Metabolic and haemodynamic responses to adrenaline in normal dogs

A. J. Drake¹, K. Herbaczynska-Cedro, L. Ceremuzynski², W. Czarnecki, and M. I. M. Noble¹

(Received June 22, 1980)

Summary

The metabolic and haemodynamic effects of adrenaline were investigated in 6 intact anaesthetized dogs, which were subjected to an infusion of adrenaline. The dose given was similar to the endogenous production rate of adrenaline in experimental myocardial infarction. Adrenaline infusion (0.8, 1.17 or 1.05 μg kg⁻¹ min⁻¹) over two hours led to a variable rise in blood level of this amine, regardless of the rate of infusion. Dogs with high blood adrenaline (over 3.5 ng ml⁻¹) exhibited haemodynamic deterioration, i.e. a rise in peripheral vascular resistance together with a fall in cardiac output and external cardiac work. Dogs with low blood adrenaline showed little change in peripheral vascular resistance, a rise in cardiac output and external cardiac work. The myocardial consumption of each of the substrates lactate, pyruvate, glucose and FFA was measured, and its equivalent oxygen consumption expressed as a percentage of the total myocardial oxygen consumption. No relationship was found between myocardial utilisation of individual substrates and the type of haemodynamic response. Thus in intact dogs exposed to adrenaline excess, similar to that found in acute myocardial infarction, the different types of haemodynamic response cannot be attributed to the type of substrate utilization by the myocardium, but to different rates of clearance of adrenaline. Low clearance rates lead to high blood adrenaline levels and an unfavourable response of the cardiovascular system.

Key words: adrenaline, metabolic response, haemodynamic response, myocardial infarction

Introduction

It has been well established that acute myocardial infarction is associated with increased blood levels of catecholamines, mainly adrenaline. This phenomenon is greatly pronounced in myocardial infarction associated with a severe clinical course, and a causal relationship has been suggested (1). Alternatively the adrenergic response might be a beneficial compensatory mechanism improving myocardial contractility (2).

At present, the notion that enhanced adrenergic activity is detrimental to the course and outcome of myocardial infarction seems to be prevailing. Adrenaline infusion in a dose imitating that released spontaneously after coronary artery occlusion results in considerable biochemical and local myocardial alterations in healthy animals (3).
The question to be answered is whether catecholamine excess causes primarily haemodynamic deterioration or metabolic alterations. In the present study, metabolic and haemodynamic effects of adrenaline were determined in intact anaesthetized dogs, subjected to infusion of adrenaline in a dose similar to that released spontaneously after coronary occlusion.

Methods

Six dogs of either sex, weighing 10.5–19 kg, were used in this study. Five of the dogs were implanted with a left atrial catheter (silastic) and right atrial pacing electrodes via a left thoracotomy, one week before the adrenaline infusion was carried out. These dogs were studied closed-chest. One dog (no. 3) was implanted acutely with a left atrial catheter and pacing electrodes at the time of the study and was studied open-chest. At the time of the studies, the dogs were anaesthetized with intravenous methohexitone sodium followed by a standard dose of chloralose (100 mg · kg⁻¹). A cannula was inserted into a branch of the femoral artery and connected to a three-way tap for blood sampling and blood pressure measurement. The left atrial catheter and pacing electrodes were exteriorized at the back of the neck. The left atrial catheter was used for injection of microspheres (for measurement of myocardial blood flow and cardiac output) and sampling of atrial blood for chemical analyses. The electrodes were connected to a Devices isolated stimulator type 2533, triggered by a Digitimer type 3290.

A cardiac catheter was introduced via the jugular vein, advanced and positioned in the coronary sinus under fluoroscopic control. The position of the catheter was checked by visualizing the coronary sinus with a bolus injection of 5.0 ml of Urografin.

Measurement of arterial pressure

Arterial pressure was measured via the arterial cannula with an Elcomatic EM750 pressure transducer. The preamplifier was a Hewlett-Packard 8650B carrier-amplifier. An electrocardiogram was obtained from a Hewlett-Packard 8811A Bioelectric amplifier. Variables were recorded on a Gould Brush 480 pen recorder.

Adrenaline infusion

Adrenaline (1 mg in 10 ml; McCarthy's Surgical) was diluted 1 in 50 in physiological saline and then infused at an appropriate rate for each dog to give doses of 0.8 (2 dogs), 1.05 (1 dog) or 1.17 (3 dogs) μg · kg⁻¹ · min⁻¹.

Measurement of metabolites

1) Lactate: approximately 1.0 ml of blood was injected into a preweighed tube containing 1.0 ml (0.7 mole · l⁻¹) ice-cold perchloric acid. The tube was immediately shaken, reweighed and centrifuged at + 4°C. The supernatant was then decanted and stored at −20°C until analysis. Lactate was measured using the lactate-dehydrogenase method (Boehringer kit).

2) Glucose 0.1 ml of the perchloric acid supernatant (see above) was taken for analysis. Glucose was measured manually using the hexokinase-UV method (Boehringer kit).

3) Free fatty acids. 5.0 ml of blood were taken for extraction of free fatty acids, the following precautions were taken to prevent lipolysis. The blood sample was immediately chilled in ice, the plasma separated at + 4°C and then stored at −20°C until analysis. The plasma was then thawed at room temperature and immediately chilled in crushed ice until assayed. Absence of these precautions could lead to a