Anti-anginal drugs and the vasodilator response to myocardial hypoxia

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Anti-anginal drugs decrease the work of the heart (Petta & Zaccheo, 1971) and promote the formation of a collateral circulation (Russell Rees & Redding, 1969). They may also have a beneficial effect on myocardial metabolism (Parratt, 1969). It is possible that their overall spectrum of activity is influenced by yet another action—the modification of the normal vasodilator response to hypoxia. This could occur with several of the more recently introduced anti-anginal drugs, since they have been shown to potentiate the dilator effects of adenosine (Raberger & Kraupp, 1971), which itself may be a mediator of physiological dilatation (Rubio, Berne & Katori, 1969).

Myocardial blood flow was measured in anaesthetized cats using a heat clearance technique (McInnes & Parratt, 1969). Vasodilator responses were obtained to reactive hyperaemia, systemic hypoxia and by intravenous infusions of adenosine (0·25 mg/kg min). Reactive hyperaemia was produced by applying tension to a loose snare round the anterior interventricular artery for 10 or 30 s. After release of the snare, blood flow remained elevated for about 2 min. Systematic hypoxia was induced by artificial respiration with 5–10% oxygen in nitrogen. It was found that marked increases in blood flow occurred when the arterial pO_2 fell below 40 mmHg.

Dipyridamole (1 mg/kg, i.v.) itself produced a shortlasting increase in myocardial blood flow, which returned to control levels after 5 min. After dipyridamole, the vasodilator effects of adenosine were markedly potentiated. This effect lasted about 45 min. No changes were observed in the dilator effects of systemic hypoxia or of reactive hyperaemia.

These results do not support the suggestion that anti-anginal drugs with a dipyridamole-like action would influence the normal vasodilator response to myocardial hypoxia.

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The effects of quazodine on myocardial blood flow in developing myocardial infarcts

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Acute ligation of a major branch of the left coronary artery in dogs markedly decreases local blood flow in the area supplied by the ligated vessel; this is partly the result of the conversion of the normal local vasodilator effect of adrenaline to vasoconstriction (Grayson, Irvine & others, 1968). In cats, the effect of noradrenaline on myocardial blood flow is much reduced following coronary artery ligation whereas the effect of isoprenaline is unchanged (Moore & Parratt, 1971). Quazodine (MJ 1988; 6,7-dimethoxy-4-ethylquinazoline) which possesses a spectrum of pharmacological activity similar to that of the β-adrenoceptor stimulants and the methylxanthines, markedly increases myocardial blood flow and contractility both in dogs (Carr, Cooper & others, 1967) and in cats (Parratt & Winslow, 1971). The purpose of this study was to determine if these effects were also present in the ischaemic myocardium and in the early stages of experimental cardiac failure.

Myocardial blood flow was assessed, in cats anaesthetized with sodium pentobarbitone, by a heat clearance technique (McInnes & Parratt, 1969). The effects of intravenous infusions of quazodine (0·5 mg/kg min^{-1}) on systemic blood pressure, heart rate, cardiac output and myocardial blood flow were determined up to 4 h after acute ligation of the anterior descending branch of the left coronary artery. In normal animals quazodine decreased systolic pressure by a mean of 7 ± 2 mmHg (from a mean control level of 135 ± 7 mmHg) and diastolic blood pressure by 14 ± 2 mmHg (from a mean control level of 92 ± 5 mmHg).