Pressure vs. volume control in COPD patients intubated due to ARF: A case-control study

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ÖZET

Akut solunum yetmezliğine bağlı entübe edilen KOAH hastalarında basınç ve volüm kontrollü ventilasyonun karşılaştırılması: Olgu-kontrol çalışması

Bu çalışmada, kronik obstrüktif akciğer hastalığı (KOAH) olan hastalarda başlangıç modu olarak volüm (VCV) ve basınç kontrollü ventilasyon (PCV)'un karşılaştırılması amaçlanmıştır. Bir vaka-kontrol çalışması olan bu çalışma Ocak 2002-Ocak 2004 tarihleri arasında solunumsal yoğun bakım ünitesi (YBÜ)'nde yapılmıştır. Akut solunum yetmezliği (ASY) olan 20 KOAH hastasına, 24 saatten fazla PCV uygulanmıştır. Bu hastalara, yaş, cinsiyet, solunumsal YBÜ'ye girişteki "Acute Physiology Assessment and Chronic Health Evaluation (APACHE)-II" skoru, pH ve $PaCO_2$ değerlerine benzer VCV uygulanan KOAH hastalarından kontrol grubu oluşturulmuştur. Her iki grubun eşleştirilme etkinliği %99 idi. Gruplar, komplikasyon gelişme ve mortalite oranı, toplam invaziv mekanik ventilasyon ve solunumsal YBÜ'de kalış süreleri bakımından karşılaştırılmıştır. Mortalite ve komplikasyon oranı ve solunumsal YBÜ'de kalış süresi bakımından gruplar benzerdi, fakat PCV grubunun ortalama mekanik ventilasyon süresi anlamlı derecede uzundu (198 ± 177 saat ve 79 ± 56 saat, p< 0.003). PCV grubunun "weaning" dönemi anlamlı olarak daha uzun saat bulundu (138.6 ± 164 vs. 34 ± 33 saat, p< 0.01), "weaning" öncesi dönem ise her iki grupta benzerdi. Verilerimize göre ASY olan KOAH hastalarında, her iki ventilasyon yöntemi uygulandığında sonuçlarının benzer olabileceği öngörülmüştür. Sonuçlarımızın desteklenmesi için randomize kontrollü çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: *ASY olan KOAH, mekanik ventilasyon modları, noninvaziv ventilasyon, invaziv ventilasyon, yoğun bakım.*

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SUMMARY

Pressure vs. volume control in COPD patients intubated due to ARF: A case-control study

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To compare volume- and pressure- controlled ventilation (VCV-PCV) as an initial ventilatory mode in chronic obstructive pulmonary disease (COPD) patients. Case-control study conducted in respiratory intensive care unit (RICU) at a large teaching hospital, between January 2002 and January 2004. PCV was applied in 20 COPD patients with ARF more than 24 hours. Their outcomes were compared with those of a control group of 20 COPD patients matched on age, sex, Acute Physiology Assessment and Chronic Health Evaluation (APACHE) II score, pH and $PaCO_2$ at the time of intubation previously treated with VCV. The effectiveness of matching was 99%. Groups were compared according to complication and mortality rates, total duration of invasive mechanical ventilation (IMV) and length of RICU stay. Mortality and complication rates, and length of RICU stay were similar in groups but, the mean duration of MV was longer in PCV (198 ± 177 h vs. 79 ± 56 h, p< 0.003). PCV group spended significantly longer IMV hours for weaning period (138.6 ± 164 vs. 34 ± 33 h, p< 0.01), pre-weaning periods of IMV were found similar. These data suggest that both ventilatory approach have similar outcomes in COPD patients with ARF. Randomize-controlled trials are needed to confirm our results.

Key Words: *COPD with ARF, mechanical ventilation mods, noninvasive ventilation, invasive ventilation, intensive care.*

Non-invasive positive pressure ventilation (NPPV) is recommended as a first-line intervention in these group patients (1-8). However, invasive mechanical ventilation (IMV) is still viable in the cases with NPPV failure or intolerance, or presence of contraindication for NPPV. The optimum ventilatory mode in patients with chronic obstructive pulmonary disease (COPD) received IMV is not well established. Volume-controlled ventilation (VCV) and pressure-controlled ventilation (PCV) have some advantages and disadvantages in COPD patients with regard to measured cardiorespiratory variables (pulmonary mechanics, gas exchange, and hemodynamics), work of breathing (WOB), and outcome (9-13). Theorically, control of pressure variable by choosing PCV is anticipated to be more beneficial in COPD patients because of, in any case, they have high airway pressure due to bronchoconstriction and airway secretions. Although PCV is thought to be more beneficial in COPD patients, there is no well-organized study in English literature that support this idea. Previously, we performed a retrospective observational study comparing COPD patients according to using initial IMV mode, either PCV or VCV, presented at European Respiratory Society (ERS) Glasgow Congress in 2004 (14). To eliminate the conflicting factors, we decided to reevaluate all cases as a case-control study. The aim of this study was to assess whether there were differences in outcomes, duration of IMV, lenght of respiratory intensive care unit (RICU) stay, complication and survival rates that could be affected with the different ventilatory modes.

MATERIALS and METHODS

Design and Setting

Case-control study conducted in RICU at a large teaching hospital, between January 2002 and January 2004.

Definitions

Cases (PCV group): Patients were admitted to the RICU according to the following inclusion criteria: presence of COPD, presence of ARF,

and the need for invasive mechanical ventilation more than 24 hour. COPD was previously diagnosed on the basis of the clinical history, physical examination, and the findings of the chest radiograph. Additional information was obtained from previous pulmonary function tests when available within 12 months before patients admitted to RICU.

Control subjects (VCV group): Sixty COPD patients with ARF previously intubated and treated more than 24 hour in our RICU who had similar baseline characteristics to those of a patient in the PCV group (ie, a case). The variables used for matching:

1. Sex,

2. Age (± 5 years),

3. Acute Physiology Assessment and Chronic Health Evaluation (APACHE) II score calculated within 24 hours just before intubation (± 5 points) (15),

4. pH just before intubation (± 0.03), and

5. $PaCO_2$ just before intubation (± 6 mmHg). The comparability of the 2 groups was further evaluated on the basis of the following data at hospital admission:

- APACHE II score at RICU admission,
- ABG,
- Hematocrite (Hct) levels,
- WBC count,
- Platelet (PLT) count,
- Serum albumine levels,
- Serum urea levels,
- Serum creatinin levels,
- Serum electrolytes levels.

Ventilatory Management

NPPV with a full-face mask was applied as the first-line intervention in 15 (70%) patients in VCV and 14 (75%) in PCV group who had no contraindication for NPPV. Endotracheal intubation (ETI) was underwent after NPPV failured in these 29 patients, and immediately on RICU admission in 11 patients had contraindication for NPPV (respiratory arrest). All patients received assist-control (A/C) ventilation initially. Decision of the initial control variable: in 2002 and in 2003, we chosed VCV because of it was more familiar to us; as our practice increased with PCV, especially using it in some acute respiratory distress syndrome (ARDS) and asthmatic patients, we chosed PCV on the last year (in 2004). The ventilatory management protocol: initial ventilator management and weaning protocol were summurized in Figure 1. In the beginning of A/C mode, in VCV group, respiratory rate: 12-14 breaths/min, moderate tidal volume (Vt) (6-8 mL/kg) and decelerating high flow pattern (60-80 L/min) were used. The A/C mode of PCV group: respiratory rate 12-14 breaths/min, inspiratory pressure (Pi) was set to acchieve Vt 6-8 mL/kg (Pi < than 30 cmH_2O. The ratio of inspiratory and expiratory times (I:E) was between 1:3 to 1:4. The acceptable levels for patient's peak airway and plateau pressures were < 40 cmH_2O and < 35 cmH_2O, respectively for VCV and PCV groups. PEEP setting was performed 2/3 of Auto PEEP of patients. The mean value of PEEP was 5-7 cmH_2O for all patients. According to the achievement values in Figure 1 extubation criterias as follows (16):

1. Fully control of underlying cause of ARF,

2. Full consciousness and cooperation,

3. Hemodynamic stability,

4. Reduction in the amount and purulence of tracheal secretions,

5. Presence of cough reflex during endotracheal aspiration,

6. An arterial oxygen saturation > 90% at a FiO_2 ≤ 0.40,

7. A hemoglobine level > 10 g/dL,

8. A core temperature < 38°C, and

9. The spontaneous rapid shallow breathing index [f/Vt, measured according to the method of Yang and Tobin (17)] < 105. Weaning duration (WD) was defined as the time (hours) from the start of weaning mode to extubation. NPPV was administered if a patient had signs of poor tole-

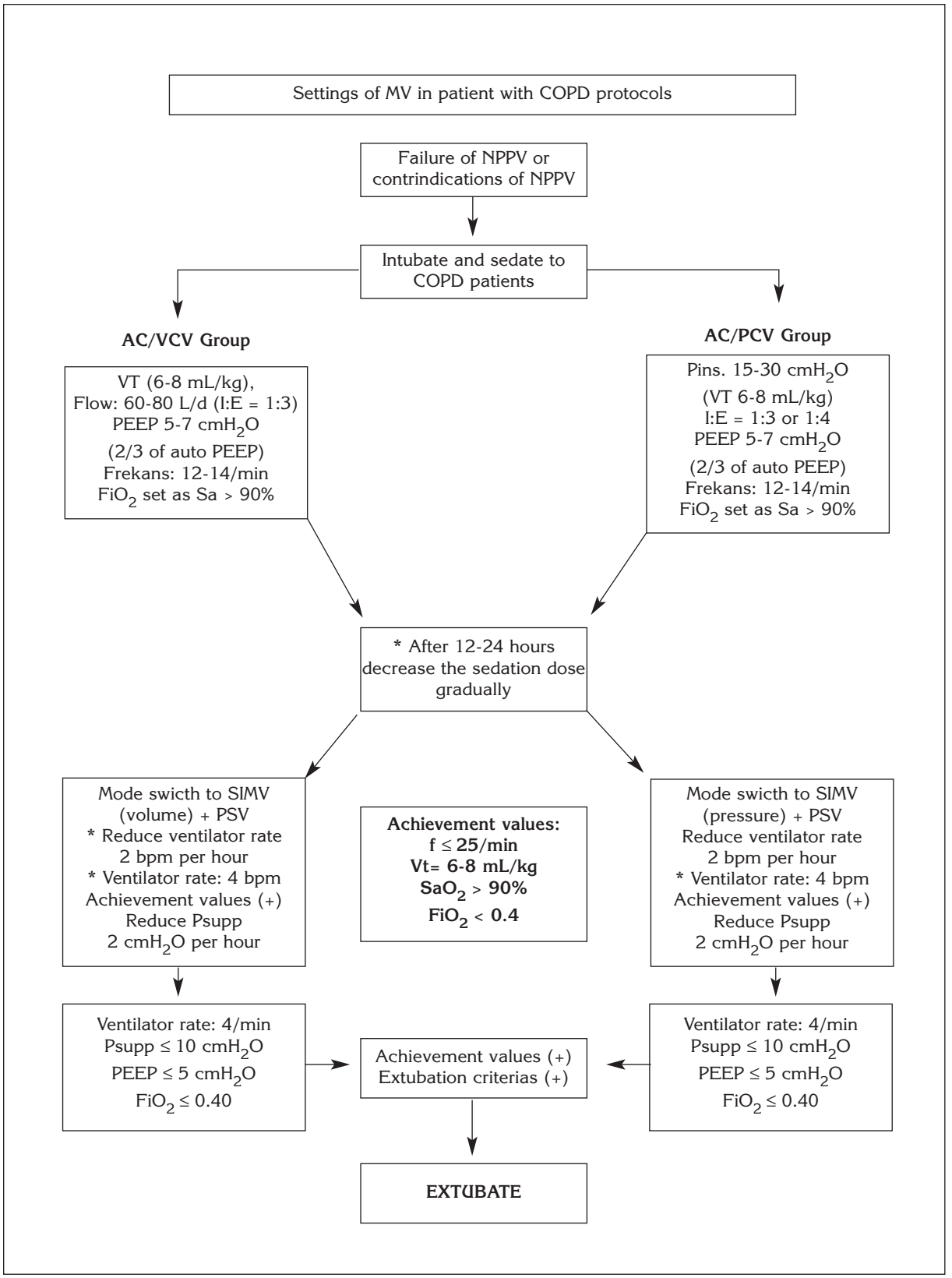

Figure 1. There was a mechanical ventilation protocol for COPD patients, written by the RICU staff physicians, and all the doctors involved in the treatment of study population act in the same way.

rance (respiratory distress, decrease in oxygen saturation or a tendency for acidosis in blood gases despite of the optimum medical treatment) at any time following extubation.

Sedation protocol: Continuous midazolam infusion (0.15-0.3 mg/kg/hour) to prevent patient-ventilator interaction and to allow the presence of endotracheal tube was given. During the first 24 hours, the rate of infusion was titrated to obtain deep sedation adequate to suppress spontaneous respiration. After the first 24 hours, to achieve the lowest midazolam dose providing comfort and cooperation for the patient, and facilitating invasive procedures, nursing care, the dose was reduced in 2 mg steps per hour. Fentanyl citrate (bolus or infusion) was given in 16 subjects for whom respiration was not suppressed despite the highest dose of midazolam, and neuromuscular blokcage (vecuronium bromide, bolus) was performed at a dose of 0.05 to 0.1 mg/kg in 2 subjects with patient-ventilator asynchrony or uncontrolled airway pressure.

Medical management: The standard treatment for an acute COPD exacerbation including bronchodilators, systemic steroids, antibiotics and diuretics as necessary was administered (18). Inhaled β_2-agonists as salbutamol was used with metered-dose inhaler (MDI) with a chamber device placed into the ventilator circuit. Dose and intervals of salbutamol was adjusted according to the patient's airway pressures and oscultation findings. Intravenous methylprednisolone (1-2 mg/kg/day) was administered to all patients at the first 3 days, than it was tapered gradually. Theophylline was administered intravenously 5-6 mg/kg over 20-30 min, followed by a continuous infusion of 0.6 mg/kg/hour.

Definitions of the Study End Points

Primary end points: 1. RICU mortality rate; and 2. complications (ie, ventilator associated pneumonia (16), pneumothorax, etc.).

Secondary end points: 1. Duration of IMV, and 2. lenght of RICU stay.

Statistics

Continuous variables were compared using paired sample Student's t test for normally distributed variables. A χ^2 test was used to analyze dischotomous variables and Fisher's exact test was used when the number of case less than 5. The difference is significant when the $p< 0.05$.

RESULTS

Patients Included in the Study

During the study period 144, 60 COPD patients admitted to our RICU were applied IMV at least 24 h. Out of 60, 20 pairs met the inclusion criteria and were therefore evaluated. The locations of the patients prior to admission to the RICU were the emergency department (PCV group, 9 patients and VCV group, 8 patients) and medical ward (PCV group, 11 patients and VCV group, 12 patients).

Effectiveness of Matching

In the matched groups, the overall effectiveness of matching for the variables used for matching was 99% (Table 1,2).

Table 1. Results of matching patients in the PCV group with patients in the VCV group using four criteria.

Criteria	Matched patients Case (PCV)/Control (VCV)	%
Sex	20/20	100
Age (± 5 yr)	20/20	100
APACHE II score (± 5)	20/20	100
pH (± 0.03)	20/19	95
$PaCO_2$ at the intubation (± 6)	20/20	100
Effectiveness of matching		99

Table 2. Matching variables*.

	Cases PCV group (n= 20)	Controls VCV group (n= 20)
Sex (F/M)	1/19	1/19
Age (year)	61.8 (9.3)	60.4 (8.8)
APACHE II	20.6 (4.0)	22.3 (4.9)
pH	7.230 (0.064)	7.234 (0.052)
$PaCO_2$ (mmHg)	92.1 (15.9)	93.7 (16.3)

* Values given as mean (SD).

Table 3. Comparison of unmatched criteria*.

	Case: PCV group	Control: VCV group	p value
COPD duration, y	10.9 (5.0)	10.1 (6.7)	0.6
Smoking status, pac/y	46.8 (23.2)	66.5 (39.8)	0.1
Comorbidity, n (%)	12 (60)	14 (70)	0.1
Cor pulmonale, n (%)	9 (45)	8 (40)	0.5
FVC, % predicted	50 (17)	44 (17)	0.1
FEV_1, mL	990 (437)	896 (360)	0.6
FEV_1/FVC	49 (10)	54 (10)	0.3
LTOT	10	12	0.52
Home-vent	3	5	0.3
NPPV case number (%)	14 (70)	15 (75)	0.9
NPPV duration, h	8.9 (15.4)	6.4 (10.1)	0.6
APACHE II** score	20.5 (4.1)	19.8 (3.5)	0.4
APACHE II*** score	11.1 (4.1)	11.4 (3.1)	0.8
pH**	7.229 (0.078)	7.255 (0.074)	0.2
$PaCO_2$**	86.3 (20.2)	97.3 (25.2)	0.2
PaO_2/FiO_2**	262.9 (116.8)	217.6 (85.7)	0.1
HCO_3**	37.2 (8.6)	43.4 (8.3)	0.012
pH***	7.444 (0.054)	7.408 (0.033)	0.044
$PaCO_2$***	50.0 (10.0)	61.4 (11.1)	0.023
PaO_2/FiO_2***	233.3 (47.2)	260.2 (66.4)	0.1
HCO_3***	34.9 (5.6)	38.9 (4.7)	0.08
GCS**	12.1 (3.3)	12.7 (2.1)	0.4
WBC**	17055 (8155)	15465 (6977)	0.4
HCT**	41.0 (6.3)	43.5 (6.2)	0.2
PLT**	248052 (110311)	249157 (125365)	0.9
Albumin**	3.4 (0.7)	3.3 (0.7)	0.8
Urea**	60.1 (30.3)	61.3 (47.4)	0.9
Creatinine**	0.8 (0.4)	1.3 (1.3)	0.1
Sodium**	137.4 (3.8)	139.7 (6.3)	0.2
Potassium**	4.5 (0.5)	4.7 (0.6)	0.1
Sedation features			
Total dose of midazolam, mg	1149.4 (1447.1)	586.0 (611.2)	0.049
Duration of midazolam, h	91.6 (117.8)	46.9 (45.9)	0.06
Fentanylcitrate administration, n	10 patients	4 patients	0.047
Systemic steroid dose, mg	636.5 (462.6)	427.0 (324.1)	0.08

* Values given as mean (SD), p> 0.05: Statisticaly non-significant.
** On admission to RICU.
*** At the time of discharge from RICU.
COPD: Chronic obstructive pulmonary disease, RICU: Respiratory intensive care unit.

Table 4. Comparison of the groups according to outcome*.

	PCV	VCV	p values
Mortality, n (%)	5 (25)	3 (15)	0.69
Predicted mortality rate, %	27	30.6	0.60
Complication rate, n (%)	9 (45)	7 (35)	0.37
Complications**			
VAP, n (%)	9 (45)	6 (30)	0.38
MOF, n (%)	6 (30)	3 (15)	0.22
Pneumothorax (%)	0	1(5)	0.90
Lower GI hemorrhage	1(5)	1(5)	1
Total IMV duration, h	197.9 (176.9)	79.2 (56.3)	0.003
A/C period, h	60.3 (44.4)	47.5 (41.6)	0.3
Weaning period, h	138.6 (163.8)	34.2 (33.1)	0.01
MV free days	2.5 (2.6)	3.8 (6.0)	0.4
Length of RICU stay, d	11.0 (7.4)	9.9 (7.4)	0.5

* Values given as mean (SD), p> 0.05: Non-significant.

** One patient have more than one complication.

The comparability of the 2 groups also was assesed by comparing some other criteria that further evaluated the severity of ARF at RICU admission and the level of cronic respiratory failure (Table 3). There was a significant difference between the groups in following variables during RICU discharge: pH, $PaCO_2$, and HCO_3 (p= 0.023, p= 0.044 and p= 0.012, respectively). Pulmonary functions were similar in both groups.

In Table 3, medical treatment features of the groups were also summarized. In PCV group, the patients required higher doses of midazolam (p= 0.049), and more patients needed fentanil sitrate administration significantly (p< 0.047). The total corticosteroid doses were similar in both groups (Table 3).

Primary End Points

1. Mortality: Overall mortality rate was 20% (8/40). Both group have similar mortality rate and have lesser mortality rate than predicted mortality rate according to APACHE II scores (Table 4). Sixteen pairs of patients had concordant outcomes (14 surviving pairs and 2 non-surviving pairs), leaving 4 pairs with disconcordant outcomes.

Among the 5 patients in PCV group who died, one had lower gastrointestinal hemorrhage, four patients had sepsis and more than 3 organ system failure. And among three patients of VCV group who died, one had lower gastrointestinal hemorrhage with MOF and other two patients had MOF.

2. Complications: Overall complication rate was 40% (13/40). The complication rates for PCV and VCV were 45% and 35% respectively (p> 0.05). Complications were recorded as VAP, MOF, pneumothorax, lower gastrointestinal hemorrhage (Table 4) (16).

Secondary End Points

1. Duration of mechanical ventilation: The total duration of mechanical ventilation was significantly lower in the VCV group (median, 53 h; range, 25 to 195 h) than in the PCV group (median, 124 h; range, 67 to 862 h) (p< 0.003). The median duration of A/C period in PCV group was 49 h (range, 17 to 190 h), and in VCV group, it was 30 h (range, 1 to 153 h) (p= 0.32). However the median duration of weaning period was 64 h (range, 8 to 672 h) in PCV group, and for VCV group it was 23 h (range, 0 to 117 h) (p< 0.01). The difference in the 15 surviving pairs was statisticaly significant (p< 0.002).

2. Lenght of RICU stay: The median lenght of stay in the RICU for patients in PCV group who survived was 8 days (range, 4 to 36 days), and the median lenght of stay of patients in the VCV group was 5 days (range, 2 to 26 days).

DISCUSSION

The main finding of this study is demonstration of similar mortality rate between COPD patients, intubated and treated with PCV and those treated with VCV after failured initial NPPV or contrindication of NPPV.

Case-Control Matching

To our knowledge, this is the first case-control study emphasizing ventilatory approach of COPD patients with ARF according to the initial IMV mode either VCV or PCV. A crucial factor for the validity of this study is the success in matching patients of the PCV group with those of the VCV group for important confounding variables. These variables were significantly related to outcome in COPD patients admitted to an ICU for ARF: age, gender, pH at the time of intubation, $PaCO_2$ at the time of intubation, and APACHE II score (20-24). The overall effectiveness of matching for these variables reached 99%. And the case patients (PCV group) were similar to control subjects (VCV group) not only in terms of the variables defined in the matching process but also in terms of further historical clinical-physiological data. It means that, many important confounding factors were similar in both group, in another words, the only difference in both group was initial MV mode. Both groups had similar auto PEEP, respiratory rate, flow rate (in VCV), I:E ratio, plato pressure and peak airway pressure at the initial A/C mode (Figure 1). Although, HCO_3 levels at RICU admission to the RICU, were significantly lower in the PCV group, it seemed to be ARF was more acute in PCV group but both groups had higher HCO_3 levels than normal.

A few studies comparing VCV and PCV modes in COPD were done only in patients with CRF rather than ARF. Schönhofer et al. Were found that PCV could maintained stability most of the patients with CRF after initial treatment with VCV (25). In the present study, overall mortality rate was similar to the other studies evaluating outcomes of COPD patients with ARF (26,27). And also our mortality rate was lower than adjusted predicted mortality rates according to APACHE II scores in both groups. Furthermore, 16 pairs of patients had concordant outcomes (14 surviving pairs and 2 non-surviving pairs), other 4 pairs had disconcordant outcomes.Our overall complication rate was 40% and both groups had similar complication rates.

Mechanical Ventilation

The duration of total ventilatory support was found significantly higher in PCV group. Although pre-weaning period had similar in both groups, weaning period was significantly longer in PCV. Sedation doses required in the patients of PCV group might be accused to longer MV duration (28). Tapering the dose of sedatives was more difficult and took longer time during the weaning period in PCV because of patients intolerance (patient with agitate and panic attack mostly in PCV group by chance).

In a review evaluating ventilatory approach in COPD patients, Davidson suggested that PCV might be more helpful for ventilation rather than VCV (9). Because PCV is more similar to normal breathing pattern, and VCV has a potential risk for patients in whom high PIP is avoided (9). Campbell and Davis emphasized that PCV offers no advantage over VCV in patients who are not breathing spontaneously, but they suggested that PCV might offer lower WOB and improve comfort for patients with increased respiratory demand (13). Cinella et al. Compared the effects on the respiratory work rate assisted ventilation. They found no difference in both ventilation modes with high VT, but with moderate VT together with decelerating high flow pattern, PCV was shown to achieve lower levels of transdiaphragmatic pressure and work of breathing (10). Chiumello et al. Studied to verify that the patient-ventilator interaction is similar regardless of mode of assisted mechanical ventilation either pressure or volume limited used (11). They reported that during assist control, tidal volume and peak inspiratory flow (set by the physician) are the main determinants of the pa-

tient/ventilator interaction. In our study, decelerating high flow pattern and moderate VT were applied. As a conclusion, these few studies comparing 2 modes, emphysized that both is possible if physician are carefull setting flow in VCV and setting I:E ratio in PCV mode, especially spontaneous breathing patients. These studies were done heterogeneous patients group. There is no any case control or randomized-controlled study to compare MV modes in COPD patients in English Literature as far as we know. This study is important for first case-control study comparing two modes in homogeneous patients group (COPD). Due to absence of ventilator monitors, we were not able to compare the wave forms making the point of these strategies.

In conclusion, after failured initial NPPV, invasive mechanical ventilation is intractable in COPD patients with ARF and the outcomes are independent of using ventilatory mode, either PCV or VCV.

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