THESIS FOR THE DEGREE OF DOCTOR OF MEDICINE

CARDIAC DYSFUNCTION AND LACTIC ACIDOSIS DURING HYPERDYNAMIC AND HYPOVOLEMIC SHOCK

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1.1 ABSTRACT

Lactic acidosis occurs during impaired tissue perfusion in both hyperdynamic and hypovolemic shock. Importantly, lactic acidosis is a key predictor of high mortality in patients. Cardiac dysfunction occurs during lactic acidosis but until recently had not been recognised to be important during hyperdynamic or hypovolemic shock.

This thesis details a series of studies in patients, in human volunteers and in large animals. Haemodynamics and left ventricular systolic and diastolic mechanics are reported during lactic acidosis, during therapies for lactic acidosis, and during hyperdynamic and hypovolemic shock. These studies do not address cardiogenic or obstructive shock.

The studies found in patients with shock and lactic acidosis, that infused bicarbonate does not improve cardiac function. In some patients, side effects of hypocalcemia and hypercapnia outweighed benefits. Transient haemodynamic effects of bicarbonate were due to the infusion of a hypertonic solution and not due to buffering. In lactic acidosis induced by hypovolemic shock (arterial pH 7.10), systolic left ventricular (LV) contractility was not decreased, perhaps due to endogenous catecholamines. Infusion of bicarbonate did not improve haemodynamics. In infused lactic acidosis (arterial pH 7.10), when catecholamines were blocked, systolic LV contractility was decreased and failed to increase after complete pH correction using bicarbonate. Histamine decreased LV contractility when measured using a non invasive technique in human volunteers (an H1 mediated effect). Histamine may therefore be an important contributor to LV dysfunction reported during anaphylaxis. TNF-α decreased LV contractility in dogs suggesting that TNF-α may be an important contributor to LV dysfunction in the early hours of septic shock. Finally, hypovolemic shock was associated with profound LV diastolic stiffness which may account for failed resuscitation in patients with prolonged hypovolemic shock.

This thesis has the unifying hypothesis that cardiac dysfunction is important in hyperdynamic and hypovolemic shock and is not caused by lactic acidosis. Accordingly, clinical therapies intended to improve cardiac function and rapidly normalise tissue perfusion in patients with shock and lactic acidosis are more likely to be successful in improving patient outcome than therapies which are intended solely to correct the acidosis.