JCSM
Journal of Clinical Sleep Medicine

SCIENTIFIC INVESTIGATIONS

Pressure-Relief Features of Fixed and Autotitrating Continuous Positive Airway Pressure May Impair Their Efficacy: Evaluation with a Respiratory Bench Model

Kaixian Zhu, MS[1,2,3]; Sami Aouf, MD[1]; Gabriel Roisman, MD, PhD[2]; Pierre Escourrou, MD, PhD[2,3]

[1]Air Liquide Healthcare, Gentilly, France; [2]Sleep Disorders Center, AP-HP Antoine-Béclère Hospital, Clamart, France; [3]Faculty of Pharmacy, Paris-Sud University, Châtenay-Malabry, France

Study Objectives: Pressure-relief features are aimed at improving the patient's comfort during continuous positive airway pressure (CPAP) treatment for obstructive sleep apnea. The objective of this study was to determine the effect of these therapy features on fixed CPAP and autotitrating CPAP (APAP) treatment efficacy.

Methods: Seven pressure-relief features applied by three CPAP devices were included in our study (Remstar Auto: C-Flex 3, C-Flex+ 3, A-Flex 3, P-Flex; AirSense 10: EPR 3; Prisma 20A: SoftPAP 2 and 3). In fixed CPAP, the devices were subjected to a 10-min bench-simulated obstructive apnea sequence (initial apnea-hypopnea index, AHI = 60/h) with and without pressure-relief features. In APAP, the sequence was lengthened to 4.2 h (initial AHI = 58.6/h). The residual AHI and mean/median pressure were compared with and without pressure-relief features.

Results: Compared to conventional CPAP, where pressure was adjusted to be just sufficient to control the simulated obstructive events, C-Flex+ 3, P-Flex, and EPR 3 failed to normalize the breathing flow and did not reduce the AHI. The mean pressures with the three features, respectively, were 1.8, 2.6, and 2.6 cmH_2O lower than the conventional CPAP. Compared to conventional APAP, similar levels of control were observed with pressure-relief features, apart from P-Flex where the delivered mean pressure was lower and residual AHI greater. The device-reported mean/median pressures in APAP with A-Flex 3, P-Flex, EPR 3, and SoftPAP 3 were higher than that measured on the bench.

Conclusions: Pressure-relief features may attenuate CPAP efficacy if not adjusted for at the time of their introduction. In clinical practice, efficacy can be ensured by increasing the therapeutic pressure delivered by fixed CPAP or by enabling the pressure-relief features prior to initial pressure titration. Device-reported pressures in APAP devices with pressure relief activated may overstate delivered pressures.

Keywords: CPAP treatment, pressure-relief features, bench test

Citation: Zhu K, Aouf S, Roisman G, Escourrou P. Pressure-relief features of fixed and autotitrating continuous positive airway pressure may impair their efficacy: evaluation with a respiratory bench model. *J Clin Sleep Med* 2016;12(3):385–392.

INTRODUCTION

Continuous positive airway pressure (CPAP) is an effective treatment for obstructive sleep apnea (OSA). However, the effectiveness of treatment mainly depends on regular use of CPAP device and the patient's tolerance to the treatment. Many factors are involved in CPAP adherence: side effects related to the equipment such as nasal discomfort and difficulty adapting to the pressure, disease severity, patient characteristics and motivation, and other surrounding factors, such as family, physician, healthcare professionals, and their interventions.[1–3]

One side effect of CPAP treatment is the difficulty of exhaling against a positive pressure, which is considered as a cause of reduced adherence to CPAP. As a solution, various CPAP delivery modalities have been developed on the basis that a lower expiratory pressure would be better tolerated. Auto-titrating CPAP (APAP) adjusts the pressure and maintains the airway patency in real time during the therapy, and the adherence of APAP has been reported as same as that of conventional CPAP.[4] Bilevel PAP is designed to provide a lower expiratory pressure to reduce the average pressure level, although no improvement in adherence has been reported.[4–7] Pressure-relief CPAP is another modality of pressure delivery, which is proposed as an optional therapy feature for the patient's comfort during the treatment and has been implemented in most fixed CPAP or APAP devices. This CPAP modality is aimed at reducing pressure during expiration to facilitate patient exhalation.

Currently, almost all CPAP manufacturers provide their own proprietary versions of pressure-relief CPAP. However, there is no instruction or caution from the manufacturers regarding the use of these features, which are often added after the initial

BRIEF SUMMARY

Current Knowledge/Study Rationale: Pressure-relief features are aimed at improving the patient's comfort during CPAP treatment for OSA. However, the effect of these therapy features on CPAP treatment efficacy is not well determined.

Study Impact: Pressure-relief features may impair the efficacy of CPAP treatment. The treatment efficacy can be ensured by increasing the therapeutic pressure or by enabling the pressure-relief features prior to initial pressure titration.

Table 1—Pressure evolution of studied pressure-relief features during one breathing cycle (summarized from the provider manuals of the CPAP devices and reference 15).

	Pressure during inspiration	Pressure during the transition to expiration	Pressure during the beginning of expiration	Pressure at the end expiration
Remstar Auto				
C-Flex Level 1, 2 and 3	Set pressure.	Set pressure.	Pressure drops proportional to expiratory flow (3 levels of settings for C-Flex and C-Flex+/A-Flex).	Set pressure.
C-Flex+ (for fixed CPAP) and A-Flex (for APAP) Levels 1, 2, and 3		Pressure drops by 1 (if set pressure = 5) or 2 cmH_2O (if set pressure ≥ 6).		1 (if set pressure = 5) or 2 cmH_2O (if set pressure ≥ 6) below the set pressure.
P-Flex (only for APAP)[a]		Pressure drops by up to 4 cmH_2O depending on the set pressure.[b]		Up to 4 cmH_2O below the set pressure.
AirSense 10 AutoSet				
EPR Level 1, 2 and 3	Set pressure.	Pressure drops by 3 levels: 1, 2, or 3 cmH_2O (3 levels of settings), but remains ≥ 4 cmH_2O.		
Prisma 20A				
SoftPAP Level 1 and 2	Set pressure.	Pressure drops depending on the set pressure (2 levels of settings).[b]		Set pressure.
SoftPAP Level 3	Set pressure with supplementary pressure support.	Pressure drops as the same way as SoftPAP 2 does.		

Set pressure: user-set pressure for fixed continuous positive airway pressure (CPAP); device-ordered autotitration pressure for autotitration continuous positive airway pressure (APAP). [a]P-Flex is exclusive for the French market. [b]Values undisclosed by the manufacturers.

titration when the patient complains of excessive pressure. In addition, most studies on such therapy feature are restricted to C-Flex (Philips Respironics, Murrysville, PA, USA), and the literature does not consistently support its usefulness.[8–16] For other pressure-relief features available on the market, the additional benefits still remain unclear.[3,17]

Bench studies have been proposed to evaluate the responses of APAP devices in different conditions, such as the presence of predefined sleep disordered breathing (SDB) patterns and air leak,[18–25] whereas no such study to date has focused on pressure-relief CPAPs and APAPs. We investigated seven pressure-relief features developed by three CPAP device manufacturers with a previously reported bench model.[25]

METHODS

Bench Model and Simulation of Obstructive Apneas

Evaluations were carried out on a previously described bench model.[25] Consisting of an active lung model and a Starling resistor, the bench model is able to simulate different SDB patterns such as obstructive apneas, hypopneas, and flow limitations. The human upper airway is mimicked by the Starling resistor, and the control of airway patency can be achieved by adjusting the pressure inside the resistor. The CPAP device and the bench are connected by a standard tubing (1.8 m long and 22 mm in diameter), and a calibrated leak port (24 L/min at 10 cmH_2O) is presented in order to mimic the intentional leak in nasal masks. Mask pressure (P_m) and airflow (V') are recorded for further analyses.

During obstructive apnea simulation, the breathing effort is generated by the piston movement. The pressure inside the Starling resistor is set at 9 cmH_2O, and the critical closing and full opening pressures were measured at around 6 and 11 cmH_2O, respectively.

Studied Pressure-Relief Features

Three CPAP devices were included in the current study: Remstar Auto P-Flex (Philips Respironics), AirSense 10 AutoSet (Resmed, Sydney, Australia) and Prisma 20A (Weinmann, Hamburg, Germany). Studied pressure-relief features and their principles are shown in **Table 1**. During the test, each feature was set at the maximum level if adjustable, i.e., achieving the maximally reduced pressure during expiration.

Pressure-Relief CPAP/APAP Efficacy

Protocol

FIXED CPAP: With simulated apneas, a manual titration of pressure was first conducted to obtain the therapeutic pressure for each CPAP device with pressure-relief features disabled (conventional CPAP): the pressure was increased from 4 cmH_2O in a stepwise manner with a minimum increment (0.5 cmH_2O for Remstar Auto and Prisma 20A, 0.2 cmH_2O for AirSense 10 AutoSet) until the breathing flow was fully normalized. Afterward, the devices were set at obtained titration pressure, and subjected to a predefined short obstructive apnea sequence with pressure-relief features enabled. The short breathing sequence lasted 10 min, which was considered

Table 2—Comparison of pressure-relief features in fixed continuous positive airway pressure mode: residual apnea-hypopnea index, apnea index, and measured pressures during a 10-min obstructive apnea sequence (initial apnea index = 60/h).

	Residual AHI (events/h)	Residual AI (events/h)	Measured mean pressure (cmH_2O)
Remstar Auto: Manual titration pressure = 11 cmH_2O			
Conv. CPAP	0	0	10.9
C-Flex 3	0	0	10.7
C-Flex+ 3	60	0	9.1
P-Flex	60	0	8.2
AirSense 10 Autoset: Manual titration pressure = 10.8 cmH_2O			
Conv. CPAP	0	0	10.8
EPR 3	60	0	8.2
Prisma 20A: Manual titration pressure = 10.5 cmH_2O			
Conv. CPAP	0	0	10.7
SoftPAP 2	0	0	9.6
SoftPAP 3	0	0	9.9

All results were identical for two independent repetitions. Titration pressure was noted as the device pressure and the pressure-relief feature was disabled during the continuous positive airway pressure (CPAP) titration. Conventional CPAP: fixed CPAP without pressure-relief feature. P-Flex is only available in autotitrating continuous positive airway pressure (APAP) mode; here the minimum pressure was set identical to the maximum to achieve a constant therapy pressure. AHI, apnea-hypopnea index; AI, apnea index.

sufficient because fixed CPAP efficacy is time-independent. A 30-sec obstructive apnea occurred every minute, i.e., total apnea-hypopnea index (AHI) = 60/h. A similar reference test was carried out without pressure-relief feature (conventional CPAP) for each device. Tests were repeated twice for reproducibility. A third test was executed if the coefficient of variance of the first two tests was higher than 10%.

APAP: The devices were set to APAP mode with open pressure range (4–20 cmH_2O), and subjected to a long obstructive apneas sequence with pressure-relief features enabled. The long breathing sequence lasted 4.2 h, including a 6-min normal breathing session at the beginning, which was considered as a baseline. A 20-sec obstructive apnea occurred every minute and thus the total AHI was 58.6/h. A similar reference test was carried out for each device without pressure-relief feature (conventional APAP). Tests were repeated twice for reproducibility. A third test was executed if the coefficient of variance of the first two tests was higher than 10%.

Data Analysis

For each test, mean or median pressure was calculated from the P_m. Also, residual AHI and apnea index (AI) were derived from the peak-to-peak flow amplitude (ΔV', derived by calculating the upper and lower envelops of the flow curve). Each residual event was scored by considering both the amplitude reduction and the corresponding duration, i.e., $\Delta V' \leq 10\%$ of baseline: apnea; $10\% < \Delta V' \leq 70\%$: hypopnea, with a duration ≥ 10 sec.[25–27] In addition, the AHI, AI, and pressure data on the device report were also noted for comparison. Results were averaged on two tests for fixed CPAP and on three tests for APAP. All the analyses were performed with MATLAB (MathWorks Inc., Natick, MA, USA).

Statistical Analysis

One-way analysis of variance, preceded by Levene's test for equality of variance, was applied to compare the AHI, AI, and pressure with and without pressure-relief feature. Kruskal-Wallis test was applied if Levene's test was positive (Medcalc Software, Mariakerke, Belgium).

Relationship between Conventional and Pressure-Relief CPAP

Different severities of upper airway obstruction were simulated by changing the pressure inside the Starling resistor from 3 to 16 cmH_2O with increment of 1 cmH_2O. At each obstruction level, the effective pressures (device pressure) obtained by the manual CPAP titration were compared between conventional and pressure-relief CPAP.

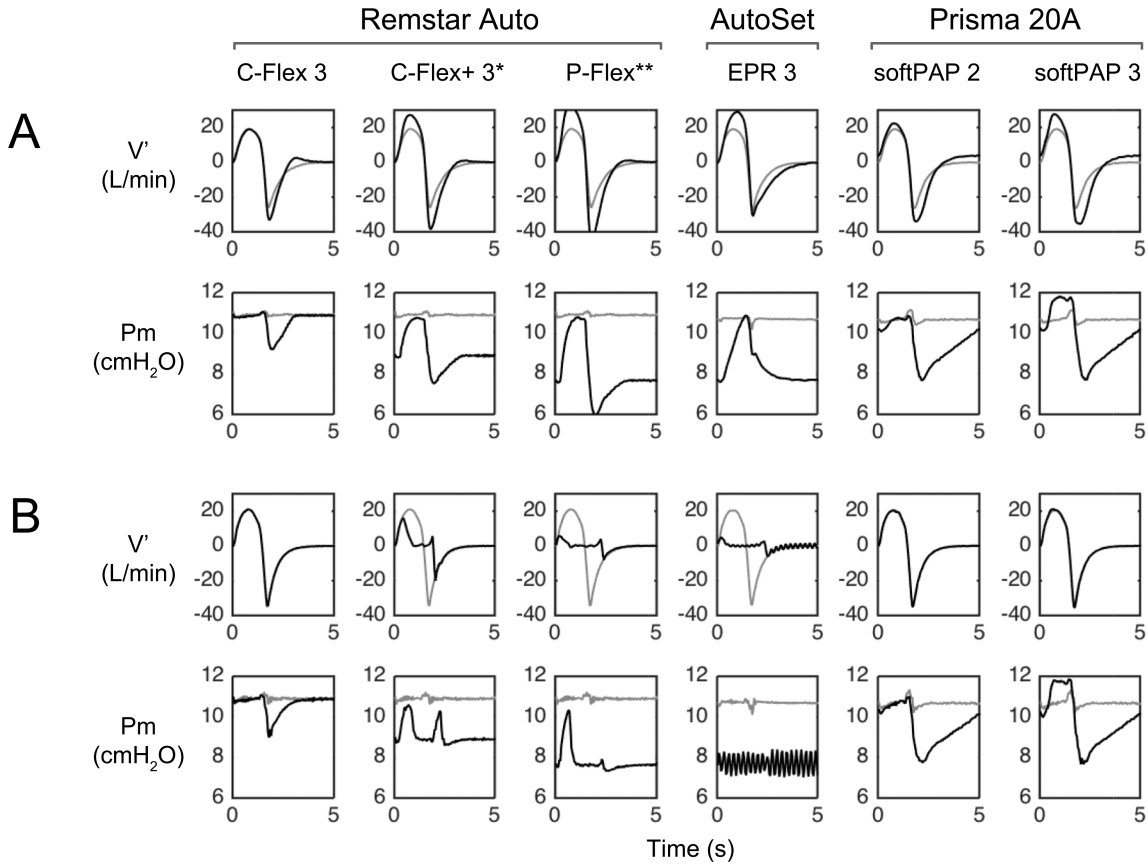
RESULTS

Pressure-Relief CPAP/APAP Efficacy

Fixed CPAP

Measured flow and pressure waveforms of each pressure-relief feature during normal breathing and obstructive apnea are shown in **Figure 1**. The residual AHI and measured pressure are shown in **Table 2**. Compared to conventional CPAP (without pressure relief), the C-Flex+ 3, P-Flex and EPR 3 pressure-relief features were ineffective to normalize the breathing flow and to reduce the AHI. The measured pressures with these features were 1.8, 2.6, and 2.6 cmH_2O respectively lower than that with the conventional CPAP. However, with C-Flex 3 and SoftPAP 2 and 3, the CPAP devices maintained the same treatment efficacy compared to the conventional CPAP and normalized the breathing flow (**Table 2**), despite the fact that their mean pressures

Figure 1—Measured mask airflow and pressure waveforms of fixed CPAP.



Measured mask airflow and pressure waveforms of fixed continuous positive airway pressure (CPAP) with (black curves) and without (gray curves) pressure-relief feature during normal breathing and obstructive apnea. For each device, the pressure was set as the same value as the manual titration pressure of conventional CPAP (without pressure-relief feature). Panel A: recordings during normal breathing. Of note, with C-Flex+ 3, P-Flex and EPR 3, the device-delivered pressure curve was shown as a pressure support accompanied by a positive expiratory pressure that was about 3 cmH_2O lower than the initial CPAP value. Panel B: recordings during obstructive apneas. The black and gray flow curves are superposed in C-Flex, and SoftPAP 2 and 3. With C-Flex+ 3, P-Flex, and EPR 3, the device-delivered pressure was around 3 cmH_2O lower than the initial setting. As a consequence, breathing could not be normalized. The pressure oscillations observed in EPR 3 was due to the upper airway patency detection with forced oscillation technique. *C-Flex+: identical to A-Flex in APAP mode. **P-Flex: only available in APAP mode. Here the minimum pressure was set identical to the maximum in order to make the device work as a fixed CPAP. Pm, mask pressure; V', airflow.

were 0.2, 1.1, and 0.8 cmH_2O lower than the conventional CPAP values.

APAP

The residual AHI, AI, and pressure are shown in **Table 3**. Regarding the bench-assessed residual AHI, no clinically significant increase was found with any pressure-relief features included in this study except P-Flex: the bench-assessed AHI increased from 9.1/h with the conventional APAP (APAP without pressure relief) to 20.6/h with P-Flex ($p < 0.05$) whereas the initial AHI was 58.6/h. Similarly, the bench-assessed AI with A-Flex 3 and P-Flex slightly increased from 0.5/h with the conventional APAP to 1.4 and 1.8/h respectively ($p < 0.05$ for both). The AI with EPR 3 slightly increased from 0.2/h with the conventional APAP to 0.7/h ($p < 0.05$).

In addition, the bench-measured mean pressure of P-Flex was 1.9 cmH_2O lower than the conventional APAP ($p < 0.05$), whereas this pressure drop was only 0.3 cmH_2O for EPR 3 ($p < 0.01$) and 0.4 cmH_2O for SoftPAP 3 ($p < 0.05$). In the device reports of A-Flex 3, P-Flex, EPR 3, and SoftPAP 3, respectively, the mean/median pressures were 1.9 ($p = 0.002$), 2.8 ($p < 0.001$), 2.5 ($p < 0.001$) and 0.9 cmH_2O ($p = 0.04$) higher than the mean/median pressures measured on the bench.

Relationship between Conventional and Pressure-Relief CPAP

Comparisons of effective treatment pressures (device pressure) between conventional and pressure-relief CPAP are shown in **Figure 2**. CPAP with C-Flex 3 (**Figure 2A**), and SoftPAP 2 and 3 (**Figure 2C**) were identical to the conventional CPAP in terms of efficacy. However, CPAP with C-Flex+ 3 (**Figure 2A**), P-Flex (**Figure 2A**), and EPR 3 (**Figure 2B**) should be set higher than conventional CPAP to achieve the same efficacy when CPAP > 4 cmH_2O.

DISCUSSION

This study demonstrates the effect of pressure-relief features on fixed CPAP and APAP treatment efficacy for OSA. Compared

Table 3—Comparison of pressure-relief features in autotitrating continuous positive airway pressure mode: residual apnea-hypopnea index, apnea index, and pressures during a 4.2-h obstructive apnea sequence (initial apnea index = 58.6/h).

	Residual AHI (events/h)		Residual AI (events/h)		Median Pressure (cmH_2O)[a]		
	Bench	Device	Bench	Device	Bench	Device	p[b]
Remstar Auto							
Conv. APAP	9.1 ± 5.7	5.0 ± 3.0	0.5	3.7 ± 2.1	10.4 ± 0.9	10.3 ± 0.8	NS
C-Flex 3	13.4 ± 4.8	5.4 ± 1.7	0.5	5.2 ± 1.7	9.7 ± 0.6	9.7 ± 0.6	NS
A-Flex 3	7.5 ± 3.7	4.6 ± 1.8	1.4*	4.6 ± 1.8	9.3 ± 0.3	11.2 ± 0.4	0.002
P-Flex	20.6 ± 0.3*	13.8 ± 2.6*	1.8 ± 0.1*	13.8 ± 2.6**	8.5*	11.3 ± 0.1*	< 0.001
AirSense 10 AutoSet							
Conv. APAP	1.3 ± 0.5	0.8 ± 0.1	0.2	0.7	10.5 ± 0.1	10.5 ± 0.1	NS
EPR 3	1.4	10.2 ± 0.6**[c]	0.7*	1.4*	10.2 ± 0.1**	12.7 ± 0.1**	< 0.001
Prisma 20A							
Conv. APAP	2.4 ± 1.3	1.0	0.5	1.0	10.0 ± 0.1	10.0	NS
SoftPAP 2	2.1 ± 1.3	2.3 ± 1.2	0.6 ± 0.1	1.0	9.9 ± 0.2	10.5 ± 0.5	NS
SoftPAP 3	4.0 ± 1.2	3.7 ± 0.6*	0.5	1.0	9.6 ± 0.2*	10.5**	0.04

Results are given as mean ± standard deviation (n = 3). [a]For Remstar Auto, mean pressure was noted instead of median pressure. Conventional APAP: APAP without pressure-relief feature. [b]For the comparison of median/mean pressures between bench and device report. Statistical analysis: one-way analysis of variance preceded by Levene's test for equality of variance; Kruskal-Wallis test was applied if Levene's test was positive. [c]Large difference in residual AHI between the bench and the device, such as observed in EPR 3, was due to the difference in the definition of baseline that applied for sleep disordered breathing event scoring: for the bench, the baseline was considered as the 6-min normal breathing session at the beginning during which the pressure-relief feature was not activated; whereas for the device such as AirSense 10 AutoSet, a real-time baseline was utilized. Of note, this baseline could later be increased by "pressure supports" that were generated by the pressure-relief features such as EPR 3. *p < 0.05; **p < 0.01: comparison between pressure-relief and conventional APAP. APAP, autotitrating continuous positive airway pressure; NS, nonsignificant.

to conventional CPAP, the residual AHI significantly increased when the following pressure-relief features were turned on: C-Flex+ 3, P-Flex, and EPR 3. Compared to conventional APAP, the residual AHI only increased with P-Flex by 11.5/h in a 4.2-h breathing sequence with successive obstructive apneas.

Pressure-relief therapy features are developed to overcome patient difficulty of exhaling against a fixed pressure during CPAP treatment and improve the treatment adherence. However, for C-Flex, better adherence has not been proved consistently in clinical studies,[4,8,9,11–14,16,17] and the majority reported similar adherence[4,9,14,17] and treatment efficacy[9] between CPAP with and without C-Flex. Adherence and treatment efficacy are not reported in the literature for the other pressure-relief features.

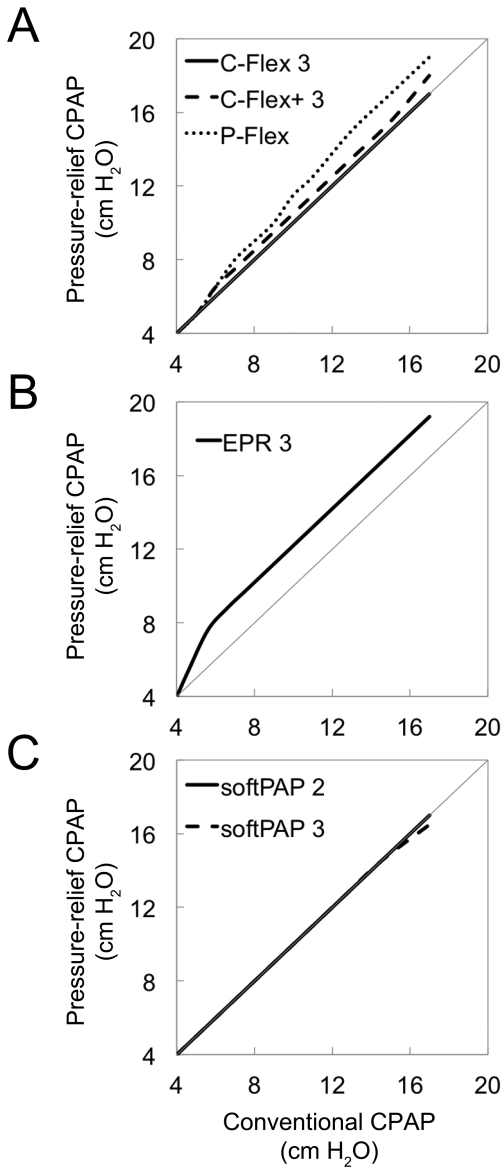
According to our results, we confirm the efficacy of C-Flex in fixed CPAP treatment.[9] However, obstructive SDB events remained untreated with C-Flex+ 3, P-Flex, and EPR 3, as a consequence of actual therapeutic pressure being lower than the titration pressure (**Table 2**). In short, these three modalities converted the pressure profiles into a "bilevel PAP" for the purpose of relieving the patient exhalation. C-Flex+ and P-Flex consist of an inspiratory positive airway pressure (IPAP) identical to the titration pressure of CPAP but an expiratory positive airway pressure (EPAP) at least 2 cmH_2O lower, with a further pressure decrease at the beginning of exhalation (**Figure 1A**). This modality of pressure delivery was not efficient to maintain the airway patency when apnea occurred (**Figure 1B**, column 2 and 3). For EPR 3, the therapeutic pressure decreased by 3 cmH_2O and apneas thus persisted (**Figure 1B**, column 4).

Because it has been demonstrated that apneas begin with upper airway narrowing at end-expiration and followed by collapse during ensuing inspiratory effort,[28] an airway pressure equal or higher than the full opening pressure, i.e., the conventionally titrated CPAP, should be applied to keep the airway patency during the end-expiration and the inspiration, as in the curves of C-Flex 3 and SoftPAP 2 and 3 shown in **Figure 1B** (Columns 1, 5, and 6). Alternatively, the airway patency can be achieved with a "bilevel PAP" pattern, with an EPAP that at least can alleviate the airway obstruction at end-expiration and allow sufficient patient-generated inspiratory airflow to trigger IPAP.[29] In this case, the EPAP must be higher than the critical closing pressure, and most importantly, the IPAP must be able to overcome the negative intraluminal pressure caused by the inspiratory effort and keep the upper airway patency during the remainder of inspiration.

In CPAP mode, C-Flex+ 3 and EPR 3 might lower the treatment efficacy on apneas if the device pressure is kept as same as that just sufficient to abolish flow limitations in conventional CPAP. As shown in **Figures 2A** and **2B**, the device pressure should be set higher to reach the same treatment efficacy as conventional CPAP. Accordingly, in the case of APAP with A-Flex 3 (A-Flex shares the same principle as C-Flex+) and EPR 3, the device autotitration pressure reported as the mean/median value was higher than that of the conventional APAP (**Table 3**) in order to compensate for the pressure reduction caused by the pressure relief. Consequently, similar bench-measured mean/median pressures and residual AHI were obtained between APAPs with and without A-Flex 3 and EPR 3 (**Table 3**). It should be highlighted that the device-reported pressures in conventional and pressure-relief APAPs are not comparable.

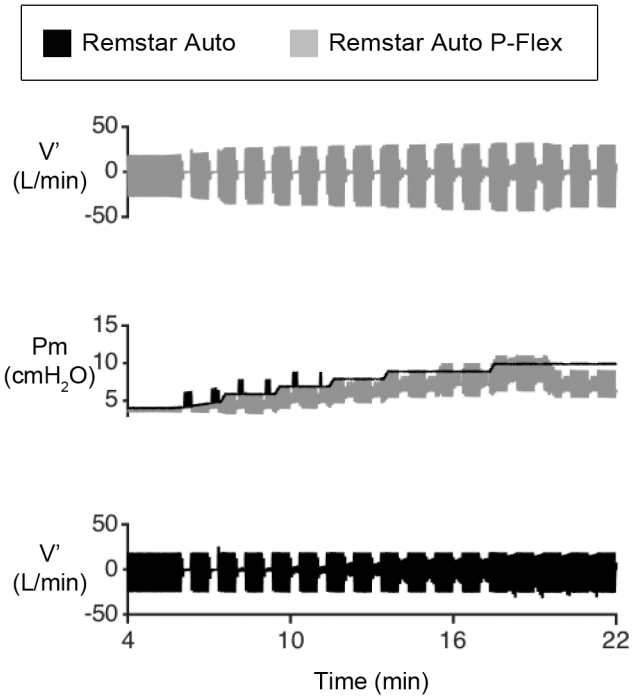
On the contrary, P-Flex APAP appeared to underperform in terms of residual AHI as well as in its response to apneas.

Figure 2—Comparisons between effective treatment pressures of the same efficacy (device set pressure) with and without pressure relief feature.



(A) Remstar Auto. **(B)** AirSense 10 AutoSet. **(C)** Prisma 20A. Conventional CPAP is continuous positive airway pressure without pressure-relief feature.

Figure 3—Mask airflow and pressure profiles of Remstar Auto with and without P-Flex at the beginning of the 4.2-h obstructive apnea sequence.



Pm, mask pressure; V', airflow.

Figure 3 shows that despite the persistent apneas the autotitration pressure of P-Flex decreased around the 19th min after a foregoing pressure increase. This is a specificity of the algorithm of Remstar Auto (P-Flex) that intends to prevent inappropriate pressure increase to central apneas and non-responding events.[30] With this specific algorithm, such improper pressure decrease may also occur during autotitration in the case of successive obstructive apneas with severe upper airway obstruction. Compared to the conventional Remstar Auto APAP, the insufficient treatment pressure with P-Flex worsened such successive apneas and led to further decrease in autotitration pressure (**Figure 3**). Thus, this inappropriate response of P-Flex APAP resulted from both the specific autotitration algorithm and the reduced CPAP efficacy with pressure-relief feature.

Regarding APAP treatment with pressure-relief features, Mulgrew et al.[10] found a nonsignificant trend of greater subjective comfort with C-Flex. Kushida et al.[31] reported an equivalency in treatment adherence and efficacy between A-Flex and conventional CPAP after either 3 or 6 mo, but a higher AHI at the initiation phase. In a recent study, Chihara et al.[15] compared the adherence between conventional APAP, APAP with C-Flex and APAP with A-Flex, and found greater adherence in APAP with C-Flex. Of note, at the initiation of the studies of Kushida et al.[31] and Chihara et al.,[15] the APAP autotitration was carried out with the allocated pressure-relief feature.

Our results have an important clinical consequence for sleep apnea treatment. In clinical practice, the problem may arise when a pressure relief feature is later added to a conventionally titrated patient without increasing the titration pressure of the device. However, the negative effects that we document in the current study may be mitigated in the case of fixed CPAP initially titrated to a pressure level that is high enough to cope with sleep in unfavorable circumstances such as supine postures and rapid eye movement sleep stage because most SDB events will be abolished; or during "CPAP exploration", when the pressure can be up to 5 cmH_2O higher than that is just sufficient to abolish SDB events.[32] Similarly, in the case of APAP our findings could be relevant if the pressure range over which autotitration was allowed to occur had an upper limit that was set close to the effective (95th or 90th centile) pressure prior to

activation of pressure relief. Thus, the treatment efficacy can be ensured by increasing the device pressure in fixed CPAP or by enhancing the full range of pressure in APAP. In the latter case, a well-functioning autotitration algorithm is indispensable. In addition, the pressure-relief features allocated for therapy should be enabled prior to the titration process. It should also be noted that the device-reported pressure in pressure-relief APAP is not comparable to that without pressure relief.

CONCLUSIONS

Pressure-relief features may lead to attenuated CPAP treatment efficacy depending on the applied settings and the device. In clinical practice, the therapy efficacy can be ensured by increasing the therapeutic pressure or by enabling the pressure-relief features prior to the manual or auto titration process. The pressures in the pressure-relief APAP device reports are not comparable to that of conventional APAPs.

ABBREVIATIONS

AHI, apnea-hypopnea index
AI, apnea index
ANOVA, analysis of variance
APAP, autotitrating continuous positive airway pressure
CPAP, continuous positive airway pressure
EPAP, expiratory positive airway pressure
IPAP, inspiratory positive airway pressure
OSA, obstructive sleep apnea
Pm , mask pressure
SDB, sleep disordered breathing
V', mask airflow
ΔV', peak-to-peak flow amplitude

REFERENCE

1. Shapiro GK, Shapiro CM. Factors that influence CPAP adherence: an overview. Sleep Breath 2010;14:323–35.
2. Weaver TE, Grunstein RR. Adherence to Continuous Positive Airway Pressure Therapy. Proc Am Thorac Soc 2008;5:173–8.
3. Wickwire EM, Lettieri CJ, Cairns AA, Collop NA. Maximizing positive airway pressure adherence in adults: a common-sense approach. Chest 2013;144:680–93.
4. Smith I, Lasserson TJ. Pressure modification for improving usage of continuous positive airway pressure machines in adults with obstructive sleep apnoea. Cochrane Database Syst Rev 2009:CD003531.
5. Marcus CL, Beck SE, Traylor J, et al. Randomized, double-blind clinical trial of two different modes of positive airway pressure therapy on adherence and efficacy in children. J Clin Sleep Med 2012;8:37–42.
6. Blau A, Minx M, Peter JG, et al. Auto bi-level pressure relief-PAP is as effective as CPAP in OSA patients–a pilot study. Sleep Breath 2011;16:773–9.
7. Powell ED, Gay PC, Ojile JM, Litinski M, Malhotra A. A pilot study assessing adherence to auto-bilevel following a poor initial encounter with CPAP. J Clin Sleep Med 2012;8:43–7.
8. Aloia MS, Stanchina M, Arnedt JT, Malhotra A, Millman RP. Treatment adherence and outcomes in flexible vs standard continuous positive airway pressure therapy. Chest 2005;127:2085–93.
9. Nilius G, Happel A, Domanski U, Ruhle K-H. Pressure-relief continuous positive airway pressure vs constant continuous positive airway pressure: a comparison of efficacy and compliance. Chest 2006;130:1018–24.
10. Mulgrew AT, Cheema R, Fleetham J, Ryan CF, Ayas NT. Efficacy and patient satisfaction with autoadjusting CPAP with variable expiratory pressure vs standard CPAP: a two-night randomized crossover trial. Sleep Breath 2006;11:31–7.
11. Kakkar RK, Berry RB. Positive airway pressure treatment for obstructive sleep apnea. Chest 2007;132:1057–72.
12. Marshall NS, Neill AM, Campbell AJ. Randomised trial of compliance with flexible (C-Flex) and standard continuous positive airway pressure for severe obstructive sleep apnea. Sleep Breath 2008;12:393–6.
13. Pépin J-L, Muir J-F, Gentina T, et al. Pressure reduction during exhalation in sleep apnea patients treated by continuous positive airway pressure. Chest 2009;136:490–7.
14. Bakker J, Campbell A, Neill A. Randomized controlled trial comparing flexible and continuous positive airway pressure delivery: effects on compliance, objective and subjective sleepiness and vigilance. Sleep 2010;33:523–9.
15. Chihara Y, Tsuboi T, Hitomi T, et al. Flexible positive airway pressure improves treatment adherence compared with auto-adjusting PAP. Sleep 2013;36:229–36.
16. Brown LK. Achieving adherence to positive airway pressure therapy: modifying pressure and the holy grail. Chest 2011;139:1266–8.
17. Bakker JP, Marshall NS. Flexible pressure delivery modification of continuous positive airway pressure for obstructive sleep apnea does not improve compliance with therapy: systematic review and meta-analysis. Chest 2011;139:1322–30.
18. Farré R, Montserrat JM, Rigau J, Trepat X, Pinto P, Navajas D. Response of automatic continuous positive airway pressure devices to different sleep breathing patterns: a bench study. Am J Respir Crit Care Med 2002;166:469–73.
19. Abdenbi F, Chambille B, Escourrou P. Bench testing of auto-adjusting positive airway pressure devices. Eur Respir J 2004;24:649–58.
20. Coller D, Stanley D, Parthasarathy S. Effect of air leak on the performance of auto-PAP devices: a bench study. Sleep Breath 2005;9:167–75.
21. Lofaso F, Desmarais G, Leroux K, et al. Bench evaluation of flow limitation detection by automated continuous positive airway pressure devices. Chest 2006;130:343–9.
22. Rigau J, Montserrat JM, Wöhrle H, et al. Bench model to simulate upper airway obstruction for analyzing automatic continuous positive airway pressure devices. Chest 2006;130:350–61.
23. Hirose M, Honda J, Sato E, et al. Bench study of auto-CPAP devices using a collapsible upper airway model with upstream resistance. Respir Physiol Neurobiol 2008;162:48–54.
24. Netzel T, Hein H, Hein Y. APAP device technology and correlation with patient compliance. Somnologie 2014;18:113–20.
25. Zhu K, Roisman G, Aouf S, Escourrou P. All APAPs are not equivalent for the treatment of sleep-disordered breathing: a bench evaluation of eleven commercially available devices. J Clin Sleep Med 2015;11:725–34.
26. Iber C, Ancoli-Israel S, Chesson A, Quan S, for the American Academy of Sleep Medicine. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications, 1st ed. Westchester, IL: American Academy of Sleep Medicine, 2007.
27. Zhu K, Kharboutly H, Ma J, Bouzit M, Escourrou P. Bench test evaluation of adaptive servoventilation devices for sleep apnea treatment. J Clin Sleep Med 2013;9:861–71.
28. Morrell MJ, Arabi Y, Zahn B, Badr MS. Progressive retropalatal narrowing preceding obstructive apnea. Am J Respir Crit Care Med 1998;158:1974–81.
29. Sanders MH, Kern N. Obstructive sleep apnea treated by independently adjusted inspiratory and expiratory positive airway pressures via nasal mask. physiologic and clinical implications. Chest 1990;98:317–24.
30. Hertegonne KB, Rombaut B, Houtmeyers P, Van Maele G, Pevernagie DA. Titration efficacy of two auto-adjustable continuous positive airway pressure devices using different flow limitation-based algorithms. Respir Int Rev Thorac Dis 2008;75:48–54.

31. Kushida CA, Berry RB, Blau A, et al. Positive airway pressure initiation: a randomized controlled trial to assess the impact of therapy mode and titration process on efficacy, adherence, and outcomes. Sleep 2011;34:1083–92.
32. Positive Airway Pressure Titration Task Force of the American Academy of Sleep Medicine. Clinical guidelines for the manual titration of positive airway pressure in patients with obstructive sleep apnea. J Clin Sleep Med 2008;4:157–71.

SUBMISSION & CORRESPONDENCE INFORMATION

Submitted for publication June, 2015
Submitted in final revised form September, 2015
Accepted for publication October, 2015
Address correspondence to: Kaixian Zhu, MS, Air Liquide Healthcare, 28 Rue d'Arcueil, 94250 Gentilly, France; Tel : +33 1 49 69 45 67; Email: kaixian.zhu@airliquide.com

DISCLOSURE STATEMENT

This was not an industry-supported study. This research was supported by a CIFRE grant to K. Zhu, from the French Ministry of Higher Education and Research. The authors have indicated no financial conflicts of interest.