Effect of Furosemide on Renal Blood Flow in the Conscious Dog[1] (34508)

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Furosemide has been reported to decrease renal vascular resistance and thereby increase renal blood flow in anesthetized dogs (1–3). Furthermore, Ludens *et al.* (2) have demonstrated that the ability of furosemide to reduce renal vascular resistance and thereby increase renal blood flow is related to the initial resistance to blood flow in the kidney. Reports by Price (4) and by Silk (5) demonstrate that renal vascular resistance is elevated in animals anesthetized with pentobarbital. Thus, these previous studies in animals anesthetized with pentobarbital may have employed a preparation that was extremely susceptible to the vasodilating action of furosemide. It is possible that the hemodynamic effect of furosemide may be limited to the high renal vascular resistance that prevails in anesthetized animals. To determine if this was indeed the case the effect of furosemide on renal blood flow was assessed in unanesthetized dogs.

Methods. Chronic animals were prepared in the following manner. Female mongrel dogs were anesthetized with pentobarbital sodium (30 mg/kg, iv). The left renal artery was approached retroperitoneally through a flank incision. An electromagnetic flow transducer (Carolina Medical Electronics; lumen size, 11-mm circumference, or *In Vivo* Metric Systems, lumen size, 3.5-mm diameter) was placed around the exposed renal artery. The transducer cable was passed through the flank muscle layers and subcutaneously to the neck region just superior to the scapulae. Here the cable was externalized with a subcutaneous connector extruding through the skin. Another small incision was made just medial to the right forelimb over the region where the omocervical artery branches from the subclavian artery in order to expose the omocervical artery. A cannula (Silastic Medical-Grade Tubing, .040 in. i.d., .085 in. o.d., Dow Corning Corp.) to be used to monitor blood pressure was inserted into the exposed omocervical artery such that the tip of the cannula was located in the subclavian artery. The cannula was passed subcutaneously to the dorsal neck region (same area in which the flow transducer was externalized) and externalized with a nylon connector (6) extruding through the skin. The animals were given an intramuscular injection of 400,000 units of Strep-Distrycillin daily for 3 days after surgery and were allowed at least 2–3 days to recover from the surgery before experimentation.

During an experiment the dogs were placed in a sling such that their feet just touched the floor. This allowed the animals to either stand in place or hang in the sling as they so desired. The externalized flow transducer cable and cannula were attached to an electromagnetic flowmeter (Carolina Medical Electronics, Model 321) and pressure transducer, respectively. Both renal blood flow and systemic blood pressure were recorded continuously on a Beckman oscillograph. A Foley bladder catheter was inserted in order to collect urinary samples. Urinary collection periods were 20 min in length. The bladder was given three 30-cc air rinses spaced by two 15-ml water rinses between collection periods. A single 20-min urinary collection period preceded and three 20-min urinary collection periods followed systemic administration of furosemide (1 mg/kg).

The data were analyzed statistically using

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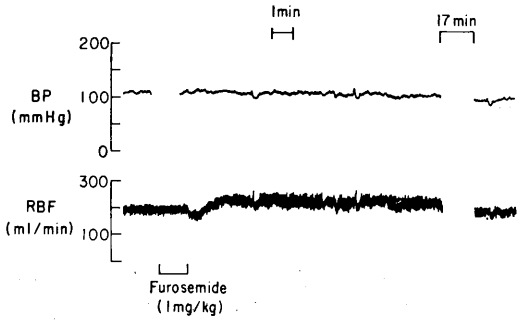

FIG. 1. Effect of furosemide (1 mg/kg) on renal blood flow in an unanesthetized dog. Blood pressure (BP) is shown by the top tracing. Renal blood flow (RBF) is shown by the bottom tracing. The bracket along the bottom indicates the duration of administration of furosemide *via* the pressure cannula.

Student's *t* test, paired comparisons (7). The 0.05 level of probability was used as the criterion of significance.

Results and Discussion. Figure 1 shows pressure and flow tracings obtained when 1 mg/kg of furosemide was administered to an unanesthetized dog. A transient decrease in renal blood flow was observed immediately after drug administration. Shortly after the slight decrease in renal flow, furosemide increased renal blood flow well above the control level of flow. The initial transient fall in renal flow produced by furosemide was not seen in all of the experiments, while the drug invariably produced an increase in renal blood flow. As can be seen by the top tracing, this dose of furosemide did not alter blood pressure. A composite of the blood flow tracings from five animals (Fig. 2) shows the characteristics of the furosemide-induced changes in renal blood flow. Renal blood flow was decreased slightly but significantly during the first few minutes after administration of the drug. At 5 min after injection, renal blood flow was increased significantly. The maximal increase in blood flow produced by the drug occurred about 10 min after drug administration. Flow returned to control level by approximately 30 min after drug administration. The results of this study show that furosemide does increase renal blood flow in the conscious animal and that the vasodilator properties of furosemide are not limited to anesthetized animals.

Quantitative results showing the effect of furosemide on sodium excretion and renal hemodynamics are shown in Table I. The values are expressed on a per kilogram total body weight basis. Sodium excretion was increased significantly upon drug administration. Furosemide given to unanesthetized dogs increased renal blood flow as renal vascular resistance was decreased significantly. Blood pressure was not altered. The results obtained in unanesthesized animals in the present study are also consistent with the previous suggestion (2) that the hemodynamic effect of furosemide is a function of initial renal vascular resistance. Initial renal vascular resistance in unanesthetized dogs was 9.1 units (Table I). Upon drug administration, renal vascular resistance changed 1.4 units as renal blood flow was increased by 2.4 ml/kg/min. An initial renal vascular resistance of 18.3 units in anesthetized animals was reported previously (2). The same dose of furosemide (1 mg/kg) in these anesthetized animals produced a greater change in resistance (6.9

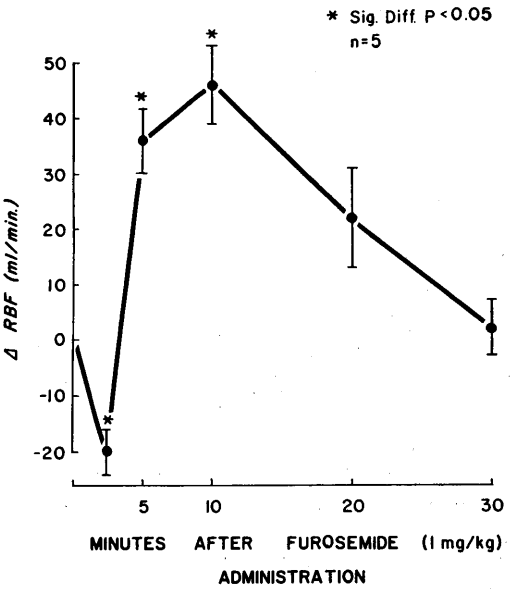

FIG. 1. Effect of furosemide (1 mg/kg) on renal blood flow in unanesthetized dogs. The tracing shows the change in renal blood flow after drug administration. Vertical lines indicate standard errors. Renal blood flow prior to furosemide administration was 211 ± 28 ml/min.

TABLE I. Effect of Furosemide (1 mg/kg) on Sodium Excretion and Renal Hemodynamics in the Unanesthetized Dog.

	Control[a]	Furosemide[b]	Difference[c]
Sodium excretion (μeq/kg/min)	3	62	59 $\pm$ 11[d]
Renal blood flow (ml/kg/min)	11.3	13.7	2.4 $\pm$ 0.4[d]
Blood pressure (mm Hg)	99	103	4 $\pm$ 3
Renal vascular resistance [mm Hg/(ml/kg/min)]	9.1	7.7	-1.4 ± 0.4[d]

[a] Control values were obtained just prior to drug administration.
[b] Furosemide values were obtained during the maximal effect of the drug on renal blood flow.
[c] Difference from control $\pm$ SE.
[d] Indicates a significant difference, $n = 5$.

units) and hence a greater change in renal blood flow (4.8 ml/kg/min). Thus, these results are consistent with the suggestion that furosemide has a greater effect on renal vascular resistance and consequently on renal blood flow in kidneys in which resistance to flow is higher.

Sodium excretion determined in a collection period obtained 40–60 min after administration of furosemide when the effect of the drug on renal blood flow was no longer apparent was still 31 μeq/kg/min greater than control values. Thus, as in anesthetized preparations, an increase in excretion can be seen when renal blood flow is not elevated by the drug.

It should be noted that the quantitative data shown here differ somewhat from the results of Vorburger *et al.* (3) They measured relative changes in renal blood flow in two conscious dogs and found that the percentage increase in renal blood flow produced by 1 mg/kg of furosemide in the two unanesthetized animals was nearly the same as the percentage increase in renal blood flow produced by the same dose of drug in anesthetized dogs. However, no values were given for renal vascular resistance. Thus, initial renal vascular resistance in anesthetized and unanesthetized animals could not be related to the change in renal blood flow produced by furosemide in anesthetized and unanesthetized animals as in the present study.

Summary and Conclusions. Furosemide was administered to unanesthetized dogs containing implanted flow transducers and pressure cannulas. The results show that furosemide increased renal blood flow in the conscious animal after an initial decrease, but that the increase in renal flow produced by 1 mg/kg of the drug was less than previously reported values obtained from anesthetized animals. It was observed that initial renal vascular resistance was lower in unanesthetized animals than the values reported for anesthetized animals. Thus, it was concluded that: (1) furosemide does increase renal blood flow in the conscious dog, and (2) the increase in renal flow produced by the drug in conscious animals is less than the increase in renal flow produced by the drug in anesthetized dogs, because initial resistance to renal flow is lower in conscious than in anesthetized animals.

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