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A Randomized Controlled Trial to Compare Adaptive Support Ventilation and Pressure Support Ventilation for Weaning COPD Patients

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ABSTRACT
Patients with COPD are frequently hospitalized for acute exacerbations (AECOPD), which may cause respiratory failure. Adaptive support ventilation (ASV) is an automatic system of ventilation, where it determines target minute ventilation based on the principle proposed by Otis et al. Weaning with ASV shows promising results, mainly in post cardiac surgery patients.
Objective: *Our study was designed to compare ASV with PSV in the weaning of AECOPD patients*
Methods: *The study was conducted on 60 mechanically ventilated AECOPD patients admitted to the Department of Critical Care Medicine, at the Alexandria Main University Hospital. Exclusion criteria included those with severe cardiac or neurological disease, those managed by non-invasive ventilation and those on tracheostomy tube. All patients were subjected on admission to complete history taking, complete physical examination and Laboratory investigations and were treated according to guidelines of treatment of AECOPD. At the time of weaning patients were randomly divided into two equal groups; Group A: patients weaned using ASV and Group B: patients weaned using PSV.*
Results: *Weaning duration was significantly shorter with ASV versus PSV [median (IQR) 24 (12-48) h versus 72 (24-144) h, $p < 0.001$]. Success rates were [(93.3%) for ASV and (70%) in PSV group B ($p = 0.042$)]. Length of stay in the ICU was also significantly shorter with ASV ($p = 0.001$).*
Conclusion: *ASV may be used in the weaning of AECOPD patients with the advantage of shorter weaning times and hospital stay.*
Keywords: *Acute exacerbation of COPD, Adaptive support ventilation, Intensive care unit, Pressure support ventilation, Work of breathing, weaning success.*

INTRODUCTION

Patients with COPD are frequently hospitalized for acute exacerbations, most commonly in association with respiratory infections. The effect of these exacerbations on survival is unclear, with estimates varying widely. [1-4]

The Global Initiative for Chronic Obstructive Lung Disease (GOLD) - a report produced by the National Heart, Lung, and Blood Institute (NHLBI) and the (WHO) defines an exacerbation of COPD as an acute increase in symptoms beyond normal day-to-day variation.[5,6]

PSV is commonly utilized and is the sole mode of mechanical ventilation used during the weaning process in, 21% of patients. [7] PSV can be used during a SBT and as a weaning mode. PSV used as the sole mode of mechanical ventilation during initial weaning attempts has been tested in two large randomised controlled trials. The study by

Brochard et al [8] involving 456 randomised patients determined that the use of PSV compared with SIMV and intermittent T-piece trials resulted in shorter duration of weaning. In 130 patients who had failed the initial SBT, Esteban et al [9] reported that either one daily trial or multiple daily trials of unassisted, spontaneous breathing (T-piece) more substantially reduced the duration of weaning than either SIMV or PSV.

Adaptive support ventilation (ASV), first described by Laubscher [10], it relies on closed-loop regulation of settings in response to changes in respiratory mechanics and spontaneous breathing, with wide-ranging, automated, pressure modes from pressure-controlled ventilation to pressure-support ventilation. [11-14]

Some studies have evaluated the use of ASV in weaning cardiac surgery patients and have shown a reduction in weaning time, a reduced need for arterial blood gas (ABG) analyses, and fewer ventilator adjustments. [15-18]

The use of ASV in patients with COPD has been described previously, [19,20] but only one study reported the use of ASV as a weaning mode for chronically ventilated patients, some of whom had COPD. [21]

Our study was therefore designed to compare ASV with PSV in the weaning of AECOPD patients.

MATERIALS AND METHODS

Patients

This randomized controlled study was conducted on 60 mechanically ventilated AECOPD patients who were admitted to the Department of Critical Care Medicine in The Alexandria Main University Hospital. The study was approved by the medical ethics committee of Alexandria faculty of Medicine. An informed consent from patients' next of kin was obtained before enrollment to the study.

Inclusion criteria:

1. A diagnosis of AECOPD. [22]
2. Patients with APACHE II score of 15-30.
3. Patients being on mechanical ventilation for at least 24 hours because of hypoxemic and/or hypercapnic respiratory failure.

Exclusion criteria:

1. Mechanical ventilation for less than 24 hours (including self extubation or death).
2. Patients with a tracheostomy tube.
3. COPD patients with coexisting severe cardiac (except cor pulmonale due to COPD) or neurologic disease as it may prolong weaning for extrapulmonary reasons.
4. Patients managed using non-invasive ventilation before intubation.

Patients of the two groups were treated according to guidelines of treatment of AECOPD. [23-26] All patients were orally intubated and mechanically ventilated using Bi PAP (Duo PAP). Initial settings were as follows: P_{INSP} achieving a tidal volume of 8mL/kg, back-up respiratory rate (RR) 12–14 breaths/min, and positive end-expiratory pressure (PEEP) of 3–5 cmH_2O. Inspiratory oxygen fraction (F_IO_2) was titrated to obtain an arterial oxygen saturation (SaO_2) 90%. Sedation was achieved with midazolam and/or fentanyl.

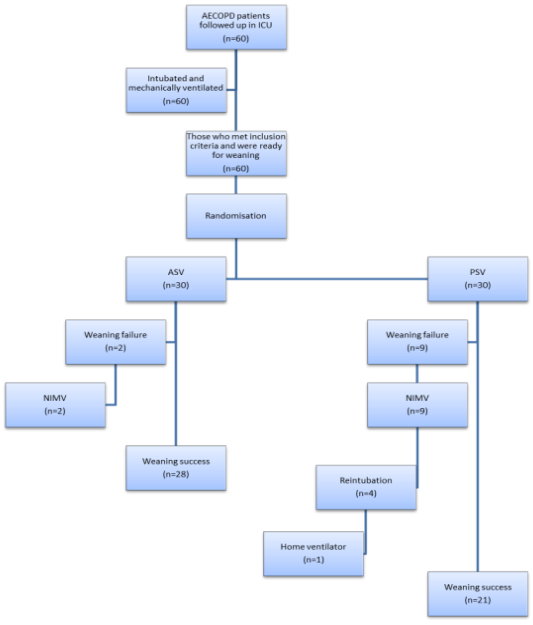

FIGURE 1. Flow chart of patients during the study. AECOPD: Acute exacerbation of chronic obstructive pulmonary disease; ICU: intensive care unit; ASV: adaptive support ventilation;

PSV: pressure support ventilation; NIMV: noninvasive mechanical ventilation.

When weaning from mechanical ventilation was decided, according to weaning criteria as defined as reversing the cause of mechanical ventilation, hemodynamic stability, heart rate < 120, RR < 35, pH >7.35, tidal volume (V_T) > 5ml/kg, minute volume < 10 L/min, PEEP < 5cmH_2O, P_aO_2 > 60 mmHg with F_iO_2<0.4, and P_aO_2/F_iO_2>150 [27,28], the studied patients were randomly enrolled using the sealed envelope method into two equal groups as shown in figure 1.

ASV description

ASV provides automatic ventilation in which minute volume is controlled via a V_T/RR combination based on respiratory mechanics. ASV assumes that the adequate ventilation of normal subjects is 100 ml/min per kg of body weight. In patients unable to trigger a breath, the ventilator generates pressure controlled breaths, automatically adjusting inspiratory pressure and timing to achieve the target V_T and RR. In patients who are able to trigger a breath, the ventilator generates pressure support breaths, automatically adjusting the level of support pressure to achieve the target V_T, and delivers additional pressure-controlled breaths if the patient's RR is below the target RR. The target V_T/RR combination is based on the equation by *Otis et al.* [29], which determines an RR that minimizes work of inspiration for a clinician-set minute volume, based on the time constant of the respiratory system. The time constant is estimated on a breath-by-breath basis by the expiratory time constant (RCexp) obtained from the expiratory flow–volume curve. [30,31]

Weaning protocols

After randomisation, the BiPAP (Duo PAP) mode was stopped and the two weaning modes (ASV and PSV) were allocated randomly using sealed envelopes. Weaning and extubation were performed by the critical care physicians who were working in the ICU.

ASV Group: weaned using ASV present in the Hamilton G-5 ventilator in the following steps: [32]

a) Setting the ideal body weight in Kg.
b) Setting the M_V at 100 ml/kg PBW.
c) ASV detected the patient's effort and automatically weaned the mandatory breath rate when the patient was ready to assume a portion of the V_m requirement through spontaneous breathing independent of the target M_V.
d) If the patient did not have spontaneous breaths, and the ABGs were accepted, reduction of $\%V_m$ by 10 to 20 % will be tried to encourage spontaneous breathing.
e) When extubation criteria were met [33]; Adequate gas exchange [Adequate arterial partial pressure of oxygen: [PaO_2/FIO_2] ratio > 150-200, appropriate pH (pH $\geq$7.25) and arterial partial pressure of carbon dioxide during spontaneous ventilation], RR < 35,Vital capacity > than 10 mL/kg, NIF > -20, Tidal Volume > 5mL/kg, Minute ventilation < 10L/min, Ability to protect airway [Appropriate level of consciousness, adequate airway protective reflexes (cough, swallow, vocal cord movement), adequate managed secretions], Hemodynamic stability, Nutritional status allowing for respiratory muscle strength, extubation was attempted directly without SBT.

PSV Group: weaned using PSV in the following steps: [34]

a) Starting at maximum PSV level (level that attains RR <20 with V_T of 8 ml/kg).
b) Decrease PSV by 5 cmH_2O.
c) If no signs of intolerance were evident for 4 hours trial, the PSV was decreased by another 5 cmH_2O for another 4 hours.
d) With any signs of intolerance, defined as RR > 35, S_aO_2<90%, HR >140, systolic BP >180 or <90 mmHg, anxiety and diaphoresis, the patient was returned to the previous level for the next 4 hours.

e) If unable to tolerate, the patient was fully rested until the next day when the process began again.
f) Once the patient was able to sustain 7 cmH_2O PSV without signs of intolerance for 4 hours, extubation was attempted.

Post-extubation failure occurring within the first 48 h was defined as pH < 7.35, an increase in arterial carbon dioxide tension of 15 mmHg from the value just prior to extubation, RR 24 breaths/min and accessory muscle use. NIMV trial with a full face mask was performed in these patients using the same ventilator in NIMV mode to avert re-intubation. [35-37] Patients who could not tolerate NIMV or showed impairment in their clinical status (unable to protect airway, inability to remove secretions, cardiac instability or loss of consciousness) or blood gas analysis (pH < 7.25 and PaO_2, 60 mmHg while receiving NIMV) were re-intubated. These patients were considered as having failed weaning irrespective of their outcomes using NIMV.

Outcomes and definitions

Weaning duration was the primary outcome, defined as the time from randomisation to extubation. Weaning success was defined as independence from mechanical ventilation (invasive or noninvasive) ≥ 48 h after extubation. Secondary outcomes were duration of mechanical ventilation and length of stay (LOS) in the ICU and the hospital. Duration of mechanical ventilation was defined as the time from the initiation of mechanical ventilation support to the permanent cessation of any form of ventilatory support (invasive or noninvasive). Duration of IMV before was defined as the time of IMV from intubation to the time of randomisation. LOS in the ICU was defined as the time from admission to the ICU until discharge or death.

Statistical Analysis: [38]

A sample size of 30 patients per each group was calculated using Medcalc program version 8.1.0.0 at a power of > 80 % and level of significance (***p***) of 0.05. Data were analyzed using SPSS software package version 18.0 (SPSS, Chicago, IL, USA). Quantitative data were expressed using median and Interquartile range (IQR), while Qualitative data were expressed in frequency and percent. Qualitative data were analyzed using Chi-square test also exact tests such as Fisher exact was applied to compare the two groups. Not normally distributed quantitative data was analyzed using Mann Whitney test for comparing the two groups. Pearson coefficient was used to analyze correlation between any two variables. A ***p***-value of ≤ 0.05 was considered significant.

RESULTS

The ASV and PSV groups were demographically similar at the time of randomisation. Factors that could affect weaning, such as the severity of patients assessed by APACHE II score, need of sedation and respiratory parameters, were also comparable between the two groups (table 1). Both groups were similar as regards arterial blood gases before extubation (table 2).

As regards the outcome measures in this study, success rate was (93%) with two cases (6.7%) of weaning failure in ASV group, while the success rate was (70%) with nine cases (30%) of weaning failure in PSV group B (p = 0.042) (table 3). Two patients in the ASV group and nine in the PSV group could not tolerate extubation and received NIMV. Four patients in the PSV needed reintubation and one of them was discharged later on with a home ventilator.

Weaning duration was significantly shorter with ASV versus PSV [median (IQR) 24 (12-48) h versus 72 (24-144) h, p < 0.001].

TABLE 1 Baseline characteristic data before randomisation

	ASV	PSV	p-value
Subject n	30	30	1
Age yrs	55 (49-74)	61 (50-73)	0.05
Males	25 (83.3)	24 (80)	0.73
APACHE II	20.5 (15-30)	23.5 (19-30)	0.08
pH	7.4 (7.35-7.41)	7.4 (7.36-7.41)	0.16
$PaCO_2$ mmHg	55 (34-58)	55 (36-60)	0.67
HCO_3 mEq/L	32 (23-40)	30 (22-39)	0.62
PaO_2/FiO_2	221 (177-406)	235 (177-406)	0.75
Duration of MV before randomisation h	36 (24-120)	48 (24-120)	0.09
Patients needing sedation before randomisation n (%)	10 (33.3)	10 (33.3)	1

Data are presented as median (interquartile range) or n (%), unless otherwise stated. ASV: adaptive support ventilation; PSV: pressure support ventilation; APACHE: Acute Physiology and Chronic Health Evaluation; $PaCO_2$: arterial carbon dioxide tension; HCO_3: bicarbonate level; PaO_2/FiO_2: arterial oxygen tension/inspiratory oxygen fraction; MV: mechanical ventilation.

Weaning duration for the two groups expressed as Kaplan– Meier curves are shown in figure 2. Total duration of mechanical ventilation was significantly shorter with ASV versus PSV [median (IQR) 50 (36-168) h versus 120 (48-192) h, p < 0.001]. LOS in the ICU was also shorter with ASV compared with PSV [median (IQR) 4 (2.5-9) days versus 6 (3-11) days, p < 0.001]. LOS in the hospital was also shorter with ASV compared with PSV [median (IQR) 5 (3-9) days versus 8 (4-12) days, p < 0.001] (table 3).

TABLE 2 Arterial blood gases before extubation

	ASV	PSV	p-value
Subject n	30	30	1
pH	7.4 (7.35-7.51)	7.38 (7.35-7.5)	0.38
$PaCO_2$ mmHg	49 (36-62)	55 (43-69)	0.22
HCO_3 mEq/L	35 (22-43)	36.5 (31-45)	0.08
SaO_2 %	96 (91-98)	96 (94-99.5)	0.46
PaO_2/FiO_2	238 (153-406)	227 (194-457)	0.32

Data are presented as median (interquartile range) or n (%), unless otherwise stated. ASV: adaptive support ventilation; PSV: pressure support ventilation; $PaCO_2$: arterial carbon dioxide tension; HCO_3: bicarbonate level; SaO_2: arterial oxygen saturation; PaO_2/FiO_2: arterial oxygen tension/inspiratory oxygen fraction.

TABLE 3 Comparison of ASV and PSV groups

Outcomes	ASV	PSV	p-value
Subject n	30	30	1
Weaning duration h	24 (12-48)	72 (24-144)	**0.001**
Weaning failure	2 (6.7)	9 (30)	**0.042**
Duration of MV h	60 (36-168)	120 (48-192)	**0.001**
LOS in ICU days	4 (2.5-9)	6 (3-11)	**0.001**
LOS in hospital days	5 (3-9)	8 (4-12)	**0.001**

Data are presented as median (interquartile range) or n (%), unless otherwise stated. ASV: adaptive support ventilation; PSV: pressure support ventilation; MV: mechanical ventilation; LOS: length of stay; ICU: intensive care unit.

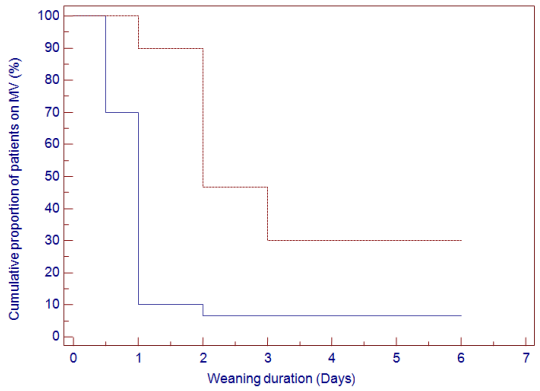

FIGURE 2. Duration of weaning expressed as a Kaplan–Meier curve in the adaptive support ventilation (——) and pressure support ventilation (------) groups. MV: mechanical ventilation. Log rank test, p = 0.001.

DISCUSSION

The major finding of this study was that, when compared with PSV in the weaning process of COPD patients, ASV was associated with a shorter weaning duration.

With similar results, Kirakli et al [39] reported a significant shorter duration of weaning with ASV than PSV in AECOPD patients [median (IQR) 24 (20-62) h versus 72 (24-144) h, p = 0.041]. ICU stay was also shorter in ASV group [median (IQR) 11 (6-15) days versus 13 (8-14) days, p = 0.5] but this difference was not statistically significant, while results from our study had significantly shorter LOS in ICU [median (IQR) 4 (2.5-9) days versus 6 (3-11) days, p < 0.001].

Of the few studies evaluating ASV in weaning, most were performed in post-cardiac surgery patients where the mean extubation time was < 6 h.

Sulzer et al [15] reported shorter duration of intubation and mechanical ventilation with ASV than synchronized intermittent mandatory ventilation (SIMV) in post-operative coronary bypass patients. Cassina et al [40] used ASV when weaning 155 cardiac surgery patients; 86% were extubated within 6 h and the mean time to extubation was 3.6 h. In a randomised controlled trial, Petter et al [16] compared ASV with SIMV+PSV when weaning 45 cardiac surgery patients and found that the duration of mechanical ventilation and the need for changing the ventilator settings were reduced with ASV. These findings suggest that ASV could be used for fast and early extubation after post-cardiac surgery. However, none of these studies included COPD patients.

Randomised controlled studies and subsequent meta-analysis indicated that spontaneous breathing trial (SBT) with T-piece or PSV are equally effective and both superior to SIMV, depending in the most part on the experience of the staff with a particular method [8,9,41,42]. Tassaux et al [19] compared ASV and SIMV+PSV patient ventilator interactions in ten patients, three of whom had acute exacerbations of COPD; they concluded that ASV could provide the same

minute ventilation with less muscle load and patient-ventilator dyssynchrony when compared with SIMV+PSV. In addition, similar levels of minute ventilation and V_T (mL)/patients (kg) ratio were achieved with ASV.

Esteban et al [43] reported weaning success rates of 70% for PSV and 63% for SBT. Their study was performed on a heterogeneous population, but 20% of the patients enrolled had COPD. Our study found weaning success rates of 93.3% and 70% for ASV and PSA respectively, similar to those in the literature.

Limitations of the study

Some studies concerning the weaning procedures suggested that SBT's with T-piece were superior to SIMV and PSV [9], while others showed that gradual reduction of pressure support was superior in patients who failed a 2-h SBT with T-piece [8]. Further studies are needed to assess the feasibility of ASV in difficult to wean patients who fail SBTs with a T-piece.

Patients with previous use of NIMV were not included in the study. However, in most situations, most patients with AECOPD are intubated after failure of NIMV. This limits the generalization of the results to all intubated patients with AECOPD.

This single centre study reflects experience of a single ICU. With 30 patients in each group we were able to detect a reduction of 1.78 days in the weaning duration ($p < 0.001$). Multicentric, higher powered studies with large sample sizes could more accurately assess the generalizability of these results to different centers and patient populations.

The lack of ICU staff prevented us from recording the number of interventions and ABG sampling needed for each group. Further studies are needed to determine the other potential benefits of ASV as patient comfort and respiratory mechanics, such as work of breathing and pressure time product with different weaning modes.

CONCLUSIONS

In light of our results we recommend that ASV may be used as a weaning mode in mechanically ventilated AECOPD patients, with the advantage of shorter weaning duration. Further studies with large sample sizes are needed to investigate the potential advantages of this mode in the weaning period and ICU stay of different patient groups.

STATEMENT OF INTEREST

None declared.

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