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Research Article

Noninvasive proportional assist ventilation may be useful in weaning patients who failed spontaneous breathing trial

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KEYWORDS

Noninvasive;
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Abstract *Background:* Endotracheal mechanical ventilation (ETMV) is accompanied with a high morbidity and mortality in intensive care unit (ICU) patients. The aim of this prospective randomized controlled study was to evaluate the effectiveness of noninvasive proportional assist ventilation (PAV) as a method of weaning in patients who could not tolerate spontaneous breathing trial (SBT).

Patients and methods: Among 112 patients presented with acute respiratory failure (ARF) admitted to Zagazig university surgical ICU, 42 patients of them failed a 2 h-SBT after they met simple criteria for weaning. Conventional invasive synchronized intermittent mandatory ventilation (SIMV) was used as the control weaning technique in 21 patients (SIMV group), and noninvasive PAV was applied immediately after extubation in the remaining 21 patients (PAV group).

Results: There was no significant difference regarding the main clinical, functional characteristics, and the physiologic parameters of the two weaning groups at the time of their admission. Gas exchange at 1-h post-randomisation was significantly improved in both groups. The duration of ventilatory support was significantly shorter in the PAV group (12.8 + 8.3 days vs 22.3 + 13.3 days in the conventional group; $P < 0.05$). Weaning success was significantly higher in the PAV group (18 patients"85%" vs 11 patients "52 %" in the conventional group $P < 0.05$). ICU survival was higher, while, reintubation rate was lower in PAV (three patients "14%" vs 10 patients "47%" in

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the conventional group; $P < 0.05$). The rate of tracheostomy was significantly lower in the PAV group (one patient "4%" vs seven patients "33%" in the conventional group; $P < 0.05$). The incidence of VAP was higher in the conventional group (eight patients "38%" vs one patient "4%"in the PAV group; $P < 0.05$).

Conclusion: Noninvasive PAV could be considered as an effective and safe method of weaning in patients who cannot tolerate 2 h-SBT.

1. Introduction

ETMV has been shown to be used successfully in patients presented with respiratory failure. Once the underlying indication of respiratory failure has been reversed, the majority of these patients can be abruptly discontinued after tolerating a 2 h-SBT [1]. However, up to 30% of those patients fail this SBT, denoting difficult weaning [2]. The causes of weaning failure in those populations should be reviewed, corrected, and screening for weanability should be attempted once daily using SBT [1].

However, persistent weaning failure is associated with prolonged MV [3] and increased risk of VAP, prolonged ICU stay, and mortality [4].

Therefore, any intervention aiming at shortening the weaning period should be encouraged.

Prophylactic noninvasive ventilation (NIV) has been used effectively to prevent respiratory failure after tracheal extubation and reduced ICU mortality in patients at risk for postextubation complications [5,6]. However the role of NIV in established postextubation respiratory failure is lacking [7,8].

On the other hand, NIV was used to facilitate weaning of patients who did not tolerate SBT in previous uncontrolled [9–11], and randomized controlled studies [12–15], as well as meta- analysis [16]. Most patients had COPD in these trials. To our knowledge, there is only one study evaluated the role of NIV in patients with respiratory failure due to other causes [17].

Bi-level positive airway pressure (BIPAP) was selected as the noninvasive modality among the majority of these trials. The efficacy of PAV, a relatively recent partial ventilator support mode, in this relatively frequent clinical situation has not been assessed as yet.

The aim of the study was to evaluate noninvasive PAV as a new method of weaning in selected populations of patients who met simple weaning criteria but failed 2 h- SBT. End points of the study were duration of ventilatory support, incidence of VAP, reintubation rate, and 30-day survival rate.

2. Patients and methods

This study included adult patients who were admitted consecutively to our 14-bed surgical ICU from July 2008 to July 2010 and were presented with ARF requiring ETMV for more than 48 h. The study was approved by the local ethical Committee, and written informed consent form was obtained by a family member for each patient.

Patients with facial trauma, recent gastric or esophageal surgery, tracheotomy, excessive respiratory secretion, lack of co-operation, or active upper gastrointestinal bleeding were excluded from the study.

A SBT was initiated once: the patient was afebrile and fully conscious with no need of sedation, and fulfilled the following criteria: reversal or some reversal of the cause of ARF that indicate ventilation support, adequate oxygenation (arterial partial pressure of oxygen (PaO_2) of >60 mm Hg on fraction of inspired oxygen (FiO_2) of $\leqslant 0.4$, and positive end-expiratory pressure (PEEP) of $\leqslant 5$ cm H_2O during pressure support ventilation (PSV) $\leqslant 8$ mm Hg), and hemodynamic stability(systolic blood pressure $\geqslant 90$ mm Hg, heart rate $\leqslant 120$ beats/min without vasopressors). At The end of the first minute of the SBT, patients were screened for readiness to wean using rapid shallow breathing index (RSBI); respiratory rate in 1 min divided by the average tidal volume (VT) in the same minute (R/TV). If it was <105, patients were considered ready to wean and SBT was extended for another 2 h.

If patients tolerate a 2 h SBTs, patients were extubated and excluded from the study. SBT was considered to be failed if: peripheral oxygen saturation (SPO_2) measured by pulse oximetry of $<90\%$ (80% in chronic respiratory failure), respiratory rate (f) $\geqslant 35$ breath/min, heart rate (HR) of >140 or <50 - beats/min (or increase or decrease of $>20\%$ in previous MV), and systolic arterial blood pressure of >180 mm Hg or <70 mm Hg (or increase or decrease of $>20\%$ in previous MV) and RSBI >105 or increased work of breathing suggested by the use of accessory respiratory muscles, paradoxical motion of the abdomen, or retraction of the intercostal spaces.

Patients who failed the SBT were randomally allocated into two groups. Patient in the first group were fully supported through SIMV mode using Servo I ventilator (SIMV group). While patients in the other group were extubated and NIV was established immediately through PAV mode (PAV group). Random assignment was done by using opaque, sealed, numbered envelopes.

In the control SIMV group, ventilatory parameters were adjusted till the previous $PaCO_2$ and pH values were reached within the first 60 min and the respiratory rate was $\leqslant 30$ - breaths/min In the PAV group, both flow and volume assist PAV were adjusted separately using "Runaway" phenomena. Runaway occurs when the pressure applied by the ventilator exceeds the opposing elastic and resistive pressure at the end of patient inspiration, and then flow and volume continue to be delivered by the ventilator during the patient's neural expiration increasing airway pressure during expiration [18–20]. Flow assist (FA) was set at 1 cm H_2O L^{-1} s^{-1} whereas volume assist (VA) was set at 2 cm H_2O L^{-1}, then VA was raised in steps of 2 cm H_2O L^{-1} until the "run-away" phenomenon occurred, then FA was raised in steps of 1 cm H_2O L^{-1} s^{-1} until the "run-away" phenomenon occurred. The values of the FA at the "run-away" minus 1 cm H_2O L^{-1} s^{-1}, and VA at the "run-away" minus 2 cm H_2O L^{-1} were assumed to reflect patients' flow resistances, and volume elastance respectively [21].

NIV was delivered continuously except during meals and for expectoration by means of a prototype portable ventilator (Respironics, Murrysville, PA, USA), through a full face mask (Respironics, Murrysville, PA, USA) with adequate size for each patient. Reintubation was performed immediately if when any of the following events occurred: hypercapnia (arterial pH < 7.35 with an increase in carbon dioxide arterial tension (Pa, CO_2) of > 20% from the time of extubation), hypoxemia (SPO_2 by pulse oximetry of < 90% with FiO_2 of 0.5, decreased consciousness rendering the patient unable to tolerate NIV, clinical signs suggestive of respiratory muscle fatigue and/or increased work of breathing as described above, inability to clear secretions, and severe haemodynamic instability without response to fluids and vasopressors.

Gradual withdrawal of ventilator support was performed in the PAV group, while SBT was done once daily in the conventional weaning group till patients can tolerate spontaneous breathing.

The patient's clinical and demographic characteristics were recorded on admission. The primary evaluation criteria were success of weaning (defined as the absence of reintubation within 3 days after extubation. Duration of MV (from the day of intubation to the day of extubation from the artificial airway before randomization plus weaning duration after randomization in the control group, and before randomization in the PAV group) was also measured. The other evaluation criteria were survival rate at 30 days, and complications related to ETMV and/or weaning procedure as septic shock, pnemothorax, and VAP.

VAP was defined as the presence of a new and persistent (> 48 h) lung infiltrate on chest X-ray combined with at least two of the following conditions: fever, peripheral leukocyte count > 10 000 cells/mm^3, and endotracheal secretion obtained by suctioning from lower respiratory tract in which a Gram stain showed one or more types of bacteria [12].

Tracheotomy was performed 14 days from initiation of ventilatory support according to our ICU protocol.

3. Statistical analysis

Data are presented as mean ± SD or percentage. Comparison of two means was performed using the Student test. Comparison of percentages was performed using the Fisher exact method. P value < 0.05 was considered significant.

4. Results

Throughout the study period, 112 patients required ETMV for more than 48 h in our ICU, 65 patients were candidate for weaning. Twenty-three patients tolerated a SBT and were excluded from the study. The remaining 42 patients failed a 2 h-SBT after they met simple criteria for weaning. These patients were randomized into PAV group (21 patients) and conventional SIMV weaning group (21 patients).

No significant difference regarding the main clinical and functional characteristics of the two weaning groups at the time of their admission (Table 1). There were also no significant differences in the physiologic parameters of patients on the day of randomization between the two groups including the breathing pattern, heart rate, systolic blood pressure, and arterial blood gases (Table 2). Gas exchange variables measured 1-h post randomization were comparable in both groups (Table 3).

Table 1 Patients characteristics.

	PAV group (n = 21)	SIMV group (n = 21)
Age (years)	71 ± 9	70 ± 10
Sex (M/F)	15/5	13/7
APPACHE II on admission	21 ± 5	20 ± 7
APPACHE II on entry into study	13 ± 4	13 ± 5
Indication of MV (n)		
Acute exacerbation of COPD	5	4
Acute pulmonary edema	3	3
Community acquired pnemonia	3	4
Postoperative respiratory failure	4	4
Thoracic trauma	3	1
Postcardiac arrest	1	2
Neuromuscular disorders	2	3

Values are presented as mean ± SD or number (percentage). PAV = Proportional assisted ventilation. SIMV = Synchronized intermittent mandatory ventilation. APACHE-II = Acute physiology and chronic health evaluation-II score.

Compared with the control group, the duration of ventilatory support was shorter in the PAV group (12.8 ± 8.3 days vs 22.3 ± 13.3 days in the conventional group; P = < 0.05). The success rate among patients weaned with invasive SIMV was significantly lower than the rate among patients undergoing noninvasive PAV (11 patients "52%" vs 18 patients "85%" in the PAV group; P < 0.05). The incidence of reintubation was significantly lower in the PAV group (three "14%" patients' vs 10 "47%" patients in the conventional weaning group; P < 0.05). Causes of renitubation were presented in Table 4.

One patient "4%" from the PAV group tracheotomized vs seven "33%" patients in the conventional-weaning group < 0.05). Compared with patients weaned conventionally, mortality rate at 30 days after admission was higher in the PAV group (19 patients' vs 15 patients in the conventional weaning group) (Table 4).

The incidence of VAP was higher in the SIMV weaning group (eight patients "38%" vs one patient "4%" in the PAV group; P < 0.05) (Table 5). The complications related to noninvasive PAV were limited to mild to moderate nasal bridge ulceration occurred in three Patients, and respiratory secretions were difficult to eliminate in two patients.

Table 2 Physiologic parameters at admission.

	PAV group (n = 21)	SIMV group (n = 21)
F (breath/min)	37 ± 8	34 ± 11
Heart rate (beat/min)	112 ± 23	113 ± 26
Systolic blood pressure (mm Hg)	142 ± 28	140 ± 32
Arterial pH	7.26 ± 0.08	7.26 ± 0.09
$PaCO_2$ (mm Hg)	116 ± 66	117 ± 59
PaO_2 (mm Hg)	44.6 ± 9.5	47.0 ± 6.6

Values are presented as mean ± SD. F = Frequency. PAV = Proportional assisted ventilation. SIMV = Synchronized intermittent mandatory ventilation. $PaCO_2$ = arterial carbon dioxide tension. PaO_2 = Arterial oxygen tension.

Table 3 Effects of weaning technique on gas exchange.

	2 h-SBT	1-h Post-randomization
Control group (n = 21)		
PaO_2 (mmHg)	72.27 ± 9.29	88.26 ± 17.22
$PaCO_2$ (mmHg)	56.14 ± 9.33	45 ± 10.90
pH	7.28 ± 0.08	7.36 ± 0.05
PAV group (n = 21)		
PaO_2 (mmHg)	74.37 ± 8.15	89.8 ± 9.92
$PaCO_2$ (mmHg)	55.68 ± 9.84	46.13 ± 11.10
pH	7.24 ± 0.11	7.35 ± 0.10

Values are presented as mean ± SD PAV = proportional assisted ventilation.
2 h-SBT = Gas exchange variables at the end of 2 h-spontaneous breathing trial.
1-h Post-randomization = Gas exchange variable 1-h from randomization in both groups.

5. Discussion

ETMV is considered a live saving intervention for patients treated from respiratory failure; however it is associated with undesirable side effects and life-threatening complications [22].

Our ICU weaning protocol includes daily SBT after testing of patients who met simple weaning criteria for weaning readiness. This daily SBT has been shown to reduce the time spent on MV and the reintubation rate [23]. However, many patients fail these SBTs and suffer difficult weaning. We tested the ability of integrating the role of NIV in our weaning protocol in selected population of these patients.

The most important finding of this study was that, for patients who had no contraindications for NIV and met simple weaning criteria but failed SBT, the combination of earlier tracheal extubation and initiation of noninvasive PAV had been associated with shorter duration of ventilatory support, lower incidence of VAP, and better ICU survival.

The shorter duration of ventilatory support encountered in the PAV group, and weaning process was similar to the studies of Nava et al. [12] and Ferrer et al. [14], however in Girault et al. [13] study, the daily ventilator duration was higher in the NIV and hospital stay was insignificantly different between the two groups that may be explained by the different patient characteristics in the study of Girault that included a higher incidence of chronic patients who in more need for ventilatory support.

Table 4 Weaning outcome variables.

	PAV group (n = 21)	SIMV group (n = 21)
Duration of ventilator support (days)	12.8 ± 8.3	22.3 ± 13.3*
Success rate, n (%)	18 (85%)	11 (52%)*
Reintubation, n (%)	3 (14%)	10 (47%)*
Causes of reintubation (n)		
Severe persistent hypoxemia	0	3
Severe dyspnea	0	3
Inability to manage secretions	2	0
Hemodynamic instability	1	0
Tracheotomy, n (%)	1 (4%)	7 (33%)*
ICU survival at 60 days, n (%)	19	15

Values are presented as mean ± SD or number (percentage). PAV = Proportional assisted ventilation. SIMV = Synchronized intermittent mandatory ventilation.
* $P = < 0.05$.

Table 5 Recorded complications.

	PAV group (n = 21)	SIMV group (n = 21)
VAP	1 (4%)	8 (38%)*
Bed sores	–	2 (9%)
PE	1 (4%)	2 (9%)
GIT bleeding	1 (4%)	2 (9%)
Pneumothorax	–	1 (4%)
Septic shock	1 (4%)	4 (19%)

Values presented as number (percentage). VAP = Ventilator associated pneumonia. GIT = Gastrointestinal. PE = Pulmonary embolism. PAV = Proportional assisted ventilation. SIMV = Synchronized intermittent mandatory ventilation.
* $P = < 0.05$.

Although, previous studies did not recommend the use of NIV to extubate non-COPD patients who fail SBT [24]. In this study, weaning success was significantly higher in noninvasive PAV group patients that was in accordance with Nava et al. [12]. The high success rate of weaning in PAV group could be explained by the well established protocol for NIV in our ICU, and well trained staff in management of this variety of ventilation. However, the main cause of success may be due to the immediate establishment of noninvasive PAV, a relatively recent synchronized partial ventilatory support that generates a proportional pressure to the patient's instantaneous effort [25].

The higher success rate in the PAV group had been associated with improved survival however it was not significant. Both had been attributed to the less incidence of VAP due to limiting the period of invasive ventilation, less incidence of reintubation and tracheostomy in this group.

The better ICU survival in the noninvasive group was in accordance with and Girault et al. [13] and Ferrer et al. [14]. Nava et al. [12] showed no significant differences in the survival between the two groups in their study that may be explained by the insignificant differences in the complications related to ETI and weaning process between the two groups specifically VAP.

The complications encountered in this study are comparable to those of Nava and colleagues [12] and Ferrer and colleagues [14]. The authors in these studies used NIV immediately and continuously after tracheal extubation. On the other hand, Girault and colleagues [13] used intermittent NIV and did not observe any significant differences in the incidence of complications.

Reintubation is a potentially hazardous complication associated with increased morbidity and mortality in mechanically ventilated patients [24].

The incidence of reintubation was significantly lower in the PAV group in the current study; this parameter was studied only in the study of Nava et al. [12]. In their study, there was no significant difference in the incidence of reintubation between noninvasive and conventional groups. The cause may be due to initiation of NIV in the conventional-weaning group if other minor criteria of spontaneous breathing failure occurred.

The higher incidence of VAP in the conventional weaning group in our study was supported by other studies [26,27]. Previous studies showed that complications related to ETMV that prolong ventilatory support are essentially related to

nosocomial pneumonia [2,12]. Moreover, endotracheal tube has been shown to be associated with the development of pneumonia by impairing cough and mucociliary clearance through accumulation of the contaminated oropharyngeal secretions above the cuff and leak around the cuff and promoting their colonization [28]. In addition, with NIV, there is a small possibility of aspiration of colonized oropharyngeal secretions, there is no airway device, and the patient have the ability to expectorate [29].

The risk for feeding aspiration increased also with invasive ventilatory support, Elpern and coworkers [30] showed that feeding aspiration was found in 50% of tracheotomized patients receiving prolonged MV. On the other hand, NIV enables patients to eat avoiding the hazards of food aspiration. In addition, these patients often are not in need for nasogastric enteral feeding that has been correlated with a high incidence of gastroesophageal reflux and aspiration [31–33], a major risk factor for nosocomial pneumonia.

Among the limitations of this study, there was no long-term follow up of both study groups. Cost evaluation was not also included in the trial.

In conclusion, Noninvasive PAV could be added safely and effectively in the MV weaning protocol for patients who meet simple weaning criteria and but failed SBT and have no contraindications to NIV.

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