CPAP period. The 37 patients who were actually switched to CPAP remained under this mode for a median (interquartile range, IQR) of 35 (33–42) days. In the patient subgroup with acceptable APAP responses after the titration night ($n = 32$), 27 patients (84%, 95% CI: 67–95%) maintained daytime $PaCO_2$ levels of ≤45 mm Hg after the home CPAP period.

Table 3 presents the baseline pulmonary function values under patients' regular NIV therapy as well as after the switch to CPAP. Blood gas parameters and lung function tests remained unchanged. In addition, there was no significant weight change between baseline and after the CPAP period ($P = 0.18$).

Table 4 demonstrates that there were no impairments in the polysomnographic measurements. As expected, the $P_{tc}CO_2$ level rose slightly under CPAP, but remained within a clinically acceptable range.

The HRQL and sleep questionnaires (Table 5) revealed no significant differences, after the CPAP switch. Nevertheless, patients may have been less anxious under CPAP therapy, as shown in the Severe Respiratory Insufficiency (SRI) questionnaire.

No patient experienced any type of decompensation during the CPAP period. The mean CPAP level used was 13.8 ± 1.8 mbar (1 mbar approximately equals 1 cm H_2O pressure). After the CPAP period, 7 of 37 patients were categorized as CPAP failure, albeit only due to mild hypercapnia (mean: 47.9 ± 2.7 mm Hg). The CPAP failure group tended to have a higher BMI (mean: 47.1 ± 10 vs 43.9 ± 6.4 kg/m^2). The required inspiratory positive airway pressure (IPAP) level on NIV was also slightly higher in the CPAP failure group (mean: 24.6 ± 5.1 vs 22.1 ± 6.6 mbar). Similarly, the required CPAP in the failure group was higher than in the CPAP success group (mean: 15 ± 2.3 vs 13.6 ± 1.6 mbar). The coexistence of COPD did not seem to lead to a higher risk of CPAP failure. Nevertheless, it must be noted that the mean baseline FEV_1 value was slightly lower in the CPAP failure group (66.1 ± 14 vs 71.6 ± 12.1% of predicted

value). Other factors such as age, gender and the reason for NIV initiation were similar in both groups.

Figure 2 shows the results of patient preferences. Overall, the majority of patients (24/37) preferred CPAP as their long-term therapy. Similarly, in five of the seven questionnaire items, CPAP was considered better, while in the remaining two items, patients reported no differences between both therapies.

DISCUSSION

This multicentre interventional trial demonstrated that stable OHS patients treated with NIV for ≥3 months can be safely switched to CPAP therapy, even if patients had an initial history of CPAP failure or acute hypercapnic respiratory failure. After 4–6 weeks of switching to CPAP therapy, the majority of patients maintained $PaCO_2$ levels ≤45 mm Hg, and there was no deterioration in polysomnographic parameters, HRQL or respiratory function. A randomized long-term study comparing outcomes between staying under NIV therapy versus switching to CPAP should be performed to validate the results of the present study.

A CPAP device is considerably cheaper and easier to set up than an NIV device. The certainty that OHS patients on home NIV can be safely switched to CPAP therapy would reduce associated healthcare costs, and minimize the requirement for highly trained health personnel. Such a treatment approach would enable greater access to therapy in areas with less favourable economies.[25]

A pilot study that probed the feasibility of switching 15 OHS patients from NIV to CPAP also reported positive results.[26] However, the patients in that study only had mild OHS. Moreover, significantly lower positive airway pressures were used in both CPAP (9.8 ± 1.4 mbar) and NIV (IPAP: 18.3 ± 3, expiratory positive airway pressure (EPAP): 7.7 ± 1.8 mbar) therapies. This could explain why 7 of 15 and 8 of 15 patients, respectively, met therapy failure criteria. In addition, CPAP titration and sleep studies were not performed.

The present study followed a standardized protocol. Patients were only switched to CPAP therapy if they were normocapnic and on optimal NIV therapy, which was assessed under PSG and $P_{tc}CO_2$.[27] This is the first trial to use APAP under PSG, as a method of CPAP titration in OHS patients[28]; it proved to be effective and very well tolerated. New studies should therefore be performed in the future to examine the clinical application of APAP titration in OHS patients.

NIV therapy is the only alternative for overcoming ventilatory insufficiency in hypoventilation conditions such as neuromuscular diseases or severe COPD. However, the majority of pathophysiological mechanisms involved in OHS can be safely corrected with CPAP. Over 90% of OHS patients suffer from concomitant obstructive sleep apnoea, where upper airway stability can be restored with CPAP.[29] Furthermore, as a consequence of central fat distribution, OHS patients present with reduced lung volumes, decreased chest wall compliance and increased work of breathing.[19,30] There is evidence that if these alterations are mild to moderate, CPAP can effectively reverse hypoventilation after a few weeks.[12,31] Furthermore, a blunted ventilatory drive response to hypoxaemia and hypercapnia has been identified in OHS patients.[18,32] Interestingly, restoration of this condition can be expected within a few months of positive airway pressure ventilation use,[19] thus allowing CPAP to become a suitable therapy.[33] However, it should be acknowledged that in some cases of severe OHS, CPAP might not be sufficient to restore normocapnia[12]; the use of NIV therapy here is therefore justified.[33]

In the present study, only a small number of patients were categorized as CPAP non-responders, albeit only in association with mild hypercapnia.

The study population cannot be regarded as representative for all OHS patients, but patients included represent the population for whom a switch to CPAP was considered feasible, and was therefore intended. Similarly, the coexistence of COPD GOLD stages I/II could be seen as a weakness of this study. However, the heterogeneity of the cohort actually mirrors the current real-life situation: OHS–COPD overlap syndrome is a new challenge that is expected to increase in the coming years. In addition, as the participants in the present study had severe obstructive sleep apnoea syndrome, the results cannot be extended to lone OHS.

To avoid a possible residual effect of NIV therapy, the inclusion of an NIV wash-out period prior to the CPAP switch was considered.[34] However, as the participants had moderate to severe OHS, it was deemed unethical to leave them without therapy. Ten different device brands were used in this patient cohort. Although different devices may not perform identically, they should not imply treatment inefficacy.[35] However, this non-uniformity amongst devices did render the download of in-built software information unfeasible. As a result of this, there are no compliance data, which is a limitation of the present study.

Unexpectedly, the majority of patients stated their preference for CPAP therapy in the long term. This despite the high CPAP levels used, and in contrast to the concern that it might be more difficult to exhale against a fixed CPAP pressure. Randomized controlled studies addressing patients' preferences for NIV versus CPAP would be welcome to validate these data.

Data availability statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Acknowledgements: The authors would like to thank the engagement of the personal at the sleep units of Cologne Merheim Hospital, Cologne, Germany; der Augustinerinnen hospital, Cologne, Germany; and Remigius Hospital, Opladen, Germany. M.P.A.-M. received a research fellowship grant from Pontificia Universidad Católica de Chile, Santiago, Chile.

Disclosure statement: S.S., J.C., M.L.D., J.S., W.W. and M.S. received funding from Phillips Respironics, ResMed, Vivisol, VitalAire, Fischer and Paykel, SenTec, Boehringer Ingelheim Pharma, Breas Medical, Linde, Weinmann, Heinen und Löwestein. M.P.A.-M. received a research grant from the Pontificia Universidad Católica de Chile.

Author contributions: Conceptualization: M.P.A.-M., W.W. Data curation: M.P.A.-M., S.S. Formal analysis: C.S. Funding acquisition: W.W., M.P.A.-M. Investigation: M.P.A.-M., C.H., S.S. Project

administration: J.H.S., C.H., M.S., W.G., J.C. Resources: W.W., M.S., W.G., J.C. Software: J.C. Supervision: W.W., J.H.S., W.G., M.S. Visualization: M.P.A.-M., W.W., M.D. Writing—original draft: M.P.A.-M., C.S. Writing—review and editing: W.W., M.L.D., C.S., M.P.A.-M., M.S.

Abbreviations: 6MWD, 6-min walk distance; APAP, auto-adjusted CPAP; CPAP, continuous positive airway pressure; EPAP, expiratory positive airway pressure; FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; GOLD, Global Initiative for Obstructive Lung Disease; HCO_3, arterial concentration of bicarbonate; HRQL, health-related quality of life; IPAP, inspiratory positive airway pressure; IQR, interquartile range; NIV, non-invasive ventilation; OHS, obesity hypoventilation syndrome; $PaCO_2$, partial arterial pressure of carbon dioxide; PaO_2, partial arterial pressure of oxygen; PG, polygraphy; pH, potential of hydrogen; PSG, polysomnography; $P_{tc}CO_2$, transcutaneous capnography; SpO_2, oxygen saturation measured with pulse oximetry; SRI, Severe Respiratory Insufficiency Questionnaire.

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Supplementary Information

Additional supplementary information can be accessed via the *html* version of this article at the publisher's website.

Appendix S1. CPAP titration.

