Bilevel Positive Airway Pressure Worsens Central Apneas During Sleep*

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Study objectives: **While most patients with sleep-disordered breathing are treated with continuous positive airway pressure (CPAP), bilevel positive airway pressure (BLPAP) is often used. Having observed that BLPAP therapy increased central apneas in some of our patients undergoing sleep studies, we conducted this study to evaluate the effects of BLPAP.**
Design: **Retrospective analysis of all sleep studies performed in an outpatient sleep center that used BLPAP over a 2-year period. We assessed the incidence and frequency of events during rapid eye movement (REM) sleep and non-REM sleep during baseline conditions, CPAP, and BLPAP. Desaturations, hypopneas, obstructive apneas, and central events, including periodic breathing (PB), Cheyne-Stokes respiration (CSR), and non-CSR central apneas were evaluated.**
Patients: **Ninety-five of the 719 patients who underwent sleep studies met inclusion criteria. Eighty of the 95 patients treated with BLPAP were also treated with CPAP.**
Results: **BLPAP was more likely to worsen than improve CSR ($p = 0.002$), non-CSR central apneas ($p < 0.001$), and CSR or PB ($p < 0.001$). CSR ($p = 0.03$) and non-CSR central apneas ($p = 0.01$) were more likely to worsen with BLPAP (24% and 23%, respectively) than with CPAP (11% and 8%). Central events ($p = 0.04$) and CSR ($p = 0.009$) were more likely to worsen during BLPAP in patients with baseline CSR or PB (62% and 48%, respectively) than develop in those without baseline CSR or PB (34% and 18%). Higher BLPAP differences worsened central events in 28% of patients, while 7% improved ($p = 0.02$). During REM sleep, central apneas improved, while hypopneas and obstructive apneas worsened ($p < 0.001$).**
Conclusions: **BLPAP often increases the frequency of CSR and non-CSR central apneas during sleep. Since CSR has adverse effects on cardiac function and sleep, it is important to consider this possible adverse effect of BLPAP.** ***(CHEST 2005; 128:2141–2150)***

Key words: bilevel positive airways pressure; Cheyne-Stokes respiration; continuous positive airways pressure; periodic respiration; polysomnography; positive pressure respiration; sleep, rapid eye movement; sleep apnea, central; sleep apnea syndromes

Abbreviations: BLPAP = bilevel positive airway pressure; CHF = congestive heart failure; CPAP = continuous positive airway pressure; CSR = Cheyne-Stokes respiration; EPAP = expiratory positive airway pressure; IPAP = inspiration positive airway pressure; OSA = obstructive sleep apnea; PB = periodic breathing; PSV = pressure support ventilation; REM = rapid eye movement; SDB = sleep-disordered breathing

Sleep disordered breathing (SDB), which includes both obstructive and central apneas and hypopneas, is very common and is associated with morbidity and mortality. Approximately 7% of adults have moderate-to-severe obstructive sleep apnea (OSA), 20% have mild OSA, and 5% > 65 years old have central sleep apnea.[1] Nearly 50% of patients with congestive heart failure (CHF) have SDB.[2] SDB is usually treated with continuous positive airway pressure (CPAP). An alternative treatment is bilevel positive airway pressure (BLPAP), which detects the patient's inspiration to "trigger" the change to the higher pressure (inspiration positive airway pressure [IPAP]), and switches to the lower pressure (expiratory positive airway pressure [EPAP]) when inspiration ends. BLPAP can be set to provide a backup rate, which changes to the higher pressure if the patient does not initiate a breath within a specified time. We observed that many patients referred for outpatient sleep studies acquired or had more frequent central apneas during BLPAP.

Central apneas occur when there is an absence of central ventilatory motor output. Central apneas

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during sleep cause repetitive arousals, increase catecholamine levels, increase BP, disrupt sleep, worsen CHF, and are associated with increased mortality in patients with CHF.[3] Cheyne-Stokes respiration (CSR) is a subset of central apneas in which there is a gradual decrease in breath size followed by an apnea, then a gradual increase in breath size. CSR is common among patients with CHF and stroke. Central apneas also include non-CSR central apneas that often occur following arousals or with sleep onset or changes in sleep state.

The standard treatment of both OSA[4] and CSR[5] is CPAP, which improves OSA by holding the airway open and improves CSR by several mechanisms. BLPAP has been reported as effective as CPAP for treating OSA[6] and central apneas.[7] We were concerned that BLPAP could worsen central apnea in many patients.

Although there has been at least one case report[8] of more frequent central apneas with BLPAP, we are unaware of any large studies. This retrospective study evaluates patients who received BLPAP to manage their SDB.

Materials and Methods

All sleep studies performed in the sleep center from January 2002 to December 2003 were reviewed. The review included 852 studies on 719 subjects. Each study began by evaluating tolerance of an interface using CPAP while awake. If sufficient respiratory events were present after a 2-h baseline period, then CPAP was begun and titrated to eliminate the respiratory events. If the patient did not tolerate CPAP because of difficulty breathing against the pressure or had persistent respiratory events with CPAP, then BLPAP was attempted. If hypoxia developed (oxygen saturation $\geq$ 4% below awake baseline) that did not improve with CPAP, BLPAP was then attempted prior to adding supplemental oxygen. BLPAP was also used for patients with known respiratory muscle weakness or previously determined to need BLPAP. If there were significant central apneas with BLPAP, then a back-up rate of 10/min was begun or CPAP resumed. Near the end of the study period, an exhalation pressure relief device (C-Flex; Respironics; Murrysville, PA) was used if there were significant central events with BLPAP. Our current practice is to use the pressure relief device prior to BLPAP. The pressure relief device detects the patient's exhalation, and makes it easier to breathe out than CPAP by lowering the pressure for approximately one third of a second at the start of exhalation. The C-flex device has three "comfort settings," which allows one to adjust the amount of pressure drop.

Our protocol for setting BLPAP pressures was to set EPAP at the level found during CPAP titration that eliminated obstructive apneas, or to 4 cm H_2O if there were no obstructive apneas, and then increase EPAP if the inspiratory efforts did not consistently trigger IPAP. The protocol for setting IPAP pressure was to start 3 cm H_2O or 4 cm H_2O higher than EPAP, and then titrate higher to eliminate hypopneas or improve saturations.

Standard criteria were used to stage sleep[9] and identify apneas and hypopneas.[4] For periods of BLPAP with a backup rate, apneas were identified by the chest and abdominal signal. The central and obstructive apnea indexes are the number of respective apneas per hour of sleep, with mixed apneas counted in both indexes.

Each study was reviewed for diagnosis. OSA had more than five obstructive apneas or hypopneas per hour. CSR had crescendo-decrescendo alterations in respiratory effort and tidal volume separated by periods of central apnea (Fig 1). Periodic breathing (PB) had periodic increases and decreases in respiratory effort without central apneas (Fig 2). Non-CSR central apneas were central apneas that were not associated with crescendo-decrescendo alterations in respiratory effort, and often occurred with sleep onset or after arousal (Fig 3)

All patients receiving BLPAP were identified (n = 127). Patients were excluded for $<$ 10 min of sleep on BLPAP (excluding 18 patients), a difference of $<$ 4 cm H_2O between inspiratory and expiratory pressures (n = 7), lack of both baseline and CPAP (n = 4), tracheostomy (n = 1), and failure to trigger BLPAP (n = 2). With these criteria, a study group of 95 patients remained.

Of the study group, 10 patients were treated with BLPAP with only a backup rate, and 3 patients were treated with BLPAP both with and without a backup rate. CPAP data were absent for 15 patients, and 1 patient had no baseline data.

The study group was evaluated for respiratory events during baseline, CPAP, and BLPAP. The indexes of obstructive apneas, central apneas, mixed apneas, hypopneas, and desaturations were determined for each condition using the periods with the highest CPAP or IPAP levels that totaled 1 h. Our analysis proceeded as follows: (1) The period with highest CPAP was identified. If the sleep time was $>$ 1 h, this was the only period included in the analysis. (2) If the sleep time was $<$ 1 h, the period with the next highest CPAP was also included. (3) This process continued until there was at least 1 h of sleep time or until all the CPAP periods were included. For BLPAP, we used a similar analysis to determine the periods with the highest IPAP to a total of 1 h of sleep. BLPAP periods with a pressure difference of $<$ 4 cm H_2O were excluded because we wanted there to be a clear difference between CPAP and BLPAP. We also determined the periods with the highest pressure difference (IPAP minus EPAP) with at least 10 min of sleep so we could test the hypothesis that higher pressure differences worsened central events. The studies were reviewed to determine the presence and effect of treatment on respiratory events. Each study was evaluated for presence of rapid eye movement (REM) periods during baseline, CPAP, and BLPAP, and whether there were no events, an increase, no change, or a decrease in obstructive apneas, central apneas, and hypopneas in REM vs non-REM sleep.

Statistical Analysis

Mean $\pm$ SD values are reported. A two-tailed Fisher Exact Test was used to compare events between groups with or without baseline CSR or PB. χ^2 test was used to determine if the numbers of patients' improving vs worsening respiratory events differed.

Results

Of the 719 patients, 638 patients had primary OSA, including 14 patients with CSR and 47 patients with non-CSR central apneas. Eighteen patients had OSA and CSR as co-equal diagnoses; 14 patients had primary CSR, including 9 patients with OSA.

The 95 patients treated with BLPAP included 77 patients with primary OSA, including 2 patients with