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A computerized decision support system to predict the variations in the cerebral blood flow of mechanically ventilated infants

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ABSTRACT

A computerized decision support system is described to predict the changes in the cerebral blood flow (CBF) of mechanically ventilated infants in response to different ventilatory settings. A CBF controller was developed and combined with a mathematical model of the infant's respiratory system to simulate the effects of ventilatory settings on the infant's CBF. The performance of the system was examined under various ventilatory treatments and the results were compared with available experimental data. The comparisons showed good agreement between the simulation results and experimental data for preterm infants. These included the results obtained under conditions of hypoventilation, hyperventilation, hypoxia, and hyperoxia. The presented decision support system has the potential to be used as an aide to the intensivist in choosing appropriate ventilation treatments for infants to prevent the untoward consequences of hazardous changes in CBF in mechanically ventilated infants such as hypoxic-ischemic brain injuries.

1. Introduction

Newborn premature infants often suffer from various respiratory disorders [1–4] and may need mechanical ventilation assistance during the first few weeks of life. However, mechanical ventilation treatment can have many side effects and may cause serious complications in neonates which include development of pulmonary interstitial emphysema, broncho-pulmonary dysplasia (BPD), and retinopathy of prematurity [5,6]. Cerebrovascular injuries are among the most serious complications that can develop during the first week of life of these infants and such complications can be caused by cerebral hemorrhage and ischemic injuries to the brain [7,8].

Disturbances in the cerebral blood flow (CBF) beyond the normal range can cause cerebrovascular injuries that may in turn lead to long-term disabilities or death among premature neonates. CBF is the ratio of the cerebral perfusion pressure to cerebrovascular resistance. Therefore, physical factors that can change these two parameters can affect CBF. Moderate changes in the mean arterial blood pressure (MABP) have not been found to cause significant changes in CBF of infants with intact cerebral autoregulation [9]. If abrupt changes in the MABP are prevented, and in the absence of hypoglycemia and anemia that can increase CBF, the most important factors affecting the CBF of mechanically ventilated infants with intact CBF autoregulation are considered to be the arterial partial pressures of carbon dioxide and oxygen [7–9].

Therefore, proper regulation of infant's blood gases through appropriate selection of ventilator settings can significantly help to reduce hazardous disturbances of CBF that can lead to periventricular hemorrhage and hypoxic-ischemic brain injuries in premature infants. In this article, a decision support system (DSS) is presented by which the effects of different ventilator treatments on infants' CBF are simulated by using a mathematical model. At this time, continuous monitoring systems utilizing non-invasive technologies such as near-infrared spectroscopy and Doppler ultrasound are available that can be used to measure or estimate the changes in the infants' CBF [8,10]. However, routine clinical application of these systems is questionable due to their limitations and practical problems [8]. In the absence of direct CBF monitoring systems, or in conjunction with such support technologies, the technique described in this article can be used at bedside to help the intensivist choose appropriate ventilator settings for infants on mechanical ventilation and avoid hazardous disturbances in CBF and their untoward consequences.

2. Methodology

A block diagram of the mathematical system used in the DSS is shown in Fig. 1. In this system, chemical control of infant's CBF is combined with a mathematical model of the infant's respiratory system [11,12] to simulate the effects of different ventilation treatments on the infant's CBF. The simulation results are

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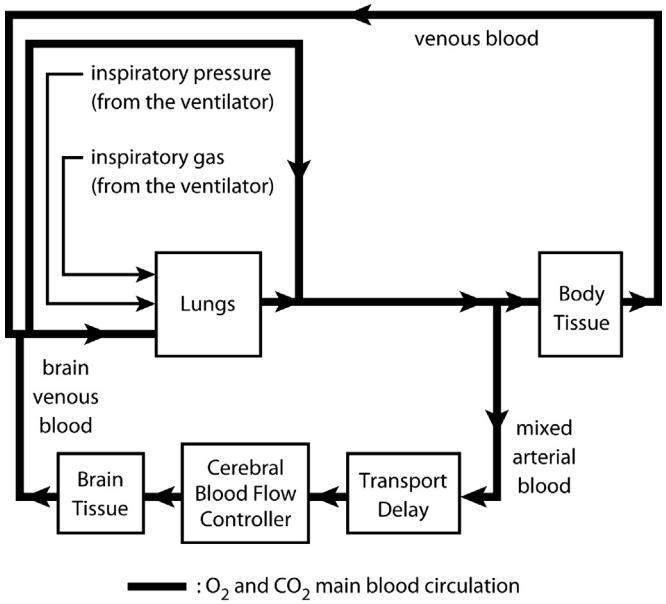

Fig. 1. A block diagram of the computerized system to predict changes in the CBF of infants in response to ventilatory settings.

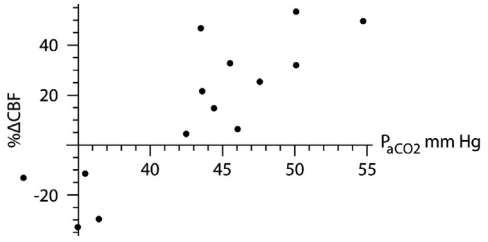

Fig. 2. %ΔCBF as a function of P_{aCO_2}.

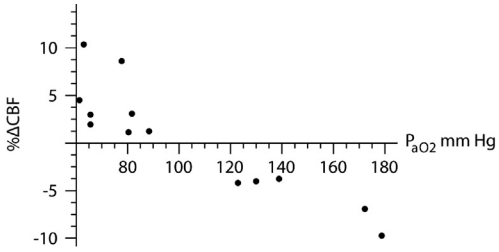

Fig. 3. %ΔCBF as a function of P_{aO_2}.

compared to reported clinical studies to assess the effectiveness of the system.

2.1. The CBF controller

To design the CBF controller, experimental data from the literature were compiled to derive mathematical relations between the infants' CBF and arterial blood gases. In compiling and analyzing the experimental data, care was taken to choose the results obtained when both the arterial partial pressure of carbon dioxide, P_{aCO_2}, and the arterial partial pressure of oxygen, P_{aO_2}, were monitored at the same time. For the CBF response to P_{aCO_2}, the results reported in several references were analyzed [13–16]. To measure the changes in CBF in response to P_{aCO_2}, Doppler ultrasound techniques were used in References [13–15], and the intravenous Xe clearance technique was employed in the experiments of Reference [16]. The experimental data obtained for mechanically ventilated infants with gestational ages ranging from 26 to 33 weeks were selected. The median gestational age in this group was 29 weeks.

For the CBF response to changes in P_{aO_2}, the experimental data reported in References [15,17] were analyzed. In both studies, Doppler ultrasound techniques were used to measure CBF. Experimental data obtained for infants under 37 weeks of gestation were used for analysis. The median gestational age of these infants was 31 weeks ranging from 25 to 36 weeks.

Percentage variations in CBF in comparison to normal CBF values were obtained and plotted as functions of P_{aCO_2} and P_{aO_2}. Normal CBF was considered at $P_{aCO_2}=40$ mm Hg, and $P_{aO_2}=100$ mm Hg. Figs. 2 and 3 show the percentage variations in infants' CBF (%ΔCBF) as compared to normal versus P_{aCO_2}, and P_{aO_2} respectively.

Curve fitting techniques and linear regression analyses were performed on the data presented in Figs. 2 and 3. The results of the linear regression analyses are

$$\%\Delta CBF = 3.67(P_{aCO_2}-40) + 2.257 \quad (1)$$

due to changes in P_{aCO_2} (with $r=0.85398$) and

$$\%\Delta CBF = 0.0933(100-P_{aO_2}) + 0.876 \quad (2)$$

due to changes in P_{aO_2} (with $r=0.90698$).

With regard to %ΔCBF response to P_{aCO_2}, a quadratic fit was found to be more accurate than a linear formula. That quadratic equation was found as

$$\%\Delta CBF = 2.41754 + 3.69354(P_{aCO_2}-40) - 0.00458(P_{aCO_2}-40)^2 \quad (3)$$

due to changes in P_{aCO_2}.

Combining Eqs. (2) and (3) yields

$$\%\Delta CBF = 0.0933[\Delta P_{aO_2}] + 3.69354[\Delta P_{aCO_2}] - 0.00458[\Delta P_{aCO_2}]^2 + 3.29354 \quad (4)$$

due to changes in blood gases where $\Delta P_{aO_2}=100-P_{aO_2}$ and $\Delta P_{aCO_2}=P_{aCO_2}-40$, and P_{aO_2} and P_{aCO_2} are in mm Hg.

Eq. (4) gives the steady state value of %ΔCBF in relation to changes in arterial blood gases. In the controller, the steady state value of CBF is found by adding %ΔCBF from Eq. (4) to normal CBF, and the instantaneous value of CBF is determined by adding a 1st order lag with a time constant of 5 s.

2.2. The mathematical model of the infant's respiratory system

The other building blocks of the system in Fig. 1 consisting of Lungs, Body Tissue, Transport Delay, and the Brain Tissue are parts of a mathematical model of the infant's respiratory system [12]. This detailed model of the human respiratory system has been used by a number of researchers to simulate the neonatal respiratory system e.g., [18–20]. The peripheral and central respiratory receptors and the respiratory controller of the model were not included in the system of Fig. 1 because in this DSS the respiratory drive signal is not provided by the infant's own respiratory control centers and is coming from the ventilator. The effects of an anatomical shunt in the lung is included in the system and the lung volume is time varying. The mathematical equations describing different building blocks of the model that have been incorporated in the DSS of Fig. 1 have been presented in Reference [12] and are not repeated here for brevity.

3. Results

Figs. 4–9 show a series of simulation results by using the presented DSS. In all the simulation tests, the patient is modeled as a premature infant of 1.8 kg weight, with respiratory distress syndrome (RDS), and a respiratory dynamic compliance of 2 ml/