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Use of noninvasive mechanical ventilation with pressure support guaranteed with average volume in *de novo* hypoxaemic respiratory failure. A pilot study

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Abstract

Background: This study was designed to determine the results associated with the use of noninvasive mechanical ventilation (NIV) using the BiPAP S/T-AVAPS ventilation strategy in subjects with mild to moderate *de novo* hypoxaemic respiratory failure.

Methods: This is a prospective study that includes subjects with *de novo* hypoxaemic respiratory failure (not produced by acute exacerbations of COPD, chronic lung disease, or congestive heart failure) with mild to moderate PaO_2/FiO_2, who were admitted to the Intensive Care Unit (ICU) of Santa Maria Clinic in Guayaquil, Ecuador.

Subjects were divided into two groups and compared according to their PaO_2/FiO_2: higher than 100 and up to 200 mm Hg (moderate ARDS) or between 200 and 300 mm Hg (mild ARDS) (both groups were ventilated with the BiPAP S/T-AVAPS strategy).

Results: A total of 38 subjects were analysed in this study. The total rate of intubation was 34.2% while the mortality rate was 28.9%. Significant differences were observed when comparing success versus failure in exhaled tidal volumes heart rate ($P = 0.04$), peak inspired pressure ($P < 0.001$), PaO_2 ($P < 0.001$), SaO_2 ($P < 0.002$), PaO_2/FiO_2 ($P < 0.002$), arterial blood pressure ($P < 0.001$), HR ($P < 0.001$), and inspiratory time ($P = 0.029$) measured at baseline and at 12-hour, 24-hour and 48-hour intervals.

Conclusion: The BiPAP S/T-AVAPS ventilatory mode can be used in subjects with *de novo* hypoxaemic respiratory failure with special vigilance concerning exhaled tidal volumes and inspired pressure.

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Key words: mechanical ventilation, noninvasive; respiratory failure, acute, *de novo*; pressure support guaranteed with average volume

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It is known that noninvasive mechanical ventilation (NIV) can be employed in subjects with hypoxaemic respiratory failure with different results [1–3]. The BiPAP S/T-AVAPS ventilatory strategy allows clinicians to use a fixed pre-programmed tidal volume, which is kept constant by virtue of inspiratory pressure variations [4]. This is achieved by programming the so-called "target volume" with a level of inspiratory positive airway pressure (IPAP); the target volume varies between the maximum and minimum IPAP range programmed in the noninvasive mechanical ventilator in order to maintain a preset target volume with a smooth transition between inspired pressure levels. The ventilatory strategy with BiPAP S/T-AVAPS is called the "hybrid mode" [5].

This ventilatory strategy has been demonstrated to be useful in patients with chronic respiratory insufficiency [6, 7] and in subjects with acute hypercapnic respiratory insufficiency [8, 9]. Briones Claudett *et al.* [8] reported the first case-control study with benefits in 11 subjects with COPD and hypercapnic encephalopathy. Cao *et al.* [9] described the results from a multi-centre randomised controlled trial comparing pressure-limited NIV versus volume-targeted NIV in 58 subjects with acute hypercapnic respiratory failure who had underlying chronic obstructive pulmonary disease (COPD). Ciftci Fatma, *et al.* [10] evaluated the feasibility of using BiPAP S/T-AVAPS. They showed that BiPAP S/T-AVAPS was effective and well-tolerated in 76.4% of cases of patients with COPD.

In subjects with acute respiratory distress syndrome (ARDS), a ventilatory strategy that delivers a small tidal volume has been demonstrated to reduce mortality [11]; however, it is difficult in daily practice to control the levels of the tidal volume setting in which NIV may depend on the levels of inspired pressures, the effort of the patient, and leakages in the system [12, 13].

The ability of the BiPAP S/T-AVAPS to combine the benefits of providing an enhanced volume, avoiding significant variation in levels of pressure in each breath, could contribute to achieving a protective ventilatory strategy.

Recent studies have emphasised the importance of using a protective ventilatory strategy during NIV. The primary disadvantage of using NIV in *de novo* hypoxaemic respiratory failure is the lack of established protocols that prevent the development of ventilator-induced lung injury [14, 15]. However, this ventilatory strategy with BiPAP S/T-AVAPS has not yet been validated in subjects with *de novo* hypoxaemic respiratory failure

This pilot study was designed in order to determine the results of the use of the BiPAP S/T-AVAPS ventilatory strategy in subjects with mild to moderate *de novo* hypoxaemic respiratory failure. The primary objective is to determine the rate of success and failure (rate of intubation), and to determine the mortality rate, duration of hospital stay, and duration of mechanical ventilation.

METHODS

This was a nonrandomised, single-centre prospective pilot study. This study was performed in accordance with the Declaration of Helsinki. This human study was approved by the Teaching and Research Committee of Santa Maria Clinic — approval: 01/12/2010 serial: 2010.14 [2]. The study's clinical trial registry number is (TRIAL REGISTER: ISRCTN13036391 DOI 10.1186/ISRCTN13036391) registered with http://www.isrctn.com/ISRCTN13036391. This study adheres to *STROBE* statement guidelines. Participant registration took place between December 1, 2010, and January 1, 2014; informed consent was obtained from the subjects, or their surrogates if any subjects were unable to respond for themselves.

The inclusion criteria were as follows: age of 18 years or older; subjects who presented signs of acute respiratory failure in the emergency room (respiratory rate (RR) > 25 breaths per minute and the use of accessory muscles; with a diagnostic of mild to moderate hypoxaemic respiratory failure with PaO_2/FiO_2 as per thresholds defined by the Berlin criteria for ARDS hypoxaemic respiratory failure [16].

The criteria of exclusion were in accordance with the British Thoracic Society Standards of Care Committee of Non-Invasive Ventilation [17]: Subjects were excluded for the following reasons: if they demonstrated haemodynamic instability; presented excess respiratory secretions; if they were noncooperative or agitated; unable to use the interface device; if the patient had undergone recent surgery of the upper airway; or if the patient had received NIV with a "Do Not Resuscitate" order.

Subjects were evaluated upon admission to the intensive care unit (ICU) and were divided into two groups according to their "de novo" hypoxaemic respiratory failure: subjects with PaO_2/FiO_2 greater than 100 to 200 mm Hg (moderate ARDS) or subjects with between 200 and 300 mm Hg (mild ARDS); both groups were treated with the BiPAP S/T-AVAPS ventilatory strategy.

All subjects were evaluated during their stay in the ICU and followed up until their discharge from hospital.

PROGRAMMED VENTILATOR PARAMETERS

The ventilatory parameters were initially programmed in the BiPAP S/T-AVAPS with maximum inspiratory positive pressure (IPAP) programmed in the 20 cmH_2O device and a minimum programmed IPAP of 12 cmH_2O with a positive expiratory pressure (EPAP) of 6 to 8 cmH_2O.

The programmed tidal volume was 6 to 8 mL kg^{-1} of one's ideal body weight (IBW) using the following formula: 55.5 ± 2.3 (height in inches — 60) for men and 45.5 ± 2.3 (height in inches — 60) for women. RR was 14–20 breaths/min; rise time was 300 to 400 ms; inspiratory time was 0.8 to

1.2 s. In addition, O_2 supplements were added through an O_2 adapter close to the mask to keep the SaO_2 remaining above 90%. Maximum IPAP, exhaled tidal volume (Vt_{exh}), V_{min}, and leakages were controlled through the ventilator software. BiPAP synchrony with AVAPS and Autotrak (*Respironics Inc., Murrysville, Pennsylvania, USA*) was used along with a series of Mirage IV (*Resmed*) face masks.

MEASUREMENTS

Arterial blood gas (ABG), vital signs, as well as the programmed and ventilatory parameters of the patient were measured at baseline (before the start of NIV) and at intervals of 1 hour, 12 hours, and 24 hours of NIV use. Each patient was evaluated by a respiratory therapist under strict supervision of NIV-trained physicians.

ABG: pH; PCO_2 (mm Hg); PO_2 (mm Hg); HCO_3 (mmol L^{-1}); SaO_2 (%); EB (mEq L^{-1}); FiO_2 (%); PaO_2/FiO_2 (mm Hg).

Vital signs: diastolic blood pressure (DBP) mm Hg; systolic blood pressure (SBP) mm Hg; heart rate (HR); respiratory rate (RR).

Ventilator parameters: tidal volume programmed — AVAPS — (mL); subject's tidal volume (mL); V_{min} (L min^{-1}); Vt_{exh} mL kg^{-1} IBW; levels of IPAP programmed maximum (cm H_2O); levels of IPAP patient (cm H_2O); levels of EPAP (cm H_2O); leakages (cm H_2O); RAMP (msec); inspiratory time (sec).

The severity of the disease was evaluated by a score of evaluation of acute illness in chronically ill subjects (APACHE II score) while the number of quadrants affected in the chest X-ray was expressed as a numeric value (0, 1, 2, 3, 4), depending on the presence of opacity or pulmonary consolidation found in each quadrant.

Complications related to mask use were also noted.

DISCONTINUATION OF NIV THERAPY

The process of NIV weaning was initiated when clinical stability was achieved, which was defined as an RR of fewer than 24 breaths per minute (RPM) and an HR of 90 beats per minute (BPM), as well as an improvement in SaO_2 with a percentage of FiO_2 lower than a range of 35% to 40%. Once the patient was stabilised, the NIV was withdrawn.

NIV WITHDRAWAL

Clinical stability was defined as: (1) RR < 25 RPM; (2) HR < 100 BPM; and (3) arterial pH compensated with SaO_2 (%) > 90% in ambient air or with low-flow oxygen (< 3 L min^{-1}).

OUTCOME MEASURES

The primary outcome was success or failure in the use of NIV (expressed as a percentage). Secondary outcomes were duration of hospitalisation (expressed in days), and mortality (expressed as a percentage of subjects).

STATISTICAL ANALYSIS

Statistical analysis was performed using MedCalc Statistical Software, version 16.4.3 (MedCalc Software bvba, Ostend, Belgium; https://www.medcalc.org; 2016). All data were expressed as a mean ± standard deviation for continuous variables and as percentages for categorical variables. The t-test for independent samples was used on data with a Gaussian distribution and similar variance (determined by homogeneity of variance or Levene's test). A nonparametric test (chi-square or Fisher's exact test) was utilised for the data with a non-normal distribution for categorical variables. A *P*-value of < 0.05 was considered statistically significant. This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

RESULTS

A total of 38 subjects were analysed in this study; they were divided into two groups and compared according to their PaO_2/FiO_2 of 100 to 200 mm Hg (moderate ARDS) or 200 to 300 mm Hg (mild ARDS). Both underwent a ventilatory strategy with BiPAP S/T-AVAPS. The most frequent age of presentation was 68.4 ± 21.7 with a mean PaO_2/FiO_2 of 182.5 ± 32.9 and an average programmed TV AVAPS of 476.6 ± 58.5, while the number of quadrants affected in the chest X-ray averaged 1.5 ± 0.6. The total rate of intubation was 34.2% while the mortality rate was 28.9%. The primary risk factors for ARDS were as follows: community-acquired pneumonia, 33 (86.8%); acute abdominal illness that required surgery, 2 (5.3%); and acute pancreatitis, 3 (7.9%). The mean APACHE II score was 22 ± 3.2 (see Table 1).

Continuous variables are presented as mean ± SD. Categorical variables are presented as No. (%). APACHE II: Acute Physiology and Chronic Health. Evaluation II; SpO_2 (%) oxygen saturation measured by pulse oximetry and risk factor of ARDS diagnosis on enrolment

Between the two groups of PaO_2/FiO_2 of 100 to 200 mm Hg (moderate ARDS) and PaO_2/FiO_2 of 200 to 300 mm Hg (mild ARDS), no differences were found in the length of stay in the ICU, the duration of non-invasive mechanical ventilation, or the mortality rate. (see Table 2).

No statistically significant differences in length of stay in ICU, number of days of non-invasive mechanical ventilation

Significant differences were observed when comparing success versus failure of the ventilatory strategy with BiPAP S/T-AVAPS in exhaled tidal volumes ($P = 0.04$), peak inspired pressure ($P < 0.001$), PaO_2 ($P < 0.001$), SaO_2 ($P < 0.002$), PaO_2/FiO_2 ($P < 0.002$), RR ($P < 0.001$), HR ($P < 0.001$), and inspiratory time ($P = 0.029$) measured at baseline and after 12 hours, 24 hours, and 48 hours (see Table 3 and Fig. 1).

Statistically significant differences are shown, where all variables, success vs. failure in PaO_2/FiO_2, PaO_2, SaO_2, FiO_2,

Table 1. Characteristics of the study population

Characteristics	Value
Age (years)	68.4 ± 21.7
Sex (M); (F)	25 (65%); 13 (35%)
Body mass, kg (IBW)	64.5 ± 11.7
APACHE II	22 ± 3.2
Risk factor of ARDS	–
Community-acquired pneumonia	33 (86.8%)
Acute abdominal illness that required surgery	2 (5.3%)
Pancreatitis	3 (7.9%)
DBP (diastolic blood pressure (mm Hg)	74.1 ± 10.1
SBP (systolic blood pressure) (mm Hg)	121.2 ± 18.9
HR (beats per min)	97.1 ± 13.8
RR (per min)	28.7 ± 3.7
pH	7.42 ± 06
PCO2 (mm Hg)	31.9 ± 5.8
PO_2 (mm Hg)	76.6 ± 11.2
HCO_3 (mmol L^{-1})	22.2 ± 4.2
BE (mmol L^{-1})	–1.6 ± 7.4
SaO_2 (%)	93.1 ± 3.4
FiO_2 (%)	0.42 ± 0.04
PaO_2/FiO_2 (mm Hg)	182.5 ± 32.9
Tidal volume programmed AVAPS (mL)	476.6 ± 58.5
Tidal volume patients (mL)	462.2 ± 128
V_{min} (L min^{-1})	11.9 ± 3.8
Levels of maximum IPAP programmed (cm H_2O)	19.9 ± 2
Levels of IPAP patient (cm H_2O)	16.8 ± 3.2
Levels of EPAP (cm H_2O)	6.1 ± 5.1
Leakage (cm H_2O)	18.1 ± 9.4
RAMP (msec)	3.2 ± 5.2
Inspiratory time (sec)	93 ± 21
Number of quadrants affected in the chest X-ray	1.5 ± 0.6
Number of days of NIV	5.9 ± 4.3
Number of days in ICU	10.7 ± 11.6
Duration of stay in hospital (days)	13.8 ± 9.1

Levels of IPAP patient, exhaled tidal volumes, peak inspired pressure; RR, HR, and inspiratory time, measured at baseline and after 12 hours, 24 hours, and 48 hours

DISCUSSION

The results of this study suggest that this ventilatory mode can be employed in subjects with *de novo* hypoxaemic respiratory failure, especially in mild cases due to the high rate of success in this subgroup.

Table 2. Characteristics of both groups

	Mild ARDS (26)	Moderate ARDS (12)	*P*-value
pH	7.41 ± 0.05	7.42 ± 0.05	0.57
PCO2 (mm Hg)	31.9 ± 6.1	31.9 ± 5.6	0.99
PO_2 (mm Hg)	86.6 ± 9.3	71.9± 10	0.0001*
HCO_3 (mmol L^{-1})	21.6 ± 4.2	22.4 ± 4.2	0.56
Base excess (mEq L^{-1})	–3.4 ± 6.1	–0.8 ± 7.9	0.32
SaO_2 (%)	0.93 ± 0.04	0.92 ± 0.03	0.58
TV AVAPS programmed (mL)	470 ± 78.5	479.6 ± 48.2	0.64
Levels of maximum IPAP programmed (cm H_2O)	19.3 ± 2.1	20.2 ± 1.9	0.19
Levels of IPAP patient (cm H_2O)	16.5 ± 2.9	17.07 ± 3,3	0.60
Levels of EPAP, (cm H_2O)	6.1 ± 0.5	6 ± 0.4	0.61
RAMP (msec)	3.4 ± 0.6	3.2 ± 0.4	0.30
Inspiratory time (sec)	0.9 ± 0.2	0.9 ± 0.2	0.84
RR (Respiratory rate)	29 ± 3.3	28.57 ± 3.9	0.74
FIO_2 (%)	0.39 ± 0.02	0.43 ± 0.04	0.003*
Vt exh (mL)	430.3 ± 158.5	477 ± 111.8	0.30
Vmin (L min^{-1})	11.5 ± 5.2	12.1 ± 3	0.62
Vt exh mL kg IBW^{-1}	7.2 ± 2.4	7.2 ± 1.6	0.42
Duration of stay in ICU	7.9 ± 4.9	11.9 ± 13.4	0.32
Number of days of NIV	4.2 ± 2.4	6.6 ± 4.8	0.10
Patient intubation rate (%)	7 (26.9%)	6 (50%)	0.17
Mortality	6 (23.8%)	5 (41.6%)	0.05

*Statistical significance at $P < 0.05$

The rate of success of NIV with BiPAP S/T-AVAPS in the group of subjects with mild ARDS was 73.1% and 50% in subjects with moderate ARDS. These results did not differ from what has been reported in other studies in which NIV was used in ARDS [18, 19]. The total rate of intubation was 34.2% while the mortality rate was 28.9%.

Variables that could help identify subjects who would benefit from NIV with BiPAP S/T-AVAPS were determined. Persistent hypoxaemia, tachycardia, tachypnoea, increased exhaled tidal volumes, and high levels of inspiratory pressure that could later reach a critical level would be determinants of success or failure in using the BiPAP S/T-AVAPS ventilatory strategy.

The BiPAP S/T-AVAPS mode may provide a better approximation of protective ventilation in a select group of subjects with mild *de novo* hypoxaemic respiratory failure and spontaneous breathing. This study showed that although better volumes were achieved, this was with a varied range of inspiratory peak pressures ($P < 0.001$) [20].

Table 3. Failure and success in patients with BiPAP S/T-AVAPS pressure support guaranteed with average volume

	PaO_2/FiO_2 (baseline)	Pa O_2/FiO_2 (12h)	PaO_2/FiO_2 (24h)	PaO_2/FiO_2 (48h)	*P*-value
Failure	186.3 ± 34.4	194.1 ± 63.4	187.5 ± 68.5	220.5 ± 127.9	< 0.001
Success	179.9 ± 32.3	266.4 ± 80.2	306.7 ± 107	343.3 ± 115.9	
	PaO_2 (baseline)	PaO_2 (12h)	PaO_2 (24h)	PaO_2 (48h)	*P*-value
Failure	78.1 ± 11.6	83.8 ± 19.9	101.3 ± 28.8	104.6 ± 33.5	< 0.001
Success	75.6 ± 12.3	104.4 ± 29	112.1 ± 33.5	120.7 ± 37	
	SaO_2 (baseline)	SaO_2 (12h)	SaO_2 (24h)	SaO_2 (48h)	*P*-value
Failure	0.92 ± 0.03	0.94 ± 0.03	0.92 ± 0.05	0.93 ± 0.05	< 0.002
Success	0.93 ± 0.03	0.96 ± 0.02	0.96 ± 0.03	0.98 ± 0.02	
	FiO_2 (baseline)	FiO_2 (12h)	FiO_2 (24h)	FiO_2 (48h)	P-value
Failure	0.42 ± 0.04	0.45 ± 0.07	0.51 ± 0.08	0.53 ± 0.11	< 0.001
Success	0.42 ± 0.04	0.40 ± 0.04	0.38 ± 0.06	0.36 ± 0.05	
	Levels of IPAP patient (baseline)	Levels of IPAP patient (12h)	Levels of IPAP patient (24h)	Levels of IPAP patient (48h)	*P*-value
Failure	17.2 ± 3.7	14.7 ± 3.2	13.1 ± 1.5	14.8 ± 2.8	< 0.001
Success	16.6 ± 2.8	16.5 ± 3.1	12.4 ± 3.2	12.2 ± 2	
	Inspiratory time (baseline)	Inspiratory time (12h)	Inspiratory time (24h)	Inspiratory time (48h)	*P*-value
Failure	0.96 ± 0.2	0.91 ± 0.2	1.06 ± 0.1	1.05 ± 0.1	0.029
Success	0.91 ± 0.2	0.93 ± 0.2	0.93 ± 0.2	0.94 ± 0.1	
	Vmin (baseline)	Vmin (12h)	Vmin (24h)	Vmin (48h)	*P*-value
Failure	11.3 ± 4	11.1 ± 4.3	12.1 ± 4.5	10.7 ± 3.2	< 0.001
Success	12.4 ± 3.6	9.6 ± 2.1	10.8 ± 3.2	11.2 ± 4.8	
	Vt exh (baseline)	Vt exh (12h)	Vt exh (24h)	Vt exh (48h)	*P*-value
Failure	473.1 ± 171	507.5 ± 159.5	524.4 ± 113.2	457.8 ± 106.6	0.04
Success	454.5 ± 88.7	494.2 ± 78.8	491.9 ± 69.7	489.8 ± 90.1	
	Vt exh (baseline) mL kg IBW^{-1}	Vt exh (12h) mL kg IBW^{-1}	Vt exh (24h) mL kg IBW^{-1}	Vt exh (48h) mL kg IBW^{-1}	*P*-value
Failure	7.2 ± 2.4	7.9 ± 2.6	8.3 ± 1.8	7.1 ± 1.7	0.006
Success	7.2 ± 1.6	7.9 ± 1.4	7.6 ± 1.2	7.5 ±1.3	
	HR (baseline)	HR (12h)	HR (24h)	HR (48h)	*P*-value
Failure	99.8 ± 15.5	99.1 ± 17.7	92.4 ± 18.5	110.7 ± 16.8	< 0.001
Success	95.2 ± 12.3	85.0 ± 14.4	83.7 ± 12.3	83.9 ± 17.8	
	RR (baseline)	RR (12h)	RR (24h)	RR (48h)	*P*-value
Failure	27.8 ± 4.4	21.4 ± 3.4	23.0 ± 5.8	25.2 ± 3.8	< 0.001
Success	29.4 ± 2.9	21.8 ± 5.7	20.8 ± 5.3	19.2 ± 4.2	

Statistical significance at $P < 0.05$

With this ventilatory strategy, we observed that, the combination of these two ventilation modes (BiPAP S/T-AVAPS) in subjects who respond to the strategy resulted in-lower inspiratory pressures with lower exhaled tidal volumes. The clinical improvement found, one that was independent of hypoxaemia as a main factor, is possibly due to better control of the effectiveness of the ventilation applied, namely BiPAP S/T-AVAPS. There are a few studies in which the BiPAP S/T-AVAPS mode has demonstrated clear benefits. Possible mechanisms lie in better rest and muscle efficiency with recruitment of hypoventilated areas [21, 22].

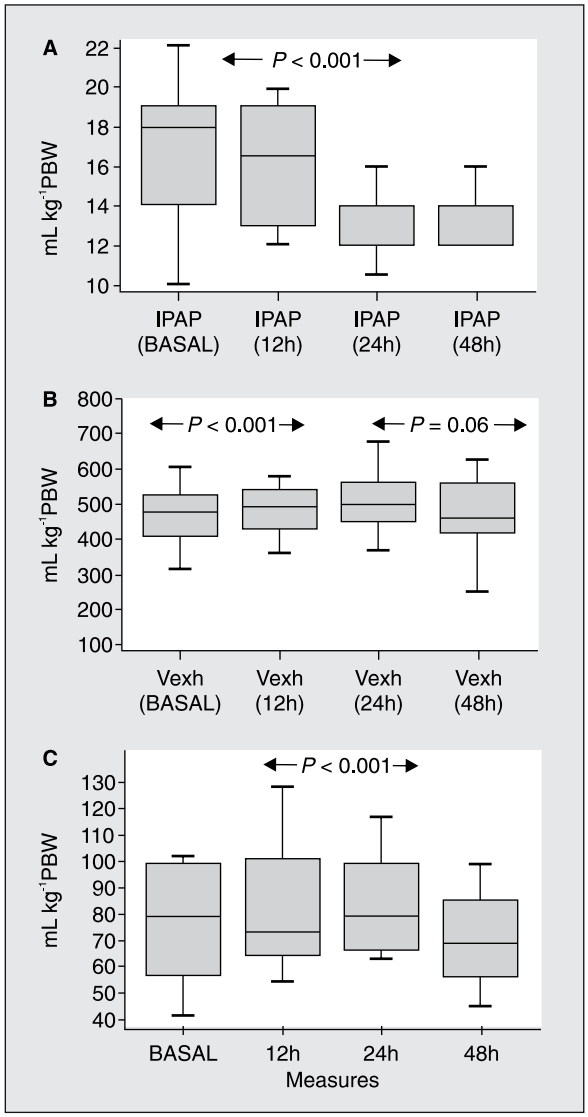

Figure 1. Statistically significant differences all variables success vs. failure in **A**) Peak inspired pressure ($P < 0.001$), **B**) exhaled tidal volumes ($P = 0.04$), and **C**) Vt exh mL kg^{-1}PBW measured at baseline and after 12h, 24h, and 48h

The direct therapeutic options in *de novo* hypoxaemic respiratory failure are limited while the main focus of such treatments is on minimising ventilator-induced lung injury (VILI) [23].

Current guidelines recommend setting the initial tidal volume to 6 mL kg^{-1} (IBW) and only increasing it to 8 mL kg IBW^{-1} if the patient experiences undesirable side effects, such as double-triggering or if positive end-expiratory pressure (PEEP) exceeds the inspiratory airway pressure [24]. Some researchers have demonstrated that only 20% of subjects achieve exhaled tidal volumes greater than 6.5 mL kg IBW^{-1} [25] and that exhaled tidal volume is an independent risk factor for NIV failure. Protective ventilatory strategies have not been reported with the use of NIV as demonstrated in a European study in which only 23% of the subjects obtained tidal volumes of between 6 and 8 mL kg PBW^{-1} during all NIV sessions [18]. In this study, tidal volumes of 10 mL kg^{-1} or greater of one's ideal weight were used in half of the subjects with hypoxaemic respiratory failure.

Our results also demonstrate that subjects with mild ARDS have better responses than subjects with moderate ARDS (26.9% as compared to 50%), which may not only be related to the severity of their disease, exhaled tidal volumes, and inspiratory pressures, but also to the levels of PEEP used for this group of subjects. A balance should be achieved when increasing PEEP levels in subjects with ARDS, since the goal of reducing lung stress and strain through improving alveolar recruitment must go in hand with the prevention of atelectrauma and end-inspiratory overdistension. However, the conditional recommendation for higher PEEP is currently based on individual patient data meta-analysis (IPDMA), which shows lower mortality in subjects with moderate ARDS and no effect on subjects with mild ARDS [26].

On the other hand, higher PEEP levels may result in a higher inspiratory plateau pressure, which presents its own risks and benefits when the plateau pressure reaches 30 cmH_2O or greater.

This study has the following limitations: (1) subjects with moderate *de novo* hypoxaemic respiratory failure had low levels of PEEP; (2) this study was conducted in a single centre; (3) a full face mask was used as the interface — other types of interfaces, such as the helmet system, which reduces the risk of depressurising, could provide different results, especially in subjects with moderate *de novo* hypoxaemic respiratory failure [27]; (4) higher synchronisation data was not available during the study; (5) comparators were not used — our study compared the BiPAP S/T-AVAPS ventilation strategy with others, such as high flow for determinant information in the clinical management of subjects [28]; (6) on the other hand, PaO_2/Fio_2 was used to define the severity of ARDS, which could be questioned by certain authors [29]. As with other ventilatory modes, the use of BiPAP S/T-AVAPS does not reduce the duration of mechanical ventilation or mortality in the ICU. As demonstrated in previous studies, the cause of mortality in subjects with this type of hypoxaemic respiratory failure may be more strongly associated with its initial severity and the development of multiorgan dysfunction as the final determinant of mortality [30].

Although this ventilatory strategy is easy to program and utilise, it is still unknown how BiPAP S/T-AVAPS could induce better protective ventilation by determining better spontaneous ventilation in subjects with mild *de novo* hypoxaemic respiratory failure. On the other hand, high inspiratory pressures and high exhaled tidal volumes could serve as guides in non-responders in order to avoid delays in intubation and higher mortality [31, 32].

More controlled and extensive studies are required to reflect the local experience of using this NIV strategy with BiPAP S/T-AVAPS for a correct evaluation of these results.

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