State Variable Model and Analysis of Birth Asphyxia

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ABSTRACT

In India, a significant percentage of high risk births, which go up to 20%, are affected by perinatal asphyxia. Birth asphyxia is associated with deficient mental and physical development, severity of which leads to mortality. It is very important that a comprehensive quantitative study of the phenomenon be undertaken and a risk index formulated. Preventive measures can then be taken to avert the emergent situation. In the present paper neuronal sequelae to neonatal asphyxia were identified and a compartmental model was developed with each compartment representing a physiological parameter. Rate constants of the model were derived from literature and other experimental studies. To obtain online data on the parameters pO₂, pCO₂, pH, cerebral blood flow, intracranial pressure and heart rate an experimental study was conducted on a monkey. Online intracranial pressure monitoring during asphyxia was done through an artificial fontanel opening. A risk index was thus formulated to determine the severity of asphyxia to enable the pediatricians take corrective action.

Keywords: Neonatal Asphyxia, Compartmental Model, Monkey, Risk Index, Simulation.

INTRODUCTION

It is well established that in newborns, asphyxia leads to morphological and functional changes in the brain. It is a major cause of infant mortality. The effects of asphyxia have been studied extensively with experiments on animals. Volpe [1] gives a detailed account of the physiological and biochemical effects of asphyxia. Studies on autoregulation of cerebral blood flow and intracranial pressure variations during pO₂ and pCO₂ changes were also reported [2][3]. But these effects have not been studied quantitatively and no comprehensive model correlating all the significant parameters exists. The earlier approaches have been confined to models that provide information about the physiological parameters and metabolic processes involved in asphyxia. It is very important that a qualitative study of the phenomenon be undertaken and a mathematical risk index evolved to determine the severity of asphyxia.

MODEL STRUCTURE

Models used for metabolic processes where the aim of modeling is to obtain information about the internal parameters are mostly described by a compartmental structure. The models assume the existence of an analogy between structure parameters and well defined physiological parameters of the actual system. Accordingly a mental model was chosen to represent the dynamics of each compartment representing a parameter. The parameters of the model that are the following:


All these parameters have been known to be adversely affected by asphyxia. The presence of coupling between any two compartments was assumed based on evidence of known cause-effect relationship between the parameters. The model thus obtained was shown in Fig. (1). Oxygen and Carbon dioxide form the inputs u and u₂ respectively to the model. Inputs u₁ = 0 and u₄ = 0 represent a condition of normalcy while the inputs u₁ = 1.0 and u₄ = 1.0 represent asphyxia.

EXPERIMENTAL STUDIES

To obtain the data for estimating the rate constants of the model, experiments were performed on a monkey and the changes in the parameters ICP, CBF, pO₂, pCO₂, pH and heart rate during asphyxia were monitored. ICP was measured by creating an artificial fontanel and monitoring the anterior fontanel tension by using a strain gauge transducer. Prior to experimentation on the monkey, the transducer was first tested on a physical model resembling a neonate skull with respirator induced pressure fluctuations. This anterior fontanel tension recording was taken as a direct reflection of the intracranial pressure [4].

pO₂, pCO₂, and pH were obtained by conducting blood gas analysis of the samples taken during normal and asphyxiated conditions. The heart rate and the CBF were monitored using the Ultrasound Doppler Velocimetry. The changes in the respiratory pulse amplitude (RPA) and the cardiac pulse amplitude (CPA) were also observed. The results of the experiments were shown in Tables (1),(2) and Fig. (2)

The coupling coefficients between the compartments were then estimated by minimizing the mean square error between the system and the model response.
Experimental Results

The model obtained was defined by the following state equations (1).

\[ x_1 = -0.0044 x_4 + 0.893 x_6 + u_1 \]
\[ x_2 = -5.5 x_3 + 0.097 x_4 + 0.034 x_5 + 0.5 x_6 + u_2 \]
\[ x_3 = 0.0628 x_1 + 0.344 x_2 + 0.856 x_7 + 0.75 x_9 \]
\[ x_4 = 0.0147 x_1 - 0.0987 x_4 \]
\[ x_5 = -0.0775 x_1 + 0.1542 x_2 + 1.03 x_4 \]
\[ x_6 = 0.3211 x_1 + 1.053 x_2 + 0.976 x_7 + 1.82 x_8 + 0.0569 x_9 \]
\[ x_7 = -0.52 x_1 + 0.89 x_2 + 1.017 x_3 - 0.0132 x_6 \]
\[ x_8 = -0.0031 x_2 + 0.0035 x_5 \]
\[ x_9 = -0.1645 x_1 - 0.5065 x_2 \]  

The eigenvalues of the system matrix were found to be 
-1.1493, 0.5323 \(\pm\) 0.9201, \(\pm\) 0.1463 \(\pm\) 0.6846, -0.17, -0.1315, -0.0052 and 0.0. It can be seen that two of the poles of the system are on the right hand side of the s-plane and the system response is unbounded for step changes in the inputs. Thus sustained severe asphyxia which is represented by inputs \(u_1 = -1.0\) and \(u_2 = 1.0\) leads to unbounded response and is fatal.

**DISCUSSION**

The variations in each state were simulated for step changes in the oxygen and carbon dioxide inputs. On simulation the model was found to predict the trends in the states due to asphyxia. To evolve a risk index the pattern changes in the cerebral blood flow and the intracranial pressure were studied. The ratio \(R_f\)

\[ RI = \frac{R_{fin} - R_{fin}}{R_{fin}} \]  

Where \(R_f\) = \(R\) during normalcy \(X^{\circ}\) = State of the model

This formula for the risk index ensures that a change in any state in isolation does not cause any change in the risk index. Mathematically the index is analogous to a correlation function between all the parameters defining the condition of asphyxia. The value of the index lies between 0 (for normalcy) and 1 for very severe asphyxia. The index as calculated from the above formula after a minute of asphyxia was 0.29 for the monkey and 0.28 when simulated using the model.

**CONCLUSIONS**

The phenomenon of asphyxia was defined and quantified using a model with nine states. A risk index was formulated to determine the severity of asphyxia. The index can be seen to be useful when compared to qualitative assessment like apgar scores which does not take into account the exact chances in the physiology. Further experimentation on animal models and testing on asphyxiated neonates should be done to establish its efficacy.

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**REFERENCES**