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Efficacy of Adaptive Servoventilation in Treatment of Complex and Central Sleep Apnea Syndromes*

Joanne Shirine Allam, MD; Eric J. Olson, MD, FCCP; Peter C. Gay, MD, FCCP; and Timothy I. Morgenthaler, MD, FCCP

Background: **Complex sleep apnea syndrome (CompSAS) is recognized by the concurrence of mixed or obstructive events with central apneas, the latter predominating on exposure to continuous positive airway pressure (CPAP). Treatment of CompSAS or central sleep apnea (CSA) syndrome with adaptive servoventilation (ASV) is now an option, but no large series exist describing the application and effectiveness of ASV.**

Methods: **Retrospective chart review of the first 100 patients who underwent polysomnography using ASV at Mayo Clinic Sleep Center.**

Results: **ASV titration was performed for CompSAS (63%), CSA (22%), or CSA/Cheyne Stokes breathing patterns (15%). The median diagnostic sleep apnea hypopnea index (AHI) was 48 events per hour (range, 24 to 62). With CPAP, obstructive apneas decreased, but the appearance of central apneas maintained the AHI at 31 events per hour (range, 17 to 47) [$p = 0.02$]. With bilevel positive airway pressure (BPAP) in spontaneous mode, AHI trended toward worsening vs baseline, with a median of 75 events per hour (range, 46 to 111) [$p = 0.055$]. BPAP with a backup rate improved the AHI to 15 events per hour (range, 11 to 31) [$p = 0.002$]. Use of ASV dramatically improved the AHI to a mean of 5 events per hour (range, 1 to 11) vs baseline and vs CPAP ($p < 0.0001$). ASV also resulted in an increase in rapid eye movement sleep vs baseline and CPAP (18% vs 12% and 10%, respectively; $p < 0.0001$). Overall, 64 patients responded to the ASV treatment with a mean AHI < 10 events per hour. Of the 44 successful survey follow-up patients contacted, 32 patients reported some improvement in sleep quality.**

Conclusion: **The ASV device appears to be an effective treatment of both CompSAS and CSA syndromes that are resistant to CPAP.** ***(CHEST 2007; 132:1839–1846)***

Key words: adaptive servoventilation; central sleep apnea; complex sleep apnea; positive pressure breathing

Abbreviations: AHI = apnea-hypopnea index; ASV = adaptive servoventilation; BPAP = bilevel positive airway pressure; BPAP-S = bilevel positive airway pressure spontaneous mode; BPAP-S/T = bilevel positive airway pressure spontaneous and timed mode; CAI = central apnea index; CompSAS = complex sleep apnea syndrome; CPAP = continuous positive airway pressure; CPAP+O2 = continuous positive airway pressure with additional oxygen; CSA = central sleep apnea; CSR = Cheyne-Stokes respiration; IQR = interquartile range; NREM = non-rapid eye movement; OAI = obstructive apnea index; REM = rapid eye movement; RERA = respiratory-related arousal

There is controversy regarding the optimal treatment of central sleep apnea (CSA) syndrome and complex sleep apnea syndrome (CompSAS).[1–4] By definition, patients with CompSAS most often begin with what appears to be classic obstructive sleep apnea but exhibit disruptive central apneas and periodic breathing on continuous positive airway pressure (CPAP).[5] In one study,[6] only 43% of CSA patients nearly resolved their sleep-disordered breathing with short-term CPAP therapy, leaving the rest with a substantially elevated apnea-hypopnea index (AHI). A prospective study[7] of CPAP therapy in patients with CSA and congestive heart failure found that the mean AHI decreased by only approximately 50% after 3 months of therapy, leaving a mean residual AHI of 20 events per hour.

Adaptive servoventilation (ASV) uses an automatic, minute ventilation-targeted device (VPAP Adapt; ResMed; Poway, CA) that performs breath-to-breath analysis and adjusts its settings accordingly.[8]

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Depending on breathing effort, the device will automatically adjust the amount of airflow it delivers in order to maintain a steady minute ventilation.

ASV has been shown to be more effective than CPAP in treating patients with CSA both in the short term[9] and over several months.[10] ASV has also been shown to be effective in resolving sleep-disordered breathing in patients with CompSAS.[11] ASV in the form of the VPAP Adapt device has only recently been available for use in the United States, and is indicated for CSA, CompSAS, mixed apnea, and Cheyne-Stokes respiration (CSR). We have employed ASV since the spring of 2006 and here report our experience with the first 100 consecutive patients undergoing ASV titration. When several treatment modalities were evaluated within one patient (*eg*, CPAP, bilevel positive airway pressure [BPAP] with or without spontaneous/timed backup rate [BPAP-S/T and BPAP-S, respectively]), we compared short-term effectiveness using polysomnographic results and expected to observe a superior response to ASV. We later obtained subjective survey follow-up data to better define treatment responses.

Materials and Methods

Definitions

Apneas and hypopneas were defined as previously described.[5] Respiratory-related arousals (RERAs) were tabulated if associated with apneas, hypopneas, or with other indicators of airflow limitation not meeting criteria for apneas or hypopneas.[12] All indexes are expressed as the number of events divided by the hours of sleep.

Obstructive sleep apnea syndrome was diagnosed if AHI was ≥ 5 events per hour, or if the patient complained of sleepiness and the number of RERAs per hour was > 10 and CPAP titration was successful in eliminating the RERAs. CSA was diagnosed if the number of central apneas per hour was ≥ 5 and at least 50% of the total AHI was central in origin. CompSAS was diagnosed if CPAP titration eliminated obstructive sleep apnea syndrome but the residual central apnea index (CAI) was ≥ 5 or the CSR pattern became predominant. CSA/CSR was diagnosed if patients showed both CSA and CSR patterns on diagnostic polysomnography.

The titration of CPAP was performed as previously described,[5] as were titrations of BPAP and ASV.[11] A successful ASV study was defined by a total AHI < 10 events per hour based on ≥ 60 min of sleep on therapy.

Patients

We identified the first 100 consecutive patients who underwent polysomnography to titrate ASV at our sleep center. All patients had undergone prior unsuccessful CPAP trials, and ASV titration (with or without other treatment modalities) was undertaken as possible alternative treatment option.

Study Design

Medical charts were reviewed, and demographic, clinical, and polysomnographic data were extracted. All polysomnograms were initially scored by a polysomnographic technologist and examined by a diplomate of the American Board of Sleep Medicine, including the diagnostic, ASV, and any other study ordered. A sleep specialist evaluated each patient before and after polysomnography, and the order and type of therapeutic trials were determined by them. The final recommendations for treatment were recorded. In addition to chart review, patients who were prescribed home ASV and available by telephone contact were later asked about their experience with ASV (Appendix). This study was approved by our institutional review board.

Polysomnography was performed using a digital polygraph (NCI-Lamont Medical Incorporated; Madison, WI; or Bio-logic Systems Corporation; Mundelein, IL). Sleep staging and arousals were scored according to standard methods as described previously.[13,14] Airflow and respiratory effort were monitored using nasal pressure transducer and respiratory impedance plethysmography during the diagnostic study, and using the flow channel from the CPAP, BPAP, or ASV plus respiratory impedance plethysmography during the positive pressure titration studies. We compared polysomnographic data, including sleep efficiency and architecture, total AHI, central and obstructive apneas, oxygen saturation and ECG findings, as well as sleep position in each of the diagnostic, CPAP, BPAP, and ASV studies.

Statistical Methods

Data analysis was done using statistical software (JMP, Version 6; SAS Institute; Cary, NC) from 1989 to 2005. Categorical variables were compared across different groups using Pearson χ^2 test or Fisher exact test as appropriate. Continuous variables were compared across groups using the Kruskal-Wallis test; when differences were detected, pairwise comparisons were made using the Wilcoxon test. Values are expressed as median (with interquartile range [IQR]) or as No. (%) unless otherwise specified.

Results

The study population was 87% male with median age of 72 years (IQR, 59 to 78). Characteristics are summarized in Table 1. The diagnoses that led to an ASV study were CompSAS in 63%, CSA in 22%, and CSA/CSR in the remaining 15%. The indication for all ASV trials was a suboptimal response to CPAP,

*From the Division of Pulmonary and Critical Care Medicine (Dr. Allam) and Mayo Clinic Sleep Disorders Center (Drs. Olson, Gay, and Morgenthaler), Mayo Clinic, Rochester, MN.
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Correspondence to: Timothy I. Morgenthaler, MD, FCCP, Mayo Clinic, 200 First St SW, Rochester, MN 55905; e-mail: tmorgenthaler@mayo.edu
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Table 1—*Characteristics of the Study Population*

Characteristics	CompSAS (n = 63)	CSA (n = 22)	CSA/CSR (n = 15)	Total (n = 100)	p Value
Median age (range), yr	70.7 (58.7–77.5)	69.3 (57.0–78.8)	78.1 (72.4–84.2)	72.3 (59.7–78.6)	0.0474*
Female gender, %	14	14	7	13	0.8312†
Congestive heart failure, %	25	32	60	32	0.0357*
Atrial fibrillation, %	25	32	53	31	0.1092
COPD, %	5	5	7	5	1.0000†
Cerebrovascular accident, %	8	5	0	6	0.8351†
Opioids, %	13	23	0	13	0.1353†
Mean body mass index (IQR), kg/m^2	31 (29–34)	29 (25–32)	30 (25–32)	31 (28–33)	0.0172*
Insomnia, %	6	5	13	7	0.5313†
Mean Epworth sleepiness scale score (IQR)	11 (6.8–14)	11 (7.8–14.3)	10 (8–15)	11 (7–14)	0.8902

*Denotes statistical significance.
†Calculated using Fisher exact test due to small numbers.

whether the CPAP trial was performed at our center or elsewhere. Patients had an average of three study segments completed, usually diagnostic polysomnography, CPAP titration, and an ASV trial. In some cases, a BPAP or CPAP with additional oxygen (CPAP + O2) trial was also added.

Overall, the study segments that were included in the analysis consisted of 93 diagnostic studies, 92 ASV titrations, 69 CPAP titrations, 22 BPAP-S/T, 11 CPAP + O2, and 5 BPAP-S. Therapeutic intervention trials < 60 min in duration were not included. The median duration of the different titrations is given in the Figure 1 legend.

During diagnostic polysomnography, the median AHI was 48.0 events per hour (IQR, 24.5 to 62.5) with a predominance of hypopneic events. The median obstructive apnea index (OAI) was 13.0 (IQR, 5.0 to 27.0), and the median CAI was 4.0 (IQR, 1.0 to 25.5). With CPAP, the median AHI decreased to 31 events per hour (IQR, 17.5 to 47.0) [p = 0.0172], the OAI diminished to 1.0 (IQR, 0.0 to 5.5), and the CAI increased to 16.0 (IQR, 6.5 to 33.0). BPAP-S tended to worsen the total AHI to 75.0 events per hour (IQR, 46.0 to 111.0). This effect, with near statistical significance (p = 0.05546), was due to the worsening in central apneic events to 40.0 (IQR, 28.0 to 57.5), while the OAI remained at 5.0 (IQR, 1.0 to 12.5). BPAP-S/T improved the total AHI to 15.0 events per hour (IQR, 11.0 to 41.5) [p = 0.0021] with the OAI at 0.0 (IQR, 0.0 to 1.0) and CAI at 1.0 (IQR, 0.0 to 3.3). With CPAP + O2, the AHI improved to 10.0 events per hour (IQR, 3.0 to 30.0) [p = 0.0003], with median OAI of 0.0 (IQR, 0.0 to 1.0) and CAI of 7.0 (IQR, 1.0 to 19.0). The most improvement occurred with ASV, which decreased the median AHI to 5.0 events per hour (IQR, 1.0 to 10.8) [p < 0.0001], median OAI to 0.0 (IQR, 0.0 to 0.0), and mean CAI to 0.0 (IQR, 0.0 to 1.0). The AHI index was significantly lower in the ASV group when compared to the BPAP-S/T group (p < 0.0001, Wilcoxon rank sum). These results are illustrated in Figure 1.

When categorized by underlying diagnoses (CompSAS, CSA, and CSA/CSR), ASV seemed to fare equally with BPAP-S/T in CSA, and worked as well as CPAP for CSA/CSR. In CompSAS, ASV remained superior to all other modalities (Fig 1).

The apnea-hypopnea events in our CompSAS subgroup occurred in non-rapid eye movement (NREM) sleep and while supine: supine rapid eye movement (REM) AHI, 0.0 events per hour (IQR, 0.0 to 0.0); nonsupine REM AHI, 9.0 events per hour (IQR, 0.0 to 26.0); supine NREM AHI, 68.0 events per hour (IQR, 33.0 to 85.0); and nonsupine NREM AHI, 12.0 events per hour (IQR, 5.0 to 46.0). ASV significantly improved the AHI in all positions and stages of sleep, and the residual events were mainly found during supine NREM sleep (Fig 2). A positional effect was also observed in the CompSAS group with the application of CPAP. Indeed, 70.2% of the CompSAS patients who underwent a CPAP titration (n = 47) showed a twofold or greater reduction in AHI in the nonsupine positions as compared to supine positions.

When compared to CPAP and BPAP-S/T, ASV improved the percentage of time spent in REM sleep in all groups (18% for ASV vs 14% and 11%, respectively, for BPAP-S/T and CPAP; p < 0.0001). ASV also significantly decreased the arousal index as well as all apneic and hypopneic events compared to CPAP and BPAP-S/T in all groups (p < 0.0001) [Table 2].

Overall, 64 patients completing > 60 min of an ASV trial achieved success, defined as a total AHI < 10 events per hour. Of these successes, 76% of patients had a diagnosis of CompSAS, 58% had CSA, and 73% had CSA/CSR. The difference in success

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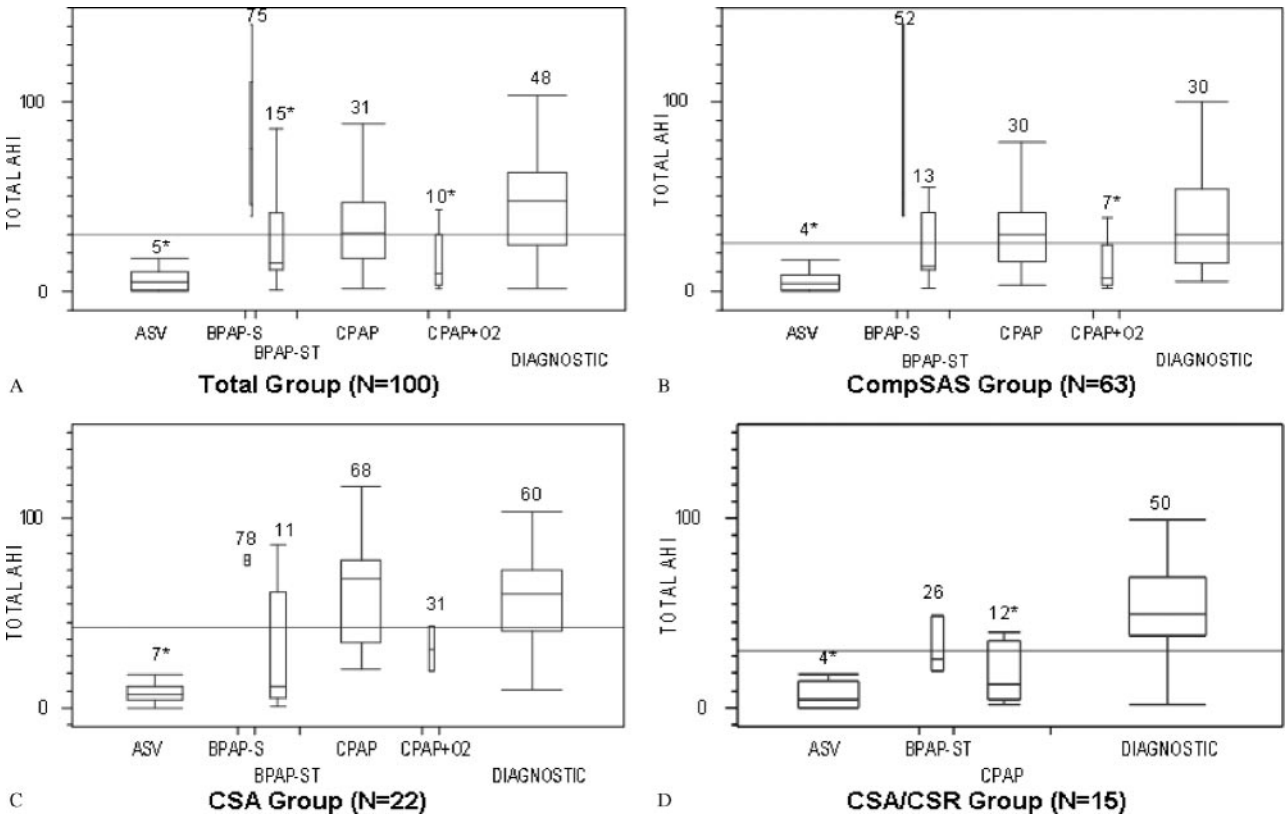

FIGURE 1. Total AHI with different positive pressure modalities. Within each panel, the box plots represent median and quartiles. They are drawn proportional to the number of studies performed. The numbers above the boxes represent medians. *Indicates statistically significant difference compared to the diagnostic study. The median duration of each of the different titrations are the following: diagnostic, 146 min (IQR, 125 to 173); ASV, 229 min (IQR, 152 to 312); CPAP, 129 min (IQR, 94 to 186); BPAP-S/T, 160 min (IQR, 121 to 366); CPAP+O2, 115 min (IQR, 80 to 147); BPAP-S, 160 min (IQR, 121 to 366). *Top left*, *A*: With all patient groups combined, ASV significantly improves the total AHI ($p < 0.0001$). Using pairwise comparisons, ASV lowered the AHI greater than CPAP, BPAP-S, BPAP-S/T, and diagnostic (all $p < 0.0001$). When comparison is made between ASV and CPAP+O2, ASV lowers total AHI and CAI more than CPAP+O2 ($p = 0.0362$ and $p < 0.0001$, respectively). *Top right*, *B*: In the CompSAS subgroup, there is significant difference between the different positive pressure modalities. Using pairwise comparisons, ASV lowered total AHI and CAI greater than all other modalities (all $p < 0.0001$). *Bottom left*, *C*: Using pairwise comparisons in the CSA subgroup, ASV is equivalent to BPAP-S/T in the control of all three variables, but superior to CPAP+O2 in reducing total AHI ($p < 0.0409$), and superior to CPAP and BPAP-S in reducing AHI, obstructive apneas, and central apneas ($p < 0.0001$). *Bottom right*, *D*: In the CSA/CSR group, ASV significantly reduces central events compared to CPAP ($p = 0.0392$) but does not reach significance in terms of total AHI control ($p = 0.0550$). Compared to BPAP-S/T, ASV significantly reduces total AHI ($p = 0.0073$) but fares equally well in preventing central or obstructive apneas (not shown).

rate between the three groups did not reach statistical significance. Fifty-three percent of patients had a successful ASV trial and were prescribed the device, 21% were prescribed the device despite having a study that did not fulfill success criteria of an AHI < 10, and 17% were not prescribed ASV despite a successful study. Of the patients in this last group, two could not tolerate ASV, two had better sleep architecture with CPAP, and four were deemed to have an equivalent treatment effect with CPAP or BPAP-S/T. The end-expiratory pressures prescribed on the ASV ranged from 5 to 10 mm H_2O median of 8 mm H_2O.

Only one of the patients studied was prescribed a benzodiazepine, three were given a sleeping aid, and six were given treatment for restless legs syndrome. Oxygen treatment was prescribed in four patients, two of them along with ASV and the other two with CPAP or as sole therapy, respectively.

Of the 44 patients who were successfully contacted for follow-up information, 37 patients (84%) were still using the ASV at the time of the survey. The median duration of use was 5 months (IQR, 3 to 6). The majority of contacted patients (32 of 44 patients) reported improvement in sleep quality and/or daytime sleepiness (Table 3). Of those who

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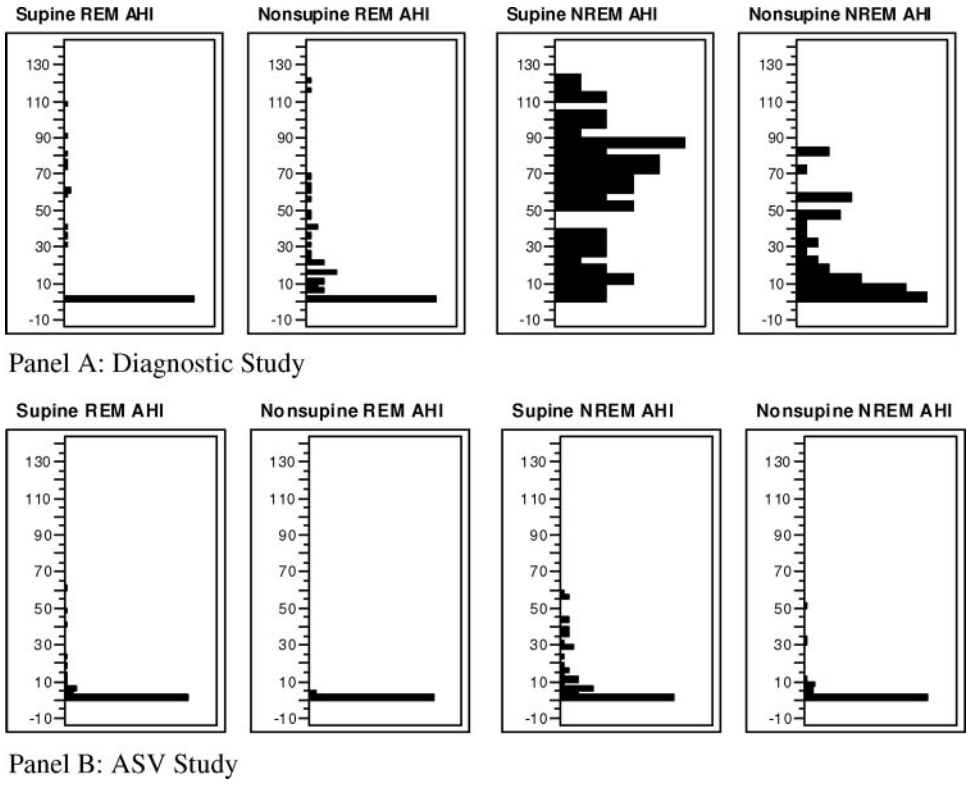

FIGURE 2. Distribution of apnea hypopnea events in the CompSAS subgroup according to sleep stage and position in the diagnostic studies and after application of ASV. *Top panels, A*: Diagnostic studies, from *left* to *right*: median AHI, 0.0 events per hour (IQR, 0.0 to 0.0), 9.0 events per hour (IQR, 0.0 to 26.0), 68.0 events per hour (IQR, 33.0 to 85.0), and 12.0 events per hour (IQR, 5.0 to 46.0). *Bottom panels, B*: ASV studies, from *left* to *right*: median AHI, 0.0 events per hour (IQR, 0.0 to 3.0), 0.0 events per hour (IQR, 0.0 to 0.0), 5.0 events per hour (IQR, 0.0 to 19.3), and 0.0 events per hour (IQR, 0.0 to 2.3).

were not using the device at the time of the survey, the majority cited comfort as a factor for their decision, whereas financial reasons were never reported to be a factor. One patient was unable to find a vendor close to home.

DISCUSSION

This is the first report of the clinical use of ASV in a consecutive series of patients. In patients with CSA, CSA/CSR, or CompSAS whose sleep-related breathing problems were not easily controlled with CPAP, we have shown that ASV resulted in a dramatic improvement in sleep-disordered breathing, as well as some improvement in sleep architecture. Furthermore, the device was very well tolerated and resulted in improvement in the symptoms of 32 of 44 contacted patients on follow-up.

CompSAS patients tend to have most apneic events during the cyclic alternating pattern of NREM sleep.[15,16] This categorization of sleep is not widely or routinely used, and we did not undertake a cyclic alternating pattern analysis of our data. Our results do confirm, though, that the majority of the apnea-hypopnea events in our CompSAS subgroup were occurring in NREM sleep and were more frequent in the supine sleep position (Fig 2). Improvement in the total AHI with position change from supine to nonsupine was observed with both ASV and CPAP. This suggests that additional positional recommendations could improve treatment effect even more. This is not surprising given that nonsupine sleep positions are known to improve both obstructive and central apneic events.[17]

An effective treatment of CSA and CSA/CSR has been reported both with ASV[9,10,18–20] and BPAP-S/T.[21] Our results confirm those findings and further show that ASV and BPAP-S/T seem to be equivalent in the treatment of CSA. Similar to the results of Teschler et al,[9] ASV appeared superior to BPAP-S/T in the treatment of CSA/CSR and controls central events better than CPAP in this subgroup (Fig 1).

CompSAS is hypothesized to be due to a dysregulation of carbon dioxide homeostasis in addition to

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Table 2—*Polysomnography Findings per Diagnostic Group With Different Positive Pressure Modalities

Variables	Total Group (n = 100)†	CompSAS (n = 63)‡	CSA (n = 22)§	CSA/CSR (n = 15)‖	p Value
AHI, events/h					
Diagnostic	48 (24.5–62.5)	30 (15–54)	60 (40.5–72.5)	50 (38–69)	0.0023¶
CPAP	31 (17.5–47)	30 (16–42)	68.5 (34.3–77.8)	12 (4.5–35.3)	0.0002¶
BPAP-S/T	15 (11–41.5)	13 (11–41.5)	11 (5.5–61)	26 (19–49)	0.4541
ASV	5 (1–10.8)	4 (1–8.8)	7 (4–11)	4 (0–14)	0.2701
p Value	< 0.0001¶	< 0.0001¶	< 0.0001¶	< 0.0001¶	
Total arousal index					
Diagnostic	47 (30.3–67.8)	44 (25.5–66.8)	53 (31–67.5)	50 (33–74)	0.6083
CPAP	37 (24.5–47)	35 (26–44)	46 (39.3–56.3)	15 (10.5–38.8)	0.0019¶
BPAP-S/T	28 (17.5–41)	30.5 (21.8–41.5)	11 (10.5–43)	26 (25–38)	0.5417
ASV	25 (17.3–34)	25 (17.8–34)	26 (21–42)	20 (16–32)	0.8158
p Value	< 0.0001¶	< 0.0001¶	0.0011¶	0.0038¶	
Respiratory arousal index					
Diagnostic	84 (61–94)	78 (52.5–93.5)	89 (74–95.5)	84 (69–97)	0.1865
CPAP	58 (32–78)	57 (31–75)	81.5 (57.8–90)	24.5 (11.8–54.5)	0.0012¶
BPAP-S/T	57 (45.3–68.5)	55 (33.5–73.8)	57 (28–62.5)	70 (64–95)	0.1568
ASV	23 (9.3–48.8)	23.5 (8.8–50.3)	30 (16–48)	11 (3–54)	0.4714
p Value	< 0.0001¶	< 0.0001¶	< l0.0001¶	< 0.0001¶	
Obstructive apnea index					
Diagnostic	13 (5–27)	12 (4–31.5)	11 (8–22)	14 (7–26)	0.9991
CPAP	1 (0–5.5)	1 (1–5)	1.5 (0–8)	0 (0–1)	0.1143
BPAP-ST/	0 (0–1)	0 (0–1.5)	1 (0–1.5)	0 (0–1)	0.6791
ASV	0 (0–0)	0 (0–0)	0 (0–1)	0 (0–1)	0.6723
p Value	< 0.0001¶	< 0.0001¶	< 0.0001¶	< 0.0001¶	
CAI					
Diagnostic	4 (1–25.5)	1 (0–8.5)	28 (15.5–51.5)	13 (1–49)	0.0001¶
CPAP	16 (6.5–33)	14 (7–28)	54 (12.5–71.5)	11.5 (0.3–22.3)	0.0137¶
BPAP-S/T	1 (0–3.25)	1 (0–3)	1 (0.5–21)	3 (0–4)	0.8001
ASV	0 (0–1)	0 (0–1)	1 (0–2)	0 (0–2)	0.3067
p Value	< 0.0001¶	< 0.0001¶	< 0.0001¶	0.0219¶	
Sleep efficiency					
Diagnostic	73 (56–83)	74 (56.5–83)	77 (58.5–88.5)	65 (40–75)	0.0545
CPAP	74 (58–80.5)	74 (58–82)	59.5 (57.5–79.8)	76.5 (72–87.3)	0.2180
BPAP-S/T	77 (57.8–90.3)	75 (56.8–83.5)	90 (74–95)	57 (50–58)	0.0757
ASV	72.5 (64.3–83.8)	74 (66–84.3)	67 (62–88)	69 (59–79)	0.4579
p Value	0.4320	0.5721	0.1084	0.1302	
Stage I, %					
Diagnostic	20 (10–39.5)	18 (9–29.5)	22 (9–41)	31 (19–55)	0.1141
CPAP	20 (9.5–27.5)	19 (10–27)	23 (19.3–44.30)	6.5 (3.3–12.5)	0.0064¶
BPAP-S/T	17.5 (8.3–26.3)	19 (12–28.3)	5 (2.5–11)	26 (16–34)	0.0134¶
ASV	12 (7–19.8)	12 (7.8–17.3)	12 (6–22)	14 (7–21)	0.8367
p Value	0.0003¶	0.0023¶	0.0107¶	0.0081¶	
Stage 2 diagnostic, %					
Diagnostic	51 (33.5–51)	52 (33.5–67.5)	50 (40–61.5)	40 (27–66)	0.7649
CPAP	54 (43–65)	54 (43–65)	61.5 (38.8–72.8)	48.5 (44–58.5)	0.5482
BPAP-S/T	56 (42.5–68.8)	60.5 (48.8–69.5)	53 (37–76.5)	41 (40–57)	0.3450
ASV	56 (46–61.8)	56 (46–62.3)	58 (51–60)	51 (34–63)	0.7788
p Value	0.1226	0.2915	0.6017	0.8836	
Slow-wave sleep, %					
Diagnostic	6 (0–23.5)	6 (0–24)	6 (0–22)	4 (0–24)	0.9076
CPAP	5 (0–16.5)	7 (0–16)	0 (0–10.5)	15.5 (4.5–30.3)	0.0510¶
BPAP-S/T	10.5 (4.3–27.3)	8 (1.5–22.5)	38 (6–49.5)	21 (0–27)	0.3799
ASV	10 (3.3–20.8)	10 (3.8–20.3)	9 (3–22)	12 (3–19)	0.9860
p Value	0.1120	0.5584	0.0321¶	0.5558	
REM sleep, %					
Diagnostic	10 (0–15.5)	11 (0–18)	10 (2.5–15.5)	2 (0–13)	0.1652
CPAP	12 (3–19)	14 (7–21)	5.5 (0–11.25)	17.5 (10–37)	0.0231¶
BPAP-S/T	11.5 (6.3–19.8)	12.5 (7–26)	7 (0–16)	8 (8–22)	0.4063
ASV	18 (12–24)	18 (13–24)	15 (3–28)	20 (5–26)	0.7724
p Value	< 0.0001¶	0.0006¶	0.2369	0.0045¶	

*Data are presented as median (IQR) unless otherwise indicated. Only those studies with total sleep time of ≥ 60 min were included in the analysis. The p values under each polysomnography variable represent the difference between the different studies; p values in the last column represent the differences between the three diagnostic groups.

†Diagnostic studies, n = 93; CPAP studies, n = 69; BPAP-S/T studies, n = 22; and ASV studies, n = 92.

‡Diagnostic studies, n = 53; CPAP studies, n = 47; BPAP-S/T studies, n = 14; and ASV studies, n = 58.

§Diagnostic studies, n = 21; CPAP studies, n = 14; BPAP-S/T studies, n = 5; and ASV studies, n = 19.

‖Diagnostic studies, n = 19; CPAP studies, n = 8; BPAP-S/T studies, n = 3; and ASV studies, n = 15.

¶Indicates significance.

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Table 3—*Follow-up Data*

Variables	Patients, No.	Patients Contacted (n = 44*), %
Using ASV	37	84
Mask discomfort	14	32
Pressure problems	5	11
Alarm problems	10	22
Leaks	14	32
Change in sleep quality		
A lot better	22	50
A little better	10	22
No change	3	6
A little worse	1	2
A lot worse	1	2
Change in daytime sleepiness		
A lot better	16	36
A little better	9	20
No change	10	22
A little worse	2	5
A lot worse	0	0

*Forty-four patients were successfully contacted of 74 patients who received ASV.

obstructive sleep apnea.[15] Patients are thought to become hypocapnic during sleep and unmask a hypocapnea-induced apnea threshold that will lead to the emergence of central apnea events. The hypocapnea is thought to be created by the recovery breaths after apneic events in patients with spontaneously developed central apneas in the latter part of the night. It can also be iatrogenically induced by the application of positive airway pressure in those patients who only unmask as CompSAS with the use of CPAP. This mechanism intuitively explains the reason behind the trend toward worsening seen in CompSAS patients with the use of BPAP-S, which is expected to eliminate obstructive events and significantly increase ventilation with a proportionate decrease in carbon dioxide, increasing further the risk for central apneas. This is exactly what we observed in our study group with CompSAS with the application of BPAP-S (Fig 1).

The present study suggests that ASV is more effective than BPAP-S/T in controlling apneic events. Furthermore, patients seem to have a good tolerance of ASV. The versatility of the ASV device with its minute ventilation-targeted settings might account for its good patient tolerance.

In 19 of our patients, the ASV device was prescribed despite a study that did not meet success criteria (AHI $<$ 10 events per hour). This is probably explained by the fact that despite an incomplete response (with AHI $>$ 10 events per hour), ASV was more successful than other modalities in these difficult patients. Nine of these 19 patients were successfully contacted, and all reported improvement in their sleep quality. This might indicate that it would be acceptable to relax the criteria for study success and actually give a trial of ASV to patients with an improvement during the overnight study.

This study has inherent limitations by its retrospective, observational, and descriptive design. There was no prospective randomization, nor blinding, nor protocol for order of application of treatment modalities, but the series was consecutive. However, all patients first underwent diagnostic polysomnography followed by an attempt at CPAP therapy. Referral bias is likely because not all patients with CSA or CompSAS were recruited to a trial of ASV. Our patient population may represent a subset of patients who are resistant to standard treatment. Even with these limitations, our data appear to be the most comprehensive presently available regarding the use and comparative efficacy of ASV in a difficult set of patients with CompSAS and central apnea syndromes.

Conclusion

ASV is a new treatment modality that has been shown effective in treating CSA, CSA/CSR, and CompSAS. Our findings clarify and extend prior observations, and suggest that ASV is an appropriate consideration to other positive airway pressure treatments and is effective for most patients with these nonobstructive sleep-related breathing disorders.

Appendix

Telephone Questionnaire: Are You Currently Using the ASV?

If yes:
- How long have you been using it?
- How many hours per night on average?

Are you having problems with:
- Mask comfort?
- Leaks?
- Alarms?
- Pressure?
- Residual snoring?
- Other problems?

Since you started using ASV, how do you feel that your sleep quality has changed?
- No change
- A little better
- A lot better
- A little worse
- A lot worse

How do you feel that your daytime sleepiness has changed?
- No change
- A little better
- A lot better
- A little worse
- A lot worse

If no:

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To what extent were the following a factor in your stopping use of the ASV (not a factor, somewhat a factor, a very big factor)?
Comfort
Financial or insurance reasons
Lack of improvement
How long did you try ASV for?
When you were using ASV, how do you feel that your sleep quality has changed?
No change
A little better
A lot better
A little worse
A lot worse
How do you feel that your daytime sleepiness has changed?
No change
A little better
A lot better
A little worse
A lot worse

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Efficacy of Adaptive Servoventilation in Treatment of Complex and Central Sleep Apnea Syndromes *

Joanne Shirine Allam, Eric J. Olson, Peter C. Gay and Timothy I. Morgenthaler

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