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Automatic adjustment of noninvasive pressure support with a bilevel home ventilator in patients with acute respiratory failure: a feasibility study

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Abstract *Objective:* To test the feasibility of applying noninvasive ventilation (NIV) using a prototype algorithm implemented in a bilevel ventilation device designed to adjust pressure support (PS) to maintain a clinician-set alveolar ventilation in patients with acute respiratory failure after initial stabilization. *Design and setting:* Prospective crossover interventional study in an intensive care unit, university hospital. *Patients:* 19 patients receiving NIV for acute hypercapnic respiratory failure (13 men, 6 women; mean age 70 ± 11 years). *Methods:* The same bilevel ventilator was used with manually adjusted PS and with the automated algorithm (autoPS), set to maintain the same alveolar ventilation as in PS. Sequence (measurements at end of each period): (a) prior to initiating NIV (baseline 1); (b) 45 min with manually set PS; (c) 60 min without NIV; (d) 45 min with autoPS; (e) 60 min without NIV; (f) 45 min with manually set PS. *Results:* The magnitude of decrease in $PaCO_2$ and increase in pH with autoPS was comparable to that of conventional PS, with the same alveolar ventilation and level of PS. No technical problem occurred in autoPS mode, and no NIV trial had to be discontinued because of patient discomfort. *Conclusions:* These results suggest that the alveolar ventilation based automatic control of PS during NIV with a bilevel device is feasible and leads to beneficial effects in patients with acute respiratory failure comparable to those of manually set PS. Further studies should now explore the potential of this system over longer periods in patients with acute and chronic respiratory failure.

Keywords Noninvasive ventilation · Pressure support · Bilevel · Automated modes

Introduction

Patient tolerance to noninvasive ventilation (NIV) is a key element to its success in avoiding intubations in acute respiratory failure (ARF) [1, 2]. Tolerance is highly dependent on the combination of the patient's spontaneous breathing activity and the ventilator's action, known as patient-ventilator interaction [3]. The latter in turn depends both on the avoidance of leaks at the mask [4, 5] and on the optimal setting of the ventilator [3, 6]. Titrating the level of pressure support (PS) is one such challenge. Unfortunately, the large number of tasks to be performed by the clinician in the setting of ARF carries the risk of insufficient attention being given to adjusting the ventilator [7].

Automation of certain ventilator settings can prove helpful in this respect. In intubated patients the automatic titration of PS by an expert-based knowledge system has been shown to improve patient-ventilator interaction [8]. Whether the automatic setting of PS during NIV is feasible remains to be seen, but it might be an attractive option. The purpose of the present study was to test the feasibility of relying on an automated algorithm based on a closed-loop control of PS designed to guarantee a user-

set minimum minute volume on a bilevel ventilator, a type of device which, although originally designed for home ventilation, has also been shown effective in performing NIV in patients with ARF [9, 10]. Findings of this study were presented in abstract form at the 2005 European Respiratory Society annual congress (Eur Respir J 2005 26:444s).

Methods

Patients

The study included 19 patients consecutively admitted to the ICU for acute respiratory failure and in whom NIV was prescribed (13 men, 6 women; mean age 70 ± 11 years); all patients were hypercapnic upon inclusion (Table 1). Patients were included if they had been stabilized with NIV after admission but had been treated in the ICU for 36 h or longer (mean 29 ± 6 h) and had received maximally four 4 NIV applications. Exclusion criteria were a very low probability of short-term survival, a do not resuscitate order, the presence of pneumothorax, severe respiratory failure or hemodynamic instability with a high likelihood of imminent intubation, impaired consciousness or absence of patient cooperation, and the presence of facial lesions precluding the use of NIV. Due to the technical limitations of the bilevel device used patients requiring an FIO_2 higher than 0.6 during NIV were also excluded. The protocol was accepted by the ethics committee of our institution. Informed consent was obtained from all patients.

Methods

All patients were ventilated with a new bilevel type device (AutoVPAP, ResMed, North Ryde, Australia) allowing two modes of bilevel PS, i.e., manually set and automatic (autoPS). A detailed description of the rules on which autoPS is based is beyond the scope of this contribution, but its basic principle can be summarized as follows. AutoPS aims to guarantee a minimum clinician-set "gross alveolar ventilation" by adjusting the level of PS within manually set boundaries (minimum and maximum inspiratory pressures). "Gross alveolar ventilation" (termed "alveolar ventilation" below for the sake of simplicity) is defined to be the portion of minute volume minus anatomical deadspace ventilation. An estimate of the anatomical deadspace is entered by the clinician. For the purpose of this study we used the accepted approximation of 2.2 ml/kg body weight for deadspace [11]. The level of PS is continuously adjusted by comparing the recent alveolar ventilation (a continuously updated estimate obtained by low-pass filtering, related mainly to the ventilation during the two preceding respiratory cycles), with the target alveolar ventilation. This means that PS responds significantly to a change in ventilation within about three breaths. Furthermore, a variable backup rate is provided in the case of apnea. However, as this function is mainly directed at patients on long-term home NIV to deal with central apnea or an inspiratory effort too weak to trigger the ventilator occurring during sleep, this function was disabled in the present study, only the automatic titration of PS being explored. Triggering is conventional,

Table 1 Patients' clinical characteristics (*BMI* body mass index, *PaCO2* arterial partial CO_2 pressure at study inclusion, *Diagnosis* main cause of acute respiratory failure, *COPD* chronic obstructive pulmonary disease)

Patient no.	Age (years)	Sex	BMI	PaCO$_2$ (mmHg)	Diagnosis
1	58	M	20	63	Empyema
2	76	F	23	65	Kyphoscoliosis
3	82	F	24	48	Pneumonia
4	85	M	28	66	Cardiogenic pulmonary edema
5	79	F	29	55	COPD
6	59	M	38	52	Pneumonia
7	78	M	22	47	Pneumonia
8	83	F	26	57	Cardiogenic pulmonary edema
9	72	M	24	45	Pneumonia
10	56	M	20	69	Pneumonia
11	64	M	26	74	Pneumonia
12	74	M	33	52	COPD
13	73	F	25	72	COPD
14	61	M	28	66	COPD
15	86	F	21	57	Restrictive disease
16	63	M	25	48	COPD
17	78	M	22	51	COPD
18	53	M	34	47	COPD
19	57	M	18	58	COPD
Mean $\pm$ SD	70.3 ± 10.9	–	25.4 ± 5.1	57 ± 9	–

based on a clinician-set flow threshold. Cycling is largely conventional, with an initial absolute refractory period followed by a threshold based on a clinician-set proportion of peak inspiratory flow, the default setting being 25%.

The difference between manual PS and autoPS on the machine therefore lies in the setting of PS and determination of target alveolar ventilation as defined above, plus the presence of a variable backup rate (which was not tested in this study). FIO_2, pressurization slope, and positive end-expiratory pressure (PEEP) are similarly set by the clinician in both modes. In both modes the maximum level of inspiratory pressure (i.e., PS + PEEP) in this prototype ventilator is 25 cmH_2O.

Design of the study

Prior to the trial, all patients had been initially stabilized with up to four runs of NIV applied by an oronasal mask (adult face mask, Vygon Schweiz, Liebefeld-Bern, Switzerland) with an ICU ventilator (Evita 4 or XL, Drägerwerk, Lübeck, Germany). The indication for NIV was as in our usual practice guidelines, based on published studies [9, 12] requiring that at least two of the following be present: worsening dyspnea over the last 10 days in cases of chronic respiratory failure; respiratory rate greater than 25/min; arterial pH less than 7.35; $PaCO_2$ higher than 50 mmHg (6.6 kPa); PaO_2 below 50 mmHg (6.6 kPa), determined from arterial blood gas measurements.

All trials with the autoVPAP device were performed by the investigating chest physiotherapist (A. B.). NIV was applied with an oronasal mask (UltraMirage Full Face Mask, ResMed). For the sake of simplicity, given that only the automatic titration of PS was tested in this study, the term "autoPS" is used below for the phase of the trial during which PS was titrated automatically, as opposed to the conventional manually set mode (PS). All trials were sequentially performed in the following order: 45 min manually set PS (PS 1), 45 min autoPS mode (autoPS), and 45 min manual mode (PS 2). To avoid a carry-over effect a 60-min period without NIV was provided between each NIV period and before PS 1. Furthermore, to avoid any interference from the automatic backup rate function in autoPS mode due to apnea, the patients' level of consciousness was continuously monitored during all three NIV phases. If any signs of sleepiness or apnea appeared, the patients were awakened and stimulated. The initial manual settings for PS 1 and PS 2 followed our usual practice guidelines for bilevel NIV: 15 cmH_2O PS, 4 cmH_2O PEEP, resulting in a PS of 11 cmH_2O. Thereafter PS was adjusted to obtain an expired tidal volume of 6–8 ml/kg and a respiratory rate below 30/min, with a minimal leak at the mask. In obstructive patients PEEP was titrated upwards until the number of ineffective inspiratory attempts either disappeared or decreased to less than 5/min. Ineffective inspiratory efforts, defined as the presence of

an inspiration initiated by the patient without any response by the ventilator, were detected by careful clinical observation. In nonobstructive patients PEEP was titrated up to 6 cmH_2O to maintain pulse-oximetry determined arterial O_2 saturation (SpO_2) at 90% or higher. Cycling was set at 25% and 40% of peak inspiratory flow in nonobstructive and obstructive patients, respectively. Once the initial settings were made, no further modification was performed. The initial autoPS settings were made as follows: the target alveolar ventilation period was set as mean minute volume during the PS 1 period minus mean deadspace ventilation, the latter defined as estimated anatomical deadspace × mean respiratory rate during the PS 1 period. The initial PS setting was identical to that set during the PS 1, the upper and lower boundaries being 25 cmH_2O (the maximum allowed by the machine) and the level of PEEP, respectively. Thereafter, PS was adjusted automatically to obtain the target alveolar ventilation. Cycling, PEEP, and pressurization slope were the same as those of PS 1.

The following measurements were taken before the start of and at the end of each NIV period (with patients still on NIV): arterial blood gases through an indwelling radial artery catheter, respiratory rate, dyspnea score (Borg visual analog scale; 0 = no dyspnea, 10 = worst possible dyspnea), expired tidal volume and minute-volume (Fleisch no. 2 pneumotachograph, Fleisch, Lausanne, Switzerland; between the Y-piece and the mask), heart rate and arterial blood pressure. During NIV all ventilatory parameters (volume, pressure, flow), leaks at the mask (computed by the device using a mathematical model based on the known characteristics of the mask and the pressure and flow signals measured at the ventilator), pulse oximetry, respiratory and heart rates, and arterial blood pressure were continuously monitored. The reported level of PS for periods PS 1 and PS 2 is that set once the patient was stabilized on the machine, and for the autoPS period it is the mean of all values automatically set by the device during the 45 min trial. Of note, although the autoPS algorithm targets alveolar ventilation, the parameter that we recorded was expired minute-volume, which is reported in the results.

Statistics

Comparisons (SigmaStat 2.0–SPSS Science) between the six time-points were made by analysis of variance, with statistical significance being determined by Fisher's protected least significance test. Differences with a p-value less than 0.05 were considered statistically significant. All results are expressed as mean ± SD.

Results

The initial ventilator settings by the physiotherapist led to mean PS and PEEP levels of 15.2 ± 3.5 and

Table 2 Respiratory and hemodynamic parameters [*HR* heart rate, *PS* level of pressure support (inspiratory pressure minus PEEP), *MAP* mean systemic arterial pressure, *RR* respiratory rate, *VE* expiratory minute-volume, *VTe* expired tidal volume, *PaCO₂* arterial partial pressure of CO_2, *PaO₂* arterial partial pressure of O_2; *baseline* values measured immediately prior to initiating NIV, *PEEP* positive end-expiratory pressure, *PS 1* and *PS 2*: NIV with manually set PS; *autoPS* NIV with automatic titration of PS]

	Baseline 1	PS 1	Baseline 2	autoPS	Baseline 3	PS 2
RR (b/min)	19.2 ± 3	16.2 ± 5	18.8 ± 5	16.5 ± 4	18.8 ± 5	16 ± 5
HR (b/min)	89 ± 19	88 ± 19	92 ± 18	85 ± 16	90 ± 16	87 ± 15
MAP (mmHg)	75 ± 16	75 ± 14	80 ± 15	77 ± 13	77 ± 14	77 ± 14
Borg scale (points)	2.3 ± 1.9	1.6 ± 0.9	1.9 ± 1.6	1.7 ± 0.9	1.8 ± 1.4	1.5 ± 0.8
VE (l/min)	n.a.	12.2 ± 3.1	n.a.	12.3 ± 2.8	n.a.	11.2 ± 3.3
VTe (ml)	n.a.	772 ± 222	n.a.	773 ± 206	n.a.	704 ± 197
PS (cmH₂O)	n.a.	15.2 ± 3.4	n.a.	15.3 ± 3.1	n.a.	15.2 ± 3.4
PEEP (cmH₂O)	n.a.	4.9 ± 0.2	n.a.	4.8 ± 0.3	n.a.	4.8 ± 0.3
Leaks (l/min)	n.a.	1.8 ± 3.5	n.a.	2.2 ± 2.8	n.a.	2.1 ± 4.4
pH	7.37 ± 0.04	$7.39 \pm 0.04^*$	7.37 ± 0.04	$7.42 \pm 0.04^*$	7.38 ± 0.04	7.43 ± 0.08
PaO₂ (mmHg)	77 ± 14	75 ± 14	73 ± 14	73 ± 9	71 ± 15	72 ± 8
PaCO₂ (mmHg)	57 ± 9	$51 \pm 10^*$	55 ± 9	$49 \pm 7^*$	56 ± 8	$49 \pm 8^*$

$^*p < 0.05$ vs. corresponding base line (analysis of variance)

5 ± 0.5 cmH₂O, respectively. The effects of NIV are outlined in Table 2. As shown, $PaCO_2$ and pH were comparably improved by both manual PS and autoPS. Individual changes in $PaCO_2$ are shown in Fig. 1. PaO_2 was unchanged by either mode. Respiratory rate decreased from its baseline values with both NIV modes, but the decrease did not reach statistical significance. Dyspnea was unchanged by either NIV mode. Expiratory minute-volume did not differ significantly between the two NIV modes. Overall the mean level of PS set either manually or by autoPS were comparable, although there were differences in some patients (Fig. 2). As seen in Fig. 3, the algorithm performed little or no change in PS in some patients (e.g., nos. 2, 7, 17, 19), whereas more frequent and/or more marked modifications were made in others (e.g., nos. 12, 14, 15), during the first 10 min of the autoPS trial. Leaks at the mask were kept at a low level, and their magnitude was comparable between manual NIV and autoPS. No apneas or ineffective inspiratory efforts were documented during any of the NIV trials, with either manually set ventilation or autoPS. No change in hemodynamics occurred during NIV (Table 2). No NIV application had to be discontinued because of patient intolerance or technical problems. No patient required tracheal intubation during the study.

Fig. 1 Individual and mean variations in *PaCO₂*. *PS 1* and *PS 2*: manually set PS; *autoPS*: automatic titration of PS. $^*p < 0.05$ vs. corresponding baseline (analysis of variance)
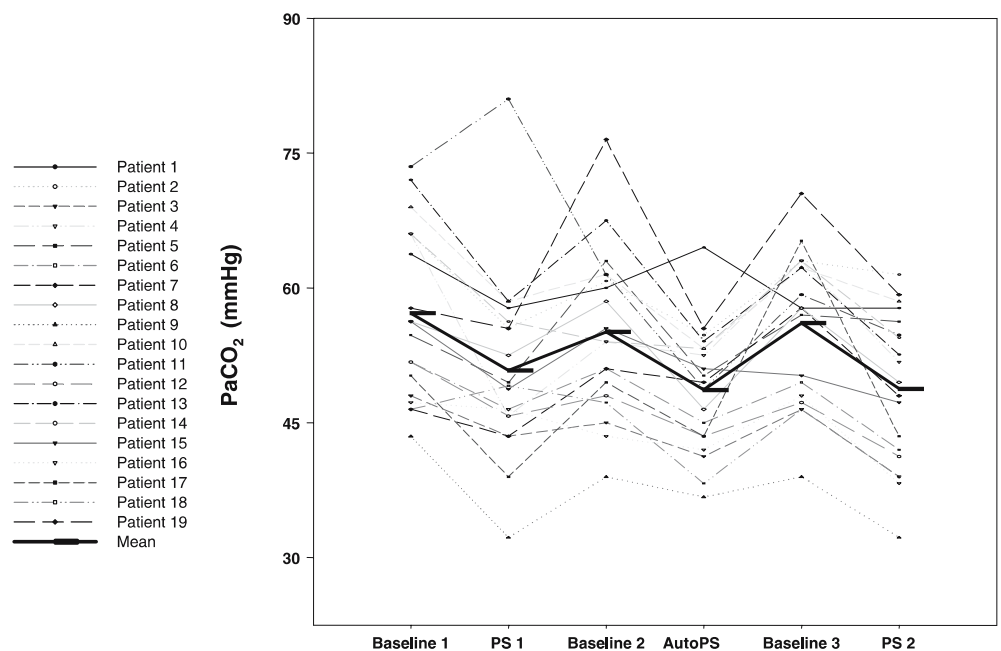
Fig. 2 Individual mean and group mean values of pressure support (*PS*, inspiratory pressure minus PEEP) during each of the three NIV periods. Values are the mean for each 45-min trial for each patient. *PS 1* and *PS 2*: manually set PS; *autoPS*: automatic titration of PS
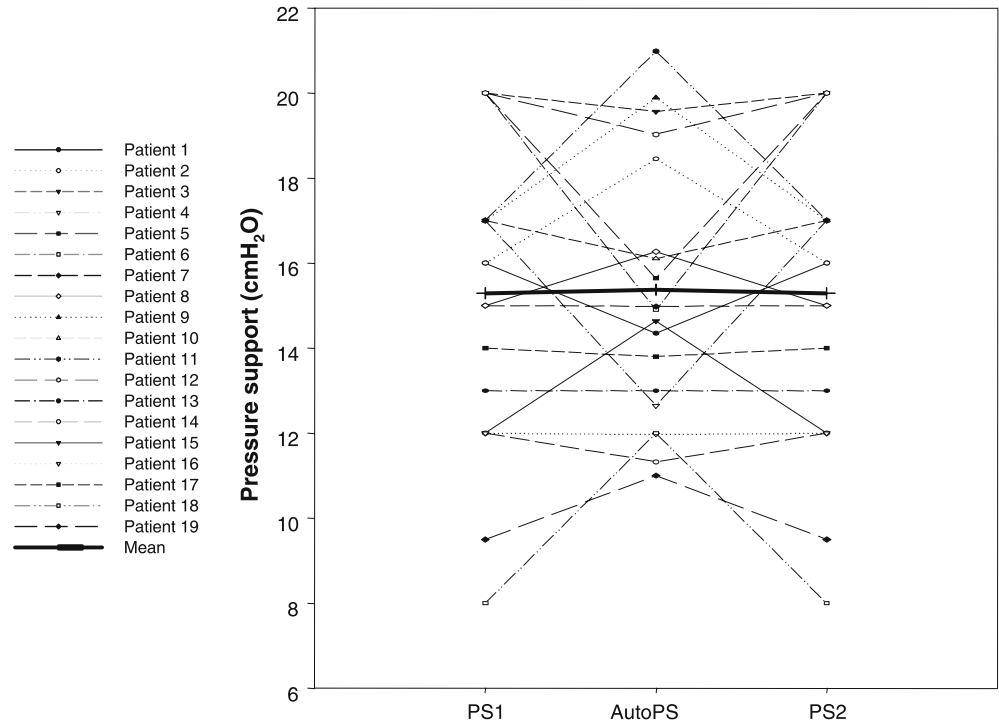

Fig. 3 Individual variation of the level of pressure support (*PS*, inspiratory pressure minus PEEP) set by the autoPS algorithm during the first 10 min of NIV, as recorded by the device; *x-axis* time in minutes; *y-axis* level of inspiratory pressure. In all patients the upper limit of inspiratory pressure (pressure support + PEEP) was 25 cmH$_2$O. The lower limit, which was equal to the PEEP level, is indicated in each patient's tracing (values in cmH$_2$O)
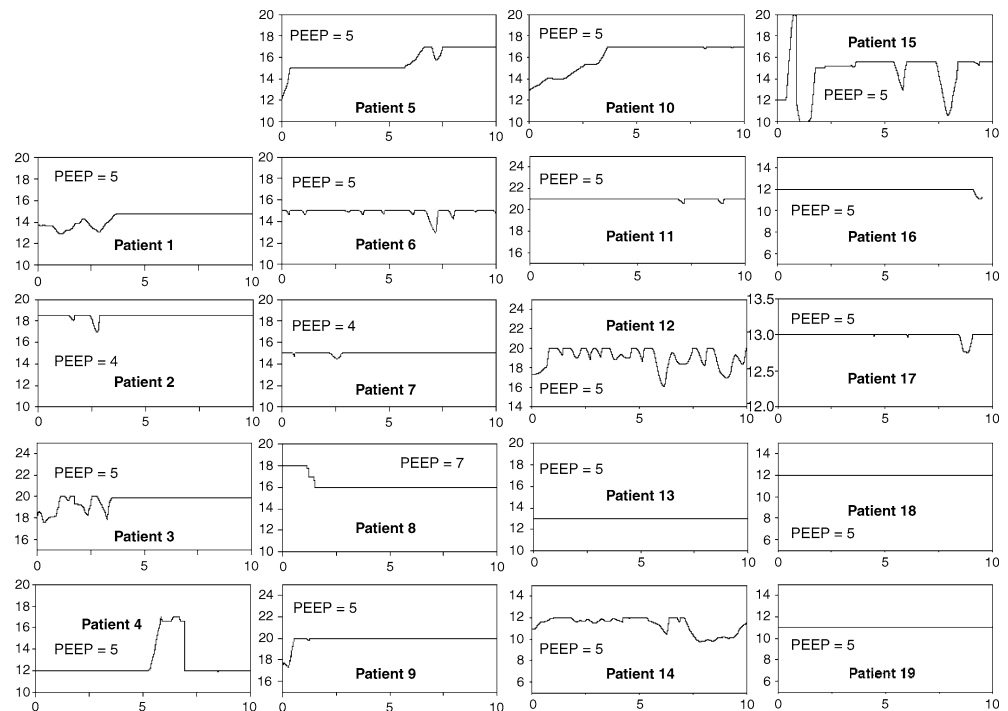
Discussion

The results of the present pilot study demonstrate the feasibility of relying on an algorithm based on volumetric closed-loop control to automatically adjust PS on a bilevel device to perform NIV in patients with acute respiratory failure, with effects comparable to those obtained by the manual setting of PS. Before discussing the implications of our results, several limitations should be outlined. First, this was a feasibility study, aimed at examining whether the concept of automatically titrating PS during NIV was possible in patients with ARF during a 45-min period and

how this compares to a manual setting approach. The duration of NIV application was in accord with that of other published trials [13, 14, 15]. However, any extrapolation as to how the system would perform over longer periods remains speculative at this time. Second, our ARF patients had been stabilized on NIV, as reflected by low respiratory rate and dyspnea score. Therefore whether the same results would have been documented in more acutely decompensated patients is unknown. Third, the settings in all three NIV applications were performed by one of the investigators (A. B.), which may have biased the results. However, safety issues mandated that an experienced therapist with in-depth knowledge of the autoPS system supervise each NIV application.

Fourth, as stated in the Methods section, the autoPS algorithm is designed not only to titrate PS but also to provide a backup rate in case of apnea. However, only PS setting was tested in the present study, given that no apnea occurred in our patients, as per our intention. Nonetheless apnea can occur both in acute NIV and chronic nocturnal home ventilation, the primary intended area of use for the device, and the performance of the algorithm in this respect remains to be evaluated, a path that we are currently exploring. Fifth, bilevel devices have been tailored mostly to the context of chronic long-term ventilation, and the relevance of using such a device in the acute ICU setting may seem questionable. However, the performance of bilevel machines has steadily increased over the years [16, 17, 18], and these devices have been used successfully in ARF [9, 10, 19]. Their much lower cost, relative ease of use, and ability to function without mural medical gas outlets makes them an attractive alternative to ICU ventilators, especially for NIV performed outside of that setting [20]. Finally, the number of patients was small and consisted of a heterogeneous group. However, the case-mix can be deemed representative of that usually found in studies on ARF requiring NIV [21].

At this stage the results of this pilot study show that the concept of automatically titrating PS support during NIV with a bilevel device is feasible, a finding which opens up possibilities in improving patient-ventilator interaction. Indeed, caring for an ICU patient involves considerable multitasking which can be a source of poor performance [22, 23]. The latter is all the more unfortunate when applying NIV since good patient ventilator synchrony, patient comfort, and minimal mask leaks are crucial in ensuring the success of the technique [1, 2]. In particular, excessive levels of PS can worsen dynamic hyperinflation in obstructive patients [24], in turn leading to an increase in the number of ineffective inspiratory efforts, heighten the incidence of gastric air intake leading to discomfort, vomiting and aspiration, and increase the magnitude of leaks at the mask [25]. This being said, there is a theoretical risk that the same excessive levels of PS could be generated by the autoPS. Therefore one must ensure that the expired tidal volume does not exceed 8–9 ml/kg, and also that the inspiratory:expiratory cycling cutoff is set at a higher level (approx. 40–50% of peak inspiratory flow) than the usual 25% default value. This last point aims to minimize delayed cycling, a common occurrence in patients with chronic obstructive pulmonary disease, and one which results in incomplete lung amptying and worsening of dynamic hyperinflation [26]. At the other end of this spectrum very low levels of PS can provide insufficient respiratory muscle assistance [27]. Of note, given that the patients had acute respiratory failure, we chose to set the upper limit at the maximum inspiratory pressure that the device can generate, to avoid insufficient PS. With these settings mean expiratory minute volume was not different during the autoPS period than in either manually set periods.

The proof of concept that automation of PS can improve patient-ventilator synchrony and comfort has been illustrated by a study in intubated patients using an expert-based knowledge system [8]. Extending these benefits to NIV is in our view an attractive prospect, although perhaps more challenging due to the presence of mask leaks and the more unstable respiratory conditions of ARF. Nonetheless, the results of this study, using a different ventilator and algorithm, suggest that such an approach is possible, bearing in mind that it is a pilot study.

In conclusion, these results demonstrate the feasibility of using an algorithm to automatically adjust PS during NIV with a bilevel device (AutoVPAP) in patients with acute respiratory failure with beneficial effects comparable to those of manually set PS. Further studies should now explore the potential of this approach over longer periods in patients with acute and chronic respiratory failure.

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