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Clinical Implications of a Quality Assessment of Transcutaneous CO_2 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, CO_2 monitoring, transcutaneous CO_2

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 (CO_2/O_2), transcutaneous monitoring of gasses ($PtCO_2$/PtO_2), ECG, etc. [2, 3]. The continuous transcutaneous measurement ($PtCO_2$) is important because CO_2 levels may change rapidly. Both severe and mild hypocapnia (low CO_2) 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 $PtCO_2$ is important. In clinical use the measurement has been shown to be influenced by many factors [7]. Often the $PtCO_2$ is used more to determine the CO_2 trend than the absolute CO_2 value. Many clinicians are uncertain about how to interpret the $PtCO_2$ data. Blood CO_2 (PCO_2) is, therefore, still used as the "gold standard" [7]. However, PCO_2 has its shortcomings. Draining the premature infants' blood is one flaw, but also rapid changes in CO_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_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_2 data by comparing it to the "golden standard" blood CO_2 data, in order to provide clinicians with a better understanding of the usefulness and limitations of transcutaneous CO_2 data in neonatal care.

2. Material and Methods

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

Table 1. Overview of the 10 children included in the study outlining the childrens' sex (M/F), gestation age in weeks (Gest), weight in gram (Wgt), and height in cm (Hgt)

Pt	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**
Sex	F	M	M	F	F	M	F	M	M	F
Gest	27	27	27	29	26	29	29	32	25	26
Wgt	600	1,190	823	1,430	765	1,259	1,075	2,375	725	630
Hgt	34	38	34	41	34	38	39	48	32	34

228 pairs of corresponding CO_2 samples were collected from the 10 children; one pair consisting of a transcutaneous CO_2 sample analysed by a TCM4 and a blood CO_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_2 and blood CO_2. A regression line is added. It can be seen that for low transcutaneous CO_2 the blood CO_2 is higher than the transcutaneously measured CO_2, and that for high transcutaneous CO_2 the blood CO_2 is lower than the transcutaneously measured CO_2. Each point in the graph represents a pair of corresponding CO_2 samples: one transcutaneous CO_2 sample and a blood CO_2 sample.

The difference between blood CO_2 and transcutaneous CO_2 as a function of transcutaneous CO_2 is shown in Figure 2. 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 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.

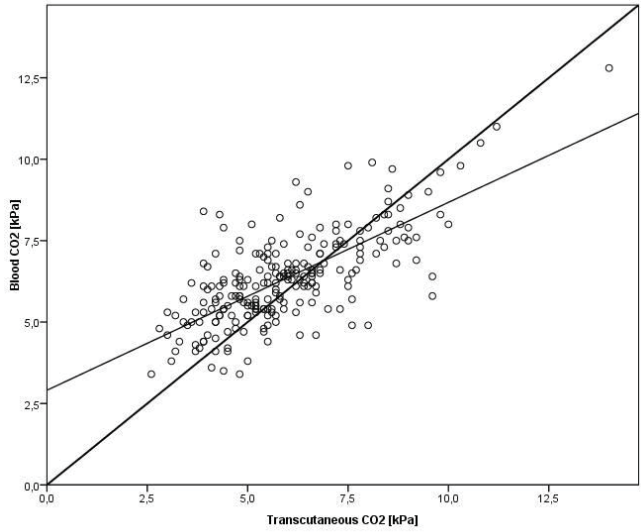

Figure 1. Transcutaneous CO_2 versus blood CO_2. A regression line (thin line) and x = y (bold line) is added

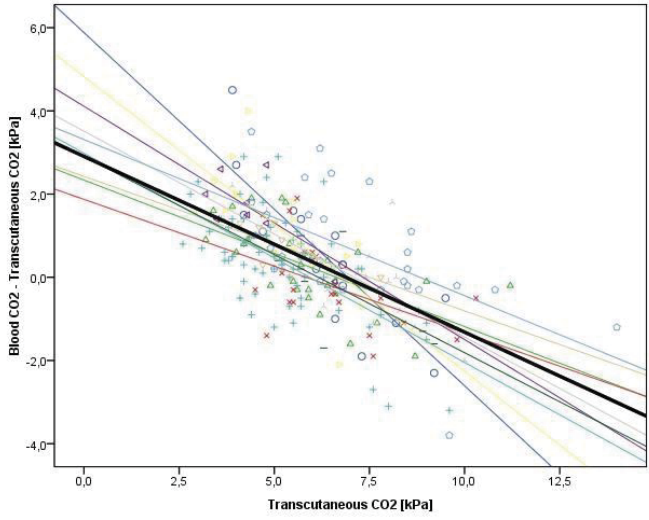

Figure 2. The difference between blood CO_2 and transcutaneous CO_2 as a function of transcutaneous CO_2

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.

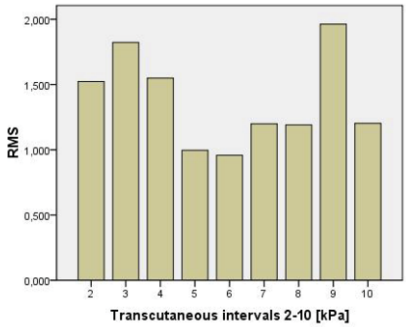

Figure 3. The RMS error as a function of transcutaneous CO_2

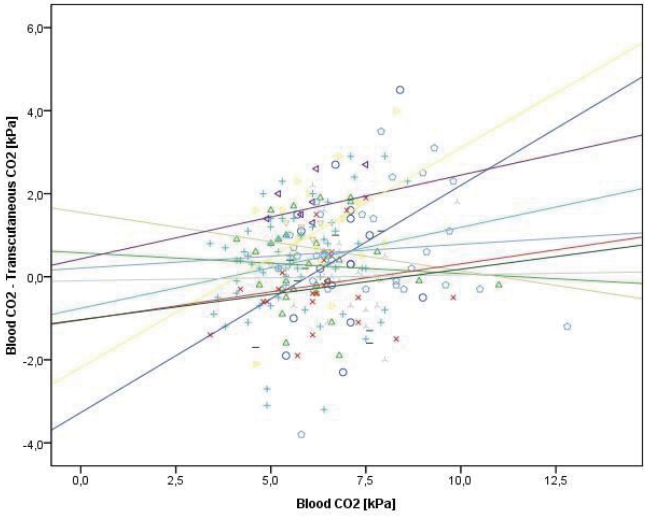

Figure 4. The difference between blood CO_2 and transcutaneous CO_2 as a function of blood CO_2

4. Discussion

From Figures 2 and 3, it can be seen that for low transcutaneous CO_2 the error is relatively high and in most cases the true CO_2, represented by the blood CO_2, which can be regarded as the "gold standard", is higher than the measured transcutaneous CO_2. In other words, most low transcutaneous CO_2 measurements are probably underestimating the CO_2. A similar argument can be used for high transcutaneous CO_2: most high transcutaneous CO_2 measurements are probably overestimating the CO_2.

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 CO_2 measurements. The blood CO_2 is regarded as the "gold standard", i.e., can be seen as being very close to the true blood CO_2, and therefore, more importantly, can be seen as the independent variable. The transcutaneous CO_2 is therefore the dependent variable. Assuming a Gaussian distribution of measured transcutaneous CO_2 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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