The influence of glucagon upon the responses of the hepatic arterial vasculature to vasodilator agents

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It had previously been demonstrated (Richardson & Withrington, 1975, 1976) that administration of glucagon into the hepatic arterial vascular bed of the dog not only causes hepatic arterial vasodilatation, but also reduces the vasoconstrictor effects of intra-arterial noradrenaline, angiotensin and vasopressin on this bed. The possibility that glucagon might either potentiate or antagonize the responses of this tissue to vasodilator agents was examined.

Under control conditions, in five chloralose-urethane anaesthetized dogs (12.3–17.5 kg) (Richardson & Withrington, 1975, 1976) the hepatic arterial perfusion pressure (PP) was 129.6 ± 7.4 (mean $\pm$ s.e. mean) mmHg. In the sympathetically innervated liver the hepatic arterial blood flow (HABF) was 54.9 ± 6.6 ml min^{-1} 100 g^{-1}, the livers weighing 348.0 ± 61.2 (mean $\pm$ s.d.) grams. The calculated hepatic arterial vascular resistance (HAVR) was 2.58 ± 0.46 mmHg ml^{-1} min 100 grams.

Isoprenaline sulphate (Macarthys) and histamine acid phosphate (BDH) were injected intra-arterially to the liver in graded doses and dose-dependent reductions in hepatic arterial vascular resistance were obtained. The complete dose/response curves to isoprenaline and histamine were constructed before, during and after the intra-arterial infusion of 10.0 µg/min glucagon (Lilly). This infusion of glucagon itself results in a fall in HAVR of $28.9 \pm 4.4\%$ ($n=6$). The decreases in HAVR due to the graded doses of isoprenaline and histamine were reduced during the infusions of glucagon compared with the control responses either before or after the infusions. If, however, the vasodilator action of glucagon was taken into account and the decreases in hepatic arterial vascular resistance due to isoprenaline and histamine during glucagon calculated from the pre-glucagon infusion level, then it was evident that there was no shift in the dose-response curves to either histamine or isoprenaline, and in one experiment, to prostaglandin E_2(PGE_2).

In previous experiments, the extent and time-course of the antagonism of the effect of noradrenaline, angiotensin and vasopressin by single intra-arterial injections of glucagon were demonstrated. In the present experiments, single doses of glucagon were injected, and control doses of the vasodilators administered at various intervals before and after the injections of glucagon. A change in response to histamine, isoprenaline and PGE_2 was apparent only during the vasodilator response to glucagon; when corrections were made for the change in background tone due to glucagon, it was evident that the reductions in HAVR due to isoprenaline, histamine and PGE_2 were unaffected by the injections of glucagon.

The experiments support the suggestion that glucagon does not modify the vasodilator effects either of the physiological vasodilators histamine and PGE_2 or the synthetic vasodilator isoprenaline on the hepatic arterial vascular bed of the dog, but emphasize the difficulties inherent in assessing the antagonistic actions of a substance which itself has agonist potency.

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References

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