Physiological Modelling of the Hemodynamic Effects of Vasoactive Drugs in Patients with Septic Shock

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We present a comprehensive computer model that can simulate the haemodynamic responses to vasoactive drugs under different pathophysiological conditions. It is based on a physiological, pulsatile model consisting of fourteen compartments describing the cardiovascular haemodynamics including the systemic, pulmonary, coronary and cerebral circulations; a drug transport model with the same number of compartments used to calculate drug concentrations in the relevant body compartments; and a drug effect model relating the concentration of drug in these different compartments to changes in the resistances and compliances of those compartments in a baseline human model of 75 Kg, a total blood volume of 5.6 liters and a heart rate of 75 beats/min.

This physiological model has been modified to study the interaction of different therapeutic interventions in patients with septic shock who typically remain hypotensive after fluid resuscitation, reproducing the key haemodynamic features of sepsis (tachycardia, vasodilatation and myocardial depression). Using these three characteristics we set the parameters for ‘mild’, ‘moderate’ and ‘severe’ cases of sepsis. The model incorporates noradrenaline, adrenaline, dobutamine, milrinone, dopamine and glyceryl trinitrate and allows for multiple drug administrations at selected infusion rates. The three models of increasing severity of septic shock in patients are considered separately to evaluate the interactions of combined infusions of noradrenaline and dobutamine.

The figure shown illustrates the haemodynamic response of a patient with ‘moderate’ sepsis: heart rate (HR) 90 beats/min; contractility ($E_{\text{max}}$) reduced by 30%; and systemic vascular resistance (SVR) reduced by 35%. Noradrenaline infused at 0.25 $\mu$g/kg/min produces a marked increase in the systemic vascular resistance due to vasoconstriction, resulting in an increased mean arterial pressure. The heart rate is increased and causes a fall in stroke volume. The variables reach steady-state. Dobutamine 2.5 $\mu$g/kg/min is introduced increasing cardiac output and HR. Simulation results show that the model reproduced successfully the therapeutic effects of noradrenaline and dobutamine as observed in clinical practice.

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Reference: 1 MA Denaï, M Mahfouf, JJ Ross. Proc. of 3rd European Medical and Biological Engineering Conference (EMBEC’05), November 20-25, 2005, Prague, Czech Republic.