Auto bi-level with pressure relief during exhalation as a rescue therapy for optimally treated obstructive sleep apnoea patients with poor compliance to continuous positive airways pressure therapy—a pilot study

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Abstract
Background Continuous positive airways pressure (CPAP) is the accepted therapy for obstructive sleep apnoea (OSA), but compliance is variable. We hypothesised that an auto bi-level device with pressure relief during exhalation (auto bi-level) would treat OSA as well as CPAP and that transitioning non-compliant CPAP patients without modifiable causes of poor compliance to this device would improve compliance and clinical outcomes.

Materials and methods OSA patients on positive airways pressure therapy with compliance below 4 h of use on ≥70% of nights over the past 3 months despite having no modifiable causes of poor compliance were transitioned onto an auto bi-level device for 10 weeks. Patients completed an Epworth sleepiness scale and Functional Outcomes of Sleep Questionnaire (FOSQ) at 15 days and 10 weeks and had their compliance and therapy data downloaded. Additionally, patients underwent polysomnography on their auto bi-level device at week 10.

Results Thirty-five patients were included. The apnoea–hypopnoea index, arousal index, sleep efficiency, total sleep time and sleep stage distribution were similar at baseline and week 10. Compliance, excessive daytime sleepiness and several FOSQ domains improved significantly at day 15 and week 10. Patients requiring an effective pressure ≥10 cmH₂O during the lead-in period on CPAP experienced greater significant improvements in compliance than those requiring an effective pressure <10 cmH₂O.

Conclusions Auto bi-level with pressure relief during exhalation treats OSA as effectively as CPAP without inducing additional arousals. Transitioning non-compliant CPAP patients without modifiable causes of poor compliance from their CPAP to this new device improves compliance and clinical outcomes over a 10-week period.

Keywords Obstructive sleep apnoea · Continuous positive airways pressure · Bi-level · Auto bi-level · BiPAP · Pressure relief · Compliance

Introduction
Obstructive sleep apnoea (OSA) is characterised by loud snoring and repeated episodes of apnoea and hypopnoea during sleep. It affects approximately 4% of middle-aged men and 2% of middle-aged women [1]. The main symptom of OSA is daytime sleepiness [2], although it is also associated with memory problems [3], a reduced quality of life [4], high blood pressure [5] and a higher incidence of cardiovascular morbidity and mortality [6].

Continuous positive airways pressure (CPAP) is the gold standard therapy for OSA, reducing snoring and the number of
improve compliance in 204 non-compliant CPAP patients.

Despite its efficacy, CPAP use is variable [11, 12]. Recent data from Weaver et al. [13] suggest that low levels of compliance may not be adequate to achieve normal function with further improvements in subjective sleepiness expected to occur up to 4 h of use per night, objective sleepiness up to 6 h per night and sleep-related quality of life up to 7.5 h per night. Similarly, blood pressure improvements are expected to occur above a threshold of 4 h of CPAP use per night [14], and optimal CPAP use of >6 h per night has been shown to increase the odds of users exhibiting normal memory function by 7.9 times when compared to patients using their CPAP for <2 h per night [8] and survival when compared to patients using their CPAP for <1 h per night [15].

Side effects to CPAP such as mask issues and upper airway symptoms are often cited as causes of poor CPAP compliance [16]; however, technological interventions targeting these complaints have only led to small improvements in compliance [17, 18]. Other interventions such as educating the patient about the short- and long-term consequences of their condition and the effects of therapy [19, 20] and intensive follow-up [21] have also been trialled with variable results.

Pressure intolerance is another common reason cited for poor CPAP compliance; however, the results of studies employing various pressure relief technologies in positive airways pressure (PAP)-naïve OSAS patients have again been variable. Aloia et al. [22] demonstrated that CPAP patients used their C-Flex device (providing flow proportional pressure relief during exhalation) for an average of 1.7 h per night more than CPAP patients over a 3 month period. However, in this study, therapy allocation was not randomised, with patients receiving the mode of therapy that was available when their therapy was allocated. In the first randomised controlled trial investigating the effects of C-Flex against CPAP, Nilius et al. [23] did not find any differences in objective or subjective compliance over 7 weeks of usage. Finally, Gay et al. [24], in a study of 27 patients with OSAS randomised to a novel bi-level therapy with pressure relief during exhalation and CPAP, demonstrated that the novel bi-level therapy with pressure relief during exhalation was as effective as CPAP for the treatment of OSAS, but offered no compliance advantages.

Whilst the evidence suggests that pressure relief technologies may not provide compliance improvements in PAP-naïve OSAS patients, there may be subgroups of CPAP patients who could benefit from their use. Ballard et al. [25] evaluated a two-phase intervention programme to improve compliance in 204 non-compliant CPAP patients. During phase 1, standard interventions to improve CPAP compliance were performed including mask optimisation, heated humidification, topical nasal therapy and sleep apnoea education. Patients that remained non-compliant then entered phase 2, a double-blind, randomised, controlled trial comparing bi-level PAP with pressure relief during exhalation and CPAP. At follow-up, 49% of patients using bi-level PAP with pressure relief and 28% of patients using CPAP achieved compliance.

The addition of an auto algorithm to bi-level PAP with pressure relief during exhalation may further increase comfort for patients with pressure intolerance. We hypothesised that an auto bi-level with pressure relief during exhalation would treat OSAS as well as CPAP and that transitioning non-compliant CPAP patients without modifiable causes of poor compliance from CPAP to this new device would improve compliance and clinical outcomes.

**Materials and methods**

**Patient selection**

OSA patients on PAP therapy with compliance below a minimally acceptable duration of 4 h of use on ≥70% of nights over the past 3 months and the ability to provide informed consent were recruited. Patients with modifiable causes of poor compliance including interface issues, nasal congestion and other symptoms requiring humidification and those with significant evidence of depression were excluded and returned to the sleep laboratory for ongoing treatment.

**Baseline assessment**

Patients underwent full polysomnography (PSG) on their current PAP device and had their arterial blood gases assessed immediately upon waking. Patients with significant evidence of periodic leg movements, restless legs syndrome, obesity hypoventilation syndrome and those with an apnoea–hypopnoea index (AHI) ≥5 were excluded and returned to the sleep laboratory for ongoing treatment.

The remaining patients had their demographic data (age, gender, height, weight, waist and neck circumference) and compliance over the past 3 months recorded before completing an Epworth sleepiness scale (ESS) and a Functional Outcomes of Sleep Questionnaire (FOSQ).

**Machine settings**

All patients were provided with an auto bi-level with pressure relief during exhalation (BiPAP Auto with Bi-Flex, Respironics Inc., Murrysville, PA, USA) and humidifier.
The minimum expiratory positive airway pressure (EPAP) was set at 4 cmH2O if the effective CPAP pressure from the previous 3 months of therapy was <6 cmH2O and 6 cmH2O if the effective CPAP pressure from the previous 3 months of therapy was >6 cmH2O. Pressure support was set at a minimum of 2 and a maximum of 8 cmH2O. Bi-Flex was set to its maximum level (level 3). Patients were given oral and written instructions on how to use their equipment before returning home and access to a helpline in case of any problems.

Follow-up

Patients were followed up at day 15 and week 10. At both time points, patients completed an ESS and the FOSQ. Compliance and therapy data were also downloaded from device. Additionally, at week 10, patients underwent full polysomnography on therapy.

Polysomnography

Full PSG was performed on therapy using an Alice 5 system (Respironics, Inc., Murrysville, PA, USA) utilising a standard montage of electrocardiogram, electroencephalogram, electro-oculogram and electromyogram signals, body position, pulse oximetry, respiratory impedance and pneumotachographically derived airflow measurements.

Scoring

Apnoeas were defined as the absence of airflow for ≥10 s. Hypopnoeas were defined as a ≥50% reduction in airflow from baseline for ≥10 s, associated with either a ≥4% oxygen desaturation or an arousal. Apnoeas and hypopnoeas were classified as obstructive if there was no/reduced flow but some discernable effort. The AHI was defined as the number of apnoeas and hypopnoeas per hour of sleep.

Subjective daytime sleepiness and quality of life

Subjective daytime sleepiness was assessed using the ESS [26]. An ESS of ≥11 indicated excessive daytime sleepiness. Quality of life was assessed using the FOSQ [27]. Patients were considered to have a reduced quality of life in each domain if: General productivity was <3.38, social outcome was <3.57, activity level was <3.34, vigilance was <3.16, intimacy was <3.84, and a reduced quality of life in general if the total score was <16.33.

Compliance

Hours of therapy use were obtained at day 15 and week 10 from a smartcard located in the side of the auto bi-level device by downloading the data into commercially available software (Encore Pro, Respironics Inc., Murrysville).

Statistical analysis

Data analysis was conducted using SPSS software. Normality was assessed using tests of skewness and kurtosis and data presented accordingly. Differences between baseline, day 15 and week 10 were assessed using Wilcoxon matched pairs signed-rank test. Differences between patients with a mean baseline PAP pressure <10 and ≥10 were assessed using Mann–Whitney U tests.

Ethics

Ethical approval was not sought for this research project as the design did not deviate from the physicians’ usual clinical routine and involved only the use of approved medical devices. However, informed written consent was obtained from each patient prior to their inclusion.

Results

Demographics

Patients were mostly male, middle-aged, obese and suffered from severe OSA. Half of the cohort smoked, but blood gases were in the normal range. The majority of patients had used autoCPAP during the lead-in period to the study (Table 1).

Trial profile

Thirty-five patients were consented onto the study, four of which did not complete. One patient was lost to follow-up, and one patient withdrew due to mask intolerance between visits 1 and 2. One patient withdrew due to mask intolerance and one due to a herniated disc between visits 2 and 3.

Table 1 Baseline demographics (n=35)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55 (46, 59)</td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>28 (80)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>33.1 (29.3, 36.6)</td>
</tr>
<tr>
<td>AHI (no. of apnoeas and hypopnoeas/hour slept)</td>
<td>39.6 (25.0, 58.6)</td>
</tr>
<tr>
<td>Smoke, n (%)</td>
<td>17 (48.6)</td>
</tr>
<tr>
<td>PaO₂ (mmHg)</td>
<td>80 (75, 88)</td>
</tr>
<tr>
<td>PaCO₂ (mmHg)</td>
<td>41 (40, 42)</td>
</tr>
<tr>
<td>Fixed CPAP, n (%)</td>
<td>9 (25.7)</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range) unless otherwise stated.
Polysomnography

The AHI was similarly controlled by the patients’ baseline therapy device and the auto bi-level device. The arousal index, sleep efficiency, total sleep time and sleep stage distribution were also similar between the devices (Table 2).

Daytime sleepiness and quality of life

Patients demonstrated excessive daytime sleepiness at baseline which improved significantly at day 15 and was maintained at week 10. All quality of life domains were abnormal at baseline. There was a significant decrease in social outcome at day 15. There was a significant improvement in general productivity, vigilance, activity level and the total FOSQ score at week 10; however, only the general productivity score returned to the normal range (Table 3).

Compliance

All compliance parameters were low during the lead-in period to the study but significantly improved by day 15. Compliance parameters remained significantly higher at week 10 when compared to baseline (Table 4). However, median values were slightly lower than at day 15, although these differences were not significant (data not shown).

Effective pressure

Patients requiring an effective pressure ≥10 cmH2O during the lead-in period on CPAP experienced greater significant improvements in mean usage/night at day 15 and week 10 than those requiring an effective pressure <10. The differences in mean usage per night between these two groups at day 15 and week 10 were statistically significant (Table 5).

Discussion

Using an observational design, this study supports the findings by Gay et al. [24] that bi-level therapy with pressure relief during exhalation effectively treats OSA without inducing arousals and Ballard et al. [25] that compliance is improved on bi-level therapy with pressure relief in non-compliant CPAP patients without modifiable causes of poor compliance. Furthermore, the finding that patients requiring an effective pressure ≥10 cmH2O during the lead-in period on CPAP experienced significantly larger improvements in mean usage/night across the study period than those requiring an effective pressure <10 cmH2O suggests that bi-level therapy with pressure relief may improve compliance in this patient group because it is a more comfortable mode of therapy than CPAP.

Whilst compliance was significantly improved on the auto bi-level device in this study at day 15 and week 10, these improvements can only be considered modest. Data

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### Table 2 Polysomnography

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=35)</th>
<th>Week 10 (n=31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Residual AHI (h⁻¹)</td>
<td>3.3 (1.1, 9)</td>
<td>2.3 (0.6, 5.9)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Arousal index (h⁻¹)</td>
<td>17.9 (9.9, 24.4)</td>
<td>14.7 (9.9, 24.9)</td>
<td>0.13</td>
</tr>
<tr>
<td>Sleep efficiency (%)</td>
<td>75.7 (64.7, 84.8)</td>
<td>72.8 (64.5, 82.3)</td>
<td>0.87</td>
</tr>
<tr>
<td>TST (min)</td>
<td>369 (293, 432)</td>
<td>379 (318.5, 431.5)</td>
<td>0.44</td>
</tr>
<tr>
<td>Stage 3 sleep (%)</td>
<td>7.5 (5.3, 13.9)</td>
<td>10 (7.1, 15)</td>
<td>0.17</td>
</tr>
<tr>
<td>Stage 4 sleep (%)</td>
<td>9.2 (3.6, 18.1)</td>
<td>10.5 (6.4, 15.9)</td>
<td>0.51</td>
</tr>
<tr>
<td>REM sleep (%)</td>
<td>19 (14.8, 23.3)</td>
<td>20.5 (16, 23.1)</td>
<td>0.99</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range)

### Table 3 Daytime sleepiness and quality of life

<table>
<thead>
<tr>
<th></th>
<th>Baseline (n=35)</th>
<th>Day15 (n=33)</th>
<th>P</th>
<th>Week10 (n=31)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESS</td>
<td>11 (7, 15)</td>
<td>7 (4, 10)</td>
<td>&lt;0.01</td>
<td>6 (3, 10)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FOSQ: General productivity</td>
<td>3.0 (2.3, 3.8)</td>
<td>3.1 (2.5, 3.8)</td>
<td>0.38</td>
<td>3.4 (2.9, 4.0)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>FOSQ: Social outcome</td>
<td>3.5 (3.0, 4.0)</td>
<td>3.0 (2.0, 4.0)</td>
<td>0.04</td>
<td>3.5 (3.0, 4.0)</td>
<td>0.85</td>
</tr>
<tr>
<td>FOSQ: Vigilance</td>
<td>2.7 (1.9, 3.3)</td>
<td>3.0 (2.3, 3.4)</td>
<td>0.15</td>
<td>3.1 (2.6, 3.6)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>FOSQ: Activity level</td>
<td>3.0 (2.2, 3.4)</td>
<td>3.0 (2.3, 3.6)</td>
<td>0.23</td>
<td>3.0 (2.8, 3.8)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>FOSQ: Intimacy</td>
<td>3.0 (2.3, 4.0)</td>
<td>3.3 (2.3, 3.3)</td>
<td>0.17</td>
<td>3.0 (3.0, 3.5)</td>
<td>0.11</td>
</tr>
<tr>
<td>FOSQ Total score</td>
<td>14.9 (11.3, 17.6)</td>
<td>14.8 (12.2, 17.4)</td>
<td>0.21</td>
<td>15.4 (13.7, 18.7)</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Data are presented as median (interquartile range)
from Weaver et al. [13] suggest that the compliance levels demonstrated in this study would yield some improvements in sleepiness and quality of life. For FOSQ, the majority of domains improved significantly over the 10-week period, but, with the exception of general productivity, did not normalise. However, the linear relationship demonstrated between compliance and FOSQ domains suggests that further improvements in sleepiness and quality of life could be achieved with higher compliance rates. It is also likely that memory [8] and survival [15] would also improve at the compliance levels demonstrated in this study.

Whilst the improvement in compliance in this study was only modest, the normalisation of sleepiness at both day 15 and week 10 may have a profound effect on the patients’ risk of road traffic accidents. Noda et al. [28] demonstrated that the risk of automobile accidents was significantly correlated with the ESS score \( (r=0.56, P<0.01) \). Furthermore, reducing sleepiness in patients with obstructive sleep apnoea through the use of positive airways pressure devices has been shown to reduce the risk back to normal levels [29].

It may be possible to further improve the compliance levels observed in this study by combining bi-level therapy with pressure relief, with psychological interventions. Recent data from Aloia et al. [30] demonstrated that although traditional education and motivational enhancement therapy (a new intervention designed from theories of behaviour change) decreased positive airways pressure discontinuation rate compared to standard care, the lowest discontinuation rate was observed when motivational enhancement therapy was combined with PAP therapy utilising pressure relief during exhalation. This finding was a secondary outcome of the study and did not reach significance, but suggests that further work should be done on this topic.

A particular criticism of systems providing pressure relief during exhalation is that they may increase the risk of upper airway collapse during exhalation due to underpressurisation. To date, two studies have demonstrated that devices providing pressure relief during exhalation correct the AHI as effectively as fixed CPAP [22, 23]. Similarly, oesophageal pressure measurements made during sleep in OSAS patients using various commercially available setting of pressure relief and fixed CPAP demonstrated no increases in the number of flow limitations [31]. Furthermore, in this study, the residual AHI on the auto bi-level with pressure relief during exhalation was significantly lower than on CPAP; however, this difference was not of clinical significance.

There are a number of strengths and limitations of this study. We believe that a population of non-compliant CPAP patients without modifiable causes of poor compliance (i.e. patients with pressure intolerance) are the correct patient population to target new, more comfortable interventions. We acknowledge that this is only an observational study and that it is possible that compliance improved in this patient group simply because of the increased attention they received. However, we believe that the differences in compliance observed between patients requiring an effective pressure \( \geq 10 \text{ cmH}_2\text{O} \) and an effective pressure <10 cmH\(_2\)O during the lead-in period on CPAP demonstrate that the dataset and comparisons we made are valid and significantly strengthen our conclusion. It is possible that the 10-week follow-up period might have been insufficient

<table>
<thead>
<tr>
<th>Table 4 Compliance</th>
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<tbody>
<tr>
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<tr>
<td>Days therapy used (%)</td>
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<tr>
<td>Days therapy used ≥4 hours (%)</td>
</tr>
<tr>
<td>Mean usage/night, all nights (h)</td>
</tr>
<tr>
<td>Mean usage/night, nights used (h)</td>
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<tr>
<td>90% CPAP/EPAP (cmH(_2)O)</td>
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<tr>
<td>90% IPAP (cmH(_2)O)</td>
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</table>

Data are presented as median (interquartile range)

<table>
<thead>
<tr>
<th>Table 5 Effective pressure</th>
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<tr>
<td></td>
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<tr>
<td>Peff &lt;10 mmHg</td>
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<tr>
<td>Peff ≥10 mmHg</td>
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<tr>
<td>P</td>
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</table>

Data are presented as median (interquartile range)
to determine what long-term compliance would be like on this device. In line with this theory, a decrease in compliance was observed between day 15 and week 10. However, it is possible that this is a statistical anomaly due to the small number of patients studied. In support of this, data from a number of studies have demonstrated that long-term compliance is established during the first weeks of therapy [12, 32].

In conclusion, this study suggests that an auto bi-level with pressure relief during exhalation treats OSAS as effectively as CPAP without inducing additional arousals and that transitioning non-compliant CPAP patients without modifiable causes of poor compliance from their CPAP to this new device improves compliance and clinical outcomes over a 10-week period.

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References


