Beta adrenoceptors in the hepatic arterial vascular bed of the dog

P.D.I. RICHARDSON &
P.G. WITHRINGTON

Department of Physiology, The Medical College of St. Bartholomew's Hospital, Charterhouse Square, London, EC1M 6BQ.

It has previously been shown that intra-arterial injections of noradrenaline cause vasoconstriction in the hepatic arterial vascular bed of the dog (Richardson & Withrington, 1975; 1976). The present communication describes a vasodilator response of the same vasculature to the intra-arterial injection of isoprenaline. The receptors responsible for this effect have been characterized using the nonselective β-adrenoceptor antagonist propranolol (Inderal, ICI), the selective β_1-adrenoceptor antagonist atenolol (ICI 66082, Tenormin; Hainsworth, Karim & Stoker, 1974), and the selective β_2-adrenoceptor agonist salbutamol (Ventolin, Allen & Hanburys; Daly, Farmer & Levy, 1971).

Eight dogs (12.3–17.5 kg) were anaesthetized with chloralose (Kuhlmann, Paris; 50 mg/kg) and urethane (BDH; 500 mg/kg i.v.), after induction with methohexitone sodium (Brietal, Lilly; 7.5–10.0 mg/kg, i.v.). The hepatic artery was dissected away from its periarterial sympathetic nerves, cannulated close to its origin from the aorta, and perfused with blood from a cannulated femoral artery. The hepatic arterial mean perfusion pressure (PP) was measured close to the cannula in the hepatic artery, and the blood flow in this system (hepatic arterial blood flow, HABF) measured with a cannulated flow probe and electromagnetic flowmeter. Since these experiments were to investigate vasodilatation, the sympathetic nerves were left intact to ensure a basal tone.

The control values (mean $\pm$ s.e. mean were: for PP, 125.6 ± 7.4 mmHg, and for HABF, 219.5 ± 14.1 ml/minute. The calculated hepatic arterial vascular resistance (HAVR) was 0.59 ± 0.06 mmHg ml^{-1} min, or 1.81 ± 0.18 mmHg ml^{-1} min 100 g, the livers weighing 316.8 ± 77.1 (s.d.) g *post mortem*.

Isoprenaline sulphate (Macarthys) was injected intra-arterially in doses from 0.01 to 100 µg, and graded reductions in HAVR obtained up to a maximum of $38.1 \pm 2.3\%$ ($n=8$).

Propranolol (100 µg/kg, i.v.) antagonized the chronotropic responses to i.v. isoprenaline (5 µg) and caused a marked, parallel shift of the dose-response curve of i.a. isoprenaline on the hepatic arterial vascular bed to the right without suppression of the maximum response (two experiments). Atenolol (100 µg/kg, i.v.) although blocking the chronotropic actions of isoprenaline (5 µg, i.v.), in contrast to propranolol caused no change in the position or shape of the dose-response curve to i.a. isoprenaline on the hepatic arterial vascular bed.

In further experiments, paired doses of isoprenaline and salbutamol were injected into the hepatic artery. It was evident that at equimolar doses, isoprenaline was always the more potent, though the maximum reduction in HAVR was the same for each. The maximum fall in HAVR for isoprenaline was $38.1 \pm 2.3\%$ and the ED_{50} was 6.3×10^{-10} mol, whilst the corresponding values for salbutamol were $38.1 \pm 3.5\%$ and 3.5×10^{-9} mol ($n=3$).

The results suggest that the adrenoceptors mediating hepatic arterial vasodilatation in the dog are predominantly of the β_2 type, and, furthermore, that isoprenaline is intrinsically a more potent stimulant of these receptors than salbutamol.

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