The pharmacological protection of mitochondrial function in hypoxic heart

WINIFRED G. NAYLER

Department of Medicine, Cardiothoracic Institute, 2 Beaumont Street, London W1N 2DX

Previous studies have established that hypoxia causes a variety of functional, biochemical and morphological changes in heart muscle. Developed tension decreases and resting tension increases (Nayler, Yepez, Grau & Slade, 1977a). The endogenous stores of adenosine triphosphate and creatine phosphate are depleted (Nayler, Grau & Slade, 1976), intracellular enzymes leak into the extracellular phase (Nayler *et al.*, 1976) and mitochondrial function is impaired (Nayler, Fassold & Yepez, 1977b). Drugs that have been shown to protect heart muscle during conditions of oxygen deprivation include verapamil (Nayler *et al.*, 1976) and propranolol (Nayler *et al.*, 1977b). Both these drugs are cardiodepressant. Methylprednisolone sodium succinate (MPSS) is also protective (Nayler & Seabra-Gomes, 1976), possibly because of its membrane stabilizing properties. In the following experiments we have investigated whether vitamin E (as α-tocopherol), an established membrane stabilizing drug, resembles MPSS in protecting hypoxic heart muscle.

Langendorff-perfused rabbit hearts were used. Hypoxia was induced by gassing the perfusate with 95% N_2 + 5% CO_2 instead of 95% O_2 + 5% CO_2. When substrate-free perfusion was required, the glucose in the perfusion buffer was replaced by mannitol. Tension development was detected by means of a Grass FTO3 transducer attached to the ventricular apex. When required, vitamin E was added to the perfusion circuit (non-recirculating) at a rate of 23.2 nM/minute. After the required period of perfusion the hearts were homogenized and the mitochondria harvested. The respiratory activity (RCI and QO_2) of the mitochondria was assayed using a Clark O_2 electrode (Lochner, Kotzé & Gevers, 1976).

Although vitamin E failed to alter peak developed tension or heart rate, it reduced the rate of CPK release during hypoxic perfusion and diminished the rate of rise of resting tension. Mitochondrial function (QO_2 ($P<0.01$) and RCI ($P<0.001$)) was also better maintained when vitamin E was present.

It is concluded that vitamin E does protect heart muscle against the deleterious effect of hypoxia.

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