The effects of practolol in the early stages of experimental myocardial infarction

R.J. MARSHALL* & J.R. PARRATT

Department of Surgery, University of Glasgow and Department of Physiology and Pharmacology, University of Strathclyde, Glasgow

It has recently been demonstrated that the cardioselective β-adrenoceptor antagonist, practolol, is capable of decreasing the severity and extent of myocardial ischaemic injury (assessed from electrocardiographic changes) after experimental coronary artery occlusion in the dog (Libby, Maroko, Covell, Malloch, Ross & Braunwald, 1973) and after acute myocardial infarction in man (Pelides, Reid, Thomas & Shillingford, 1972). This reduction in infarct size may well be due to a more favourable balance between myocardial oxygen supply and demand and the purpose of the present work was to determine the effects of practolol in a canine preparation which allows blood flow and oxygen consumption to be measured simultaneously in both normal and acutely ischaemic myocardial regions (Ledingham, Marshall & Parratt, 1973; Marshall, Parrat & Ledingham, 1974).

The chosen dose-level of practolol (0.5 mg/kg) caused an 18-fold parallel shift in the positive chronotropic and inotropic responses to intravenously administered isoprenaline and, when administered 2-3 h after acute coronary artery ligation, significantly decreased heart rate, cardiac output and LV dP/d *max* (Table 1). These changes were associated with a modest, but significant, decrease in blood flow and oxygen consumption in the normal myocardium. However, in the ischaemic region, neither blood flow nor oxygen consumption were affected by practolol although there was evidence that oxygen utilization by the ischaemic tissue was more efficient. For example ST-segment depression was markedly reduced, lactate production was reversed to extraction and there was also a marked temperature decrease in the ischaemic region. It is suggested that practolol, by decreasing heart rate and perhaps by decreasing myocardial contractility in the ischaemic region, might help to conserve chemical energy for those energy-consuming reactions that are important for the preservation of cellular integrity, thereby delaying the development of necrosis.

Table 1 The effect of practolol (0.5 mg/kg) on systemic haemodynamics and on blood flow and oxygen consumption in both normal and ischaemic areas of myocardium. (± s.e. mean, $n = 8$).

	Pre-drug	*10 min post-drug*
Mean blood pressure (mmHg)	120 ± 7	109 ± 8
Heart rate (beats/min)	198 ± 13	151 ± 7**
Cardiac output (litres/min)	2.0 ± 0.3	1.2 ± 0.2**
Left ventricular dP/dt *max* (mmHg/s)	2412 ± 324	1288 ± 172**
Left ventricular end-diastolic pressure (mmHg)	12 ± 5	17 ± 5*
External cardiac work (kgm/min)	3.4 ± 0.6	1.8 ± 0.4**
Blood flow (normal myocardium); ml/min	134 ± 20	102 ± 21*
Oxygen consumption (normal myocardium); ml/min	24.0 ± 3.9	15.2 ± 2.1*
Mean peripheral coronary pressure (mmHg)	35 ± 3	31 ± 5
Blood flow (ischaemic myocardium); (ml/100 g)/min	28 ± 6	28 ± 5
Oxygen consumption (ischaemic myocardium); (ml/100 g)/min	4.9 ± 1.1	4.6 ± 0.8

** $P < 0.005$; * $P < 0.01$; (paired t-test).

References

LEDINGHAM, I.McA., MARSHALL, R.J. & PARRATT, J.R. (1973). Drug-induced changes in blood flow in normal and ischaemic regions of the canine myocardium. *Br. J. Pharmac.*, 47, 626-627P.

LIBBY, P., MAROKO, P.R., COVELL, J., MALLOCH, C.I., ROSS, J. & BRAUNWALD, E. (1973). Effect of practolol on the extent of myocardial ischaemic injury after experimental coronary occlusion and its effects on ventricular function in the normal and ischaemic heart. *Cardiovasc. Res.*, 7, 167-173.

MARSHALL, R.J., PARRATT, J.R. & LEDINGHAM, I.McA. (1974). Changes in blood flow and oxygen consumption in normal and ischaemic regions of the myocardium following acute coronary artery ligation. *Cardiovasc. Res.*, 8, 204-215.

PELIDES, L.D., REID, D.S., THOMAS, M. & SHILLINGFORD, J.P. (1972). Inhibition by β-blockade of the ST-segment elevation after acute myocardial infarction. *Cardiovasc. Res.*, 6, 295-301.