CLINICAL FEASIBILITY OF AN AUTO-ADJUSTING BI-LEVEL PAP DEVICE FOR THE TREATMENT OF OBSTRUCTIVE SLEEP APNEA

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КЛИНИЧЕСКИЕ ВОЗМОЖНОСТИ АВТОМАТИЧЕСКОЙ ДВУХФАЗНОЙ ВЕНТИЛЯЦИИ С ПОЛОЖИТЕЛЬНЫМ ДАВЛЕНИЕМ В ДЫХАТЕЛЬНЫХ ПУТЯХ (ДФВ) ДЛЯ ЛЕЧЕНИЯ ОБСТРУКТИВНОГО АПНОЭ СНА

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Summary. Background. Bi-Level positive airway pressure (BPAP) is an effective alternative to continuous positive airway pressure (CPAP) in patients with obstructive sleep apnea (OSA) who could not tolerate CPAP. An automatically titrating BPAP device has recently been developed, BPAP Auto[®] with BiFlex™ (BPAPauto). The primary aim of this study was to examine the performance of this new device during attended polysomnography (PSG).

Methods. This was a prospective case series study. Participants with OSA currently using CPAP or BPAP therapy were recruited and undergo in-lab PSG study with BPAPauto.

Results. A total of 27 participants met the criteria, enrolled the study. All participants received BPAPauto therapy during an attended PSG. Sleep and respiratory data were examined. The mean apnea hypopnea index was found 2.2 ± 2.5 events/hour. SaO_2 (oxygen saturation) was 94.0 ± 1.8. The mean inspiratory positive airway pressure (IPAP) abolish respiratory events was 14.1 ± 3.4 cmH_2O and that of expiratory positive airway pressure (EPAP) was 10.7 ± 3.9 cmH_2O.

Conclusions. The new developed BPAPauto is able to establish an appropriate Bi-Level PAP and control oxygen saturation without excessive disruption of sleep. Further studies using randomized control design are needed to examine potential roles and advantages of BPAPauto for treatment of OSA.

Key words: Obstructive sleep apnea, Continuous positive airway pressure, Bi-level positive airway pressure

Резюме. Проблематика: двухфазная вентиляция с положительным давлением в дыхательных путях (ДФВ) является действенной альтернативой режиму вентиляции с помощью непрерывного положительного давления в дыхательных путях (СИПАП) у пациентов с обструктивным апноэ сна (СОАС), которые не могут переносить СИПАП. Не так давно было разработано устройство автоматического титрования BPAP Auto[®] с BiFlex™ (BPAPauto). Основной целью данного исследования стало изучение эффективности данного устройства с сопутствующей полисомнографией (ПСГ).

Методы: осуществлялось проспективное исследование серии случаев. Участники исследования были набраны среди пациентов с СОАС, лечащихся при помощи СИПАП или ДФВ терапии, которые затем прошли лабораторное исследование ПСГ при помощи BPAPauto.

Результаты: в общей сложности, параметрам исследования подошли 27 пациентов. Все участники исследования проходили BPAPauto терапию с сопутствующей ПСГ. Были изученные данные периода сна, а также дыхательных путей. Средний индекс апноэ гипопноэ был составил $2,2 \pm 2,5$ события / час. SaO_2 (насыщение кислородом) составило $94,0 \pm 1,8$. Средний показатель положительного давления в дыхательных путях на вдохе без респираторных событий составил $14,1 \pm 3,4$ смH$_2$O, в то время как показатель положительного давления в дыхательных путях на выдохе (ИВЛ) составил $10,7 \pm 3,9$ смH$_2$O.

Вывод: новый разработанный BPAPauto способен поддерживать необходимую двухфазную вентиляцию с положительным давлением в дыхательных путях и контролировать насыщение кислородом без чрезмерного нарушения сна. Для изучения потенциальных возможностей и преимуществ BPAPauto для лечения СОАС необходимо проводить дальнейшие исследования.

Introduction. Obstructive sleep apnea syndrome is a common clinical problem effecting approximately 2% and 4% of the adult population [1]. It is characterized by intermittent and recurrent upper airway occlusion during sleep [2]. The resulting airway narrowing and/or closure restrict airflow and can produce repeated oxyhemoglobin desaturations, sleep fragmentation, or both. Continuous positive airway pressure (CPAP) is a standard treatment for patients with OSA [3,4] . Positive airway pressure (PAP) is a very effective treatment but only if it used on a regular basis [5]. A comprehensive review of CPAP literature found non-acceptance rates to vary from 5 to 50%, with the average approximately 20%. Another 12 to 15% can be expected to stop PAP treatment with in 3 years. Of those using PAP, adherence rates (>4 h use for 70% of days) have varied from 40 to 80% [6,7]. A major challenge facing clinicians is improving adherence to PAP treatment [8]. While the literature mainly supports CPAP therapy, BPAP is an optional therapy in some cases where high pressure is needed and the patient experiences difficulty exhaling against a fixed pressure [4,9,10]. Bi-level PAP delivers a separately adjustable lower expiratory positive airway pressure (EPAP) and higher inspiratory positive airway pressure (IPAP) [9,11].

The new 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. 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 [5].

The primary aim of this study was to examine the performance of BiPAP Auto® with BiFlex™ (BPAPauto)(respironics corporation) device during attended polysomnography (PSG) for the treatment of OSA. Specifically; 1.To automatically adjust EPAP and IPAP pressure to maintain a therapeutic apnea hypopnea index (AHI), 2. To automatically adjust EPAP and IPAP pressure to maintain airway potency, 3.To maintain low average treatment pressure, 4.To maintain acceptable sleep architecture.

Methods. Participants: Subjects with OSA currently using CPAP or BPAP therapy were recruited from the University of Pittsburgh Medical Center (UPMC), Sleep Medicine Center where they have been diagnosed with OSA and are currently being treated with fixed PAP. Patients who met all criteria for participation and provided informed consent were scheduled to undergo in-lab PSG study with BPAP auto with BiFlex. Participants were also asked to bring their own mask and accessories in order to maximize their comfort. Inclusion criteria of the study were; 1. Fixed CPAP users with a prescription $\geq$ 8 cmH2O or fixed BPAP users with any Bi-Level prescription, 2. The Sleep disordered breathing events were required to be primarily obstructive in nature (> 50%), 3. Age $\geq$ 18 years, 4. No weight change in excess of $\pm$ 15 pounds since last titration (< 1 year), 5. Able to follow instructions, 6. Able to provide inform consent. Exclusion criteria were; 1. CPAP prescription of < 8 cmH2O , 2. An artificial airway, 3. Current acute upper respiratory infection, encephalitis, sinusitis or middle ear infection, 4. Acute dermatitis or other skin lesions or trauma interfering with the application of a mask, 5. Co-morbid conditions including cardiopulmonary diseases, COPD, heart failure or receiving anticoagulants. The study was approved by Western Institutional Review Board (WIRB) and UPMC Clinical Trials Office (CTO) (the ethics committee approval number: 201047). All participants provided informed consent prior to participation in the study.

Design. This was a prospective case series. Participants were recruited from the Sleep Evaluation Center at UPMC, where they have been evaluated and treated for OSA. After obtaining

institutional Review Board (IRB) approved informed consent, 27 subjects who met inclusion/exclusion criteria evaluated with BPAP Auto Flex device during attended PSG.

Auto Bi-Level with Bi-Flex. Auto Bi-Level PAP delivers spontaneous Bi-level therapy with automatically adjusting EPAP and IPAP levels. The device is capable of responding to apnea, hypopnea, vibratory snoring, and large air leak events. The Auto Bi-level therapy also incorporates a "pro-active" search algorithm that responds to early indications of airway obstructions. During therapy, the auto Bi-Level PAP device continues to monitor breathing and searches for vibratory snoring, apneas, hypopneas, of flow limitations. The pressure is adjusted in response to an event. Usually, a change occurs over a 15 second period. This approach is based upon a titration protocol that increases EPAP related to obstructive apnea events and increases Pressure Support (PS) based upon obstructive hypopnea, snoring and flow limitation events. The level of pressure support (PS) delivered is determined by the difference between the IPAP and EPAP settings (PS = IPAP - EPAP). In a sleep lab, EPAP is usually adjusted first as the patient goes through various sleep stages and body positions to ensure that obstructive apneas are eliminated under worst-case conditions. PS is then adjusted to eliminate partial airway closure such as hypopneas and snoring. The auto Bi-Level device included a pressure relief feature called Bi-Flex. The Bi-Flex mode provides pressure relief during the latter stages of inspiration and during active exhalation (the beginning part of exhalation). In the Figure1, comfort feature of Bi-Flex was presented graphically. Bi-Flex levels of 1, 2, or 3 progressively reflect increased pressure relief that take place at the end of inspiration and at the beginning of expiration.
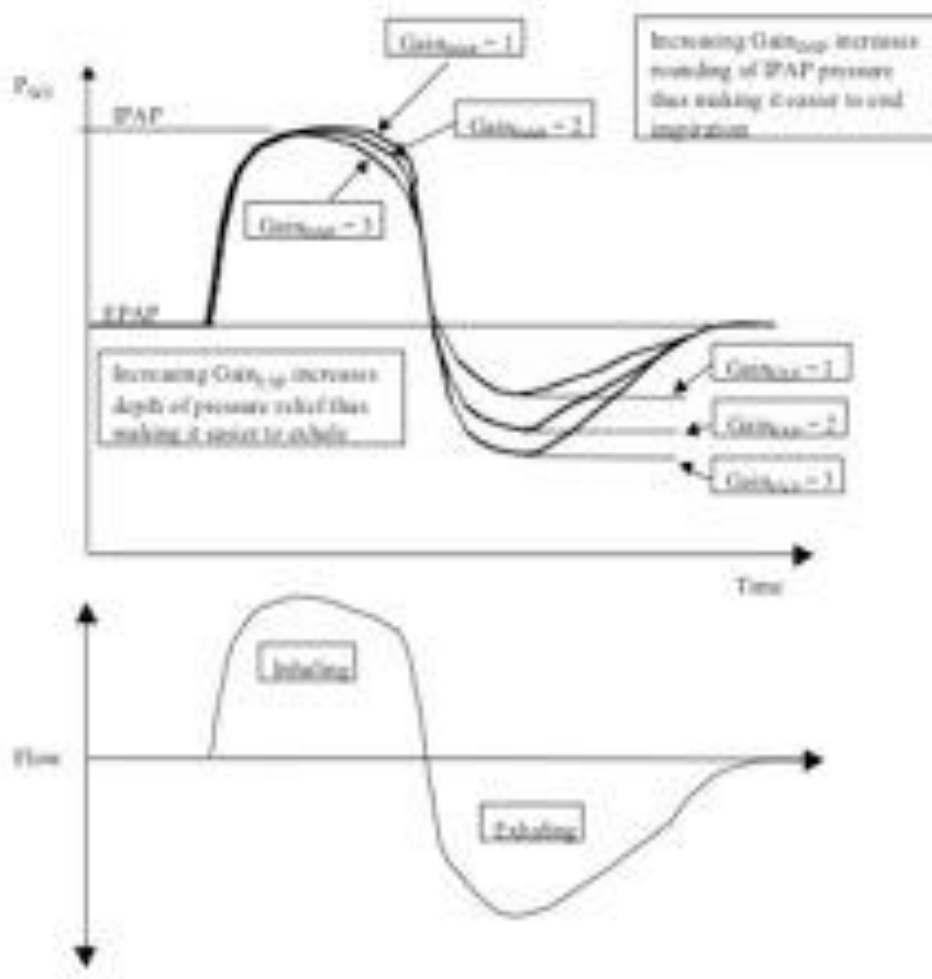

Рисунок 1 - Comfort feature of Bi-Flex

The device was set to deliver between 4 and 25 cmH2O for both the inspiratory (IPAP) and expiratory (EPAP) positive airway pressures. IPAP and EPAP were adjusted independently as determined by the device's algorithm. The minimum allowable difference between IPAP and EPAP was 2 cmH2O and a maximum difference was 8 cmH2O. The device's algorithm determined therapy pressure requirements for the duration of the PSG. Participants received therapy with the auto Bi-Level with Bi-Flex comfort feature.

Polysomnography. Full PSG performed using the SomnoStar Pro ™ system (Viasys[®] Healthcare). Channels monitored and recorded with surface electrodes included electroencephalogram, electrooculogram and submental electromyogram. Arterial oxygen saturation was recorded by digital pulse oximetry. Chest and abdominal effort were recorded using inductance plethysmography. Airflow was recorded with a pressure transducer attached to the Bi-Level device's pressure outlet . Apnea was defined as complete cessation of airflow for at least 10 seconds; hypopnea was defined as a 50% decrease in airflow and a 4% drop in oxygen saturation. American Academy of Sleep Medicine (AASM) sleep scoring criteria was used for scoring the diagnostic PSG [12] .

Statistical Analysis. Standard sleep parameters were collected and analyzed. Baseline demographic data was summarized. For continuous variables such as weight, the mean, standard deviation and range was presented. For categorical variables such as gender, the proportion of participants in each category was presented. Data were analyzed using SPSS statistical software (macintoch version 20.00, serial number; 10229569, SPSS Inc, Chicago, IL, USA)

Results. The entire study population comprised 82% (22/27) male and 18% (5/27) female participants. The mean age was 54±16 years and BMI (body mass index) was 33.0±9.1 kg/m^2.

The mean AHI (apnea hypopnea index) of entire study population obtained from the baseline diagnostic sleep study was 47.0±31.5 events/hour. Thirteen of the 27 participants currently had been using CPAP with a mean pressure of 12.0±3.1cmH2O. Fourteen of the 27 participants were on BPAP treatment. The mean IPAP pressure was 11.4±2.4 cmH$_2$O and the mean EPAP pressure was 7.6±2.1 cmH2O. To evaluate performance of BPAPauto device, PSG with BPAPauto was performed.

The mean total sleep time was 263.4±50.8 and sleep efficiency was 74.5±13.6%. The mean duration of rapid eye movement (REM) sleep was 43.6±25.0 minute. The mean AHI was 2.2±2.5 events/hour. The mean SaO$_2$ (oxygen saturation) was 94.0±1.8. The mean IPAP pressure required to abolish respiratory events was 14.1±3.4 cmH$_2$O and that of EPAP pressure was 10.7±3.9 cmH$_2$O. Figure 2, shows the representative waveform of BPAP auto signal performance.
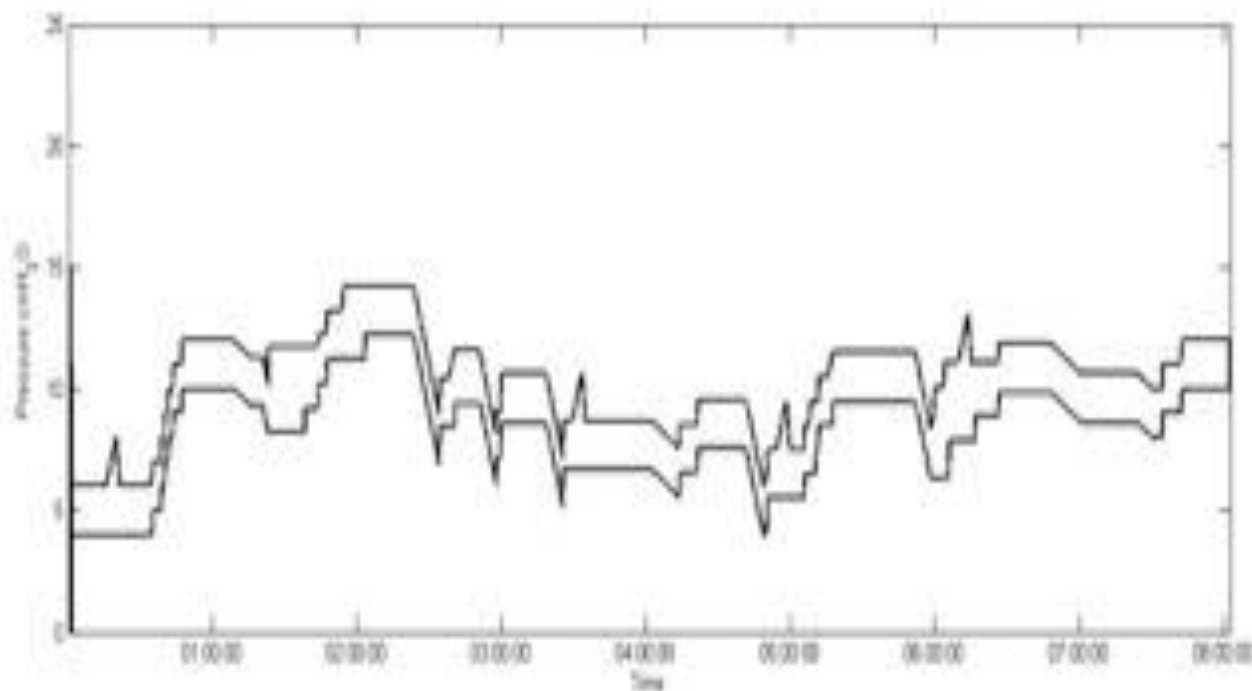
Рисунок 2 - Representative waveform of BPAP auto signal performance

Discussion. Data obtained from this study showed that BPAPauto is able to determine appropriate Bi-Level positive airway pressure and control oxygen saturation without excessive disruption of sleep. In 1981, nasal continuous positive airway pressure , which acts as a pneumatic splint, was introduced as a treatment of OSA and has been considered the gold standard for treatment of OSA since [13] . Several clinical trials have shown that CPAP eliminates apneic and hypopneic events, improve day time function, quality of life, sustained attention and mood and decrease cardiovascular risk factors[14-17]. Although highly effective, only half of the patients use CPAP as prescribed [18]. Pressure intolerance could be one of the reasons for decreased adherence [11,19]. Improving patient tolerance of PAP is one of the main driving forces for the development of alternative modes of PAP. A change in PAP mode may dramatically improve adherence in individual patients [5]. However studies showed that BPAP or APAP treatments do not result in higher adherence [9,20].

In one study use of C-flex device provided a statistically significant improvement in adherence [21]. BPAPauto was developed to potentially increase comfort and adherence to therapy. In a BPAPauto validation study, Wylie et all[22] showed that the BiPAP Auto with Bi-Flex provided adequate clinical resolution of the obstructive apnea and hypopnea events, with lower mean IPAP pressure and the effect on sleep continuity and architecture was comparable to that experienced during manual titration as determined during attended in-laboratory polysomnographic evaluation.
In our study BPAPauto performed well with respect to sleep efficacy, total sleep time, proportion of sleep stages as well as AHI and oxygen saturation during attended PSG. It is known that, a number of factors such as body position, sleep stage, nasal patency, ingestion of alcohol or hypnotic agents can affect the level of PAP required to keep upper airway open during sleep [23] . Instead of fixed IPAP/EPAP pressures, BPAPauto adjusts to an EPAP and an IPAP that are most comfortable for the patient. The Bi-Flex feature provides pressure relief in the transition period between the end of IPAP, and the beginning of EPAP and allows for a more comfortable delivery of PAP therapy. This mode could potentially be useful in pressure intolerant patients or patients who have considerable variability in the pressure requirement throughout the night [5]. This new device could be helpful to increase the adherence of patients to the therapy. The advantages of BPAPauto over other PAP modes remain to be demonstrated.

Limitations of this study include is the small study population and the lack of a control group.

In conclusion; BPAPauto is able to determine appropriate Bi-Level positive airway pressure and control oxygen saturation without excessive disruption of sleep. Further studies using randomized control design are needed to examine potential roles and advantages of BPAPauto for treatment of OSA.
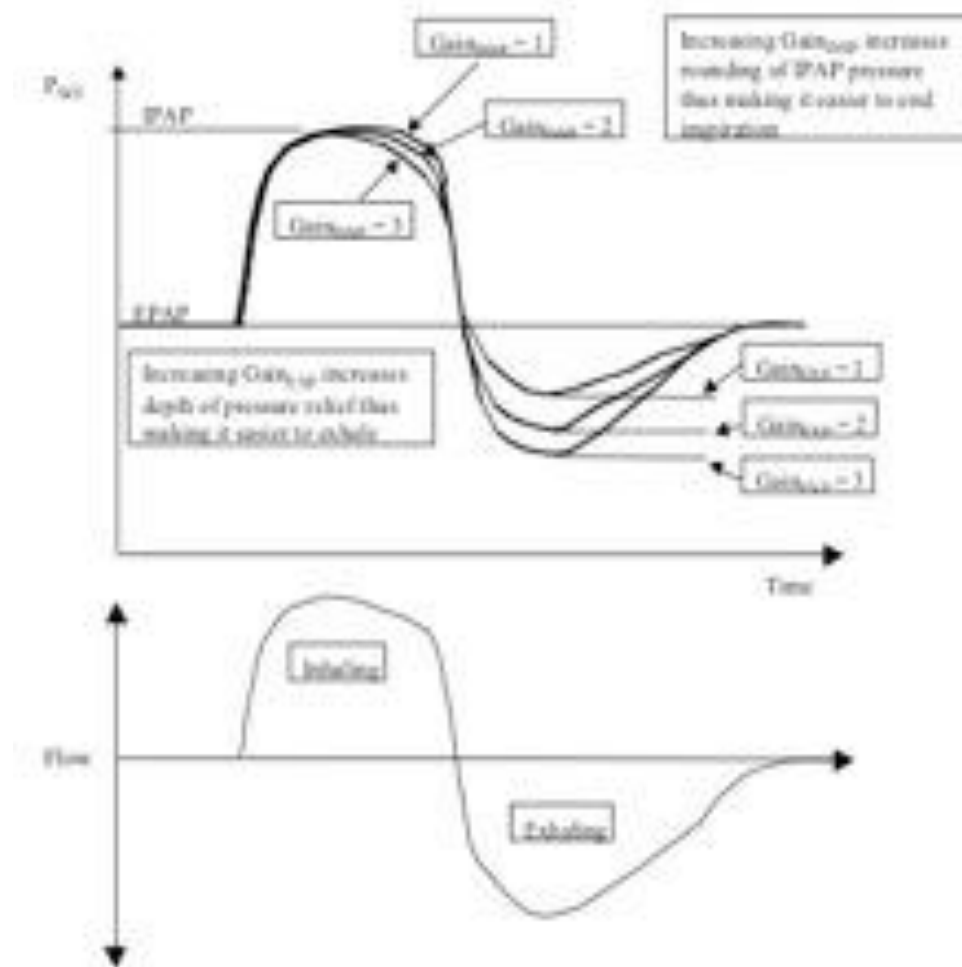
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