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A novel approach towards noninvasive monitoring of transcutaneous CO₂

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Abstract

The continuous monitoring of transcutaneous gases is an integral part of neonatal intensive care. Present monitors measure the equilibrating values of these gases by raising the skin temperature to 42°C or above. Because neonatal skin is very sensitive and delicate, this often leads to serious skin injuries. In this work, we present a new approach to the noninvasive measurement of transcutaneous partial pressure of carbon dioxide (tcpCO₂) based on the initial pseudo steady state diffusion rates instead of the mass-transfer equilibrium. Because we are following initial diffusion rates, each measurement takes no more than a few minutes. Additionally, raising the surface temperature is not required, thus, skin irritation and burns are highly unlikely. A dual-chamber diffusion vessel with either porcine skin or dialysis membrane placed between the two chambers was used to mimic neonatal skin. LI-820 CO₂ Analyzer was used to measure the CO₂ diffusing through the membrane or skin. Initial experiments on adult human skin under varying physical activities, food intake and breathing patterns showed a strong influence of the various conditions on the amount of CO₂ diffusing through skin. These initial findings suggest that this method can be used not only on neonates but to a wider population of patients.

Keywords

noninvasive monitoring; sensors; preterm neonate; diffusion; transcutaneous gases

1. Introduction

Partial pressures of arterial oxygen (PaO₂) and carbon dioxide (PaCO₂) are two of the most important respiratory parameters in the treatment of critically ill neonates. Extremes of these two factors account for hyperoxia and hypoxia, or hypercarbia and hypocarbia, respectively. Continuous monitoring of transcutaneous oxygen tension (tcPO₂) in neonates requiring oxygen therapy could reduce the incidence and acuteness of retinopathy of prematurity by

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Competing interests: None declared.

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preventing the occurrence of hyperoxia [1–4]. Continuous monitoring of CO₂ may prevent chronic lung disease and conditions like periventricular leucomalacia. Hypocarbica leads to intraventricular hemorrhage, cerebral palsy, cognition developmental disorder, and auditory deficit whereas severe hypercapnia can cause intracranial hemorrhage, consciousness alterations, cataphora, and hyperspasmia [5–7].

Considered as a scientific breakthrough in the late 1970s, transcutaneous blood gas monitors were rapidly adopted for routine use in neonatal intensive care to measure O₂ (tcpO₂) and CO₂ (tcpCO₂) dissolved in tissue that approximated arterial values. These monitors require heating the skin underneath the sensor to 43°C, which can result in skin burns, necessitates frequent sensor site changes as well as re-calibration. Plagued by technical problems, pulse oximetry emerged as an alternative during the 1980s. Pulse oximetry has the advantages of not requiring heating the skin or calibration, ease of use and low-cost. However, false alarms occur frequently due to motion artifacts. Additionally, while pulse oximetry is acceptable at low and normal oxygenation, it is limited in the detection of hyperoxia. In delicate neonates, long term use can cause development of finger ischemia or necrosis due to the applied pressure. Current commercial transcutaneous blood gas analyzers use electrochemical cells as sensors based on the principle of amperometry. But they incorporate high maintenance cost and replenishing major working units [8,9]. In this study we have focused upon a novel rate-based approach of transcutaneous measurement, which can give us a quick and efficient estimate safely.

2. Materials and Methods

2.1. Materials

Porcine ear skin, accepted as a well-suited model for premature neonatal skin, was used in this study [10–12]. The porcine ear skin was carefully cut off the cartilage and excessive fat was removed. The average thickness of one layer of porcine skin was measured as 1 mm. Regenerated cellulose dialysis membrane with a MWCO (molecular weight cut off) of 10K (Thermo Scientific) was utilized for comparison in the diffusion rate studies. The average thickness of a single layer dialysis membrane was 25 µm. A dual-chamber system comprising of a measurement and a feeding chamber was made of poly (methyl methacrylate) (PMMA). The porcine skin or the dialysis membrane was placed between the two chambers to mimic the transcutaneous gas diffusion. The low concentrations of CO₂ in the measurement chamber were measured by a LI-820 CO₂ Analyzer. Human studies were carried out on an adult for the measurement of transcutaneous CO₂ under various circumstances and conditions.

2.2. Experimental setup and operation procedure

The studies recorded by James et al. [13] give the dimensions of the preterm neonate foot measuring the foot length, occipital-frontal head circumference, crown-rump, and crown-heel length of 123 neonates of gestational ages 26–42 weeks. Based on these data, the basic design of the chambers in terms of volume, dimensions and surface area was optimized. The inner diameter of the chambers (Fig. 1) is 37.5 mm. The feeding chamber (top) has a volume of 44.2 ml while the volume of the measurement chamber (bottom) is 6.6 ml. The device was built using a laser cutter and a milling machine along with design software like Corel Draw and Google Sketch Up.

The N₂-CO₂ mixture with varying CO₂ concentrations is continuously passed through the feeding chamber. The inlet of the measurement chamber on the bottom was connected to either a N₂ supply or the outlet of the LiCor CO₂ analyzer through a multi-way valve. The outlet of the measurement chamber was connected to the inlet of the LiCor through a pump. The entire system was placed inside an incubator and the temperature was maintained at

37°C. To make a measurement, the chamber was first purged with N₂ to drive away any trace of CO₂ present in the system. The multi-way valve was then switched to recirculation. The data were recorded continuously throughout the process. Various feed concentrations of CO₂ were passed as feeds to record the amount of gas diffusing through the membrane or the porcine skin.

In the human study, the feeding chamber and the porcine ear skin or the dialysis membrane was removed. The forearm of the healthy adult human subject was then tightly placed on the measurement chamber. After N₂ purging, a continuous measurement of transcutaneous CO₂ was obtained. The study was conducted under various conditions.

2.3. Calculation of the pseudo steady state diffusion rate

The mass balance equation for the whole recirculation system including the measurement chamber, the inside volumes of the pump, the LiCor CO₂ analyzer, and the tubing can be written as follows

$$V \frac{dC}{dt} = kA (C_f - C) \quad (1)$$

where V is the total volume of the system, C is the CO₂ concentration in the measurement chamber, t is time, k is the mass transfer coefficient, A is the total mass transfer area, and C_f is the CO₂ concentration in the feeding chamber. At the beginning of the recirculation ($t = 0$), the CO₂ concentration in the measurement chamber is zero. Integration of equation (1) from the beginning of the recirculation gives

$$C = C_f (1 - e^{-at}) \quad (2)$$

where $a = V/kA$. a is a constant for a specific patient subject. The function e^{-at} can be expanded into a Taylor series at $t = 0$:

$$e^{-at} = 1 - at + \frac{1}{2}at^2 - \frac{1}{6}at^3 + \dots \quad (3)$$

Because the transcutaneous mass transfer resistance is usually large, $a \ll 1$ (for example, $a = 8.46 \times 10^{-6} \text{ s}^{-1}$ for a single layer of porcine ear skin), the third and later items can be negligible. Thus,

$$e^{-at} \approx 1 - at \quad (4)$$

Substitution of equation (4) into equation (2) gives

$$C \approx aC_f t \quad (5)$$

From the above equation, we know that the CO₂ concentration in the measurement chamber increases linearly with time. The slope of the trend line, which is the pseudo steady state CO₂ diffusion rate, is equal to aC_f , i.e.,

$$\text{Slope} = aC_f \quad (6)$$

Obviously, the slope of the CO₂ trend line is linearly proportional to the CO₂ concentration in the feeding chamber (C_f). By fitting the pseudo steady state CO₂ concentration trend line to a linear equation, the pseudo steady state CO₂ diffusion rate can be easily obtained. It should be noted that it takes a little time (less than 1 minute depending on the thickness of the skin) to reach the pseudo steady state diffusion because the skin is not infinitely thin.

3. Results and discussion

The response curves for the single and double layers of porcine ear skin are shown in Fig. 2. It can be seen that the CO₂ concentration in the measurement chamber increases linearly with time since the beginning of the recirculation as described by equation (5). Fig. 3 shows the plots of the pseudo steady state CO₂ diffusion rates (the slopes of trend lines in Fig. 2) across the porcine ear skin vs. the feed CO₂ concentrations. It can be seen that the CO₂ level in the feeding chamber is linearly proportional to the pseudo steady state diffusion rate, which is in agreement with equation (6). Thus, by measuring the pseudo steady state diffusion rate, the CO₂ level in the feeding chamber can be obtained in less than a few minutes. Comparatively, the traditional equilibrium-based transcutaneous gas monitors need at least 15 minutes to get a stabilized value even at an elevated temperature (usually 42°C). The double layers of porcine ear skin shows lower CO₂ diffusion rate owing to the increased mass transfer resistance. Experiments using single layer and double layers of dialysis membrane were also conducted and similar results were obtained (results not shown).

After the system was tested using dialysis membrane and porcine ear skin as a mimic, it was tested on adult skin to measure the pseudo steady state transcutaneous CO₂ diffusion rate. The blood flow rate for a healthy adult human being is 0.11–0.14 ml/min. Gas exchange occurs through the epidermis of the skin by diffusion. The main variables for the transcutaneous measurements are blood flow rate and gas concentration or pressure of the arterial blood, although studies have shown that metabolism and skin structure show influences too. Fig. 4 shows the pseudo steady state transcutaneous diffusion rate of an adult after food intake. As expected, the metabolism rate is a little bit higher at noon. The CO₂ diffusion rate reaches its highest at 1.5 hours after food intake, about 0.5 hours behind the highest blood glucose concentration, which usually occurs 1 hour after food intake. Sudden hypercapnia or varying breathing disorders might arise in a premature neonate due to the underdeveloped lungs in the body. Transcutaneous CO₂ diffusions through the skin under various breathing conditions were simulated by holding breath, breathing continuously in a closed bag, and hyperventilation. The former two breathing patterns significantly increase the blood CO₂ levels, as shown by a rise in the pseudo steady state diffusion rate of transcutaneous CO₂ diffusion (Fig. 5). On the other hand, hyperventilation decreases the blood CO₂ level.

As the pseudo steady state transcutaneous diffusion rate can be affected by the thickness and mass transfer properties of the skin, a calibration procedure is required in order to interpret the diffusion rates as blood gas concentrations. Due to the linear nature of the relationship between the two variables, a single-point calibration is possible.

4. Conclusions

Dialysis membrane and porcine ear skin were used as a model to study the characteristics of initial diffusion of transcutaneous gases. Results show that a pseudo steady state diffusion was established in less than a minute. The feed CO₂ concentrations are linearly proportional to the pseudo steady state diffusion rates. The porcine skin offers more resistance to the mass transfer of the gases than the dialysis membrane because of its structure, thickness and deposition of fat in the stratum granulosum. Preliminary human studies using the developed

device show that different physical activities, food intake and breathing patterns have a strong influence on the amount of CO₂ evolving from the human skin.

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Fig. 1.
Schematic of the experimental setup.

Fig. 2.
CO₂ trend lines with single layer (left) and double layers of porcine ear skin (right).

Fig. 3. Slope of CO₂ trend line vs. CO₂ feed concentration for 1 layer and 2 layers of porcine ear skin. The error bars are the standard deviations of 3 repeated measurements.

Fig. 4.
Slope of the CO₂ trend line measured on an adult after food intake.

Fig. 5. Slope of the CO₂ trend line measured on an adult for different breathing patterns including normal breathing, breathing in a closed bag, hyperventilation, and holding breath. The error bars are the standard deviations of 3 repeated measurements.