Sleep and Breathing (2021) 25:1867–1873
https://doi.org/10.1007/s11325-021-02291-6

SLEEP BREATHING PHYSIOLOGY AND DISORDERS • ORIGINAL ARTICLE

Combination of positional therapy with positive airway pressure for titration in patients with difficult to treat obstructive sleep apnea

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Received: 19 October 2020 / Revised: 30 December 2020 / Accepted: 5 January 2021 / Published online: 23 January 2021

Abstract

Introduction Positional therapy has been described as add-on therapy to a mandibular advancement device, but the efficacy of combination of positional therapy and positive airway pressure (PPAP) has not been documented. We have found PPAP therapy as an effective method of titration in patients with difficult to treat OSA (obstructive sleep apnea).

Methodology This retrospective analysis was done in patients who had difficult to treat OSA, i.e., in whom titration in the supine position was *unacceptable* with any PAP device (CPAP or bilevel PAP) and could only be successfully titrated with a PAP device in the lateral position. This study describes our experience of PPAP therapy. Baseline characteristics and polysomnography data of patients who were successfully titrated in supine v/s lateral positions were compared.

Results Of 272 consecutive patients with OSA selected for analysis, 218 patients (191 and 27 with CPAP and bilevel PAP, respectively) could be successfully titrated in supine position. Further 54 (20%) patients in whom titration in supine position was *unacceptable* were titrated in lateral position. Patients titrated with PAP in the lateral position therapy group had higher BMI, higher neck and waist circumference, and lower awake sPO_2 and nadir sPO_2 during sleep, and spent more time in sleep with $sPO_2 < 90\%$.

Conclusion Combination of positional therapy and PAP device is an effective way of titration for difficult to treat OSA patients. It can be tried in patients who fail titration in supine position.

Keywords Obstructive sleep apnea · Continuous positive airway pressure failure · Bilevel positive airway pressure · Titration · Positional therapy · OSA in India

Introduction

Obstructive sleep apnea (OSA) is a breathing disorder during sleep which creates a mismatch in airflow and efforts for breathing [8]. OSA is often associated with significant cardiovascular conditions, derangement in the quality of life such as fatigability, excessive daytime sleepiness, insomnia, nocturia in adults and poor attention span, enuresis, and poor academic grades in children [5, 9, 10]. The main underlying pathophysiology of OSA is hypoxemia and inflammation.

Currently, best available treatment of OSA is continuous positive airway pressure (CPAP) which is usually effective for most OSA patients. Positional therapy is also an alternative for some of the patients who have almost normal sleep in non-supine position. These patients have been described as younger, with lower BMI and smaller neck, waist, and hip circumferences and with less prevalence of hypertension compared to patients with non-positional OSA [17].

According to the American Academy of Sleep Medicine (AASM) titration guidelines, patients with OSA should be first titrated with CPAP and if apnea or hypopnea could not be abolished till 15 cm H_2O, then the patient can be titrated with bilevel PAP [11]. The maximum pressure recommended with bilevel PAP is 30 cm H_2O in adults. AASM has graded titration on basis of consensus into four types: optimal, good, adequate, and inadequate. Titration is defined as optimal when "apnea-hypopnea index (AHI) is reduced to less than 5 per hour for at least a 15-min duration and should include supine REM sleep at the selected pressure." Good titration is defined as when "AHI is reduced to ≤ 10 per hour or by 50% if the baseline AHI < 15 per hour and should include supine REM

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sleep." An adequate titration is defined as "one that does not reduce the overnight AHI ≤ 10 per hour but does reduce the AHI by 75% from baseline, or one in which the titration grading criteria for optimal or good are met with the exception that supine REM sleep did not occur at the selected pressure." An unacceptable titration is one that does not meet any one of the above grades.

In some patients with severe OSA, optimal or good titration cannot be achieved with maximum CPAP pressures and then they are titrated with bilevel PAP in supine position. If optimal or good titration could not be achieved, then AASM recommends repeating titration. At our referral sleep lab, we often find some difficult to treat OSA (dOSA) patients in whom optimal or good titration cannot be achieved with either CPAP or bilevel PAP (even with maximum inspiratory pressure of 30 cm H_2O) in supine position. In these patients, supine REM could not be achieved, and AHI could not be decreased by 75% from baseline, i.e., they do not even match the criteria for adequate titration. We have found that the only way these patients can be managed is by titrating them in lateral position. Position therapy has been advised as an important treatment option in isolation and in combination with therapies like a mandibular advancement device [2] [6], but its combination with any PAP device has never been described in literature. In our experience, positional positive airway pressure (PPAP) is effective for titration of difficult to treat OSA patients. This study describes our experience of PPAP therapy in our sleep lab.

Material and methods

Design and settings

A retrospective medical record review study was done in OSA patients who were diagnosed in the sleep laboratory of AIIMS Bhopal Hospital. Records of consecutive patients diagnosed between June 2015 and July 2019 were extracted from our sleep registry.

Data abstraction process

We maintain an electronic record for every patient undergoing polysomnography (PSG). This record consists of clinical history, examination, biochemistry, and ABG reports; Epworth sleepiness score assessment was done by a sleep physician. It also has information on routine investigations including complete hemogram, pulmonary function tests, thyroid function tests, and results of PSG. Data was retrieved from an electronic database by a sleep physician. Detailed history for sleep symptoms, clinical examination for anthropometry, and biochemical investigations were taken for analysis. All patients performed spirometry according to the American Thoracic Society/ERS guidelines using Cosmed Quark PFT [13]. Indian reference values were used [4]. All patients who had $FEV_1/FVC < 0.7$ were labeled as obstructive lung disease and were excluded from the sample size.

Anthropometry

The waist was defined as the point midway between the iliac crest and the lower costal margin. Waist measurement was done during normal breath out with tape snugly fitted and horizontal to the floor while the subject is standing. Hip circumference was measured around the widest portion of the hips with tape snugly fitted and horizontal to the floor while the subject is standing with arms at the sides and feet close together. Neck circumference was measured at the level of the cricothyroid membrane with tape while the patient in standing position.

Polysomnography

Level I polysomnography (PSG) was done with Alice 6 PSG lab (Philips Respironics, USA). EEG, cEMG, Leg EMG, EOG, sPO_2, and chest and abdominal movements with zRIP belts and body sensor were used in all patients. AASM 2012 criteria for scoring apnea and hypopneas were used [3]. Apnea was defined as the cessation of airflow through the nose ≥ 10 s. Hypopnea was defined as the reduction in airflow ≥ 30% associated with a decrease in oxygen saturation measured by pulse oximetry (sPO_2) ≥ 3% and/or associated with arousal.

Titration protocol followed at our sleep lab (Fig. 1)

We do manual titration with OmniLab Advanced (Philips Respironics, USA) in all our patients. All patients with moderate or severe OSA (AHI > 15) undergo titration with CPAP, which starts @ 4 cm H_2O.

Failure of titration

We try to achieve optimal or good titration in our sleep lab according to AASM criteria, which is defined as the presence of supine REM at adequate pressure and final AHI < 5 (optimal) or AHI < 10 (good titration). If the patient's AHI cannot be decreased below 10/hour and the patient does not achieve supine REM for more than 15 min, even with maximum CPAP titration (i.e., 18 cm H_2O), it is considered a failure of titration with CPAP. Then, these patients undergo titration with bilevel PAP according to AASM titration guidelines [11]. If a patient could not be successfully titrated (optimal or good titration as earlier described) even with maximal pressure of IPAP 30; then, the patient is retitrated in a lateral position and titration is started at CPAP of 4 cm H_2O.

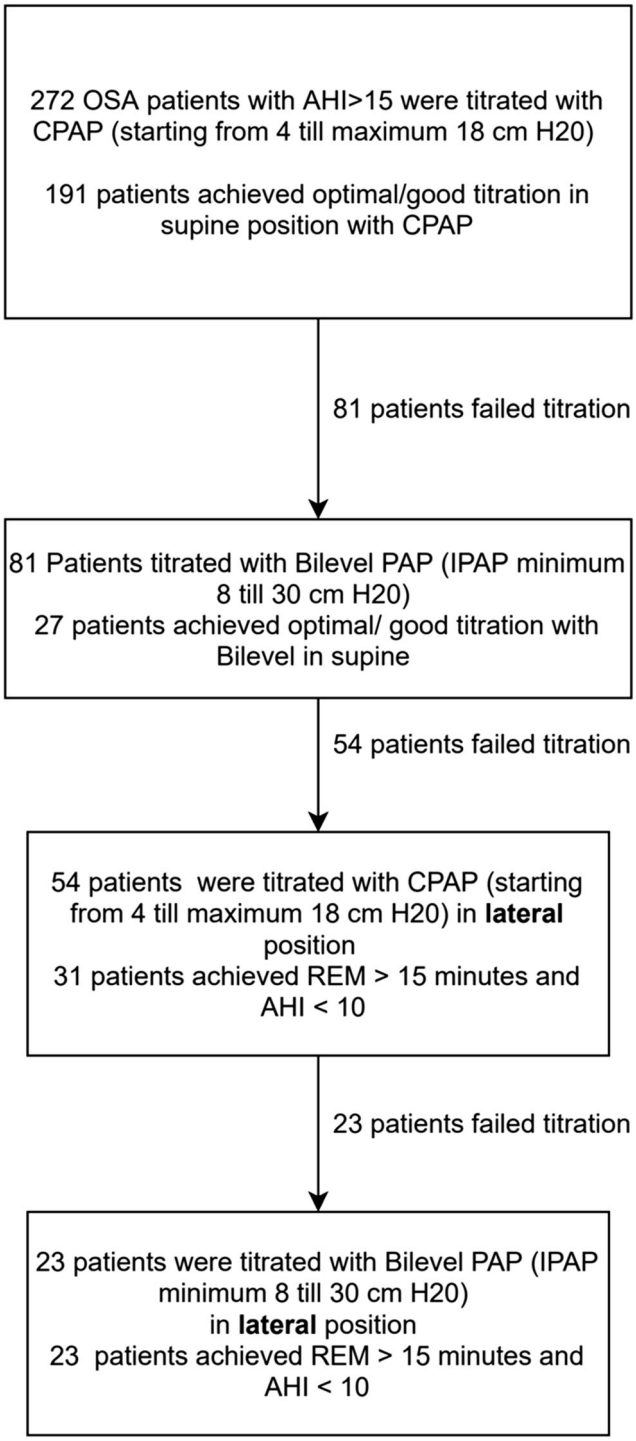

Fig. 1 Sequential titration protocol followed in our lab

Titration in lateral position is called successful if AHI can be decreased < 10 and achieve REM for more than 15 min. Patients are titrated with CPAP till a maximum of 18 cm H_2O and if the AHI does not fall below 10 or REM > 15 min is not achieved, then these patients are titrated with bilevel PAP in lateral position therapy. In lateral position, titration with CPAP and bilevel PAP is done as recommended by AASM titration guidelines. With this protocol, we were able to achieve target AHI < 5 in 80% and < 10 in 100% of OSA patients.

The prescribed pressure should be given for at least 30 min, out of which a minimum of 15 min should be in the REM stage. In our lab, bilevel PAP-S is used in patients with OSA and bilevel-S/T mode was used only in patients with hypoventilation like OHS or associated COPD. For positional therapy, we use an indigenously made positional device made up of hard pillows and a belt.

Measurement of hypoventilation

According to our protocol, we perform arterial blood gases (ABG) in all suspected OSA patients after taking consent. For ABG analysis, an ABG analyzer (Radiometer, Bronshoj, Denmark) was used. From ABG, direct measurement of PaO_2, $PaCO_2$ values, and calculated values of HCO_{3-} were noted.

We measure $etCO_2$ (lofloetCO_2 capnography sensor, Philips Respironics, USA) for detecting nocturnal hypoventilation in our sleep lab. Nocturnal hypoventilation was scored when the $etCO_2$ was > 55 mmHg for ≥ 10 min or there was an increase in the $etCO_2$ ≥ 10 mmHg (in comparison with an awake supine value) to a value exceeding 50 mmHg for ≥ 10 min[6]. Obesity-related hypoventilation was described according to ERS definition [16].

Data analysis

We have used IBM SPSS Statistics for Macintosh, Version 26.0 (Armonk, NY: IBM Corp.) for analysis. For descriptive statistics, we used count and proportion to summarize nominal variables and mean and standard deviation for numerical variables. The difference in numerical variables across supine and positional groups was tested by the unpaired *t*-test for normally distributed numerical variables or Mann-Whitney *U*-test for skewed variables. The distribution of nominal variables was compared by using the chi-square test. For all analyses, statistical significance was determined at *p* value less than 0.05.

Results

During the study period, 474 patients underwent sleep study and 440 patients had AHI > 15. Out of these 440, 366 patients underwent titration with PAP. Out of these patients, 94 patients were excluded from this analysis due to the presence of airway obstruction on spirometry.

A total of 272 patients were finally included in the analysis. Out of these, 191 patients were successfully titrated with CPAP in the supine position. In those patients in whom optimal/good titration could not be achieved with CPAP (*n* = 81), 27 patients were successfully titrated with bilevel PAP

Table 1 Frequency of patients who were successfully titrated with CPAP/bilevel PAP in supine or lateral position

	Frequency	%	Cumulative percent
CPAP supine	191	70	70
Bilevel supine	27	10	80
CPAP lateral	31	11	91
Bilevel lateral	23	9	100.0
Total	272		100.0

CPAP: continuous positive airway pressure device; PAP: positive airway pressure device

in the supine position. Further patients in whom optimal/good titration could not be achieved in the supine position with either CPAP or bilevel PAP (n = 54) were first titrated with CPAP in the lateral position. Thirty-one patients were successfully titrated (AHI < 10 and REM > 15 min) with CPAP in the lateral position. Further 23 patients could only be successfully titrated (AHI < 10 and REM > 15 min) with bilevel PAP in lateral position (Fig. 1, S1 : Figs. 1 and 2 and Table 1).

The analysis was done for baseline characteristics in patients who were successfully titrated in supine position (optimal or good) with either CPAP or bilevel PAP (henceforward called as the supine PAP group) and patients who could be successfully titrated (AHI < 10 and REM > 15 min) only in lateral position with either CPAP or bilevel PAP (henceforward called as the positional PAP or PPAP group) (Table 2).

Patients in the PPAP group (n = 54; 20%) were more obese: higher BMI (p = 0.016), higher neck circumference (p = 0.005), and waist circumference (p = 0.002). These patients also had significantly lower awake sPO_2 (p = 0.017) (Table 2 and Fig. 2). Although the difference in AHI did not reach a statistically significant difference, other markers of OSA severity like nadir oxygen during sleep and T90 (percentage of total sleep time spent with sPO_2 < 90%) were significantly different between the two groups (p = 0.015 and 0.002, respectively).

Approximately 1/3 of patients who were diagnosed with obesity hypoventilation syndrome (OHS) (n = 55) could be successfully titrated (with AHI < 10 and REM > 15 min) only in the lateral position with PAP. Other baseline characteristics were not different between these two groups. History of sleeping position was available in only 230 individuals (out of 272). Out of 158 patients who gave a history of sleeping preferably in the lateral position at home, 125 (80%) could be titrated in the supine position. Similarly, 89% of patients who prefered to sleep in the supine position at home were titrated in the supine position. Twelve out of 53 in the PPAP group and 73 out of 217 in the supine PAP group had positional OSA, respectively, on diagnostic sleep study, with no significant difference seen (Table 2).

Discussion

This study shows our initial experience with combination of positional therapy and PAP (PPAP) in titration of patients with difficult to treat OSA (dOSA). With PPAP therapy, we

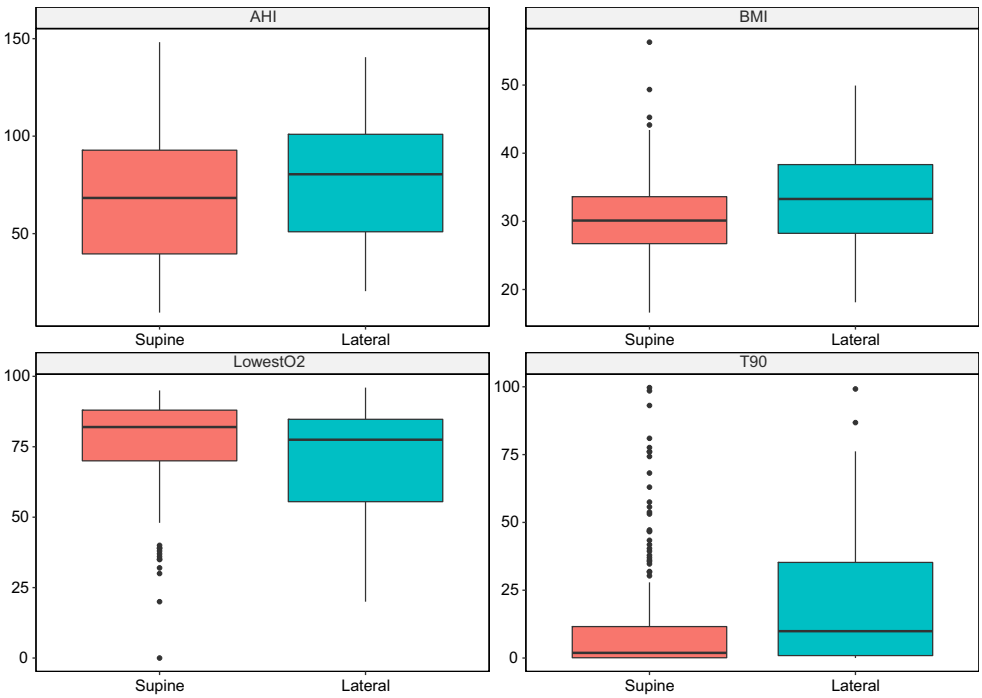

Fig. 2 Box plot showing differences in AHI, BMI, nadir O_2, and T90 in groups (supine PAP and positional PAP). AHI: apnea-hypopnea index; BMI: body mass index; T90 : percent sleep time spent with sPO_2 < 90%

Table 2 Baseline characteristics of patients in supine PAP and positional PAP group

Variables	Supine PAP Mean (SD); median	Positional PAP Mean (SD); median	*p* value
Age	50.4 (11.3); 51.5	51.6 (12.6); 52	0.537
Males Females	144 (83.2) 56 (81.2)	29 (16.8) 13 (18.8)	0.700
Body mass index	30.7 (5.5); 30.4	33.7 (7.1); 33.9	0.016
Epworth sleepiness scale	9.2 (4.9); 9	9.2 (4.6); 9.5	0.964
Awake sPO_2	95.6 (3.7); 96	93.9 (4.1); 95	0.017
Neck circumference	15.9 (1.4); 16	16.6 (1.4); 16	0.005
Waist circumference	41.4 (5.1); 42	44.1 (5); 43.8	0.002
Hip circumference	42.4 (5.1); 42	43.6 (4.5); 43	0.161
Fasting blood sugar	112.4 (73.5); 99	128.8 (119.1); 102.5	0.226
Forced vital capacity%	79.4 (17); 80	79.4 (23.1); 83	0.667
FEV1 %	84.2 (19.3); 85	85.4 (25.6); 88	0.541
AHI	69.2 (34.1); 69.3	79.7 (31.4); 81.4	0.054
REM AHI	42.8 (38.4); 43.6	45.6 (40.7); 50	0.719
NREM AHI	67.9 (35.7); 68.8	78.8 (32.8); 79.1	0.053
Supine AHI	78 (36.5); 82.3	88.1 (37.6); 90.8	0.124
Lt AHI	38.3 (44.6); 19.2	37.1 (44.2); 0	0.595
Rt AHI	49.2 (44.8); 38.6	61.1 (42.4); 56.9	0.066
Lowest oxygen level	76.1 (16.3); 82	69.6 (18.8); 76	0.015
T90%	11.3 (20.4); 2	23.7 (28.8); 12.3	0.002
No OHS OHS	167 (84.8) 37 (67.3)	30 (15.2) 18 (32.7)	0.003
Position history-supine (n = 72) Position history-lateral (n = 158)	64 (88.9) 125 (79.1)	8 (11.1) 33 (20.9)	0.072
POSA on PSG (n = 85) No POSA on PSG (n = 185)	73 (85.9) 144 (77.8)	12 (14.1) 41 (22.2)	0.167

AHI: apnea-hypopnea index; sPO_2: saturation by pulse oximetry; T90: percent sleep time spent with $sPO_2 < 90\%$; OHS: obesity hypoventilation syndrome; FEV1: forced expiratory volume in 1 s; REM: rapid eye movement; NREM: non-rapid eye movement; PAP: positive airway pressure device; POSA: positional OSA; PSG: polysomnography

were able to successfully treat patients who failed conventional titration in the supine position.

Patients with positional OSA (POSA) are described as those with severe disease in the supine position and much less severe in the lateral position. They are usually younger, thinner (lower BMI, waist, hip, and neck circumference), lower chances of hypertension, lower ESS, and lower STOPBANG scores compared to patients with non-positional OSA. On PSG, they usually sleep in the lateral position; they have better sleep efficiency, more total sleep time, lower AHI, and lower ODI compared to non-positional OSA patients. Recently, a new classification system for positional sleep apnea was described, in which POSA was classified into three types, the most severe being type III: patients with an overall AHI ≥ 40 who can theoretically achieve a > 25% reduction of their AHI with positional therapy (PT) only [7]. The authors suggested that positional therapy can be used in combination with existing therapies, and thereby improving compliance. They have also mentioned that patients' CPAP pressure requirement can also be reduced if POSA is used in this subtype III. Our study also suggests the same point that some patient who do not achieve either optimal or good titration in spite of maximum pressure (up to IPAP of 30 cm H_2O) in the supine position can be managed with much lower pressure in the lateral position.

Previously, Dieltjens et al. did a study in post-mandibular advancement device (MAD) residual supine predominant OSA (i.e., POSA persisting after MAD) and did PSG on two consecutive nights: one with Sleep Position Trainer (SPT) and next with MAD-SPT combination [6]. They demonstrated the combination of MAD and SPT was most effective in reducing median overall AHI (from 20.9/h to 5.5/h) in comparison to individually MAD and SPT which were also able to reduce AHI from baseline (from 20.9/h to 11.6/h and 12.8/h, respectively). With combination therapy, 95% of subjects achieved a minimum of > 50% or more reduction in AHI.

Out of 15 subjects, 7 patients preferred combination therapy. Similarly, Benoist et al. showed that additional PT in patient population with residual POSA after upper airway surgery can improve the mean disease alleviation from 39.5% (effect of surgery alone) to 65.6% (effect of combining surgery and PT) [2].

At our referral sleep lab, we often find some patients with difficult to treat OSA (dOSA) in whom optimal or good titration cannot be achieved with either CPAP or bilevel PAP in the supine position. In these patients, supine REM could not be achieved, and AHI could not be decreased by 75% from baseline. We have found the combination of positional + PAP (PPAP) therapy as a good treatment option for patients with dOSA. AHI could be decreased to < 10/h, and stable REM could be achieved in these patients in the lateral position only. By conventional definition, this does not fit into optimal or good titration, as supine REM is mandatory criteria for both of these, but for these patients, this is the best that could be achieved with PAP therapy.

Our study shows that patients who require PPAP are more obese (higher BMI, neck, and waist circumference). In the supine position, gravity further narrows the retroglossal area causing more obstruction and less airflow; that is probably why these patients respond well to the combination of positional and PAP therapy. Patients requiring PPAP have also more severe OSA. Although AHI difference was not statistically different, among the other severity markers, patients with PPAP had much lower nadir oxygen and they spent more time below 90% during sleep. Also, it was shown that OHS patients were more difficult to treat in the supine position with PAP and around 1/3 of OHS patients ultimately could be successfully titrated (AHI < 10 and REM > 15 min) in the lateral position only with PAP.

It is important to note that neither history of sleeping in the lateral position nor presence of positional OSA was associated with failure of titration in the supine position in our lab.

Central events were seen in few patients in the supine position, but central events were surprisingly not seen while titrating in the lateral position. We have also reported positional central sleep apnea which did not improve with maximum pressures in the supine position [14, 15].

The tennis ball technique and other positional sleep trainers have been shown to be variably effective in POSA. In various trials in mild-moderate patients with OSA, positional therapy has been shown to be an effective alternative to CPAP therapy. But its long-term adherence (10–38%) is even worse than that for CPAP therapy [17]. Newer vibratory sleep trainer devices have been shown to have better adherence (89% at three months).

Adherence to either CPAP or position therapy is poor, so expecting a patient to use both position device and PAP device during the night requires substantial determination from the patient. So we do a one-to-one session for all these patients to counsel them regarding the importance of positional therapy as well as PAP. These patients are sicker than routine OSA patients, and we have seen that patients who are sicker or have more complications usually are more adherent to combination therapy [8]. We use lateral therapy with an indigenously developed pillow technique (costing $2–3) in which two hard (albeit softer than a tennis ball) small pillows are sewn in a cloth and tied around the waist during sleep. We have been prescribing this SPT for the last three years, and we have seen good results with it. Patients are usually adherent to using positional therapy along with CPAP and according to patients they "train themselves" to sleep in lateral position with the help of positional devices. This SPT technique is simple and unsophisticated, but we cannot quantitatively measure the adherence of usage of a positional device unlike newer positional devices (cost around $600), where we can have compliance download.

One of the main limitations of this study is non-availability of adherence data for combination therapy. However, in our experience, patients use both the therapies if they are counseled properly. We are collecting follow-up data for this combination treatment and long-term efficacy which would be subsequently published. Another limitation is that it was done from a single referral center in central India and the rates of suboptimal titration were higher than usually reported in literature. This could be due to craniofacial structure difference in different ethnicities. Asians have been shown to have more severe OSA compared to Caucasians with the same BMI [12]. Although it is speculative, this could be the reason for higher rates of suboptimal titration, and it would be interesting to do multiethnic studies to see levels of optimal pressure in different countries.

Recently, Benjafield et al. described the potential benefit from switching from CPAP/APAP to bilevel PAP for patients struggling with PAP adherence [1]. Our current study also shows that with CPAP, only 70% of patients can be treated optimally. The remainder of the patients will require bilevel PAP (10%), CPAP in the lateral position (11%), or bilevel PAP (9%). It will be interesting to see if adding lateral position therapy to AutoPAP for patients with poor AutoPAP acceptability is beneficial.

Conclusion

The combination of positional therapy and a PAP device (PPAP) is an effective way of titrating patients with difficult to treat OSA.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11325-021-02291-6.

Acknowledgments We want to thank Mr. Senthil Kumar, RPSGT, and Mr. Amit Sen for doing the scoring and data collection of OSA patients.

Author contributions AG: Conceptualized, data collection, analysis, and manuscript writing
AP: Data collection and analysis
RS: Analysis and manuscript writing
AK: Data collection and analysis
PC: Conceptualized and data collection
All authors have seen and approved the manuscript.

Compliance with ethical standardsConflict of interest

AG, AP, AK, PC, and RS have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. This is a retrospective analysis study, and a waiver of this study was taken from the ethical clearance committee.

Informed consent Informed consent was obtained from all individual participants included in the study.

Supplementary Information The online version contains supplementary material available at https://doi.org/10.1007/s11325-021-02291-6.

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