Effects of Prostaglandin B_2 on Renal Hemodynamics and Excretion[1] (37445)

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Johnston, Herzog and Lauler (1), in 1967, reported an increase in renal plasma flow (RPF), sodium excretion ($U_{Na}V$) and urine flow (V) following the renal arterial infusion (ia) of prostaglandin E_1 (PGE_1), 10–2000 ng/min, in dogs. In 1968, Vander (2) infused both PGE_1 and PGE_2, 10–5000 ng/min, ia, and observed an increase in total RPF, $U_{Na}V$ and V in the absence of changes in mean arterial pressure (MAP). Vander noted that the increase in $U_{Na}V$ was highly variable and did not correlate well with the increase in RPF. McGiff and co-workers (3) found that both intravenous and intraaortic infusions of PGA_1 and PGA_2 produced an increase in total renal blood flow (RBF) and V without changes in MAP. A threshold dose of 1.0 ng/kg/min was observed for PGA_1 infused into a renal artery. An inability to dissociate the changes in V from changes in RBF led the investigators to suggest that these are related.

It is thought that prostaglandins B_1 and B_2 may be metabolites of PGA_1 and PGA_2, respectively (4). PGB_2 has been reported to be a weak dilator relative to the E and A prostaglandins (5) and PGB_1 and PGB_2 produce little or no decrease in blood pressure in rats (6). However, recent experiments have indicated that PGB_2 significantly lowers MAP in anesthetized normotensive dogs (7). In order to investigate possible direct effects on total RBF and excretion similar to those of the E and A prostaglandins, PGB_2 was infused directly into a renal artery of anesthetized dogs.

Methods. Mongrel dogs of either sex weighing between 16 and 22 kg were anesthetized with pentobarbital sodium (30 mg/kg, iv) and the trachea was intubated. MAP was monitored with a pressure transducer (Statham P23AA) via a carotid artery catheter. The femoral artery and vein were catheterized for the collection of blood and administration of solutions, respectively. An infusion of 0.4% inulin, 0.08% *p*-aminohippurate (PAH) in 0.9% NaCl, was administered at a rate of 0.25 ml/kg/min. A kidney was approached via a retroperitoneal flank incision and the ureter catheterized. If more than one renal artery was encounted, the contralateral kidney was used. A flow probe was placed around the renal artery and connected to a square wave electromagnetic flowmeter (Carolina Medical Electronics). This provided a direct measurement of total RBF. MAP and RBF were recorded continuously on a Beckman Type R dynagraph. A 23 gauge scalp needle was passed retrograde into the renal artery for drug administration. A solution of NaCl (0.9%) was infused continuously at a rate of 1.0 ml/min.

When urinary volume had stabilized, three 5-min control urine samples were collected. PGB_2 was then infused, during the next three 5-min collection periods, directly into the renal artery. The PGB_2 concentration was adjusted to allow the different doses to be given at the same infusion rate. Blood was collected at the midpoint of each collection period. Four animals were studied at each dose. Significant differences from control were determined by Student's t test (paired comparison) (8). Dose–response curves were tested by an analysis of variance test for linear regression and deviation from linearity (8). In addition, RBF and $U_{Na}V$ were

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analyzed for possible correlation (8).

Renal vascular resistance (RVR) is expressed as resistance units (RU) and was calculated by dividing MAP (mm Hg) by RBF (ml/min). Filtration fraction (FF) was calculated by dividing glomerular filtration rate (GFR) by C_{PAH}. GFR was estimated from the clearance of inulin. Inulin was determined by the method of Schreiner (9) and PAH was determined by the method of Smith *et al.* (10). Sodium and potassium concentrations were determined with an IL flame photometer. All parameters are expressed in units per kilogram of body weight.

A stock solution of PGB_2 (Upjohn Co.) (5 mg/ml) was prepared in 95% ethanol and stored in a freezer. The appropriate dilution was made just prior to infusion.

Results and Discussion. The data indicate that the renal arterial infusion of PGB_2 (250–1000 ng/kg/min) increases total RBF and $U_{Na}V$ in a dose related manner. The results for each parameter are shown in Table I. Infusion of 250 ng/kg/min produced a significant increase in RBF and $U_{Na}V$ and a significant decrease in RVR and FF. Infusion of 500 ng/kg/min produced a significant increase in RBF, C_{PAH} and $U_{Na}V$. Infusion of 1000 ng/kg/min produced a significant increase in V, RBF, C_{PAH} and $U_{Na}V$ and a significant decrease in RVR and FF. An analysis of variance test for linear regression showed that the slope of the regression lines for RBF and $U_{Na}V$ were significantly different from zero and that there was no significant deviation from linearity (Fig. 1). Although V appeared to be increasing in a dose related manner, the slope of the regression line was not significant. It should be noted that at no dose was there a significant change in MAP or GFR. Furthermore, there was no significant correlation between the increase in RBF and $U_{Na}V$ following PGB_2 infusion which is comparable to the results of Vander (2) following the infusion of PGE_1 and PGE_2.

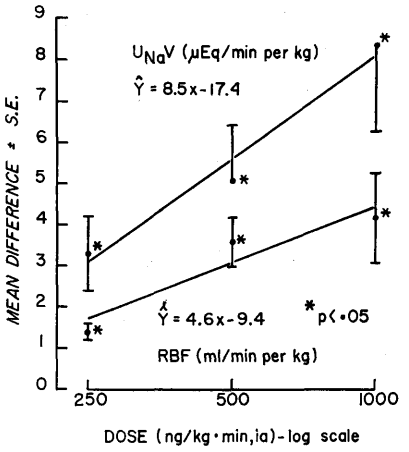

FIG. 1. Dose–response curves of renal blood flow (RBF) and sodium excretion ($U_{Na}V$) during intra-arterial infusion of PGB_2. Each point represents 4 animals; * a significant difference from control.

Four of five dogs receiving PGB_2 at either 2000 or 5000 ng/kg/min had less than expected increases in RBF and only slight in-

TABLE I. Effect of PGB_2 on Renal Hemodynamics and Excretion Expressed per kg Body Weight (Mean Difference from Control ± SE).[a]

	ng/kg min, ia		
	250	500	1000
V (ml/min)	0.02 ± 0.01	0.03 ± 0.01	0.04 ± 0.01[b]
RBF (ml/min)	1.4 ± 0.2[b]	3.6 ± 0.6[b]	4.2 ± 1.1[b]
MAP (mm Hg)	−0.2 ± 0.1	0.3 ± 0.2	−0.08 ± 0.08
RVR (RU)	−0.004 ± 0.001[b]	−0.015 ± 0.005	−0.01 ± 0.003[b]
GFR (ml/min)	0.2 ± 0.1	0.4 ± 0.2	0.08 ± 0.08
C_{PAH} (ml/min)	0.8 ± 0.4	2.3 ± 0.5[b]	1.8 ± 0.2[b]
$U_{Na}V$ (μEq/min)	3.3 ± 0.9[b]	5.1 ± 1.6[b]	8.4 ± 2.1[b]
U_KV (μEq/min)	0.4 ± 0.2	0.6 ± 0.2	1.0 ± 0.4
FF	−0.04 ± 0.01[b]	−0.04 ± 0.02	−0.05 ± 0.01[b]

[a] $n = 4$.
[b] $p < 0.05$.

creases or decreases in V and $U_{Na}V$. The only dog in which RBF increased to the expected level had a 40% reduction in V and $U_{Na}V$. Furthermore, one of the two dogs that received 5000 ng/kg/min PGB_2 had an initial transient increase in RBF followed by a sustained decrease of 2.8 ml/kg/min (31% reduction) which returned to control following the infusion. This apparent transition to a vasoconstriction with increasing dose of PGB_2 may account for the increasing variability of RBF and $U_{Na}V$ shown in Fig. 1, and the lack of a dose related effect on RVR and C_{PAH}.

Summary and Conclusion. The infusion of PGB_2 into canine renal arteries produces a dose related increase in total RBF and $U_{Na}V$. The increasing variability in RBF and $U_{Na}V$ with increasing dose may be due to a transition from vasodilator to vasoconstrictor action. The results obtained demonstrate that PGB_2 affects renal hemodynamics and excretion qualitatively the same as PGE_1, PGE_2, PGA_1 and PGA_2.

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