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Cardiovascular actions of prostacyclin (PGI_2) in chloralose anaesthetized dogs

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Prostacyclin (PGI_2 or PGX) is an unstable intermediate of arachidonic acid metabolism, which strongly inhibits aggregation of human platelets (Moncada, Gryglewski, Bunting & Vane, 1976) and relaxes several isolated vascular preparations (Bunting, Gryglewski, Moncada & Vane, 1976; Dusting, Moncada & Vane, 1977). Prostacyclin is the predominant active metabolite of the cyclic endoperoxides in all vascular tissues studied, including bovine coronary arteries (Dusting *et al.*, 1977). We have now measured the cardiovascular effects of prostacyclin in anaesthetized open-chest dogs.

Anaesthesia was induced with thiopentone (20–25 mg/kg) and maintained with chloralose (50 mg/kg, i.v.) supplemented (5 mg/kg i.v.) as required. The dogs were artificially ventilated; arterial Po_2 was maintained above 100 mmHg and Pco_2 in the range 28–40 mmHg. Electromagnetic flow probes (Statham Instruments Inc.) were fitted to the ascending aorta (5 dogs) and to the left circumflex artery (8 others). Cardiovascular parameters were recorded as previously described (Hughes, 1971). Mean coronary flow (over 4 s intervals) and coronary vascular resistance were also computed. Drugs were infused into the right femoral vein, into a cannula in the left atrial appendage, and in some experiments via a fine catheter in the left circumflex artery distal to the flow probe.

Intravenous infusion of prostacyclin for 3 min (50–1,000 ng kg^{-1} min^{-1}) caused dose-dependent decreases in systemic blood pressure, total peripheral resistance, and coronary vascular resistance and moderate increases in stroke volume and cardiac output (maximum increase $72 \pm 20\%$, mean $\pm$ s.e. mean). Heart rate changes were variable. The stable metabolite of prostacyclin, 6-oxo-$PGF_{1\alpha}$ had no effect (up to 10 μg kg^{-1} min^{-1}).

The cardiovascular effects of prostacyclin were similar after intravenous or left atrial infusions. Whereas prostaglandin E_1 (left atrial infusions) was slightly more potent than prostacyclin, it was about one tenth as potent when given intravenously.

Intravenous infusion of prostacyclin (50–500 ng kg^{-1} min^{-1}) increased peak phasic coronary flow only at the highest infusion rate. However, mean coronary flow did not change significantly at any infusion rate although coronary vascular resistance was substantially reduced. Direct injection of prostacyclin (50–1000 ng) into the left circumflex artery increased both phasic and mean coronary flow and decreased coronary vascular resistance (for 1–4 min) without any change in systemic blood pressure or heart rate. Similar effects with PGE_1 were more persistent (up to 8 min) whereas PGE_2 was less potent.

After indomethacin (5 mg/kg i.v.: 4 dogs) or sodium meclofenamate (2 mg/kg i.v.: 2 dogs) there was a slow increase in systemic blood pressure and coronary vascular resistance, and a reduced phasic and mean coronary flow. Indomethacin and meclofenamate potentiated the coronary dilator effects of the smaller intravenous infusions of prostacyclin but did not alter the hypotensive effects. Thus, the sensitivity of the coronary vascular bed *in vivo* is enhanced when endogenous biosynthesis of prostaglandin-like substances is inhibitied.

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