Automatic Bi-level Positive Airway Pressure Delivery with Flow-Directed Pressure Modulation and Expiratory Pressure Relief – an In-laboratory Comparison with Conventional Bi-level Positive Airway Pressure Therapy

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Study Objectives: To evaluate the therapeutic effect of Automatic Bi-level Positive Airway Pressure with flow-matching and early expiratory pressure relief (BiPAP® Auto with Bi-Flex®) to treat adult obstructive sleep apnea/hypopnea. The study also evaluated the therapeutic efficacy of BiPAP Auto with Bi-Flex as compared to manually titrated conventional Bi-level Positive Pressure Therapy for reduction of the Apnea/Hypopnea Index in adult OSAH patients, and the "optimum" therapeutic pressures derived from the night therapy.

Study Design: Prospective cross-over, blinded analysis.

Setting: Sleep disorders center (Arkansas Center for Sleep Medicine, Little Rock AR, Sleep Center of Greater Pittsburgh, Pittsburgh, PA).

Participants: 20 patients with previously diagnosed OSAH (within 12 months), and successful accommodation to chronic CPAP therapy at home.

Measurements and Results: Three nights of in-laboratory full polysomnography were performed, using conventional bi-level therapy being manually titrated, BiPAP set at therapeutic pressure levels, BiPAP Auto with Bi-Flex set at operational pressure ranges.

Conclusions: The BiPAP Auto with Bi-Flex adequately treats OSAH, provides a 90% pressure that is comparable to the 'fixed' pressure level derived during manually titrated conventional bi-level therapy.

Abbreviations: BiPAP – Bi-level Positive Airway Pressure, OSAH – Obstructive Sleep Apnea Hypopnea, AHI – Apnea/Hypopnea Index, TST – Total Sleep Time, TIB – Time in Bed, WASO – Wake after sleep onset, SOL – Sleep Onset Latency, SEI – Sleep Efficiency Index

Key Words: sleep-disordered breathing, obstructive sleep apnea - hypopnea syndrome, BiPAP therapy, Automatic BiPAP, Bi-level, Bi-Flex.

INTRODUCTION

The prevalence of obstructive sleep apnea – hypopnea syndrome is estimated to be between 2-4%[1]. The disorder remains largely undiagnosed and under-treated[2]. The disorder is associated with an increased risk of development of psychosocial as well as physiologic sequela. Effective treatment for the OSAH has been shown to improve not only directly sleep-related consequences, but the blood pressure consequences of OSAH[3]. Therapy most commonly begins with a course of continuous positive airway pressure (CPAP). This therapy has been demonstrated to serve as an effective treatment of the OSAH syndrome[4].

Reduced compliance reduces physiologic benefits of CPAP therapy. Strategies to improve compliance have been evaluated, and many have been implemented in clinical practice (i.e., education, follow-up contact, heated humidification, etc.). Another factor may be the sensation of high pressure on exhalation. Both conventional CPAP and Auto-CPAP therapy present elevated pressures during exhalation, and may be a reason for similar compliance rates for the two applications.

Patients who have demonstrated persistent non-compliance to CPAP therapy may receive a program of compliance improvement techniques (i.e., reassessment, counseling, mask fitting, behavioral training, etc.). Patients with non-compliance that is resistant to such conventional intervention (up to 75%)[5] may be placed on Bi-level PAP therapy to improve compliance. This transition often presents significant logistic challenges, as many patients are not initially titrated to both a CPAP and a bi-level prescription. Clinicians may try empiric initiation with bi-level therapy with BiPAP, but such intervention must be closely monitored for success or failure.

BiPAP with Bi-Flex offers a unique form of bi-level therapy by which Bi-Flex provides flow-directed modification to the transition into and out of the IPAP phase, and dynamic expiratory pressure relief[5]. The amount of expiratory pressure relief is determined by the patient's expiratory flow. Accordingly, the pressure returns to therapeutic levels prior to the initiation of the next breath's inspiratory phase. The pressure relief offers a more comfortable expiratory experience for the patient, and may impact favorably on perceptions of therapy as well as potentially long-term acceptance to therapy.

Automatically titrating CPAP therapy (Auto-CPAP) has been shown to effectively treat patients with OSAH[6]. Auto-CPAP may be used when access to titration is limited or to re-titrate patients in whom there are questions about the effectiveness of their current therapy level. Further, Auto-CPAP can be used to treat patients with highly variable

pressure requirements (e.g., REM-related or body-position dependent OSA)[7]. These Auto-CPAP algorithms have been employed in a new BiPAP device. By offering an Auto BiPAP alternative in this case, extensive re-titration and follow-up empiric pressure modification may be avoided.

This study was performed to provide a series of basic validations for the new BiPAP Auto with Bi-Flex technology. The study was to determine if the therapy would provide adequate resolution to the underlying OSAH. The BiPAP Auto with Bi-Flex was compared to conventional manually titrated BiPAP therapy to also evaluate the ability of the new technology to offer clinicians both a meaningful 'fixed-CPAP' therapy pressure as well as a reliable AHI.

METHODS

Twenty chronic CPAP patients were recruited for this study. Subjects with polysomnographically-determined OSAH and with demonstrated successful compliance to CPAP therapy were approached for participation. The research was approved by an Institutional Review Board, and all subjects gave written, informed consent.

Patients underwent three nights of PSG, scheduled no more than ten nights apart. Subjects used their current interface (i.e., nasal mask) and were prepared for standard polysomnography (PSG) for a titration study. PSG measures included evaluation of sleep state (central and occipital electroencephalogram, electro-oculogram, sub-mental electromyogram), respiration (chest and abdominal respiratory effort, respiratory airflow, and pulse oximetry), body position, ECG, leg EMG, snoring, and technician comments. Therapy for all nights was provided by the BiPAP® Pro 2 with Bi-Flex® (Respironics, Inc., Murrysville, PA). Device therapy data were recorded on the PSG from the therapy device (device pressure, flow, and breathing events) via the Analog Output Module (Respironics, Inc., Murrysville, PA). Patients were studied in an attended, conventional clinical sleep lab setting.

On the first night, subjects were randomized to either a manual bi-level positive airway pressure therapy titration or to therapy titration using the BiPAP Auto with Bi-Flex.

On the manual titration night, pressures were adjusted by an experienced sleep technologist to eliminate obstructive apnea events, hypopneas and snoring. EPAP and IPAP were maintained between 4 and 25 cm H_2O for each patient. The principal investigator determined the optimal IPAP and EPAP pressures which were to be used on the fixed therapy pressure night. If the patient had the auto-titration PSG prior to the manual titration PSG, the principal investigator was blinded to the results of the BiPAP Auto with Bi-Flex PSG.

On the BiPAP Auto with Bi-Flex titration night, the auto-titrating algorithm was activated and the device treated the patient with minimal interference from the sleep technologist. During Auto Bi-level therapy, EPAP and IPAP were set between 4 and 25 cm H_2O for each patient. The IPAP and EPAP difference (i.e., Pressure Support) was set at a minimum of 2 cm H_2O and a maximum of 8 cm H_2O. For savvy patients who are already accustomed to higher CPAP therapy and who experienced sleep onset delay due to intolerance of lower pressure, there was a one-time manual intervention to allow the subject to initiate sleep with a higher EPAP pressure.

On the third night (Fixed Pressure Night), patients were treated for the entire night at the optimal bi-level pressure that was determined on the previous manual titration night at the pressures determined by the principal investigator using the sleep laboratory's standard protocol for bi-level pressure titration.

The PSG studies were then manually scored, using standard scoring criteria for both sleep state[8] and respiratory events[9]. A standard PSG report was generated for each sleep study. Pressure data from the device were recorded on a separate PC.

The statistical approach was based on a null hypothesis so that any significant differences could be attributed to differences between the auto-titrating and fixed pressure PSG nights. As each subject served as his/her own control, comparisons were made using a paired t-test (MedCalc software, Version 7.5; Belgium), examining for differences in major variables of sleep duration, sleep stage, sleep continuity, arousals from sleep, and AHI. Comparisons were made between the best pressure on the manual titration night and the 90% pressure determined using the BiPAP Auto with Bi-Flex in the Auto Bi-level mode. Post-hoc analyses focused on differences between the AHI at the time of initial presentation of the patient and the titration pressures determined on the two nights.

RESULTS

Demographics

The twenty subjects (5 female, 15 male) had a mean age of 56 ± 9 years. Other demographic characteristics are presented in Table 1. Nineteen of the twenty patients were using CPAP prior to entering the study. (Table 1).

Table 1.

Gender	**5 female , 15 male**
Age (years)	56 ± 9
BMI (kg/m2)	37 ± 6
Diagnostic AHI (hr^{-1})	41 ± 27
Time Elapsed since initiating CPAP treatment (days)	196 ± 399

Sleep Quality

Sleep parameters for each PSG night were analyzed. Subjects slept a comparable duration during the three study nights. There were no significant differences in Time in Bed (TIB), Total Sleep Time (TST) in hours, Sleep Latency, or Sleep Efficiency. Arousal rates were comparable between all three nights. (See Table 2).

Table 2.

	Manual Bi-level Therapy Titration	BiPAP Auto with Bi-Flex Therapy	Fixed Pressure Bi-level Therapy	Sig.
TIB (min)	400.7 ± 30	413.5 ± 23.2	400.2 ± 37	NS
TST (min)	352.4 ± 29	364.4 ± 48	335.1 ± 49	NS
Sleep Onset Latency (min)	6.6 ± 7.3	8.4 ± 12.6	8.0 ± 8.8	NS
Sleep Efficiency (%)	88.1 ± 5.9	87.1 ± 9.6	87.6 ± 8.6	NS
Stage 3/4 Sleep (min)	21.2 ± 25.8	20.8 ± 25.4	14.1 ± 20.6	NS
REM Sleep (min)	60.6 ± 29.5	65.9 ± 35.5	63.7 ± 33.3	NS
Arousal Index (hr^{-1})	25.6± 33.3	15.8 ± 8.4	14.4 ± 9.7	NS

THERAPY PERFORMANCE

Residual AHI, apnea index and hypopnea index were comparable between the titration nights. No significant differences were seen in minimum oxygen saturation (Table 3).

Table 3.

	Manual Bi-level Therapy Titration	BiPAP Auto with Bi-Flex Therapy	Fixed Pressure Bi-level Therapy	Sig.
Residual AHI (hr^{-1})	4.5 ± 3.9	3.2±2.8	2.9± 3.6	NS
Apnea Index (hr^{-1})	1.3 ± 1.5	0.9 ± 1.2	1.2 ± 1.9	NS
Hypopnea Index (hr^{-1})	3.2 ± 3.1	2.3 ± 2.0	1.6 ± 2.5	NS
Min SpO_2 (%)	89.5±3.1	89.9±2.9	89 ± 8.2	NS

Figure 1 shows the relationship between residual AHI from the manually titrated bi-level night, and the BiPAP Auto with Bi-Flex night. There is a good correlation between the two titration methodologies.

Figure 1.

AHI- Manual Titration Night vs. BiPAP Auto with Bi-Flex Night

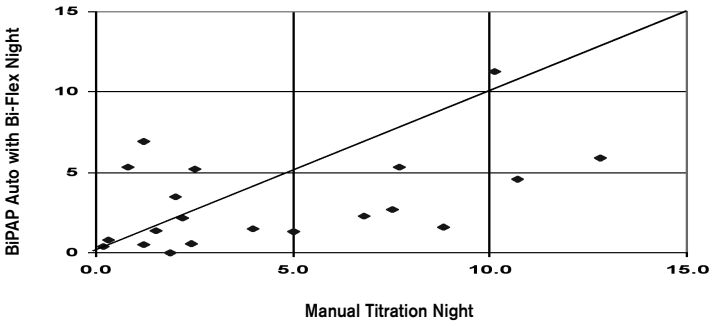


Figure 2 is a Bland-Altman plot comparing the AHI from the manually titrated bi-level night and the BiPAP Auto with Bi-Flex night.

Figure 2.

Bland & Altman Plot – AHI Auto vs. AHI Manual

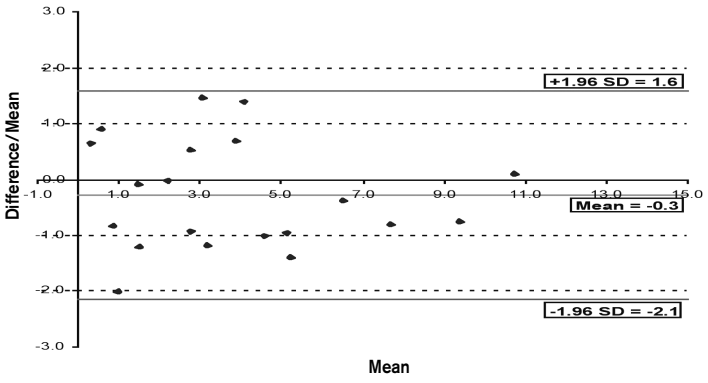


Figure 3 shows the BiPAP Auto with Bi-Flex residual AHI vs. the fixed pressure night residual AHI.

Figure 3

AHI- Fixed Bi-level Pressure Night vs. BiPAP Auto with Bi-Flex Night

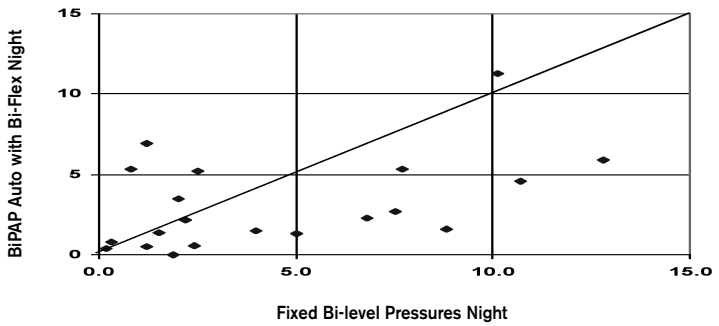
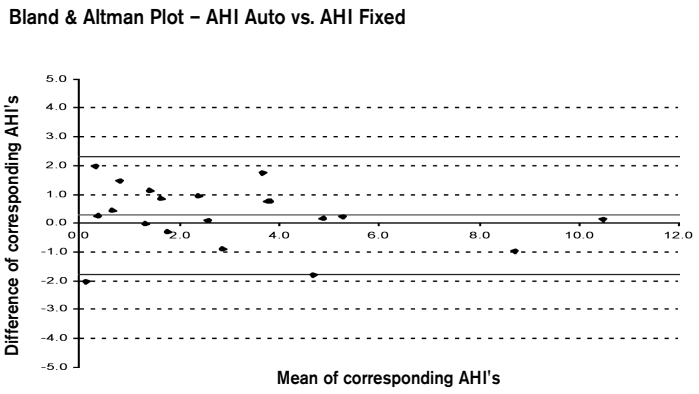


Figure 4 shows the Bland-Altman plot for BiPAP Auto with Bi-Flex residual AHI vs. the fixed pressure night residual AHI.

Figure 4.



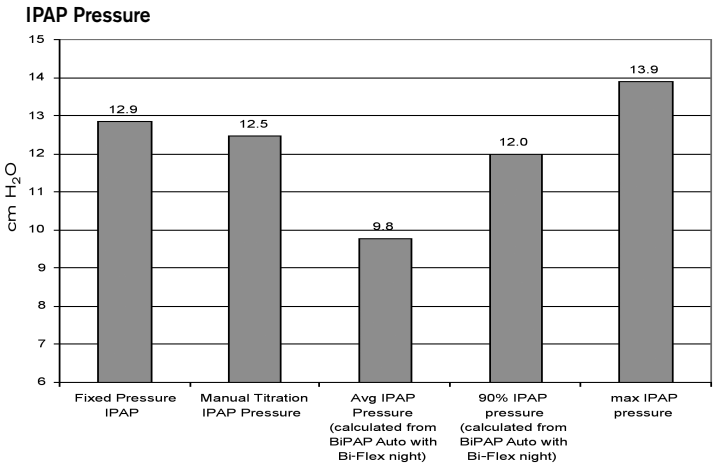
These data demonstrate that the BiPAP Auto with Bi-Flex achieves therapy efficacy comparable to that achieved with manual titration and during manually titrated fixed pressure bi-level therapy. No significant differences were seen between BiPAP Auto with Bi-Flex and the other nights with regards to sleep parameters and amelioration of breathing events.

THERAPY PRESSURE COMPARISON

IPAP Analysis

Figure 5 illustrates the IPAP pressures from the manual titration night, the fixed pressure night and the 90% pressure, the highest pressure, and the average pressure from the auto-titration night.

Figure 5. (IPAP mean values)



An initial analysis using ANOVA revealed significant differences between the IPAP mean values ($p = 0.002$). (Table 4)

The mean, average IPAP pressure (determined for the entire night by the auto algorithm) was significantly lower than the average, manual titration IPAP (determined during manual titration) ($p < 0.001$). The average, maximum IPAP pressure (determined by the BiPAP Auto with Bi-Flex during the auto-titration night) was significantly higher than the device determined mean, average IPAP (the mean value of IPAP for the entire night determined by the auto algorithm) ($p< 0.001$). The average maximum IPAP pressure trended to be higher compared to the average 90% IPAP pressure but barely failed to be significant ($p = 0.053$).

Table 4.

	Manually Titrated IPAP Pressure	Fixed Pressure IPAP Pressure	BiPAP Auto with Bi-Flex Therapy Average IPAP Pressure	BiPAP Auto with Bi-Flex Therapy 90% IPAP Pressure	BiPAP Auto with Bi-Flex Therapy Maximum IPAP Pressure
Mean	12.9*	12.5	9.8**	12.0	13.9**
SD	2.9	2.9	2.7	3.6	3.6
p value (ANOVA)	**0.002**				

** p < 0.001, Manually Titrated IPAP compared to average IPAP*

*** p < 0.001, Average IPAP compared to maximum IPAP*

These data demonstrate that the BiPAP Auto with Bi-Flex algorithm determines IPAP pressure in a manner similar to manually titrated IPAP pressure. Although the algorithm determined highest pressure was higher than the manually titrated IPAP pressure, the average IPAP pressure was significantly lower than the manually titrated, best (or the IPAP pressure that would have been prescribed) IPAP.

EPAP ANALYSIS

Figure 6 illustrates the EPAP pressures from the manual titration night, the fixed pressure night and the 90% pressure, the highest pressure, and the average pressure from the auto-titration night.

Figure 6. (EPAP mean values)

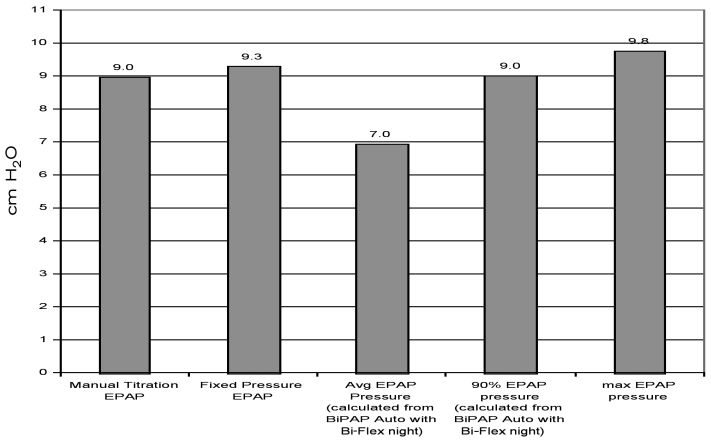


Table 5 presents the analysis of the mean EPAP values from each PSG night.

Table 5.

	Manual Best Rx EPAP Pressure	Fixed Pressure EPAP Pressure	BiPAP Auto with Bi-Flex Therapy Titrating Average EPAP Pressure	BiPAP Auto with Bi-Flex Therapy Titrating 90% EPAP Pressure	BiPAP Auto with Bi-Flex Therapy Titrating Maximum EPAP Pressure
Mean	9.3	9.0	7.0	9.0	9.8
SD	3.2	3.3	2.7	3.7	3.8
p value (ANOVA)	**NS**				

Using ANOVA, no significant differences were revealed between any of the EPAP pressures although the mean, average EPAP pressure (the average EPAP for the entire night determined by the device) trended to be lower than the other EPAP pressure values.

DISCUSSION

The ability of the BiPAP Auto with Bi-Flex in the auto-titrating mode to reduce obstructive apnea and hypopnea as effectively as manually adjusted bi-level positive airway pressure titration is demonstrated in this subject set. With very low residual AHI's, the BiPAP Auto with Bi-Flex meets accepted criteria for therapeutic success[10]. The BiPAP Auto with Bi-Flex provided comparable therapy as compared to manually titrated, Bi-level positive airway pressure.

The average IPAP pressure value over the entire night was significantly lower than the average IPAP on either the manual titration night or the fixed pressure night. The highest IPAP pressure deemed necessary by the auto-titrating algorithm was not significantly different from the manual titration or the fixed pressure IPAP. The EPAP pressures did not differ significantly between any of the therapeutic modes. As is seen with auto-titrating CPAP devices, therapeutic efficacy is achieved with lower pressures on average.

The duration of sleep and sleep architecture for the three nights were similar. Patients on BiPAP Auto with Bi-Flex had sleep that was similar to that experienced during a comparable in-laboratory titration on two separate therapy nights. This indicates that auto-titrating bi-level positive airway pressure with Bi-Flex does not negatively affect sleep quality.

Consequences of the apnea and hypopnea events, arousals and desaturations, were comparable during use of the BiPAP Auto with Bi-Flex in the auto-titrating mode night as during the manual titration and fixed pressure nights.

In certain medical environments, BiPAP Auto with Bi-Flex may be utilized in hospitalized or disabled patients as well as those in whom a re-titration might be indicated because of poor adherence or CPAP therapy. The ability to offer the patient an alternative pressure profile from the BiPAP Auto with Bi-Flex device, and determine compliance changes, are essential for such an application. These data suggest that the 90% pressure from the BiPAP Auto with Bi-Flex can serve to reach decisions for setting 'fixed' BiPAP with Bi-Flex pressures, if so desired.

CONCLUSION

The BiPAP Auto with Bi-Flex provides effective therapy in this group of 20 OSAS patients. With the mean residual AHI of less than 5 hr^{-1} sleep, the BiPAP Auto with Bi-Flex provides adequate clinical resolution of the obstructive apnea and hypopnea events, with lower mean IPAP pressure, as determined during attended in-laboratory polysomnographic evaluation. The effect on sleep continuity and architecture is comparable to that experienced during manual titration. BiPAP Auto with Bi-Flex provided therapeutic information (breathing events, average pressures, 90% inspiratory and expiratory pressures) comparable to that derived by conventional bi-level titration. This initial evaluation demonstrates the efficacy of the BiPAP Auto with Bi-Flex technology as a method to either treat or determine pressure requirements for patients with obstructive sleep apnea.

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