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Carbon dioxide mandatory ventilation (CO2MV): A new method for weaning from mechanical ventilation

Description and comparative clinical study with I.M.V. and T. tube method in COPD patient

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Summary

We describe a new technique specially designed for weaning from mechanical ventilation: carbon dioxide mandatory ventilation (CO2MV). CO2MV is based on feedback between end tidal expired partial pressure of carbon dioxide and ventilatory mode, controlled or spontaneous. In order to evaluate its real interest we performed a randomized prospective study, CO2MV vs Intermittent Mandatory Ventilation (IMV) and T. Tube Method (TTM). Fourty-two adult patients with chronic obstructive pulmonary disease entered this study at the end of acute respiratory failure requiring mechanical ventilatory support. We observed a better stability of arterial blood gas during weaning with CO2MV and an increase in success rate (CO2MV 13/14 - IMV 5/14 - TTM 10/14). From this study CO2MV seems available for weaning of COPD patients. Nevertheless, further studies are required to appreciate its real clinical interest.

Introduction

Despite numerous criteria for weaning from mechanical ventilation the decision to discontinue respiratory support is one of the most difficult problems in critical care.

Newer generation of ventilators provide sophisticated techniques like, intermittent mandatory ventilation (IMV) [7], minute mandatory ventilation (MMV) [11] and pressure support.

However, several publications have not supported the interest of these technical developments. Advantages and disadvantages of IMV have been previously discussed [28]. IMV could increase ventilatory work and oxygen consumption [21] and requires more monitoring. A low IMV rate requires an increase in patient's own spontaneous ventilation to prevent acute hypercapnia. MMV could be more convenient, however, minimum minute ventilation can be reached by increasing tidal volume as well as respiratory rate. The consequence could be an increased dead space ventilation. So we have designed a new technique based on a feedback between end tidal partial pressure of expired carbon dioxide (PET CO2) and the mode of ventilation, controlled or spontaneous.

We called this technique carbon dioxide mandatory ventilation (CO2MV). In order to evaluate its clinical interest we performed a randomized study, CO2MV vs IMV and T.tube method (TTM), during weaning of chronic obstructive pulmonary disease (COPD) patients at the end of an acute respiratory failure (ARF).

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Description of the CO2MV technique

CO2MV background

Theoretical background of CO2MV is the following:

- In COPD patients, there is an individual correlation between PaCO2 and PETCO2. The gradient D(a-ET)CO2 is not changed by CO2 production [17] or cardiac output increase [19]. It is only slightly modified by mechanical ventilation or during variation of minute ventilation. It may be dramatically increased by acute cardiac or respiratory complications, but, in the contrary, may be considered as a constant value in steady state. So, during the weaning and without acute circulatory or respiratory complications, D(a-ET)CO2 allows estimation of PaCO2 from PETCO2.
- Recent studies have focused on muscle fatigue and measured respiratory work involved in spontaneous breathing during weaning. Muscle fatigue is an important factor in ARF [2] and in the occurrence of hypercapnia [18]. During weaning, increased hypercapnia is rather due to hypoventilation than to acute ventilatory circulatory ratio mismatching. Experimental data have shown that diaphragmatic contractility is decreased by acute hypercapnia and respiratory acidosis [13].

Thus, keeping PaCO2 at a constant level during weaning in COPD patients could be of great interest.

Principle of CO2MV

The basic principle is that spontaneous (SV) or controlled (CV) ventilatory mode is automatically selected by the MVCO2 device, depending on PETCO2 level. PETCO2 is each cycle determined and compared with three limits selected by the operator: PETCO2 maximum (PETmax), PETCO2 minimum (PETmin), PETCO2 intermediate (PETint).

- PETmax is the maximum threshold of PETCO2 while the patient breathes spontaneously. Up to PETmax CV mode is automatically selected after a time delay T1 (Fig. 1).
- PETint is the maximum threshold of PETCO2 while the patient is in controlled ventilation. Down to PETint SV mode is automatically selected after a time delay T2.
- PETmin is the minimum threshold of PETCO2. It is a safety limit in case of apnea or cardiac arrest under which CV mode is continuously maintained.

PETmax and PETint are selected depending on the difference between PETCO2 and arterial partial pressure of CO2 (D(a-ET)CO2)) and expected PaCO2 during SV and CV. For example, in order to wean a COPD patient we want the patient to have PaCO2 within 40 to 50 mmHg. Expected maximum PaCO2 are 50 in SV and 40 in CV. As the weaning starts D(a-ET)CO2 is determined at 10 mmHg. So PETmax will be:

PETmax = expected SV PaCO2 – D(a-ET)CO2, that is 40 mmHg, and PETint = expected CV PaCO2 – D(a-ET)CO2, that is 30 mmHg.

PETmin is automatically set at 25 per cent of PETmax but must always be higher than 10 mmHg. In figure 1, the weaning starts in SV. Over PETCO2, CV mode is activated after T1 (T1 = fixed time 20s) is elapsed. CV is maintained for the time the patient needs to decrease PETCO2 under PETint plus time T2. T2 is an additional time of controlled ventilation giving the patient a resting time. After T2, SV is selected again.

In order to avoid tachypnea during SV and a dramatic increase of D(a-ET)CO2 as a result, a maximum respiratory rate (RR) must be entered into the device (RRmax).

To summarize, SV mode is kept as long as PETCO2 is less than PETmax and RR less than RRmax. CV mode is automatically activated during the following circumstances:

- out of PETmax – PETmin ranges,
- out of RR limits (from 5 to RRmax),
- in case of malfunction of the capnigraph or/and the computer,
- on operator's request.

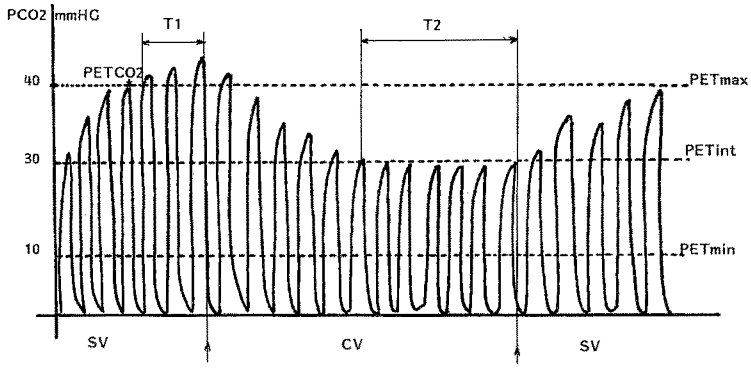

Fig. 1. Principle of CO2MV. PETCO2: end tidal partial pressure of CO2; SV: spontaneous ventilation; CV: controlled ventilation; T1: delay time; T2: CV time; PETmax: maximum limit of PETCO2 during spontaneous ventilation; PETint: Intermediate limit; PETmin: minimum safety limit. See text for additional information.

Actual configuration and blockdiagram of the system

CO2MV module is inserted in serial between an infrared capnigraph (Capnolog Dräger) and the ventilator (UV2 Dräger).

Hardware configuration uses a Motorola microprocessor (6802 – 2 K RAM – 8 K EPROM). Analog to digital conversion is performed by an 8 bits A/D convertor at 100Hz. A 6840 timer generates interrupt every 10ms permitting acquisition of the signal, display of the results and management of the keyboard (Fig. 2).

A criterion for recognizing a CO2 signal and for validating a cycle is one way passage of CO2 signal through PETmin twice within 12 seconds. Whenever it is impossible to determine a valid cycle within 12 sec, CV is automatically selected.

Several digitals display the settings (PETmax and int, RRmax, T2) and calculated data (PETCO2, RR and the ratio between the time the patient has been in SV and the time elapsed since initialization (TSV/T)).

A standby key stops the system during nursing and holds it in previous mode of ventilation. An emergency key restores instantaneously the CV mode. The current running mode is clearly indicated.

Clinical validation

Figure 3 shows a simultaneous recording of PETCO2 and transcutaneous partial pressure of CO2 (PTCCO2). The main feature is the parallel evolution of PETCO2 and PTCCO2. This leads us to believe that the CO2MV mode permits a perfect control of PaCO2 and avoids risk of acute hypercapnia and respiratory acidosis. The patient gradually establishes himself in the SV. Our two-year-long experience suggests that, when the ratio TSV/T is higher than 80 per cent for two hours, the patient may be extubated.

Clinical evaluation

Method

We performed a comparative study of CO2MV vs IMV and TTM in our medical intensive care unit (ICU). Fourty-two adult patients entered this prospective study, 7 females and 35 males, 62 ± 8 years old.

Criteria of inclusion were: previously documented COPD (FEV less than 1 $l.s.^{-1}$ measured at least previous year), ARF with hypercapnia (PaCO2 superior to 50 mmHg) and hypoxia (PaO2 inferior to 60 mmHg $F_iO_2 = 0.21$ – SV), respiratory support with conventional CV required for four days at least.

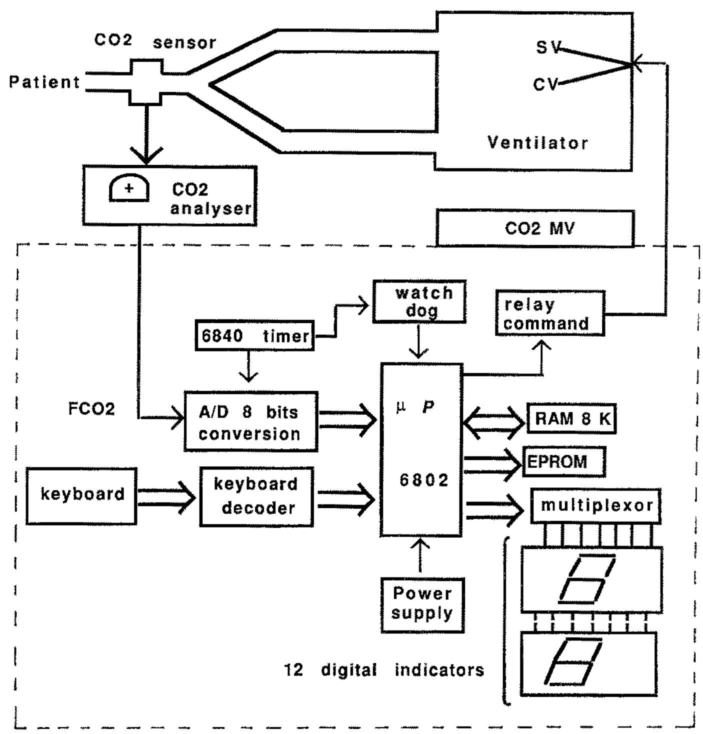

Fig. 2. Block diagram of the system.

Criteria of exclusion were: starvation (less than 50 kg body weight (BW) or obesity (more than 100 kg BW), age superior to 75, hematologic or neoplasic diseases, severe sepsis during ARF and home tracheostomized patients.

Criteria for weaning were: normal consciousness, body temperature below 38° C, stable hemodynamical state, no acute respiratory complication, no metabolic acute disorder and PaCO2 lower than 50 mmHg and PaCO2 higher than 60 mmHg. During CV (F_iO_2 = 0.3, VT = 10 ± ml.kg^{-1}, RR = 15 c.mn^{-1} – T1/TE = 1/2). At the start of the weaning, the patients were all on CV mode with the same type of electronical ventilator (UV2, Dräger).

They were randomized in three groups (n = 14 each), G1: TTM, G2: IMV, G3: CO2MV, using a permutation table with serial equilibration.

In G1, the mode CV was abruptly removed and the patient placed under a weaning circuit with T piece, oxygen and aerosol therapy. In G2, the IMV rate began at 7 c.mn^{-1} and reduced at a rate of 2 c.mn^{-1} at a 6 hours interval. In G3, the patients used the CO2MV mode with T2 (CV time) of 10 ± 3 mn and PETCO2 limits chosen according to the method described above.

The same physiotherapist helped the patients, two hours a day. The glucose intake rate allowed was 3 g.kg^{-1}/24 h.

During the weaning, the patients were monitored for clinical and biological data every six hours. For all patients, F_iO_2 was measured by a mass spectrometer and kept constant at 0.3. Arterial blood gas (ABG) were sampled through a radial artery catheter at T0 and every six hours (T6, T12, T18, T24) and were immediatly analyzed (Corning 178) for blood gas determination. At T48, another sample was taken and analyzed if the extubation has been successful.

Criteria of extubation for the three groups under study were: patient's own respiratory rate lower than 30 c.mn^{-1}, cardiac rate lower than 120 b.mn^{-1}, PaCO2 lower than 50 mmHg and PaO2 higher than 60 mmHg (F_iO_2 = 0.3) for two

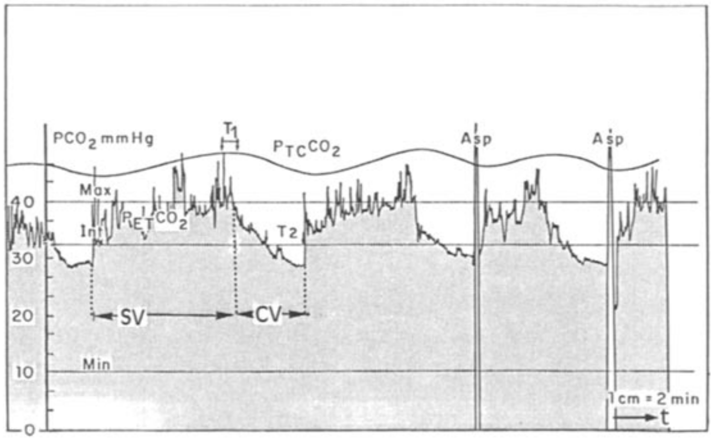

Fig. 3. Simultaneous recording of transcutaneous partial pressure of CO2 (PTCCO2) and expired tidal partial pressure of CO2 (PETCO2).

successive analysis of ABG sampled during SV. SV was defined as ventilation through the T piece (G1), as ventilation through the respirator circuit with IMV rate (G2) or as spontaneous ventilation period with CO2MV (G3). In addition, in G3, patients had to have established themselves in the SV mode for more than two hours.

Criteria of success and failure: all patients who required return to the CV mode before discharge from the ICU were considered as failure. Return to CV was decided on the following circumstances: worsening clinical status (RR>30, CR>120, consciousness deterioration) and PaCO2 higher than 60 mmHg and/or PaO2 lower than 60 mmHg.

Statistical analysis used one way analysis of variance and Chi square test with Yate's correction. Results are expressed as mean ± 1SD and considered significant for $p<0.05$.

Results

The three randomized groups were homogeneous regarding etiologies of ARF, mean age, mean duration of controlled ventilation before weaning and biological data (Table 1).

The success rate in G1 was 10/14. Six patients have been extubated at T12, two at T18, two at T24 (mean = 14 ± 6H). One patient required return to CV at T12, another one at T18, two at T24.

The success rate in G2 was 5/14. Two patients have been extubated at T18, three at T24 (mean 16 ± 17H). Nine patients required return to CV, five at T12, two at T18.

The success rate in G3 was 13/14. Six patients have been extubated at T12, three at T18, four at T24 (mean = 19 ± 6H). One patient required return to CV at T18.

ABG obtained during the weaning in each group are reported in Table 2. At T0, ABG were in normal ranges for all the patients without any significant difference comparing the three groups. Mean pH were comparable (G1: 7.45 ± 0.05, G2 = 7.43 ± 0.06, G3 = 7.45 ± 0.06, NS). Arterial pH became significantly lower in both G1 and G2 compared to G3, related to respiratory acidosis occurring in the G1 and G2.

At T24, pH were: G1 = 7.30 ± 0.02, G2 = 7.34 ± 0.05, G3 = 7.40 ± 0.02 ($p<0.05$). At T48, G1 = 7.34 ± 0.05, G2 = 7.33 ± 0.05, G3 = 7.41 ± 0.06 ($p<0.05$).

Discussion

Several systems based on feedback between PET-CO2 and minute ventilation have been previously described and used on animals and healthy humans

Table 1. Etiologies of acute respiratory failure (ARF), mean age, controlled ventilation time before weaning trial and arterial blood gas (ABG) during spontaneous ventilation (SV) on admission in the ICU.

n = 42	G1 n = 14	G2 n = 14	G3 n = 14	S
Etiologies of A.R.F.*				
• acute bronchitis	6	6	7	
• bronchospasm	5	3	3	NS
• cardiac failure	2	4	3	
• metabolic disorders	1	1	1	
Mean age (years)**	65 ± 2	60 ± 8.7	62 ± 8	NS
C.V. Time (days)**	5.7 ± 2.1	5.2 ± 1.2	5.3 ± 2.4	NS
A.B.G. on admission (S.V.-FIO2 = 0.21)**				
• pH	7.33 ± 0.08	7.35 ± 0.08	7.33 ± 0.09	NS
• PO2 (mmHg)	52.3 ± 16.3	54 ± 22.4	55.1 ± 10.1	NS
• PCO2 (mmHg)	62.4 ± 7.6	63 ± 10.9	61.3 ± 8.4	NS

* Chi square test
** Analysis of variance
TTM: T. Tube Method; IMV: intermittent mandatory ventilation; CO2MV: carbon dioxide mandatory ventilation; Data are expressed as mean ± S.D.; NS: non significant($p>0.05$).

Table 2. Evolution of ABG value in each group.

	CV	Weaning period				Extubation
	T0	T6	T12	T18	T24	T48
G1 = T. Tube Method						
• PCO2 (mmHg)	39 ± 6	47 ± 5	47 ± 6.2	55 ± 10	50 ± 6.7	52 ± 7.1
• PO2 (mmHg)	90 ± 22	63 ± 13	60 ± 12	66 ± 12	76 ± 24	62 ± 9
• n	14	14	14	13	12	10
G2 = I.M.V.						
• PCO2 (mmHg)	42 ± 5.1	50 ± 7.2	52 ± 7	53 ± 4	54 ± 7.5	54 ± 9
• PO2 (mmHg)	94 ± 29	89 ± 31	90 ± 19	78 ± 15	97 ± 30	64 ± 15
• n	14	14	14	9	7	5
G3 = CO2 M.V.						
• PCO2 (mmHg)	37 ± 4	46 ± 3.4	46 ± 4.1	47 ± 8	47 ± 3.1	45 ± 4
• PO2 (mmHg)	93 ± 18	90 ± 21	86 ± 18	86 ± 24	84 ± 16	73 ± 18
• n	14	14	14	14	13	13
PCO2 G1–G2		NS	NS	NS	NS	NS
PCO2 G1–G3	NS	NS	NS	+	NS	+
PCO2 G2–G3		+	+	+	+	+
PO2 G1–G2		++	+++	+	NS	NS
PO2 G1–G3	NS	+++	+++	+	NS	NS
PO2 G2–G3		NS	NS	NS	NS	NS

FIO2 = 0.3
G1: T. Tube Method; G2: IMV; G3: CO2 MV. During weaning period ABG were sampled in G3 in Spontaneous Ventilation (SV) and in G2 in selected IMV rate.
ABG at T0 were sampled during Controlled Ventilation (CV) with FiO2 = 0.3.
Data are expressed as mean ± SD – Analysis of variance (F)
+ = $p<0.05$; ++ = $p<0.01$; +++ = $p<0.001$.

[4, 8, 17]. Such systems increased minute ventilation according to the patient's needs [3, 25]. But their response was questionable in the case of variation of the respiratory function, requiring to modify the feedback. CO2MV is not so sophisticated a system.

However, the CO2MV technique rests on the absence of variations of D(a-ET)CO2 during the weaning. Without acute cardiac or respiratory complications responsible for an increase in dead space effect, D(a-ET)CO2 can be assumed to hold at a constant level.

D(a-ET)CO2 is not modified by an increase of CO2 production, an infusion of bicarbonate and an increase of cardiac output [9–17]. The influence of ventilatory mode has been previously documented. Hill demonstrated that D(a-ET)CO2 is identical during SV and CV in normal lung anesthetized patients [21].

In group of thirty-one COPD patients we did not find a significant difference of the D(a-ET)CO2 obtained during SV and CV (Table 3).

Perrin [19], in a study of eleven COPD patients, mechanically ventilated at different levels of minute ventilation pointed out that it is possible to estimate PaCO2 from PETCO2, with a mean predictive error of 2.8 ± 1.9 mnHg ($n = 76$ determinations).

Nevertheless D(a-ET)CO2 could increase dramatically in case of complications, i.e. bronchospasm, pneumothorax, pulmonary embolism, acute cardiac failure, cardiac arrest.

Table 3. Comparison between D(a-ET)CO2 obtained during spontaneous ventilation (SV) and controlled ventilation (CV) in a group of 31 COPD patients.

	V.S.		V.C.
PaCO2 mmHg	42 ± 6.6	p<0.01	37 ± 5.1
PETCO2 mmHg	31 ± 5.8	p<0.01	24 ± 3.8
D(a-ET)CO2 mmHg	11.2 ± 4.7	NS	10.6 ± 4.5

n = 31; male = 25. female = 6. mean age = 53 ± 17
Data are expressed as mean ± SD – Student's test for paired observations.
NS: non significant (p>0.05).

In case of cardiac arrest or acute circulatory failure PETCO2 drops below PETmin and CV is restored.

In other circumstances variations of PETCO2 depend on simultaneous variations of PaCO2 and D(a-ET)CO2. Acute hypoventilation (i.e. bronchospasm) in spontaneous mode usually induces acute hypercapnia and an increase of PETCO2 despite the increase of D(a-ET)CO2. CV mode is activated by overtaking PETmax. In addition CV is held on as long as PETCO2 is over PETint.

Acute increase of dead space effect (i.e. pulmonary embolism, air embolism) increases D(a-ET) CO2 as a result. That is the weak point of CO2MV. But tachypnea usually occurs during these acute complications. So a judicious choice of RRmax is one of the most important settings of the device.

It could be objected that, in this study, we did not use more sophisticated criteria for weaning [22, 23] like vital capacity, VD/VT ratio, maximum negative inspiratory pressure, mouth occlusion pressure. These criteria are not always valid [26] and are still debatable. So we choose to use criteria on clinical and biological data.

In this study, the greater success rate of weaning was observed with CO2MV. One patient only failed the weaning trial in G3. The difference is significant between IMV group and CO2MV group ($p<0.05$) and between IMV group and T.tube ($p<0.05$). These results are questionable when one considers that the number of patients success rate of the weaning with IMV is only 5/14. We have to take into account the fact that IMV was closed in a strict protocol and might have been disadvantaged in this study. However advantages and disadvantages of IMV have been previously pointed out by several authors [14–20–28]. IMV can increase respiratory work and oxygen consumption [21]. Downs claimed on the contrary that disadvantages of IMV are very often due to bad setting and indications [6]. In our experience, IMV seems to be difficult to use especially in COPD patients at the end of an ARF, requiring meticulous controls and monitoring. The decrease of IMV rate is not always followed by an expected increase in patient's own

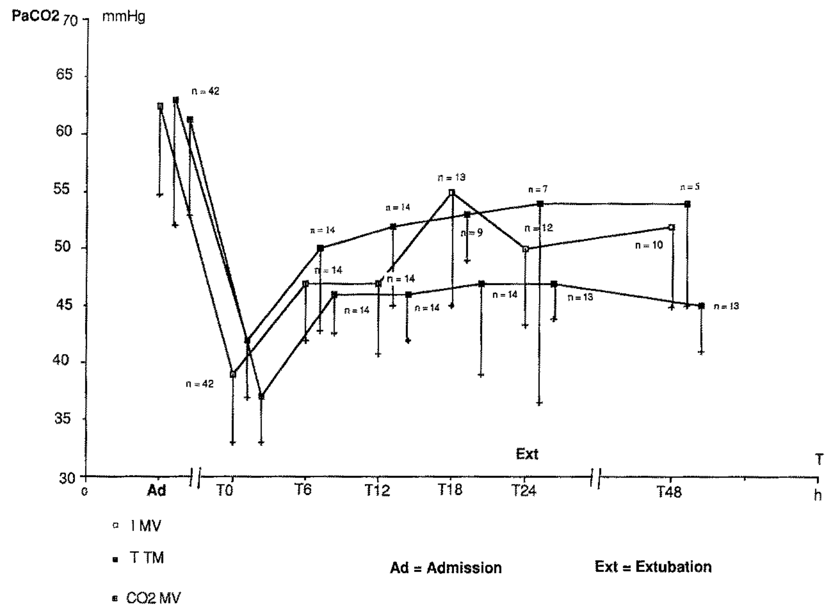

Fig. 4. Evolution of PaCO2 during the weaning period studied. TTM: T. Tube Method; IMV: intermittent mandatory ventilation; CO2MV: CO2 mandatory ventilation.

ventilation. Therefore CO2 elimination only depends on controlled cycles and acute hypercapnia can occur.

The aim of CO2MV is to maintain PaCO2 between acceptable ranges during weaning trials. Figure 4 shows that in G1, PaCO2 tended towards increase and was unstable with great individual variation. In G2, PaCO2 increased gradually in accordance with the decrease of controlled cycles rate. PaCO2 was more stable and significantly lower in G3 than in the other two groups.

At T48 (extubated patients) PaCO2 was significantly lower in G3. It may be that supporting patients at an acceptable level of PaCO2 during the whole weaning trial, increases muscular ventilatory performance [13].

CO2MV seems to increase the weaning time: the shortest was observed in G2 and the longest in G3.

Conclusion

From our study we can conclude that CO2MV seems to be a new available method for weaning. Indications of this technique must be determined by further studies. COPD patients are surely a good indication but we are presently unable to specify its true interest in others as ARDS or post-operative patients. In addition, CO2MV doesn't compete with other methods for weaning but, on the contrary, could be coupled with IMV and pressure support.

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