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Efficacy of Flow- vs Impedance-Guided Autoadjustable Continuous Positive Airway Pressure*

A Randomized Cross-over Trial

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Study objectives: Autoadjustable continuous positive airway pressure (CPAP) devices are increasingly used in the treatment of obstructive sleep apnea (OSA). Since different measurements of upper airway obstruction are applied, it is uncertain whether these devices are equally effective in controlling sleep-disordered breathing. Hypothesizing that differences in therapeutic efficacy were to come out, we compared the performance of the AutoSet device (ResMed; Sydney, Australia), which features autoadjustable positive airway pressure (APAP) guided by detection of flow limitation (APAPfl), with the SOMNOsmart device (Weinmann; Hamburg, Germany), which features APAP guided by the forced oscillation technique (APAPfot).
Design: A double-blind, randomized, cross-over trial.
Setting: The sleep disorders center and sleep laboratory of a university hospital.
Patients and interventions: An overnight CPAP autotitration procedure was performed in 30 patients with OSA. A split-night protocol allowed that each patient used both devices.
Measurements and results: Using polysomnography, sleep, indexes of sleep-disordered breathing, snoring, and CPAP levels were recorded. No significant differences were found in conventional sleep variables. While the apnea-hypopnea index (AHI) was lower with APAPfl (3.5 ± 5.6/h) as compared to APAPfot (9.9 ± 31.0/h), the difference was not statistically significant (mean ± SD). The snoring index, however, was significantly lower with APAPfl (35.3 ± 53.7/h vs 111.6 ± 175.4/h, respectively; $p = 0.01$). The median and 95th percentile pressure levels rose from wakefulness to sleep in APAPfl, but decreased in APAPfot. Higher pressure variability was present in the latter method.
Conclusions: These findings suggest that the APAPfl is superior to APAPfot in the control of snoring. While a lower AHI was achieved with APAPfl, at the expense of a higher median pressure but less pressure variability, the difference with APAPfot was not statistically significant.

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Key words: AutoSet; continuous positive airway pressure; obstructive sleep apnea; snoring; SOMNOsmart

Abbreviations: AHI = apnea-hypopnea index; AI = arousal index; APAP = autoadjustable positive airway pressure; APAPfl = autoadjustable positive airway pressure guided by detection of flow limitation; APAPfot = autoadjustable positive airway pressure guided by the forced oscillation technique; CPAP = continuous positive airway pressure; OSA = obstructive sleep apnea; P_{50} = median positive airway pressure; P_{95} = 95th percentile of positive airway pressure

For > 2 decades, nasal continuous positive airway pressure (CPAP) has been the cornerstone in the treatment of patients with moderate-to-severe obstructive sleep apnea (OSA).[1] Over the years, the therapeutic end points of CPAP application have evolved from abolishing respiratory events, including apneas, hypopneas, and snoring, to controlling respi-

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ratory event-related arousals, and finally to normalize airflow and respiratory effort.[2]

Most commonly, for treatment of OSA, based on results of a formal sleep study, a fixed positive pressure level is established by means of manual pressure titration. However, the efficacy of this method is uncertain because manual titration methods have never been standardized. Furthermore, overnight CPAP requirements may be quite variable due to a variety of reasons, such as changes in body position and sleep stage,[3] and consumption of alcoholic beverages.

In more recent years, new devices have been developed that are designed to deliver autoadjustable positive airway pressure (APAP), meeting the patient's immediate pressure needs.[4] These devices have the theoretical advantage of stabilizing the upper airway during changing physiologic conditions, thereby circumventing the methodologic issues of manual pressure titration.

Although commercially available APAP devices have been shown to be useful in the assessment of CPAP requirements both in the sleep laboratory and at home,[5] it is still unknown whether the implicated APAP technologies are equally effective.[6] It has been shown that devices that run on different pressure-driving algorithms respond differently to changing pressure demands.[7] Therefore, we hypothesized that differences in the ability of various devices to stabilize sleep-disordered breathing should likewise occur. We compared two devices whose operation is based on different modes of sensing incipient upper airway obstruction. The operational characteristics of the AutoSet device (ResMed; Sydney, Australia) feature APAP guided by detection of flow limitation (APAPfl) of inspired air and the subsequent pressure adaptation.[8] The SOMNOsmart device (Weinmann, Hamburg, Germany) features APAP guided by the forced oscillation technique (APAPfot).[9] Pressure adjustments are based on changes in the measured impedance, and aim at keeping the resistance below a given percentage of wakefulness values. Favorable outcomes have been reported on the use of both aforementioned APAP devices regarding pressure titration in the sleep laboratory,[9–14] as well as unattended use in the home environment.[15,16] The present study was designed to compare the efficacy of these two APAP technologies in terms of effects on sleep quality, respiratory disturbance, and snoring indexes. Since adequate control of sleep-disordered breathing should be achieved at the lowest possible pressure level, it was also evaluated if the pressure output was appropriate in terms of magnitude and variability.

Materials and Methods

Subjects

Patients who demonstrated an apnea-hypopnea index (AHI) > 20/h plus an arousal index (AI) > 30/h (ie, Belgian criteria for reimbursement of nasal CPAP) were enrolled. Exclusion criteria included a history of prior uvulopalatopharyngoplasty, signs of severe nasal obstruction, excessive sleep disruption due to non-respiratory causes, and COPD (ie, $FEV_1/FVC < 65\%$). None of the patients had symptoms and signs of congestive heart failure. No one refused to enter the study. Five patients had to be excluded after the registration because of intolerance or technical problems. Twenty-seven male and 3 females subjects (mean age, 53.8 ± 10.1 years; body mass index, 30.5 ± 4.5; FEV_1/FVC, 0.76 ± 0.06; AHI, 52.9 ± 27.2/h; AI, 50.4 ± 19.8/h) successfully completed the study (± SD). The study ran from January 2001 until July 2001. The participants gave written informed consent, and the trial was approved by the Ethical Review Board of our institution.

Sleep Studies

Polysomnography was carried out using a 19-channel digital polygraph (Morpheus; Medatec; Brussels, Belgium). A standardized sleep recording procedure was carried out, as previously described.[17] To record airflow, thermocouples plus nasal pressure cannulae were used during baseline studies. During the APAP trial, airflow was evaluated by measuring the respiratory pressure fluctuations in the nasal mask, which was connected via 4-mm-diameter flexible tubing to the built-in manometer (model 164PC01D37; Honeywell; Freeport, IL). Respiratory movements were recorded using thoracic and abdominal piezo-sensors (Sleepmate Technologies; Midlothian, VA). Sleep and respiratory events were manually scored in epochs of 30 s. Sleep stages were identified according to standard criteria.[18] The scoring of arousals was based on published guidelines.[19] The AI, the AHI, and the snoring index (ie, count of inspiratory snores per hour of sleep) were assessed according to previously described methods.[17] The CPAP level was also assessed manually in epochs of 30 s. A pressure value and corresponding sleep stage were allocated to each epoch.

Trial Protocol

Before carrying out a CPAP titration procedure, the patients were habituated on fixed CPAP home treatment. The CPAP was empirically set at a predicted pressure value of 7.9 ± 1.8 cm H_2O.[20] The CPAP compliance before the titration study was 4.7 ± 2.5 h/night. The CPAP habituation period was 90.5 ± 69.2 days. The patients were subsequently hospitalized to carry out an overnight study in which the AutoSet and SOMNOsmart devices were used in randomized order. The devices were covered in identical boxes for blinding purposes. After 4 h, the mask was disconnected from the first device and attached to the next device, which was then used for another 4 h. Both devices were programmed to a pressure range between 4 cm H_2O and 14 cm H_2O. The APAP devices were compared regarding their effect on relevant sleep and respiratory variables. The median positive airway pressure (P_{50}) and 95th percentile of positive airway pressure (P_{95}) values were computed differentially for the states of sleep and wakefulness. Finally, the P_{50}/P_{95} ratio was calculated. The lower the index, the greater the difference between P_{50} and P_{95}, which is indicative of increased pressure variability.[4] Scoring was done by one skilled technician, and reviewed by the first author of this article. Both were blinded to the treatment conditions.

Table 1—*Sleep Parameters in Both Treatment Conditions* *

Parameters	APAPfl	APAPfot
Time in bed, min	238 ± 36	228 ± 41
TST, min	180 ± 41	177 ± 53
Sleep efficiency, %	76 ± 16	77 ± 17
Wakefulness, min	58 ± 45	53 ± 38
NREM stage 1, min (% TST)	21 ± 14 (13 ± 9)	20 ± 15 (13 ± 9)
NREM stage 2, min (% TST)	103 ± 37 (65 ± 23)	98 ± 33 (62 ± 21)
NREM stage 3–4, min (% TST)	19 ± 21 (12 ± 13)	17 ± 17 (10 ± 11)
REM sleep, min (% TST)	40 ± 23 (25 ± 14)	37 ± 27 (23 ± 17)
AI, events/h	3 ± 3	9 ± 24

*Data are presented as mean ± SD. The paired t test showed no significant differences between APAPfl and APAPfot methods in any of the listed variables. NREM = non-rapid eye movement; REM = rapid eye movement; TST = total sleep time.

Statistical Analysis

The paired t test was applied for evaluating differences between treatment conditions. To analyze whether the APAP devices behave differently in the sleep vs wake state, analysis of variance for repeated measurements was applied. This statistical procedure can be used to evaluate the interaction between different predictor variables (*ie*, the treatment condition and the sleep vs wake state) on therapeutic outcome (*ie*, pressure level). SPSS version 11.0 statistical software was used (SPSS; Chicago, IL). All presented data are mean ± SD unless otherwise specified.

RESULTS

Comparison of the two APAP devices showed no significant differences in the various sleep parameters, including time in bed, total sleep time, sleep efficiency, sleep stages, and AI (Table 1). While the AHI was lower with the use of APAPfl (3.5 ± 5.6/h)

as compared to APAPfot (9.9 ± 31.0/h), the difference was not statistically significant (p = 0.27). In contrast, the snoring index was significantly lower with the application of APAPfl in comparison with APAPfot (35.3 ± 53.7/h vs 111.6 ± 175.4/h, respectively; p = 0.01). Analysis of variance for repeated measurements showed a highly significant interaction between the treatment condition (APAPfl vs APAPfot) and the sleep vs waking condition with respect to pressure output (p = 0.004). While P_{50} and P_{95} were significantly higher during sleep with APAPfl as compared with APAPfot, both variables rose from wakefulness to sleep in APAPfl, but decreased in APAPfot (Fig 1). During sleep, the P_{50}/P_{95} was significantly lower with APAPfot as compared with APAPfl (0.65 ± 0.15 vs 0.79 ± 0.11, respectively; p < 0.001), indicating increased pressure variability in the former method. A typical example of pressure variability in a patient is shown in Figure 2.

DISCUSSION

The present study is one of the first clinical reports to compare the efficacy of two devices that are driven by different mechanisms for detection of upper airway obstruction. In this double-blind, randomized, cross-over trial, APAPfl (AutoSet device) and APAPfot (SOMNOsmart device) methods were compared. APAPfl provided a significantly better control of snoring, and resulted in a lower AHI (though not significantly) than APAPfot. These differences in respiratory parameters were best explained by differences in pressure profiles of the two devices. The median and 95th percentile of pressure levels rose significantly from wakefulness to sleep when using APAPfl, but fell paradoxically in the APAPfot treatment arm. In addition, APAPfot was
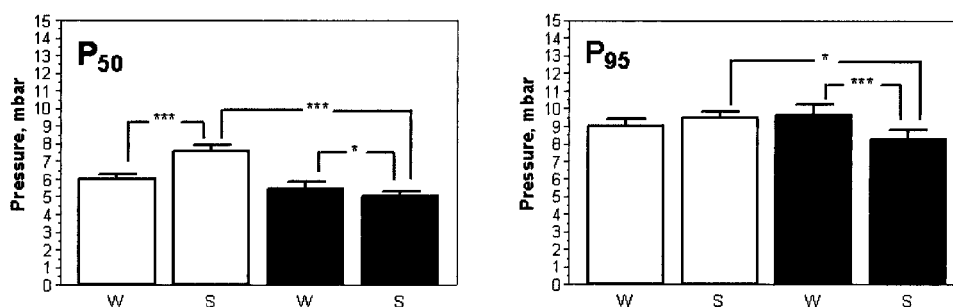

FIGURE 1. Changes of pressure output in APAPfl (AutoSet device) [white bars] as compared with APAPfot (SOMNOsmart device) [black bars] from wakefulness (W) to sleep (S). *p < 0.05; ***p < 0.001. The error bars represent SEM. P_{50} and P_{95} are significantly higher during sleep with APAPfl as compared with APAPfot. P_{50} and P_{95} increase from wakefulness to sleep in APAPfl. The opposite is true with APAPfot.
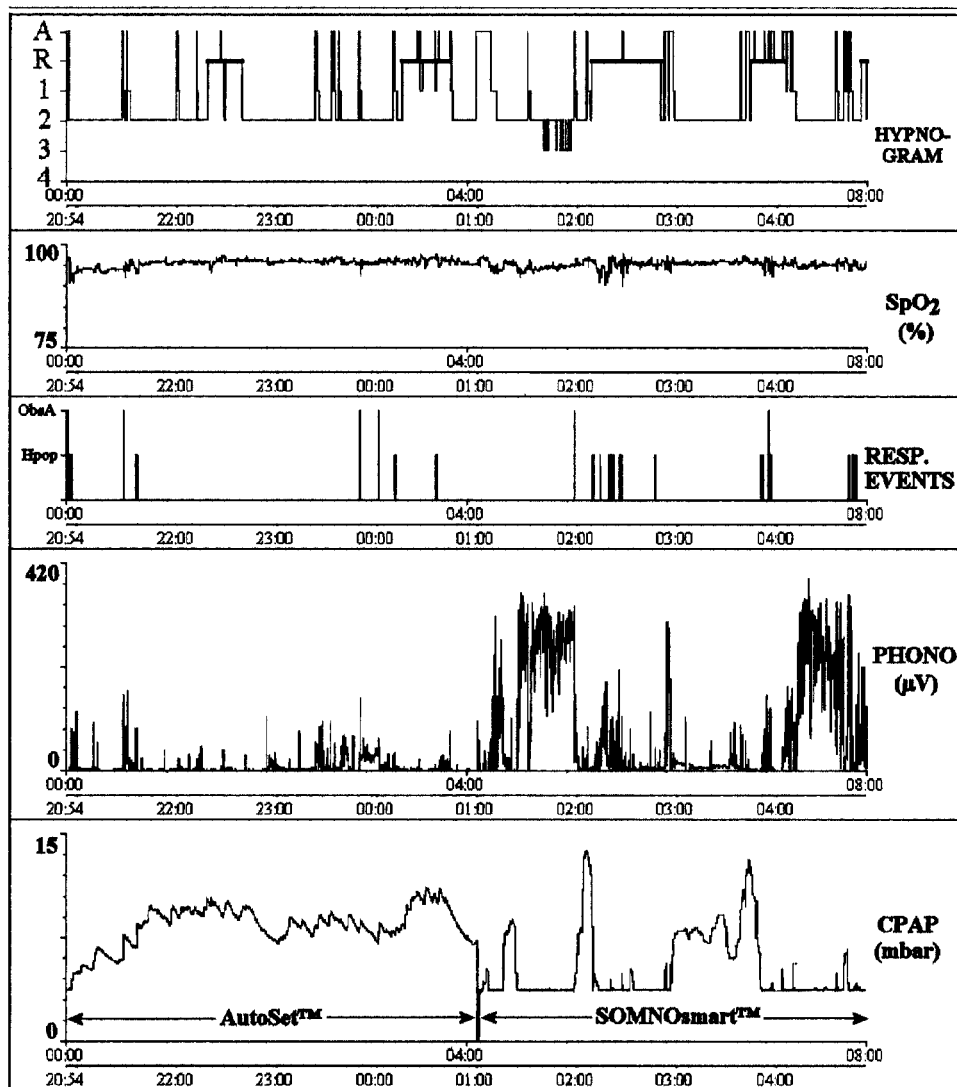
FIGURE 2. Split-night trends showing the effects of both APAP methods in a typical patient. *Top panel*: hypnogram (A = awake; R = rapid eye movement sleep; 1 to 4 = NREM stages 1 to 4). *Second panel*: oxyhemoglobin concentration (SpO_2) measured with a pulse oximeter. *Middle panel*: occurrence of disturbed respiratory (RESP) events (ObsA = obstructive apnea; Hpop = hypopnea). *Fourth panel*: snoring sound measured with a microphone (PHONO) at the level of the larynx. *Bottom panel*: pressure trends of APAPfl and APAPfot. Note the increased pressure and limited pressure swings in APAPfl ($P_{50}/P_{95} = 0.90$). In contrast, APAPfot shows large pressure swings and failure to increase baseline pressure during episodes of loud snoring ($P_{50}/P_{95} = 0.38$).

subject to significantly higher pressure variability, which was indicated by a lower P_{50}/P_{95} ratio.

Both the measurement of respiratory impedance based on forced oscillations applied to the upper airway, and the detection of inspiratory flow limitation have been used for monitoring of residual airway obstruction during CPAP titration. Lorino et al[21] demonstrated that the former method is more sensitive than the latter. Accordingly, the responses to the detection of disturbed breathing may be different in APAPfot and APAPfl methods. Another important difference between the two methods are the reaction times (change in pressure/change in time) that determine the rate at which the pressure adjustment will be completed. The slope of adaptation is steeper in both lowering and increasing the pressure in response to certain respiratory events with the APAPfot method. While a more sensitive and faster response to respiratory changes may predispose the APAPfot method to greater variability in pressure output, the handling of unphysiologic signals by the APAPfot method is also dissimilar from the APAPfl method. The AutoSet device, in contrast to the SOMNOsmart device, has a built-in system for the

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continuous monitoring of bias flow. The system is able to compensate for pressure drops due to excessive air leakage up to a flow rate of 0.4 L/s.[11] Since mask and/or mouth leaks often occur during sleep, this may in part explain why higher median positive pressure levels were found in the AutoSet device.

The pressure data from the present trial correspond to previously published results. The mean pressure values in a report[9] on the SOMNOsmart device are similar to our current findings. In that study, Randerath et al[9] reported that the SOMNOsmart device produced significantly lower pressure values in comparison with a manual titration procedure. As in our study, snoring was not eliminated in the APAPfl arm of the trial. Moreover, the P_{50} and P_{95} values of the AutoSet device are quite similar to previously published data on patients with a comparable severity of OSA and body mass index.[15] Since it is known that the pressure required to abolish snoring exceeds the pressure required to eliminate apneas by 2 cm H_2O in $> 90\%$ of the patients,[22] it is evident that the better control of snoring obtained with APAPfl in this study is explained by the median CPAP level, which was on average 2.5 cm H_2O higher than the median pressure produced by the APAPfot method.

From the present study, several issues emerge regarding our understanding of the operational features of APAP technology. The observation that the AHI, the principle outcome measure of this study, was not significantly different in two devices with markedly different pressure profiles requires further consideration. We hypothesize that there is a margin of pressure tolerance around an optimal CPAP level in a given patient at a given time. While obstructive breathing events will reappear when the pressure is reduced below a critical lower limit, raising the pressure above an upper threshold will induce air leakage and bring on unwarranted side effects. While essentially no data on the hypothetical upper pressure limit exist, it is known from the literature that "sham" nasal CPAP levels as low as 2 cm H_2O may induce significant improvements in markers of sleep-disordered breathing.[23] Hence, the corresponding margin of pressure tolerance may comprise several centimeters of water. Within this conceptual margin, however, pressure adjustments will not appreciably affect sleep or breathing outcomes. We believe that the two APAP devices under study operated to a large extent in the presumed zone of pressure tolerance, which provides an explanation for the absence of a significant difference in effect on the AHI. Also in this concept, the absence of residual disturbed breathing at a given CPAP level does not by itself mean that this is the result of appropriate pressure adaptation. Second, it is unclear whether one measure of upper airway narrowing is sufficient to reliably titrate CPAP. It has been suggested that obstructive breathing events identified by the forced oscillation technique should not be scored unless corroborated by the concurrent presence of impaired ventilation, which requires the use of a pneumotachograph.[4,24] Improved results, *ie*, normalization of the AHI at lower and more stable CPAP levels, might be obtained from the combined use of both techniques. Third, knowledge regarding the appropriate rate of pressure adjustment is lacking. From the present study it is clear that a fast pressure response is not necessarily synonymous with improved stabilization of breathing. On the contrary, excessive pressure variability may lead to inadequate control of snoring and sleep-disordered breathing.

In conclusion, the results of the present study show that a significantly better suppression of snoring is achieved by APAPfl than with APAPfot. Furthermore, AHI was lower with APAPfl than with APAPfot, although this difference was not statistically significant. The pressure profile of AutoSet device was strikingly different from the SOMNOsmart device in that AutoSet device had a higher median pressure but less pressure variability than the SOMNOsmart device. The difference in pressure profile best explains the differences in snoring and AHI observed with these two devices.

References

1 Sullivan CE, Issa FG, Berthon-Jones M, et al. Reversal of obstructive sleep apnoea by continuous positive airway pressure applied through the nares. Lancet 1981; i:862–865

2 Montserrat JM, Ballester E, Olivi H, et al. Time-course of stepwise CPAP titration: behavior of respiratory and neurological variables. Am J Respir Crit Care Med 1995; 152:1854–1859

3 Oksenberg A, Silverberg DS, Arons E, et al. The sleep supine position has a major effect on optimal nasal continuous positive airway pressure: relationship with rapid eye movements and non-rapid eye movements sleep, body mass index, respiratory disturbance index, and age. Chest 1999; 116:1000–1006

4 Levy P, Pepin JL. Autoadjusting continuous positive airway pressure: what can we expect? Am J Respir Crit Care Med 2001; 163:1295–1296

5 Series F. Is treatment of obstructive sleep apnea syndrome with auto-CPAP useful? Sleep 2000; 23:S161–S165

6 Berry RB, Parish JM, Hartse KM. The use of auto-titrating continuous positive airway pressure for treatment of adult obstructive sleep apnea. Sleep 2002; 25:148–173

7 Farre R, Montserrat JM, Rigau J, et al. Response of automatic

continuous positive airway pressure devices to different sleep breathing patterns: a bench study. Am J Respir Crit Care Med 2002; 166:469–473

8 Berthon-Jones M, Lawrence S, Sullivan CE, et al. Nasal continuous positive airway pressure treatment: current realities and future. Sleep 1996; 19:S131–S135

9 Randerath WJ, Parys K, Feldmeyer F, et al. Self-adjusting nasal continuous positive airway pressure therapy based on measurement of impedance: a comparison of two different maximum pressure levels. Chest 1999; 116:991–999

10 Lloberes P, Ballester E, Montserrat JM, et al. Comparison of manual and automatic CPAP titration in patients with sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1996; 154:1755–1758

11 Teschler H, Berthon-Jones M, Thompson AB, et al. Automated continuous positive airway pressure titration for obstructive sleep apnea syndrome. Am J Respir Crit Care Med 1996; 154:734–740

12 Teschler H, Farhat AA, Exner V, et al. AutoSet nasal CPAP titration: constancy of pressure, compliance and effectiveness at 8 month follow-up. Eur Respir J 1997; 10:2073–2078

13 Gagnadoux F, Rakotonanahary D, Martins de Araujo MT, et al. Long-term efficacy of fixed CPAP recommended by Autoset for OSAS. Sleep 1999; 22:1095–1099

14 Ficker JH, Fuchs FS, Wiest GH, et al. An auto-continuous positive airway pressure device controlled exclusively by the forced oscillation technique. Eur Respir J 2000; 16:914–920

15 Teschler H, Wessendorf TE, Farhat AA, et al. Two months auto-adjusting versus conventional nCPAP for obstructive sleep apnoea syndrome. Eur Respir J 2000; 15:990–995

16 Randerath WJ, Schraeder O, Galetke W, et al. Autoadjusting CPAP therapy based on impedance efficacy, compliance and acceptance. Am J Respir Crit Care Med 2001; 163:652–657

17 Pevernagie D, Hamans E, Van Cauwenberge P, et al. External nasal dilation reduces snoring in chronic rhinitis patients: a randomized controlled trial. Eur Respir J 2000; 15:996–1000

18 Rechtschaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Washington DC: U.S. Government Printing Office, 1968

19 American Sleep Disorders Association. EEG arousals: scoring rules and examples; a preliminary report from the atlas task force of the American Sleep Disorders Association. Sleep 1992; 15:173–184

20 Miljeteig H, Hoffstein V. Determinants of continuous positive airway pressure level for treatment of obstructive sleep apnea. Am Rev Respir Dis 1993; 147:1526–1530

21 Lorino AM, Lofaso F, Duizabo D, et al. Respiratory resistive impedance as an index of airway obstruction during nasal continuous positive airway pressure titration. Am J Respir Crit Care Med 1998; 158:1465–1470

22 Hoffstein V, Oliver Z. Comparing pressures required to abolish snoring and sleep apnea. Can Respir J 2001; 8:427–430

23 Loredo JS, Ancoli-Israel S, Dimsdale JE. Effect of continuous positive airway pressure vs placebo continuous positive airway pressure on sleep quality in obstructive sleep apnea. Chest 1999; 116:1545–1549

24 Badia JR, Farre RO, John KR, et al. Clinical application of the forced oscillation technique for CPAP titration in the sleep apnea/hypopnea syndrome. Am J Respir Crit Care Med 1999; 160:1550–1554

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