Responses of the hepatic arterial and portal venous vascular beds of the dog to intra-arterial infusions of noradrenaline and adrenaline: inhibition of the hepatic arterial vasoconstrictor responses by intraportal infusions of glucagon

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

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

Intra-arterial (i.a.) injections of noradrenaline and adrenaline elicit hepatic arterial vasoconstriction followed by vasodilatation, due to α- and β_2-adrenoceptor stimulation respectively (Richardson & Withrington, 1977). In addition, such i.a. injections of noradrenaline elicit hepatic portal vasoconstriction, an effect not dependent upon recirculation (Richardson & Withrington, 1978a).

The purpose of the present experiments was to determine the predominant hepatic arterial and portal vascular responses to intra-arterial infusions of low doses of either adrenaline or noradrenaline and to assess the effect on these responses of the concomitant intraportal infusion of glucagon. previously shown to inhibit the hepatic arterial responses to many vasoconstrictor agents (Richardson & Withrington, 1976).

Control values in 6 chloralose-urethane anaesthetized dogs were similar to those reported previously for preparations in which both the hepatic artery and the portal vein were perfused *in situ* (Richardson & Withrington, 1978a). Noradrenaline and adrenaline were infused separately into the hepatic artery on a total of 29 and 30 occasions respectively in doses from 0.1–10.0 μg/min. Noradrenaline infused i.a. only increased the hepatic arterial vascular resistance (HAVR) and there was a positive and significant ($P<0.001$) correlation between the $\log_{10}$ increase in hepatic arterial noradrenaline concentration and the increase in HAVR. In contrast, adrenaline infused i.a., at doses resulting in an increase in hepatic arterial blood concentration of 0.5–10 ng/ml, reduced the HAVR by up to 24± 4% (mean ± s.e. mean). Higher arterial concentrations of adrenaline caused progressively smaller falls in HAVR leading in 3/6 experiments to increases in HAVR. However the intra-arterial infusions of each catecholamine only increased the hepatic portal vascular resistance (HPVR).

Glucagon was infused into the portal venous bloodstream once in each of 6 experiments (dose = 0.2–1.0 μg/min) resulting in calculated initial increases in portal blood glucagon concentration of 1.1 to 4.3 ng/ml. These infusions inhibited the hepatic arterial vasoconstrictor responses to noradrenaline and the higher doses of adrenaline where hepatic arterial vasoconstriction had occurred in the absence of glucagon.

In 3 experiments, increasing the hepatic arterial noradrenaline concentration by 10 ng/ml evoked increases in HAVR of 42 ± 6% under control conditions and during intraportal infusions of 0.5 μg/min glucagon (portal blood glucagon concentration increased by 2.5 ± 0.4 ng/ml.), the increase in HAVR was 20 ± 5%. In 5 experiments, there was a positive significant correlation between the $\log_{10}$ increase in portal blood glucagon concentration (calculated as infusion rate/blood flow) and the attenuation of the hepatic arterial vasoconstrictor effect due to increasing the hepatic arterial blood noradrenaline concentration by 10 ng/ml ($r = 0.918$; $P<0.05$). The increase in HPVR due to the same intra-arterial noradrenaline infusions was unchanged by the intraportal glucagon infusion.

The present experiments reveal that elevated portal concentrations of glucagon inhibit the hepatic arterial vasoconstrictor responses to intra-arterial infusions of adrenaline and noradrenaline whilst the portal vasoconstrictor responses remain unaltered, an effect of glucagon similar to that observed on the responses of the two hepatic vascular beds to sympathetic nerve stimulation (Richardson & Withrington, 1978b).

References

RICHARDSON, P.D.I. & WITHRINGTON, P.G. (1976). The inhibition by glucagon of the vasoconstrictor actions of noradrenaline, angiotensin and vasopressin on the hepatic arterial vascular bed of the dog. *Br. J. Pharmac.*, **57**, 93–102.

RICHARDSON, P.D.I. & WITHRINGTON, P.G. (1977). The role of β-adrenoceptors in the responses of the hepatic arterial vascular bed of the dog to phenylephrine, isoprenaline, noradrenaline and adrenaline. *Br. J. Pharmac.*, **60**, 239–249.

RICHARDSON, P.D.I. & WITHRINGTON, P.G. (1978a). Pressure-flow relationships and effects of noradrenaline and isoprenaline on the simultaneously-perfused hepatic arterial and portal venous vascular beds of the dog. *J. Physiol. (Lond.)*, (in press).

RICHARDSON, P.D.I. & WITHRINGTON, P.G. (1978b). The effects of intraportal infusion of glucagon on the responses of the simultaneously-perfused hepatic arterial and portal venous vascular beds of the dog to periarterial nerve stimulation. *J. Physiol. (Lond.)*, (in press).