Microvascular responses produced by the prostaglandin endoperoxide PGG_2 *in vivo*

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We have investigated the effects of PGG_2 on microvessels *in vivo* using microscopic and isotopic techniques.

The hamster cheek pouch preparation was set up as described by Lewis & Westwick (1975). Changes in arteriolar diameter (25–45 μm) were monitored continuously using a photometric technique (Hutchings, Lewis, Sabikowski & Westwick, 1976).

PGG_2 (stored at −20°C in acetone, 500 μg/ml) was diluted either in saline or acetone at 0°C and applied immediately (0.5–5 μl) via a microsyringe onto the vessel being viewed under the microscope. The PGG_2 solutions were assayed simultaneously using isolated vascular strips (Bunting, Moncada & Vane, 1976).

On arterioles having a low vascular tone, PGG_2 (25–100 ng) produced a short lasting vasoconstriction reaching a maximum at 30 to 60 s, e.g. PGG_2 (25 ng) produced 93 ± 2% constriction (mean ± s.e. mean, $n=6$). Repeated doses of PGG_2 rapidly induced tachyphylaxis which was not observed on the isolated vascular strips. In comparison, noradrenaline (NA) produced 57 ± 3% ($n=5$), and 80 ± 2% ($n=5$) vasoconstriction in doses of 0.1 ng and 1.0 ng respectively. Doses of NA equiactive with PGG_2 were of longer duration and were not tachyphylactic.

On vessels having a high tone induced by a continuous superfusion of NA (0.5 ng ml^{-1} min^{-1}), PGG_2 produced a much smaller vasoconstriction (PGG_2, 100 ng, 45 ± 7%, $n=4$) followed by a protracted phase of strong vasodilatation (60–100% with 25–100 ng PGG_2). Control applications of cold saline or acetone produced a small vasoconstriction (4 ± 2%, $n=6$). In these concentrations of PGG_2 white body formation was not observed.

Similar two-phase vascular responses to PGG_2 were observed in rabbit skin using a ^{133}Xe clearance technique to measure blood flow (Lewis, Peck, Williams & Young, 1975). PGG_2 in acetone mixed with ^{133}Xe in saline (250 ng PGG_2/50 μl injection) was injected into dorsal skin and ^{133}Xe washout monitored every 10 s for 15 min using a γ-detector. The means of six sets of observations were compared with six controls (acetone/^{133}Xe in saline). Reduced flow (i.e. reduced ^{133}Xe washout) was apparent for the first 70 seconds. The count at 70 s as a percentage of the initial count was: PGG_2 89.15 ± 0.85%; control, 82.10 ± 1.29%. This was followed by a protracted phase of increased flow; the count at 360 s was: PGG_2, 8.61 ± 1.22%; control, 20.88 ± 0.98%). The initial reduced flow was less in magnitude and duration than that produced by 10 ng of noradrenaline.

Because of the dominance of the vasodilatation produced by PGG_2, a pro-inflammatory effect on bradykinin-induced plasma exudation would be expected (Williams, 1976a). Using the method of Williams (1976b) marked potentiation was observed with PGG_2. The mean plasma accumulation per injection site produced by bradykinin (500 ng dose) was 15.99 ± 2.71 μl, and by PGG_2 (250 ng) 5.60 ± 2.13 μl, whereas for the mixture of bradykinin and PGG_2 the accumulation was 57.02 ± 5.35 μl ($n=6$).

The significance of these observations depends on the site and nature of PGG_2 production under physiological or pathological conditions. Under the conditions of our experiments, PGG_2 produced a transient vasoconstriction followed by a protracted phase of vasodilatation. The dilator effect results in potentiation of bradykinin-induced exudation. The observed effects could be due to PGG_2 itself or products of PGG_2.

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