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BRIEF REPORT

Nectaria Xirouchaki
Eumorfia Kondili
Maria Klimathianaki
Dimitris Georgopoulos

Is proportional-assist ventilation with load-adjustable gain factors a user-friendly mode?

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N. Xirouchaki · E. Kondili · M. Klimathianaki · D. Georgopoulos (✉)
Department of Intensive Care Medicine, University Hospital of Heraklion, Medical School, University of Crete, Heraklion, Crete, Greece
e-mail: georgop@med.uoc.gr

Abstract *Objectives:* The aim of this study was to compare the number of interventions (ventilator settings and sedatives, analgesics and vasoactive medication dose manipulations) between critically ill patients on proportional-assist ventilation with load-adjustable gain factors (PAV+) and those on pressure support (PS). *Design:* Retrospective analysis of data from a previous randomized clinical trial. *Methods:* A total of 208 patients who were mechanically ventilated on controlled modes and met criteria for assisted breathing were randomized to receive either PS ($n = 100$) or PAV+ ($n = 108$). Changes in ventilator settings and in the dose of sedatives, analgesics, and vasoactive medications were identified during the period in which the patients were ventilated either with PS (30.4 ± 17.4 h) or PAV+ (30.0 ± 18.1 h) and classified as changes to facilitate weaning (CFW) or changes to respond to deterioration (CD). *Results:* The mean number of changes in ventilator settings was significantly higher with PS than that with PAV+ (10.7 ± 5.7 vs. 8.9 ± 4.6). With PS the proportion of these changes classified as CFW was significantly lower than that with PAV+ (59.8% vs. 69.2%). Dyssynchrony as a cause of CD was more likely to occur with PS than with PAV+ (42 vs. 3%). The mean number of changes in the dose of sedatives, analgesics, and vasoactive medications was higher with PS than with PAV+, the difference being significant only for sedatives (4.06 ± 3.8 vs. 2.82 ± 3.4). *Conclusions:* Compared to PS, PAV+ is associated with fewer intervention in terms of ventilator settings and sedative dose changes.

Keywords Ventilator settings · Sedatives · Analgesics · Vasoactive medications · Critically ill

Introduction

Proportional-assist ventilation with load-adjustable gain factors (PAV+) is a mode of support in which the ventilator pressure is proportional to instantaneous flow (flow assist) and volume (volume assist) [1, 2]. Flow and volume assist are automatically adjusted so that they always represent constant fractions of resistance and elastance of the respiratory system, as measured by the ventilator software [2–4].

In a recent randomized study [5], we showed that PAV+ may be used as a main mode of support in critically ill patients. Compared to pressure support (PS), PAV+ increases the probability of remaining on assisted or unassisted spontaneous breathing, whereas it considerably reduces the incidence of patient-ventilator asynchronies.

Although PAV+ is an efficient modality of ventilatory support [5], it is not known whether it is a user-friendly mode. Contrary to PS, with PAV+ the patient exclusively

drives the ventilator. This functional principle imposes two main advantages compared to PS; first, with PAV+ only four variables are manipulated (1) fractional concentration of O_2 (FIO_2), (2) positive end-expiratory pressure (PEEP), (3) threshold for triggering and (4) assist level [5], whereas with PS, in addition to the above variables, rising time and cycling off criterion should be taken into account [6, 7]. Second, PAV+ is associated with better patient-ventilator synchrony than PS [2, 5]. Thus, to minimize patient-ventilator dyssynchrony, the caregiver may change the ventilator variables more often with PS than with PAV+. It is also possible that due to dyssynchrony, modification in analgo-sedation administration might be different. Conversely, the same functional principle may prove disadvantageous for PAV+. For example, during PAV+, low respiratory drive may result in very low tidal volume (V_T) and inefficient gas exchange [1]. Consequently, PEEP/assist level may be increased and analgo-sedation decreased to correct these abnormalities. Therefore, the aim of this study was to compare the number of interventions between the two modes of support (PAV+ or PS). We retrospectively collected detailed data from files of patients enrolled in our previous randomized trial [5] that had not previously been collected. Specifically, we examined in each patient the number of and reason for changes in ventilator settings and changes in dose of sedatives, analgesics, and vasoactive medications during the period of assisted mechanical ventilation.

Methods [see also electronic supplementary material (ESM)]

Participating patients were randomly assigned to receive either PS ($n = 100$) or PAV+ ($n = 108$) using a Puritan-Bennett 840 ventilator (Nellcor Puritan Bennett LLC, Covidien, Boulder, CO). Specific written algorithms were used to adjust the ventilator settings in each mode. PAV+ or PS was continued for 48 h unless the patients met predefined criteria for either switching to controlled modes or breathing without ventilator assistance. In both groups, identical algorithms for titration of sedatives, analgesics, and vasoactive drugs were followed [8–10].

The medical chart of each patient was examined for interventions (related to ventilator settings, analgo-sedation, and vasoactive medications) during the period in which the patients were ventilated with either PS or PAV+. The changes in ventilator settings pertained to (1) FIO_2, (2) flow threshold for triggering, (3) assist level (PS or % of assist), (4) PEEP, (5) cycling off criterion, and (6) rising time. The changes in cycling off criterion and rising time applied only to PS.

Interventions were classified as either (1) changes to facilitate weaning (CFW) or (2) changes to respond to deterioration (CD) of the patient's status (i.e., respiratory distress, inefficient gas exchange, patient-ventilator dyssynchrony, agitation, etc.). Any change from baseline value in flow threshold for triggering, cycling off criterion, and rising time and any increase in FIO_2, assist level, and PEEP was classified as CD. A decrease in assist level was classified as CD if the change was due to dyssynchrony, otherwise it was considered as CFW. Any increase in the dose of sedatives, analgesics, or vasoactive medications was considered as CD, whereas any decrease in dose was considered as CFW.

Summary descriptive statistics are given as mean ± SD. Proportions were compared using χ^2 test or the Fisher's exact test when required. Continuous variables were compared between the two groups with unpaired t-test.

Results

During the study period, patients randomly assigned to PS were ventilated for 30.4 ± 17.4 h and patients randomly assigned to PAV+ were ventilated for 30.0 ± 18.1 h. The mean number of changes in ventilator settings was significantly higher with PS than with PAV+, mainly due to changes classified as CD (Table 1). Among the ventilator settings examined, the number of changes in assist level and triggering threshold were significantly higher with PS than with PAV+.

In the PAV+ group, the proportion of changes in ventilator settings classified as CFW was significantly higher than in the PS group (69.2 vs. 59.8%) (Table 2). Further analysis of the causes of changes in ventilator settings revealed that patient-ventilator dyssynchrony was reported as the primary reason for the change in 41% of interventions classified as CD with PS versus only 3% with PAV+ (Fig. 1).

The mean number of changes in the dose of sedatives, analgesics, and vasoactive medications was higher with PS than with PAV+, the difference being significant only for sedatives (Table 3). The proportion of changes in sedatives, analgesics and vasoactive medications classified as CF and CD did not differ between the two modes (ESM).

Discussion

The main finding of this study is that compared to PS, PAV+ is associated with less manipulation of ventilator settings and the dose of sedatives. Furthermore, with

Table 1 Mean number of changes in ventilator settings

	PS	PAV+	Δ (95% CI of Δ)	*P*
All settings	10.66 ± 5.7	8.88 ± 4.6*	1.78 (0.37–3.19)	0.000
CFW	6.37 ± 3.3	6.15 ± 3.5	0.22 (−0.70–1.15)	0.636
CD	4.29 ± 3.5	2.73 ± 2.3*	1.56 (0.75–2.37)	0.000
FIO_2	2.51 ± 2.1	2.54 ± 1.7	−0.03 (−0.60–0.50)	0.920
CFW	1.57 ± 1.4	1.73 ± 1.3	−0.16 (−0.53–0.21)	0.387
CD	0.94 ± 1.1	0.81 ± 1.0	0.13 (−0.15–0.42)	0.350
Assist level	4.71 ± 2.4	3.92 ± 2.4*	0.79 (0.14–1.45)	0.018
CFW	3.20 ± 1.7	2.89 ± 1.9	0.31 (−0.53–0.21)	0.210
CD	1.51 ± 1.6	1.03 ± 1.2*	0.48 (0.10–0.86)	0.013
PEEP	2.43 ± 2.2	2.37 ± 1.7	0.06 (−0.48–0.60)	0.827
CFW	1.60 ± 1.3	1.53 ± 1.2	0.07 (−0.26–0.41)	0.673
CD	0.83 ± 1.2	0.84 ± 0.9	−0.01 (−0.30–0.27)	0.930
Triggering	0.29 ± 0.46	0.06 ± 0.23*	0.23 (0.13–0.33)	0.000
Rising time/cycling off	0.72 ± 1.1	NA	NA (NA)	NA

Values are mean ± SD

PS pressure support; *PAV+* proportional assist ventilation with adjustable gain factors; *Δ* difference between PS and PAV+; *CI* confidence interval of Δ; *NA* not applicable; *FIO_2* fractional concentration of O_2; *PEEP* positive end-expiratory pressure; *CFW* changes performed in order to facilitate weaning; *CD* changes performed because of patient's status deterioration

Table 2 Total number of changes and number of changes (% of total) classified as CD and CF in ventilator settings

	PS			PAV+		
	Total	CFW	CD	Total	CFW	CD
Ventilator settings (all)	1066	637 (59.8)	429 (40.2)	959	664 (69.2)*	295 (30.8)*
FIO_2	251 (23.5)	157 (14.7)	94 (8.8)	274 (28.6)	187 (19.5)	87 (9.1)
Assist level	471 (44.2)	320 (30.0)	151 (14.1)	423 (44.1)	312 (32.5)	111 (11.6)
PEEP	243 (22.8)	160 (15.0)	83 (7.8)	256 (26.7)	165 (17.2)	91 (9.5)
Triggering threshold	29 (2.7)		29 (2.7)	6 (0.6)		6 (0.6)
Rising time/cycling off	72 (6.8)		72 (6.8)	NA		

*Significantly different from PS (proportions comparison)

PAV+ the proportion of changes in ventilator settings performed to facilitate the weaning progress was significantly higher than with PS.

The ventilator settings were modified approximately 11 times over a 48-h period in patients on PS versus 9 times in patients on PAV+. Although this difference is of questionable clinical significance, it clearly shows that PAV+, compared to PS, is a user-friendly mode. Patient-ventilator dyssynchrony was reported as the primary reason for the change in 41% ($n = 176$) of interventions classified as CD with PS versus only 3% ($n = 9$) with PAV+. These results are expected because in our previous study [5] we observed a considerably higher incidence of major patient-ventilator dyssynchrony with PS than with PAV+, and by protocol, specific actions [6, 7, 11, 12] were taken to improve patient-ventilator synchrony. In addition, with PS but not with PAV+, V_T is highly dependent on the assist level [5, 13, 14], and as we demonstrated in the current study, this influenced the number of support-level manipulations.

One may argue that the higher number of changes in ventilator settings with PS is rather artificial, because of the specific algorithms (see ESM) designed to minimize

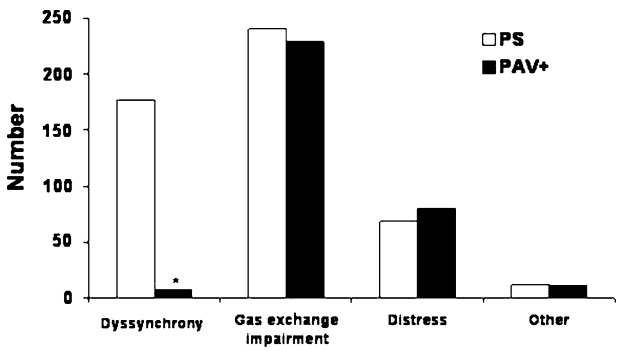

Fig. 1 Distribution of the various causes that resulted in modification of ventilator settings performed because of patients' status deterioration. *PS* pressure support; *PAV+* proportional assist ventilation with adjustable gain factors. *Significantly different from PS

the patient-ventilator dyssynchrony. However, recent data indicate that patient-ventilator dyssynchrony may affect the outcome of critically ill patients. Studies have shown that dyssynchrony is associated with a longer duration of mechanical ventilation [14] and disrupted sleep [15], an

Table 3 Mean number of changes in sedative, analgesic, and vasoactive medications

	PS	PAV+	Δ (95% CI of Δ)	*P*
Sedatives	4.06 ± 3.8	2.82 ± 3.4*	1.23 (0.25–2.23)	0.015
CFW	2.13 ± 2.1	1.60 ± 1.8	0.53 (0.01–1.06)	0.050
CD	1.93 ± 2.1	1.2 ± 1.9*	0.71 (0.16–1.26)	0.011
Analgesics	3.44 ± 3.2	3.04 ± 2.7	0.39 (−0.42–1.20)	0.340
CFW	1.86 ± 1.7	1.73 ± 1.5	0.13 (−0.30–0.56)	0.557
CD	1.58 ± 1.9	1.31 ± 1.6	0.27 (−0.21–0.74)	0.276
Vasoactive medications	4.02 ± 4.9	2.87 ± 4.1	1.15 (−0.09–2.39)	0.069
CFW	2.45 ± 3.1	1.60 ± 2.1*	0.85 (0.13–1.57)	0.021
CD	1.57 ± 2.1	1.27 ± 2.3	0.30 (−0.29–0.90)	0.319

PS pressure support; *PAV+* proportional assist ventilation with adjustable gain factors; *Δ* difference between PS and PAV+; *CI* confidence interval of Δ; *CFW* changes performed in order to facilitate weaning; *CD* changes performed because of patient's status deterioration

*Significantly different from PS

important and often unrecognized determinant of outcome in patients on mechanical ventilation. In addition PAV+, which is associated with less patient-ventilator dysssynchrony, increases the probability of remaining on spontaneous breathing [5]. All these findings suggest that dysssynchrony between patient and ventilator should be identified and corrected. Nevertheless, because causality between dyssynchrony and outcome is not entirely clear, further studies are needed to resolve this issue.

In our previous study we observed that the total amount of sedatives, analgesics, and vasoactive medications received within the period of assisted ventilation was similar between groups [5]. The current study showed that the dose of these medications changed more frequently with PS than with PAV+; the difference being significant only for sedatives. These findings indicate that with both modes the titration of sedatives to predefined goals [8, 9] may be achieved with comparable total drug amount but necessitates different caregiver actions. Although the reasons for this difference were not entirely clear, the higher incidence of major patient-ventilator dyssynchrony with PS could be a factor [16].

A potential limitation of this study is that data were extracted by following a hypothesis generated after the results of the first study were known. This may increase the risk of bias in formulating the hypothesis and analyzing the data. We tried to minimize any bias by defining all the variables of interest before starting the review of the medical records. In addition, all patients in this study underwent strict random assignment to the two modes. Also, detailed predefined algorithms [5] were used to adjust the ventilator settings and the dose of sedatives, analgesics, and vasoactive medications in each mode, which are important steps in eliminating the bias that would confound a truly retrospective study.

A final limitation of this study, inherent in its retrospective design, is the accuracy of information extracted from the patients' medical charts. Although due to the original study design the changes as well as the reason for a change in ventilator settings should be recorded in the patients' chart, the possibility that some changes were either not reported or not adequately explained still exists. However, we believe that these errors, if any, should be small and apply to both modes of support.

In conclusion, this study showed that when using a specific protocol, PAV+ is a user-friendly mode associated with fewer manipulations of ventilator settings and fewer changes in sedative dosing compared to PS.

Conflict of interest statement Dimitris Georgopoulos received 3000 Euros in 2008 and 1500 Euros in 2009 for speaking at conferences sponsored by Tyco, and 20000 Euros in years 2007–2009 from Nellcor Puritan Bennett as a research grant for conducting clinical trials. Tyco or Nellcor Puritan Bennett was not involved in any aspect of the design or conduct of the study, the data analysis, or the manuscript preparation and presentation. None of the other authors has a financial relationship with a commercial entity that has an interest in the subject of this manuscript.

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