Quantitative Analysis of the Effect of Prolonged Mechanical Ventilation on Capnographic Indices

Carmen Caroline Rasera[1], Pedro Miguel Gewehr[1] and Adriana Maria T. Domingues[2]
[1]*Biomedical Engineering Programme, Parana Federal University of Technology (UTFPR) Parana, Brazil*
[2]*Department of Cardiac Intensive Care Unit, Pequeno Principe Hospital, Parana, Brazil*

Keywords: Monitoring Device, End-tidal Carbon Dioxide Pressure, Capnogram, Invasive Mechanical Ventilation.

Abstract: The monitoring of carbon dioxide pressure through Capnography has been clinically used as a continuous and non-invasive measurement of alveolar ventilation. The patients with lung disease, respiratory and hemodynamic instability and when in mechanical ventilation have a significant alteration in the waveform of the capnogram. In this study, quantitative analysis between capnographic indices of the patients under prolonged mechanical ventilation were obtained and compared to waveforms of spontaneously breathing patients. The measurements were performed at the 10th day of invasive mechanical ventilation and 48 hours after tracheal extubation, totalling 52 capnographic curves. $PaCO_2$ and $PetCO_2$ measurements maintained a significant correlation in spontaneously breathing patients ($r^2 = 0.97$, $p<0.001$) and a weak correlation in patients during prolonged mechanical ventilation ($r^2 = 0.86$). Four waveform parameters (intermediate slope, alpha angle, beta angle and area ratio) were identified as altered. These altered parameters can provide guidance to physicians about the physiological interpretation of capnograms and clinical decision. Proper interpretation of the capnogram can alert a clinician to important changes in mechanical ventilatory parameters in order to obtain a capnographic wave closest to normal thereby improving the lung function of patients.

1 INTRODUCTION

Capnogram is the graphical waveform which describes the carbon dioxide (CO_2) concentration throughout respiration, it is a curve obtained by continuous and non-invasive recording of the CO_2 partial pressure in a sample of expiratory air, providing a measurement of alveolar ventilation (You et al., 1994); (Roy et al., 2007). Besides it is useful to assess respiratory disorder in patients under invasive mechanical ventilation (IMV), capnography is also capable to detect changes in pulmonary blood flow, monitoring the function alveolar and CO_2 production (Belpomme et al., 2005); (Cheifetz and Myers, 2007).

The information provided by the capnography, as end-tidal CO_2 pressure ($PetCO_2$) and the waveform capnogram can be used as a tool to diagnose pulmonary problems and respiratory monitoring during the time that the patient remains in IMV (Thompson and Jaffe, 2005); (Roy et al., 2007). The device can also be used to monitor patients in emergency response situations, during anesthesia procedure and pediatric intensive care unit (ICU) (Langhan, 2009).

The normal capnogram has a rectangular wave model, measured by alternating inspiratory and expiratory phases (Gravenstein et al., 2011). Expiration itself consists of three stages as follow: Phase I represents the anatomical dead space, during phase II occurs a mixture of anatomical and alveolar dead space and phase III represents the expiration of CO_2 rich gas (Figure 1) (Cheifetz and Myers, 2007).

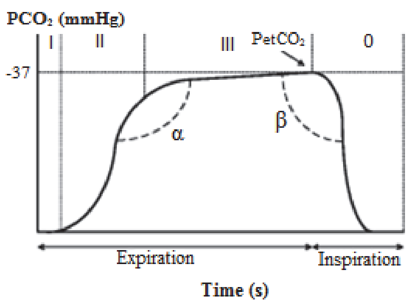

Figure 1: Example of a normal capnogram with the inspiratory (phase 0) and expiratory phases (I, II and III), α and β angles and $PetCO_2$ value.

Rasera C., Gewehr P. and T. Domingues A..
Quantitative Analysis of the Effect of Prolonged Mechanical Ventilation on Capnographic Indices.
DOI: 10.5220/0004229102530256
In *Proceedings of the International Conference on Biomedical Electronics and Devices* (BIODEVICES-2013), pages 253-256
ISBN: 978-989-8565-34-1

The maximum value reached at the end of phase III is referred to $PetCO_2$, which precedes the start of the following inspiration. These three phases are separated by two well-defined transitions: α and β angles (Thompson and Jaffe, 2005).

Waveform indices of CO_2 can be easily calculated. Furthermore, trends could provide useful information for pulmonary diagnostic from patient. However, it should be noted that their values cannot be uniquely linked to physical respiratory parameters. Other approaches to calculate waveform parameters are necessary in pediatric practice (Benallal and Busso, 2000); (Op Den Buijs et al., 2006). Thus, the aim of this paper is to establish the quantitative relationship between shape indices of the patients under prolonged IMV after cardiac surgery and the waveforms obtained 48 hours after tracheal extubation of these patients in ICU.

2 METHODS

This study was approved by the ethics committee of Pequeno Principe Hospital, Curitiba, Brazil. The research was carried out in the hospital's cardiac ICU between September 2011 and January 2012. Informed consent was obtained from the parents or the caregivers responsible for the patients.

A total of 52 infants were evaluated from 2 days to 3 months of age, both sexes. The characteristics of the patients are presented in table 1. Patients who had sepsis, some respiratory complication (e.g. pneumonia and pleural effusion) or the children who passed away were excluded.

The capnographic curves were analyzed in two moments during the period that the patient remained in ICU: A) Prolonged IMV: measurements were performed at the 10^{th} day of mechanical ventilation; B) Spontaneously breathing: measurements were performed two days after tracheal extubation with the spontaneously breathing infant.

Table 1: Characteristics of the patient.

Characteristic	Patient (n = 52)	
Age (month)	1.37 ± 0.6	
Sex (male/female)	19/33	
Weight (kg)	2.32 ± 1.6	
Vital Parameters	Instant A	Instant B
Cardiac Frequency	79.3 ± 3.8	80.1 ± 1.4
Respiratory Frequency	28 ± 2.3	18 ± 2.1
Body temperature (ºC)	36.1 ± 1.2	36.7 ± 1.3
Pulse Oxygen Saturation (%)	92.4 ± 3.2	99.2 ± 1.2

Values are expressed as mean ± standard deviation or number of patients.

Patients undergoing IMV were ventilated by Inter 5 Ventilator (Intermed, São Paulo, Brazil), using limited pressure, time-cycled ventilators in assistcontrol mode.

Samples for arterial blood gas analysis were obtained from a catheter in the radial artery by using a heparinised syringe (Monovette LH, Nümbrecht, Germany). The blood gas measurements were obtained using a Cobas B121 system (Roche, Mannheim, Germany) that was calibrated daily.

$PetCO_2$ was monitored using a sidestream capnography module (Figure 2) (CO_2CGM OA1000, Ronseda, Shenzhen, China) placed between endotracheal tube and the circuit of ventilator through an airway adapter in moment A; and it was adapted to nasal catheter in moment B. The CO_2 monitoring began immediately after calibration.

Figure 2: Sidestream capnography module.

In order to measure the deformation of capnogram related to time; some variations of waveform parameter were calculated; they were defined in relation to the beginning of expiration (T_0), i.e. from the start of phase II on the capnographic curve.

Six waveform indices have been tested from a single capnographic curve (Figure 3):

Three indices measured the capnogram slope during the expiration period. The slopes were obtained by linear regression of CO_2 *versus* time:

- S_1: initial slope measured from 0 to 0.2 s (phase II);
- S_2: intermediate slope measured from 0.8 to 1.2 s (beginning of phase III);
- S_3: final slope measured at the end of expiration during half second preceding the end of expiratory peak (end of phase III).

Three indices were measured indirectly:

- The α angle between the intermediate and the initial slopes $(S_2/S_1) \times 100$;
- The area ratio (AR) under the curve at angle α (A_1) to the area of the rectangle in which it is inscribed;

- The β angle was defined by the prolongation of the line between the terminal slope (phase III) and the descending slope (phase 0).

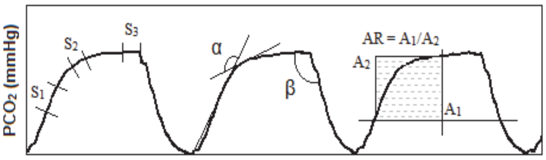

Figure 3: Schematic description of the capnographic indices measured on a normal capnogram. See text for details.

For comparison and quantitative analysis of CO_2 waveforms in two moments of each patient, it was necessary to select good quality cycles according to criteria of amplitude, duration and, when possible, regularity of the curve. In this study, we systematically eliminated the cycles that did not meet the following criteria: 1) validity lasting between 1 and 4 seconds; 2) symmetry for at least 5 cycles; and 3) good regularity of expiratory phases.

The data recorded were analyzed statistically; the association between $PetCO_2$ and arterial carbon dioxide pressure ($PaCO_2$) values was analyzed using the Pearson product-moment correlation coefficient (r). Analysis of variance (ANOVA) was performed to compare waveform parameters between infants under prolonged IMV and 48 hours after tracheal extubation. Significance was defined for two-tailed values of $p<0.05$. Statistical analysis was performed using MedCalc Statistical Software version 10.4.5.

3 RESULTS

The waveform analysis was assessed at the 10th day of IMV in postoperative cardiac patients. For the 52 measurements, $PaCO_2$ was 39.4 ± 3.2 mmHg and $PetCO_2$ was 37.6 ± 3.2 mmHg. The correlation between $PaCO_2$ and $PetCO_2$ measurements was $r^2 = 0.8618$ ($p<0.001$) throughout the study period. The mean $P(a–et)CO_2$ was 1.82 ± 1.2 mmHg with values that ranged from –0.7 to 4 mmHg.

The mean period that the patients remained in IMV was 16 days, the minimum and maximum time of IMV were 12 and 19 days, respectively.

For the measurements in spontaneously breathing patients the mean values for $PaCO_2$ and $PetCO_2$ were 40 ± 3 mmHg and 39.5 ± 3 mmHg, respectively. The $PaCO_2$ and $PetCO_2$ measurements maintained a significant correlation ($r^2 = 0.9787$, $p<0.001$) throughout the study period.

Six quantitative waveform parameters were determined for each patient. In addition $PaCO_2$ and $PetCO_2$ values also have been measured for statistical analysis (Table 2). Significant differences were noted between the mean of prolonged IMV and spontaneously breathing patients for four waveform parameters: intermediate slope, α and β angles, and area ratio.

Table 2: Waveform parameter data.

Waveform parameter	Instant A	Instant B	p-Value
S_1	15	13.4	0.08
S_2	0.25	0.57	< 0.001*
S_3	0.17	0.20	0.10
α angle	100.5º	117º	0.04*
β angle	90.7º	106.4 º	0.02*
AR	80.3	67	< 0.001*
$PetCO_2$	39.5	37.6	< 0.001*
$PaCO_2$	40	39.4	0.17
$P(a\text{-}et)CO_2$	0.5	1.8	< 0.001*

The CO_2 measurements are expressed in mmHg.
* Statistically significant.

Patients under prolonged IMV had a steeper ascending slope and a higher alpha angle, a fast descent in phase III and larger descending angle presented on 1 and 2 curves of Figure 4. The curve 3 found only in 6 patients at the 10th day of IMV indicates asynchrony between patient and ventilator.

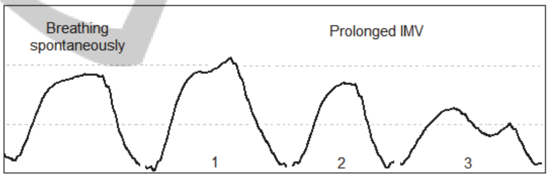

Figure 4: A sample recorded waveform from infant in two different conditions; breathing spontaneously and prolonged mechanical ventilation (10 days mean).

4 DISCUSSION

Capnography has become the standard of care for basic respiratory monitoring for all intubated patients in the ICU; the extension of this technique to intubated infants has been limited by technical problems associated with the capnographic indices.

Waveform analysis of infant patients has been used to demonstrate several parameters that correlate with the respiratory condition of intubated patients for a long period. Alpha angle, alveolar plateau slope and area ratios can be used clinically for estimating the alveolar ventilation and the pulmonary involvement in infants (Hagerty et al., 2002); (Roy et al., 2007).

As expected there was a significant difference in the $PetCO_2$ measurements and $P(a–et)CO_2$ gradient in patients under prolonged IMV when compared with spontaneously breathing patients. The P(a–et)CO_2 gradient is essentially an indicator of alteration in ventilation/perfusion due to cardiopulmonary causes and is directly proportional to degree of dead space (Domingo et al., 2010).

You et al. (1994) found larger differences among the indices in asthmatic patients than healthy subjects, but the strongest differences were observed analyzing indices in the intermediate phase of the capnogram. These results are similar to the ones found in our research for infant patients without respiratory alteration but under prolonged IMV.

In 2002, Hagerty et al. carried out a study with 20 newborn patients who were receiving mechanical ventilation for pulmonary diseases and for postoperative condition and they found four waveform parameters (ascending slope, alveolar angle, alpha angle and descending angle), which independently differentiated patients with pulmonary disease from control group.

The analysis of CO_2 pressure through capnography during prolonged IMV of neonates is less documented in the pediatric literature (Thompson and Jaffe, 2005). The additional dead space, mechanical problems, low weight, small flow and respiratory pressure may limit the clinical value of capnography with infants.

In order to reduce these limitations we have used the sidestream capnograph that requires a small sample cell and, therefore, a low flow rate (50 ml/min). For the neonate with high respiratory rates and low tidal volumes, this rate of gas avoids the dilution of alveolar CO_2. Thus, the device provides precise measurements in newborns patients.

In this study, patients under prolonged IMV had a steeper ascending slope and a higher alpha angle, a rapid descent in phase III and little alveolar plateau if any. These may be explained by the fact that although the patients do not have respiratory disease, the fact that they were submitted to IMV for a prolonged period associated with high mechanical ventilator parameters produces a commitment of lung function, as well as a smaller dead space and higher respiratory rate.

5 CONCLUSIONS

We have analyzed capnograms from our subjects, and it was determined that the infant under prolonged IMV can significantly alter the characteristic waveform.

Patients under prolonged IMV had a steeper ascending slope and a higher alpha angle, a rapid descent in phase III and larger descending angle (beta) than the normal waveform parameters found in patients 48 hours after tracheal extubation.

The present results could be a guideline for clinicians in the physiological interpretation of the capnogram and it could help clinicians to get accurate respiratory information about the infant patient.

The knowledge of alteration in the CO_2 waveform can help the health professionals to change the mechanical ventilatory parameters in order to obtain a capnographic wave closest to normal thereby improving the lung function of patients.

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