Clinical Implications of a Quality Assessment of Transcutaneous CO₂ Monitoring in Preterm Infants in Neonatal Intensive Care

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Abstract. More than 1% of infants are born premature. Many of these children require special treatment because of immature organs and body functions. CO₂ is an important parameter to monitor in order to avoid serious brain damage. Blood sampling of CO₂ has several shortcomings and non-invasive transcutaneous CO₂ is being investigated in order to assess its potential to contribute with the same type of information as blood CO₂ measurements. The present study assesses the quality of transcutaneous CO₂ data by comparing it to the “golden standard” blood CO₂ data, in order to provide clinicians with a better understanding of the usefulness and limitations of transcutaneous CO₂ data in neonatal care. The study shows that for low transcutaneous CO₂ the error is relatively high and in most cases the true CO₂, represented by the blood CO₂, which can be regarded as the “gold standard”, is higher than the measured transcutaneous CO₂. The opposite is the case for high transcutaneous CO₂. It is discussed how this is not due to any systematic error in the equipment, but due to the natural behaviour of noisy data.

Keywords. prematurity, neonatal care, CO₂ monitoring, transcutaneous CO₂

1. Introduction

In Denmark approximately 700 infants are born premature each year, i.e., born before the 32nd week of gestation, which is approximately 1.4% of all births [1]. Many of these children require special treatment because of immature organs and body functions [2, 3]. In particular, complications of the respiratory system are often seen due to less developed surfactant systems [2, 3]. Treatment includes surfactant infusion, high frequency ventilation (HFV), continuous positive airway pressure (CPAP), blood gas analysis (CO₂/O₂), transcutaneous monitoring of gasses (PtCO₂/PtO₂), ECG, etc. [2, 3]. The continuous transcutaneous measurement (PtCO₂) is important because CO₂ levels may change rapidly. Both severe and mild hypocapnia (low CO₂) is risky particularly in neonates [4]. Hypocapnia has been associated with the development of brain damage – intraventricular haemorrhage, periventricular leucomalacia and death [4–6].

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The precision of the PtCO\textsubscript{2} is important. In clinical use the measurement has been shown to be influenced by many factors [7]. Often the PtCO\textsubscript{2} is used more to determine the CO\textsubscript{2} trend than the absolute CO\textsubscript{2} value. Many clinicians are uncertain about how to interpret the PtCO\textsubscript{2} data. Blood CO\textsubscript{2} (PCO\textsubscript{2}) is, therefore, still used as the “gold standard” [7]. However, PCO\textsubscript{2} has its shortcomings. Draining the premature infants’ blood is one flaw, but also rapid changes in CO\textsubscript{2} levels are not discovered, and invasive intervention is not desirable for more reasons [7, 8]. Better precision and better understanding of how to interpret the transcutaneous CO\textsubscript{2} measurements may help the clinical staff to give the patient a better treatment and to prevent hypocapnia.

The present study assesses the quality of transcutaneous CO\textsubscript{2} data by comparing it to the “golden standard” blood CO\textsubscript{2} data, in order to provide clinicians with a better understanding of the usefulness and limitations of transcutaneous CO\textsubscript{2} data in neonatal care.

2. Material and Methods

Data from ten premature children were collected from the Department of Pediatrics, Aalborg Hospital. Table 1 gives an overview of the 10 children – 5 male and 5 female.

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228 pairs of corresponding CO\textsubscript{2} samples were collected from the 10 children; one pair consisting of a transcutaneous CO\textsubscript{2} sample analysed by a TCM4 and a blood CO\textsubscript{2} sample analysed by an ABL400, both from Radiometer. Data were analysed and visualised using SPSS, version 16.0.

3. Results

Figure 1 shows the correlation between transcutaneous CO\textsubscript{2} and blood CO\textsubscript{2}. A regression line is added. It can be seen that for low transcutaneous CO\textsubscript{2} the blood CO\textsubscript{2} is higher than the transcutaneously measured CO\textsubscript{2}, and that for high transcutaneous CO\textsubscript{2} the blood CO\textsubscript{2} is lower than the transcutaneously measured CO\textsubscript{2}. Each point in the graph represents a pair of corresponding CO\textsubscript{2} samples: one transcutaneous CO\textsubscript{2} sample and a blood CO\textsubscript{2} sample.

The difference between blood CO\textsubscript{2} and transcutaneous CO\textsubscript{2} as a function of transcutaneous CO\textsubscript{2} is shown in Figure 2. Each point represents the difference between a pair of corresponding samples (one transcutaneous CO\textsubscript{2} sample and a blood CO\textsubscript{2} sample), and for each patient a regression line is shown and a regression line for all 10 patients is also added (shown in bold). For all ten patients the regression line has a negative slope.
In Figure 3 the RMS error is shown as a function of transcutaneous CO$_2$. For low and high transcutaneous CO$_2$ the RMS error is in the range 1.20–2.00 kPa, and for the normal CO$_2$ range (4.9–6.0 kPa) the RMS error is 0.95–1.00 kPa.

The difference between blood CO$_2$ and transcutaneous CO$_2$ as a function of blood CO$_2$ is shown in Figure 4. Each point represents the difference between a pair of corresponding samples (one transcutaneous CO$_2$ sample and a blood CO$_2$ sample), and for each patient a regression line is added. For seven out of the ten patients the regression line has a positive slope.
4. Discussion

From Figures 2 and 3, it can be seen that for low transcutaneous CO₂ the error is relatively high and in most cases the true CO₂, represented by the blood CO₂, which can be regarded as the “gold standard”, is higher than the measured transcutaneous CO₂. In other words, most low transcutaneous CO₂ measurements are probably underestimating the CO₂. A similar argument can be used for high transcutaneous CO₂: most high transcutaneous CO₂ measurements are probably overestimating the CO₂.

One might be tempted to try to correct this problem by applying a linear correction derived from the regression line for all 10 patients shown in bold in Figure 2. However, before doing this, one should consider the nature of the two types of CO₂ measurements. The blood CO₂ is regarded as the “gold standard”, i.e., can be seen as being very close to the true blood CO₂, and therefore, more importantly, can be seen as the independent variable. The transcutaneous CO₂ is therefore the dependent variable. Assuming a Gaussian distribution of measured transcutaneous CO₂ relative to the true...
(blood) CO$_2$, it can be seen that due to the ‘noise’ the transcutaneous CO$_2$ will tend to be more widely spread than the blood CO$_2$ – for example a true CO$_2$ of 4 kPa can lead to a transcutaneous CO$_2$ measurement of both 3 kPa and 5kPa with the same probability. Or in other words, the low transcutaneous CO$_2$ measurements represent the left tales relative to the true CO$_2$ (the right tales being ‘hidden’ by the other measurements in the middle CO$_2$ range) and the high transcutaneous CO$_2$ measurements represent the right tales relative to the true CO$_2$. Trying to correct the low and high transcutaneous CO$_2$ measurements by a linear function will adjust both the visible and the ‘hidden’ tales – even though adjusting the visible tales will improve the prediction error, adjusting the ‘hidden’ tales will work in the opposite direction. Due to the nature of the calculation of the RMS error it can be shown that the net result of such an adjustment will be an increased RMS error.

Another way of describing this dilemma is to illustrate the data as shown in Figure 4. Even though from a clinical point of view it may be natural to have the measured transcutaneous CO$_2$ on the x-axis and analyse the error relative to the transcutaneous measurement (which may be right in front of the clinician), the independent variable should be on the x-axis. Showing the difference between blood and transcutaneous CO$_2$ as a function of the blood CO$_2$, illustrates the point. Instead of the negative slopes of the regression lines seen in Figure 2, the regression lines for seven out of ten patients in Figure 4 has a positive slope, and the overall picture in Figure 4 is that the data is insufficient to make any conclusion regarding the correlation between blood CO$_2$ and the error. There is no clear indication of any systematic error.

From a clinical point of view the analysis shows how most low transcutaneous CO$_2$ measurements are probably underestimating the CO$_2$, and how most high transcutaneous CO$_2$ measurements are probably overestimating the CO$_2$. However, it is important to understand that this is not due to any systematic error in the equipment, but due to the natural behaviour of noisy data. Assuming Gaussian noise, this is in fact what will be seen in any measurement system where true physiological variables are sampled.

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References