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Use of DELTA-CO_2 as Predictor of Ventilatory Failure

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ABSTRACT

The ventilatory failure after a programmed extubation is defined as the inability to maintain spontaneous ventilation within a period of 72 hours of surveillance. The incidence of this problem is approximately 15%, and causes related to respiratory problems include 28% of the total being the principal cause of ventilatory failure and left ventricular dysfunction is the second cause. The criteria used to determine the possibility to extubate a patient only include respiratory factors; from the cardiac point of view only contemplates the use of amines. So far there is no a reliable noninvasive marker that can predict heart failure as a cause of ventilatory failure. Considering that the increase in ventilatory mechanics defines the majority of cases of ventilatory failure after extubation, it is possible that a tissue hypoperfusion marker could discern those patients with the possibility of ventilatory failure. In situations with low tissue perfusion, the difference in carbon dioxide is seen as an increase in CO_2 in the venous blood and related to a decrease in cardiac output according to Fick equation. The amount of CO_2 in venous blood is dependent on blood flow. For this reason, an increase in the venous-arterial CO_2 difference reflects a decrease in blood flow and tissue hypoperfusion that could be used as a predictor of failure in extubation. We propose delta CO_2 as a risk marker for ventilatory failure after extubation.

Introduction

Mechanical ventilation (MV) has been the main therapeutic support in patients with respiratory failure, especially in patients admitted to the intensive care unit. Despite advances in the management of MV, mortality in these patients remains high and costs continue to be very high[1]

The first published studies about mechanical ventilation coincide with the appearance of the first intensive care units. The first study in patients with mechanical ventilatory assistance admitted to the intensive care Unit (ICU) was published in 1989, where it was found that the percentage of patients admitted to the ICU who require mechanical ventilation is 49%. More than half of them start in the first 24 hrs of admission[2].

The main targets of mechanical ventilation are to improve systemic oxygenation as well as rest of the respiratory muscles, in such a way that the hemodynamics of the patient can be maintained.[3]

Basic Concepts of Mechanical Ventilation

The objectives of invasive mechanical ventilation are aimed to meliorate the physiological conditions of the patient: enhancing gas exchange, maintaining lung volume, reducing respiratory work and therefore improving the availability of arterial oxygen. To achieve these objectives, goals have been set during ventilatory assistance whose compliance will determine the possibility to extubate the patient.[4]

Weaning of Mechanical Ventilation (MV)

The criteria established for initiating mechanical ventilation status are the patient's clinical state, gasometric status, ventilatory parameters as well as comorbidities that affect the response to the established treatment.[5] This determines the duration of the MV and the patient's prognosis. There are several protocols to initiate it. The criteria for predicting the success of patients who are undergoing spontaneous testing must be objective and measurable to make the correct decision.[6]

Weaning of mechanical ventilation in most patients is a relatively simple process.[6] The method of choice is to initiate a spontaneous unassisted breathing test, on a daily basis, which may be with the use of a T-piece (without positive pressure at the end of expiration), CPAP (continuous positive pressure), or a test of pressure Ventilation (PVT). The decision of which of them using is based mainly on the experience and knowledge of each doctor. Spontaneous tests should be performed while the patient is awake and without

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sedation.[7,8,9] The variables that predict that the patient is suitable for initiation of spontaneous test are presented in (Table 1).[7,8,9,10]

Table 1. Variables that Predict that the Patient is Suitable for Initiation of Spontaneous Test.

CLINICAL ASSSESMENT
Intact airway reflexes
Resolution of pathology that cause the beginning of mechanical ventilation
No continuos sedation or adequate mentation
OBJECTIVE MEASUREMENTS
Heart rate ≤140 beat/minute
Cardiovascular stability (absence of vassopresors)
Hemoglobin level ≥ 8 gr/dl
Systolic blood pressure ≥ 90 -160mmHg
No or minimal vasopressor
ADEQUATE OXYGENATION
Tidal volume ≥ 5 ml/kg
Vital capacity ≥10 ml /kg
Proper respiratory effort
PEEP ≤ 8 mmHg
No significant respiratory acidosis (pH ≥ 7.30)
Maximal inspiratory pressure (MIP) - 20 — - 25mmHg
O2 saturation > 90 % on FiO2 < 0.4 (or $PaCO_2$ / FiO_2 ≥200)
Rapid Shallow Breathing Index (Respiratory frequency / tidal volume) ≤105
FiO2, Inspiratory fraction of Oxygen / PEEP: positive pressure at the end of expiration / PaO2: partial pressure of oxygen. Modified from Zein et al; Ventilator Weaning and Spontaneous Breathing trials; an educational review. [10]

For spontaneous breathing to be successful, the patient must breathe spontaneously for at least 30 minutes, and must not have any of the following: a respiratory rate greater than 35 rpm for more than 5 minutes, an oxygen saturation of less than 90%, and / or a heart rate of more than 140 bpm, a sustained change in heart rate of 20%, or systolic blood pressure of 180 mm Hg or less than 90 mm Hg. Neither should you present anxiety or diaphoresis [10]

Once the patient has successfully passed the spontaneous test, the amount of secretions must be taken into account: abundant secretions are not factors of good prognosis for extubation, as well as the strength of the cough reflex.[10]

The indexes that predict success in the extubation of the patient, once they have successfully passed the spontaneous test are presented in (Table 2).[7,8,10]

Table 2. The Indexes that Predict Success in the Extubation After a Successfully Spontaneous Breathing Test.

Good tolerance to spontaneous breathing trials
FiO2 ≤0.4
PaO2/FiO2: > 200
Vital Capacity: > 10 ml/kg
Tidal Volume (VT): >5ml/kg
RR/Tidal volume: <105 r/min/ml
Pmáx: < -20 - -30 cmH2O
RR: < 35 rpm
HR: <130 lpm
Oxygen saturation > 90 %

PaO2: Partial oxygen pressure, RR: respiratory rate,
FiO2: inspiratory fraction of oxygen; Pmáx: maximum inspiratory pressure
HR: Heart rate

Hemodynamic changes in the MV

The MV produces hemodynamic changes caused by the increase in intra-thoracic pressure that leads to a decrease in venous return.[11] This causes important changes in both cardiac chambers. The changes produced in the right ventricle are mainly: decrease in preload, increase in afterload due to an increase in pulmonary venous resistances. In the left ventricle: decreased preload, decreased blood pressure and increased cardiac output during positive pressure ventilation (PPV).

When the weaning of the MV is decided, increments of the preload is produced and after suspending the intra-thoracic positive pressure the systemic venous return increases and decreases in the left ventricle afterload. On the other hand, increased respiratory effort intensifies cardiac output and oxygen consumption. During this stage, there is an increment in the pulmonary artery wedge pressure and a decrease in the central venous saturation of O_2.[12] In this way, in patients with low cardiac reserve even in those with subclinical heart failure, they may be intolerant to this increase in cardiac work and consequently present failure in extubation due to heart failure and not due to a respiratory problem.

Extubation Failure

It is defined as failure in extubation when the patient is unable to hold the breath spontaneously after the MV suspension and therefore it is necessary to restart it within the first 72 hrs.[13, 14, 15, 16]

The incidence of extubation failure has an average of 15% [16], depending on the etiological factors associated. Nevertheless, according to Krinsley et al, [16] the "optimal" rate of extubation failure should be between 5-10%, so the rate presented in the study of Epstein et al, [17] might be inappropriately high. According to Epstein, extubation failure is associated with a 43% mortality compared to those in which extubation was successful with a 12% risk.[17]

It is relevant to determine the pathology that causes the failure in extubation, due to its association with mortality.[19] According to Esteban and colleagues, the percentage of mortality associated with failure in extubation secondary to upper airway obstruction was 7%, compared to those patients who presented respiratory failure, in which it was 30%. Table 3 [20]

Table 3. Main Causes of Failure in Extubation.

Causes of Failure in Extubation.	%
RESPIRATORY FAILURE	28%
HEART FAILURE	23%
EXCESS OF SECRETIONS	16%
UPPER AIRWAY OBSTRUCCION	15%
ENCEPHALOPATHY	9%
OTHERS	8%

Modified from Robert C. Rothaar. Current Opinion in Critical Care 2003 20

Table 4. Criteria for Extubution Failure.

OBJECTIVE MEASUREMENTS
Increase in $PaCO_2$ >10mmHg
Decrease of pH > 0.10
PaO2 < 60 mmHg
SatO2 % < 90 con FiO2% 50-100%
CLINICAL ASSESSMENT AND SUBJECTIVE INDICES
Tachycardia
Agitation and anxiety
Diaphoresis
Depressed mental status
Use of accessory muscles
Abdominal- thoracic dissociation
Upper airway obstruction
Poor secretion management

PaO2: partial pressure of Oxygen, Sat%: oxygen saturation

Modified from Arnaud W.Thille, MD, PhD, et al; Crit Care Med. 2011.[22]

After weaning from MV, there are clinical and gasometrical markers indicative of extubation failure (Table 4) [18] which can be used as criteria for the restart of mechanical ventilation [21]. Ai-Chin Cheng et al; in their study, they found that patients who had failure in extubation had significantly longer ICU stay as well as days of hospital permanence, increased incidence of tracheostomy, higher in-hospital mortality and higher costs [22] Esteban and colleagues found that the main complications after reintubation were: pneumonia, arrhythmias, atelectasis or pulmonary collapse, myocardial infarction and cerebral vascular event.[20]

So far, the criteria used to determine the possibility of weaning of mechanical ventilator assistance are basically respiratory type. Among the most studied are the rapid surface respiration index (RR / TV), [17] relation of the occlusion pressure and maximum inspiratory pressure, the minimum recovery time of ventilation, respiratory work, liver-spleen displacement, leakage, laryngeal ultrasound with measurement of aerial column, among others. Left ventricular dysfunction is the second cause of extubation failure, [21] but myocardial function is not evaluated routinely. And although it is often difficult to determine the isolated participation of left ventricular dysfunction as a cause of failure in extubation, it is important to know the degree of myocardial reserve in order to be able to foresee the possibility that extubation fails.

Delta Co_2 and Ventilation Failure

Every day about 15,000 to 20,000 mmol of carbon dioxide (CO_2) are produced throughout the body. The CO_2 balance is achieved when the quantity produced by the cellular metabolism is transported by the circulation and excreted by the lungs[23] The production of CO_2 can be in two forms: aerobic or anaerobic. The aerobic generation of CO_2 is a final product of mitochondrial oxidative phosphorylation. Under normal conditions, the formation of total CO_2 is related to the total O_2 consumption. In this way, aerobic CO_2 formation is proportionally related to the increase in oxidative metabolism and to the overall consumption of O_2. On the other hand, anaerobic formation is related to tissue hypoxia. In this context, we find two main sources: 1) increase of lactic acid and therefore a buffer effect with bicarbonate is initiated increasing the formation of CO_2; 2) the presence of anaerobic decarboxylation of some substrates such as alpha-cetoglutarate and oxaloacetate, where CO_2 production is lower.[24]

Carbon dioxide (CO_2) is found in circulation in three forms: dissolved, like bicarbonate and bound to proteins, from which the carbamino compounds are formed. Because CO2 is twenty times more soluble than oxygen (O_2); the dissolved form plays a more important role under normal conditions. Carbamino compounds are formed by the union of a CO_2 molecule plus a terminal amino group of blood proteins, mainly reduced hemoglobin, which is more akin to CO_2 than HbO_2. In such a way that the total concentration of CO_2 and the partial pressure of CO_2 ($PaCO_2$), are influenced by the amount of hematocrit, saturation of O_2 and blood pH, mainly.

In the Fick equation, related to CO_2, it is indicated that the excretion of CO_2 with a constant production equals the product of cardiac output (CO), with the following gradient:

$\Delta CCO_2 = (CvCO_2 - CaCO_2)$.
$VCO_2 = CO \times (CvCO_2 - CaCO_2)$
Where:
VCO_2 = Total production of CO_2
CO = Cardiac output
$CvCO_2$ = Venous concentration of CO_2
$CaCO_2$ = Arterial concentration de CO_2

In this way, if we invert the values, we substitute the CO_2 concentration (CCO_2), by partial pressure of CO_2,

(PCO_2) and we clear the venous-arterial differential gradient of CO_2, we obtain the following modified Fick equation:

$\Delta PCO_2 = kVCO_2 / CO$

In this context k, refers to the global CO_2 formation constant.

In this equation it is observed that delta or venous-arterial CO_2 gradient is directly related to the formation of CO_2 and inversely proportional to the cardiac output.[24,25]

As previously explained, the production of CO_2 can be related to anaerobic metabolism, clinically associated with pathologies such as: circulatory failure secondary to myocardial dysfunction, hypovolemia or sepsis. The venous-arterial difference of $PaCO_2$ has been considered a marker of the capacity of the cardiovascular system to eliminate CO_2 produced in peripheral tissues.[24]

Under normal tissue perfusion conditions, delta CO_2 is relatively stable and less than 6mmHg (0.8 Kpa) .[26]

Different studies have shown that a delta CO_2 > 6mmHg persistent for more than 24 hours could signal the persistence of peripheral hypoperfusion [24]. In situations in which tissue perfusion decreases, for example, in shock or due to altered distribution of blood flow, the difference in venous and arterial CO_2 increases due to an increase in CO_2 in venous blood related to a decrease in cardiac output, according to the Fick equation. This is related to the fact that the amount of CO_2 in venous blood is dependent on blood flow, unlike arterial blood, in which the amount of CO_2 depends on gas exchange at the pulmonary level. For this reason, an increase in the venous-arterial CO_2 difference reflects a decrease in blood flow.[27]

Mecher et al, compared patients with and without septic shock status and observed that patients with septic shock had a delta CO_2> 6mmHg in addition to having an inverse relationship with cardiac output. The authors concluded that patients with septic shock had decreased blood flow.[28]

In the study by Bakker et al, they studied the relationship of the CO_2 delta in septic shock as well as the acid-base status and its relation to cardiac output. They studied 64 patients and observed that at the beginning the patients with septic shock had a delta of CO_2 greater than 6mmHg with a lower cardiac index, with p less than 0.01. The patients with high delta CO_2 had a higher mortality and concluded that high CO_2 delta in a patient with septic shock is related to a decreased cardiac output also related to a degree of pulmonary alteration. [29]

Vallée et al. Tested the hypothesis that the CO_2 delta can be used as a global indicator of low tissue perfusion in patients with septic shock despite a central venous saturation of O_2 ($ScvO_2$) greater than 70%. They showed that patients who had a blood lactate concentration> 2 mmol / L were associated with a high CO_2 delta (> 6 mmHg), on the other hand, patients with low levels of ΔPCO_2 had a greater lactate decrease and had a reduction significantly higher of the SOFA score. [30]

In general terms, delta CO_2 is a marker of low tissue perfusion and under a suitable clinical context it can translate some degree of left ventricular dysfunction. During spontaneous ventilation, the post-extubation state represents a challenge to myocardial function, which explains why the second cause of extubation failure is precisely left ventricular dysfunction. In this case it is possible that the CO_2 delta is able to identify those patients with low tissue perfusion secondary to left ventricular dysfunction as a cause of extubation failure.

Conclusions

Invasive ventilation assistance is one of the most frequent therapeutic resources offered to patients in critical condition. It represents a great economic cost and in turn also a major source of complications. On the other hand, throughout history the process of weaning of mechanical ventilation has posed serious challenges especially for the rates of extubation failure after extubation and the need for re-intubation. Morbidity and mortality increases up to 43% in the re-intubation. Hence, the need to identify in a safe way those patients with the possibility of failing extubation becomes important. The criteria stated so far are based primarily on ventilation parameters, but there is no specific criterion (except for the absence of the use of amines) that is defined as a cardiovascular risk factor as a predictor of post-extubation ventilation failure.

Once a patient has reached a successful spontaneous ventilation test and is candidate for extubation, in theory he has a compensated hemodynamic state. But when it develops extubation failure, the presence of left ventricular dysfunction represents an important cause, only behind the respiratory causes. The increase of ventilation effort after extubation causes an increase in cardiac output to face the increasingly important metabolic needs of the respiratory musculature. This closes the circle - to greater respiratory work, greater cardiac output - and this happens once the orotracheal cannula is removed secondary to the increase in the resistances imposed by the airway. Given this situation, a left ventricle with little reserve will to fulfill this increase in work by participating in the development of extubation failure.

The determination of a delta CO_2 can be useful in selecting those patients who may fail in spontaneous ventilation and thus re-evaluate the process of extubation.

Currently we are evaluating this possibility in a controlled prospective study.

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