Effect of Prostaglandins E_1 and A_1 on the Gastric Circulation in Dogs[1] (36318)

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Roberts *et al.* (12, 13) first reported that intravenous infusions of prostaglandins E_1 (PGE_1) and A_1 (PGA_1) inhibit gastric acid secretion in conscious dogs and rats. Wilson and Levine (18) demonstrated that PGE_1 decreases both gastric mucosal blood flow and histamine-induced gastric secretion in conscious dogs treated with chlorpromazine. They postulated that the antacid action of PGE_1 is caused by the decrease in the gastric mucosal blood flow induced by PGE_1. Jacobson (5) also found that PGE_1 decreases both gastric mucosal blood flow and gastric secretion, which is stimulated by either histamine or pentagastrin in conscious dogs. However, he concluded that the decrease in the gastric mucosal blood flow is the result rather than the cause of the inhibition of gastric secretion by PGE_1. It remained uncertain, however, whether PGE_1 exerted a vasoconstrictor action in the gastric vascular beds since both groups of workers indirectly measured the gastric mucosal blood flow employing the aminopyrine clearance technique (6). The present study was undertaken to elucidate the direct effect of intraarterially and intravenously injected PGE_1 and PGA_1 on the gastric peripheral vascular beds in dogs.

Methods. Eight dogs weighing between 19 and 24 kg were anesthetized with intravenous sodium pentobarbital (30 mg/kg). Under a midline laparotomy, the stomach was exposed and all of the branches of the coeliac artery except those to the stomach were ligated. In all experiments, 2.5 mg/kg of sodium heparin were administered intravenously before cannulation of the blood vessels; and this dose was repeated every 0.5 hr. After the coeliac artery was cannulated distally, the entire stomach was perfused at constant and known rates with blood bypassed from a femoral artery by means of a Sigmamotor pump (Model TM-2). The gastric arterial blood flow (pump rate) was regulated so that the gastric arterial perfusion pressure exceeded systemic arterial pressure by 10 mm Hg. In this technique, the changes in the gastric peripheral vascular beds can be readily evaluated by measuring the changes in the arterial perfusion pressure with a Statham pressure transducer (P23AA) connected to a catheter in the distal tubing of the pump. Systemic arterial and gastric venous pressures also were measured with Statham pressure transducers (P23AA) connected to catheters inserted into the brachiocephalic artery via the left thoracic artery and into a small branch of a gastric vein, respectively. Gastric peripheral vascular resistance was computed by the following formula:

> Gastric peripheral vascular resistance (mm Hg/ml/min) = [mean gastric arterial perfusion pressure (mm Hg) — gastric venous pressure (mm Hg)/gastric arterial blood flow (ml/min).

The experimental data in this study were evaluated statistically using Student's t test (15); t values of less than 0.05 were accepted as indicating a significant difference between compared values.

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TABLE I. Effect of the Intravenous Injection of PGE_1 and PGA_1 on Mean Systemic Arterial Pressure (MSAP), Mean Gastric Arterial Perfusion Pressure (MGAPP), Mean Gastric Venous Pressure (MGVP), and Gastric Peripheral Vascular Resistance (GPR) in 8 Dogs in Which the Gastric Arterial Blood Flow Was Maintained Constant by Means of a Sigmamotor Pump. Values denote mean change ± SEM.

(μg/kg)	MSAP (Δmm Hg)	MGAPP (Δmm Hg)	MGVP (Δmm Hg)	GPR (Δmm Hg/ml/min $\times 10^3$)
PGE_1, 1	−12.1 ± 2.0[a]	−21.7 ± 4.6[a]	−1.9 ± 0.7	−27 ± 3[a]
PGA_1, 1	−47.2 ± 7.4[a]	−45.1 ± 10.6[a]	−3.7 ± 1.3	−304 ± 70[a]

[a] A significant difference from the control value.

Results. The effects of intraarterial and intravenous injections of PGE_1 and PGA_1 were studied in 8 anesthetized dogs. The results are summarized in Tables I and II. The intravenous injection of a single dose (1 μg/kg) of PGE_1 or PGA_1 decreased, significantly, systemic arterial pressure, gastric arterial perfusion pressure, and gastric peripheral vascular resistance; whereas gastric venous pressure remained essentially unchanged (Table I). The magnitude of the hemodynamic changes induced by intravenously injected PGA_1 was significantly greater than that induced by intravenously injected PGE_1. On the other hand, as shown in Table II, the intraarterial injection of either of two doses (2.5 or 10 ng/kg) of PGE_1 or PGA_1 decreased, significantly, gastric arterial perfusion pressure and gastric peripheral vascular resistance without producing any significant change in systemic arterial pressure and gastric venous pressure. The magnitude of the decreases in gastric arterial perfusion pressure and in gastric peripheral vascular resistance induced by intraarterially injected PGE_1 was significantly greater than that induced by intraarterially injected PGA_1.

Discussion. From the present study, it is evident that either the intravenous or the intraarterial injection of PGE_1 and PGA_1 decreases significantly gastric peripheral resistance in anesthetized dogs, indicating the potent vasodilator action of PGE_1 and PGA_1. This is in agreement with the previous observations from this laboratory (8, 11) and others (4, 7, 17) in which both PGE_1 and PGA_1 dilate blood vessels and increase blood flow in almost all organs and tissues studied. It has been shown that the direct vasodilator action of PGE_1 in the femoral artery is significantly greater than that of PGA_1 in dogs (8). However, as reported by some investigators (4, 7), the hemodynamic effects of intravenously injected PGA_1 are markedly greater than those of intravenously injected PGE_1 in dogs and rats. It has been well established that prostaglandins are effectively inactivated to their corresponding 15-keto-PG compounds by 15-hydroxyprostaglandin dehydrogenase in the lungs (1, 2, 7, 9, 10). Since PGE_1 is a better substrate than PGA_1 for this enzyme, PGE_1 is more effectively inactivated by a single circulation through the lungs (3, 4, 7). The present study also confirms this postulate and shows that the vasodilator effect of intravenously injected PGA_1 on the gastric peripheral vascular beds is significantly greater than that of intravenously injected PGE_1. On the other hand, the direct vasodilator effect of intraarterially injected PGE_1 is markedly greater than that of intraarterially injected PGA_1 in dogs.

Robert *et al.* (12, 13) first showed that the intravenous injection of both PGE_1 and PGA_1 inhibits gastric secretion in dogs and rats. Wilson and Levine (18) postulated that the inhibitory action of PGE_1 on histamine-induced gastric secretion is due to decreased blood flow in the gastric mucosa in conscious dogs. Jacobson (5) also observed that PGE_1 decreased the gastric mucosal blood flow in dogs, the gastric secretion of which had been stimulated markedly with either histamine or pentagastrin. He concluded that the decrease in the mucosal blood flow produced by

TABLE II. Effects of the Intraarterial Injection of PGE_1 and PGA_1 on Mean Systemic Arterial Pressure (MSAP), Mean Gastric Arterial Perfusion Pressure (MGAPP), Mean Gastric Venous Pressure (MGVP), and Gastric Peripheral Vascular Resistance (GPR) in 8 Dogs in Which the Gastric Arterial Blood Flow Was Maintained Constant by Means of a Sigmamotor Pump.

Values denote mean change ± SEM.

(ng/kg)	MSAP (Δmm Hg)	MGAPP (Δmm Hg)	MGVP (Δmm Hg)	GPR (Δmm Hg/ml/min × 10^3)
PGE_1				
2.5	−0.6 ± 0.4	−31.8 ± 4.8[a]	+1.5 ± 0.8	−433 ± 12[a]
10	−2.8 ± 0.7	−30.0 ± 5.9[a]	+1.3 ± 0.8	−461 ± 16[a]
PGA_1				
2.5	−2.6 ± 1.7	−16.3 ± 3.6[a]	−0.5 ± 0.2	−138 ± 24[a]
10	−1.8 ± 0.7	−21.6 ± 4.2[a]	−0.2 ± 0.2	−209 ± 40[a]

[a] A significant difference from the control value.

PGE_1 may not be the cause but the result of the antacid action of PGE_1. The present study in which PGE_1 and PGA_1 dilate the gastric arterioles appears to be in disagreement with the previous observations made by Wilson and Levine (18) and by Jacobson (5). Presently, no satisfactory explanation can be entertained from the present study. However, it is conceivable that Wilson and Levine, and Jacobson by markedly stimulating gastric secretion also probably induced a marked vasodilatation of the gastric vascular beds. Hence, PGE_1 might not be able to directly dilate the vascular beds further, but might indirectly decrease the gastric mucosal blood flow as the systemic arterial blood pressure decreases. An alternative explanation is that PGE_1 may cause a redistribution of the gastric blood flow from the mucosal layer to the other layers of the stomach.

Robert *et al.* (12, 13) observed that the antacid action of intravenously injected PGE_1 is greater than that of intravenously injected PGA_1. It can be concluded that the antacid action of the prostaglandins is most likely unrelated to their action on the gastric blood flow since this study shows that the vasodilator action of intravenously injected PGA_1 is greater than that of intravenously injected PGE_1 in dogs. Recently, more clear-cut evidence for the underlying mechanism responsible for the antacid effect of PGE_1 has been provided. *In vitro,* PGE inhibits histamine-stimulated gastric secretion in the isolated rat and bullfrog gastric mucosa, where gastric blood flow is not involved (14, 16).

Summary. The effect of intravenous and intraarterial injections of PGE_1 and PGA_1 on the gastric peripheral vascular beds was studied in anesthetized dogs, in which the total gastric arterial system was perfused at a constant rate of blood flow by a Sigmamotor pump. By both routes of administration, both PGE_1 and PGA_1 decreased the gastric arterial perfusion pressure and the gastric peripheral vascular resistance, while the gastric venous pressure remained essentially unchanged. This study indicates that PGE_1 and PGA_1 are potent vasodilators on the gastric circulation in the dog.

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