Effect of potassium on renal vascular resistance and urine flow rate

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Effect of potassium on renal vascular resistance and urine flow rate. Am. J. Physiol. 197(2): 305-308. 1959.—The effect of potassium chloride upon renal vascular resistance and urine flow rate was studied in anesthetized laparotomized dogs. Potassium chloride was infused directly into the renal artery with the rate of blood flow to the kidney held constant and with flow rate not controlled. Resistance progressively decreased when serum potassium level in the kidney was elevated by infusing 0.11-0.69 mEq K+/min. It progressively increased when the infusion rate exceeded 0.69 mEq/min. This relationship was unaltered by the adrenergic blocking agent phentolamine. Urine flow rate increased both before and after denervation of the kidney when potassium was infused at the rate of 0.6 mEq/min. This increase was not apparent when the rate of blood flow was held constant. These findings indicate that a local potassium excess in amounts which might occur naturally leads to dilatation of renal vessels and increase of urine flow rate. The latter probably is related to the former.

A number of studies (1-15) suggest that arteriolar tone and sensitivity are in part determined by concentrations of cations. If this be true, then it is possible that the concentrations of cations are important determinants of the level of the blood pressure normally and in conditions characterized by malfunction of the adrenal cortex, neurohypophysis and kidney. Unfortunately, the above studies do not indicate the direct effect of a physiological change of concentration upon arterioles in intact vascular beds. In all except one of the above studies, concentrations were either changed in a bath surrounding an isolated strip of smooth muscle, in an artificial solution perfusing a vascular bed or generally within the intact animal. The tone of an isolated strip or vascular bed perfused with other than blood may not be applicable to arterioles in intact beds. Changes of arterial pressure in an intact animal in which the concentration of a cation has been changed generally also may not indicate changes in arteriolar tone. Pressure may change either because of change of vascular caliber or cardiac output. Further, this method does not permit separation of direct and indirect effects. For example, potassium may produce a discharge of catecholamines from the adrenal medulla (4, 16-21). Hence, a general change in potassium concentration might produce caliber changes which are not the direct effect of potassium upon the arteriole.

In order to determine the direct effects of cations upon intact blood perfused vascular beds, a study was initiated in which various cation salts were separately infused into the arterial supply of a bed at a rate which was sufficient to raise concentrations in the bed but insufficient to significantly raise concentrations generally within the animal. Such a study has been previously reported for the intact vascular bed of the dog foreleg (22-24). Caliber changes were separately measured in large arteries, small vessels and large veins. The arterioles of the foreleg dilate as a function of sodium or magnesium concentration and constrict as a function of calcium concentration. The response to potassium salts is more complex. The leg arterioles dilate as potassium concentration is raised over the range 3-8 mEq/l. However, large arteries progressively constrict as the concentration is elevated above 8 mEq/l. The net result is a falling resistance to flow over the lower range of concentrations but a rising resistance over the higher concentrations. In the same preparation, the local effect of increasing the hydrogen ion concentration is arteriolar dilatation (25).

The present study represents an extension of the above study to the renal vascular bed. Renal vascular resistance and urine flow rate were measured as potassium concentration was progressively elevated in the dog kidney. Resistance changes were similar to those observed in the dog foreleg.

METHODS

The effects of potassium chloride upon renal vascular resistance and urine flow rate were studied in anesthetized laparotomized dogs. Potassium chloride was infused directly into the renal artery with the rate of

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FIG. 1. Renal vascular resistance as a function of potassium infusion rate. Average of 9 kidneys before (solid circles) and during (open circles) infusion of 100 μg/min. phentolamine methanesulfonate in the renal artery. Potassium infusion rates achieved by infusing a solution of potassium chloride containing 0.5 mEq K+/ml into renal artery. Pressures were measured in the renal artery and vein after they became stable. This was obtained about 30 seconds after changing the rate of infusion. Blood flow rate was held constant throughout, the average values being 89 and 94 ml/min. before and during infusion of phentolamine respectively. Average values for renal arterial pressures were 74, 70, 68, 66, 67, 73, 96, 114, and 86, 89, 79, 75, 73, 73, 79, 104, 133 mm Hg with the various infusion rates in the absence and in the presence of phentolamine respectively. Venous pressure remained constant.

Blood flow to the kidney held constant or not controlled. Pressures were measured in the renal artery and vein in the former experiments and in the aorta and renal vein in the latter experiments. Caliber changes in renal vessels were inferred from changes in calculated resistance. Changes in caliber were correlated with changes in urine flow rate. These methods have been described in detail previously (26-28).

The study includes a total of 43 dogs. Their weights ranged from 30 to 40 lb. They were anesthetized with sodium pentobarbital, 33 mg/kg, and anticoagulated with heparin, 70-100 mg. Hydration was accomplished with a continuous intravenous infusion of 5% glucose in water at the approximate rate of 5 ml/min. The right kidney was surgically exposed and the artery, vein and ureter isolated. In one series of experiments, pressures were measured in the aorta and renal vein and urine collected from the pelvis before, during and after potassium administration. Solutions of potassium chloride, containing 0.2, 0.6 and 1.0 mEq K+/ml, were infused (Constant Infusion Machine, model ES-4B, Engineering Specialties, Madeira, Ohio) into the renal artery at the approximate rate of 1 ml/min. for 5 minutes. The infusions were repeated following section of extrinsic nerves in the hilus. Potassium chloride was also infused into the renal artery with the rate of blood flow held constant. A precalibrated blood pump (Sigmamotor Gump, model T-6, Sigmamotor, Inc., Middleport, N. Y.), whose output under the conditions of this experiment was independent of pressure, was interposed in the renal artery. The flow rate was set at a value which produced a mean pressure in the renal artery of about 60-80 mm Hg. At this pressure, flow rate ranged from 50 to 118 ml/min. in individual animals but was maintained constant throughout.

Complete sequence in any given animal. Pressures were measured in the outflow arm of the pump tubing and in the renal vein. Urine was collected from the renal pelvis. Potassium chloride was infused into the outflow tubing of the pump both before and after section of nerves in the hilus. In addition, potassium was administered to some kidneys during infusion of the adrenergic blocking agent, phentolamine methanesulfonate, into the renal artery at the approximate rate of 100 μg/min. This infusion rate was selected because it is sufficient to completely prevent a vascular response in the foreleg following a challenging injection of 1 μg norepinephrine into the brachial artery (25). The potassium level in renal vein serum was determined by flame photometry. Renal vascular resistance was calculated by dividing the pressure drop from renal artery to renal vein by the blood flow rate.

Results

Figure 1 shows that renal vascular resistance decreased moderately and then increased greatly as a function of the infusion rate of potassium. The resistance decrease was apparent in seven of nine and the resistance increase in nine of nine kidneys tested. Resistance returned almost to the control value within 30 seconds of stopping the infusion. The concentration of potassium in renal venous serum was measured in two animals with the potassium infusion rate at 0.00, 0.27, 0.69, 0.98, 1.50, 1.89 and 0.00 mEq/min. in that order. The values obtained were 3.9, 7.2, 10.8, 15.4, 22.0, 30.0, 12.0 and 3.0, 5.6, 9.6, 8.8, 16.6, 20.0, 12.6 mEq/l. respectively. It is apparent that reversal of the direction of the curve occurs at about a concentration of 10 mEq/l. Further, the higher infusion rates elevate the serum potassium level in the animal as a whole. Since the latter finding introduced the possibility that the rise in resistance might be related to an adrenal discharge (4, 16-21), the experiments were repeated during a constant infusion of phentolamine into the renal artery. The response was not significantly different from that obtained in the absence of phentolamine.

With this data as a background, the effect of potassium chloride upon urine flow rate was studied in kidneys not perfused with the blood pump. Potassium infusion rates of 0.2, 0.6 and 1.0 mEq/min. were selected because these rates elevate serum potassium concentration in the kidney to levels which might occur naturally and because they include the range over which the dilator response was observed. Further, a previous study showed that serum potassium concentration in the animal as a whole did not change measurably during 5-minute periods of infusion at rates of 0.2 and 0.6 mEq/min. (29).

Infusion of potassium increased the rate of urine flow both before and after denervation. The increase was most
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![Graphs showing the effect of potassium chloride on urine flow rate.](image)

**Fig. 2.** Effect of potassium chloride upon urine flow rate. Average of 12 animals. Ten also studied following surgical denervation of the kidney. Solutions of potassium chloride, containing 0.2, 0.6, 1.0 mEq K+/ml, were infused into the renal artery at the rate of 1 ml/min. for 5 minutes. Urine was collected for 1 minute just prior to onset of infusion, between the 3rd and 5th minute of the infusion and 3-5 minutes after stopping the infusion. Pressures were measured at the same times. P value for change less than 0.01 in those starred once and between 0.5 and 0.01 in those starred twice.

regular during administration of 0.6 mEq/min. (fig. 2), the same approximate rate that produced the maximum decrease of resistance (fig. 1). With this infusion rate, urine flow rate increased in 11 of 12 kidneys before denervation and 10 of 10 kidneys after denervation. In neither instance did aortic pressure change. Less regular changes were observed with 0.2 and 1.0 mEq/min. With the latter infusion rate, aortic pressure increased significantly.

In order to determine whether the rise in urine flow rate might be related to an increase in blood flow rate subsequent to vascular dilatation, the above sequence was repeated with the renal blood flow held constant. Though resistance decreased in 9 of 10 innervated kidneys infused with potassium at the rate of 0.6 mEq/min., urine flow rate did not change significantly. The average urine flow rate before potassium infusion was 1.5 ml/min. It increased in six and decreased in four, the mean change ± S.D. being 0.02 ± 0.26 ml/min. Urine flow rate also failed to change following section of nerves in the hilar region. Neither resistance nor urine flow rate changed regularly when potassium was infused at the rates of 0.2 and 1.0 mEq/min. An irregular increase of urine flow rate was observed during infusion of 1.0 mEq/min. Urine flow rate increased in seven and decreased in two before denervation (mean change ± S.D. = +0.21 ± 0.29 ml/min. \( P = 0.05-0.01 \)) and increased in eight and decreased in two after denervation (+0.37 ± 0.39 ml/min. \( P = 0.05-0.01 \)).

Ten separate innervated kidneys, perfused with blood at a constant rate, were studied before and during infusion of phenolamine methanesulfonate at the rate of 100 \( \mu g/\text{min.} \). As in the above group, infusion of potassium did not significantly change the rate of urine flow. Mean changes of urine flow rate during infusion of potassium at 0.2, 0.6 and 1.0 mEq/min. were \( -0.05 \pm 0.18 \), \( +0.14 \pm 0.43 \) and \( +0.12 \pm 0.24 \) ml/min. before phenolamine and \( +0.09 \pm 0.38 \), \( +0.02 \pm 0.17 \) and \( +0.18 \pm 0.55 \) ml/min. during phenolamine infusion, respectively.

**Discussion**

These studies show that potassium has a direct effect upon calibers of blood vessels in the dog kidney. It causes active dilatation when serum concentration is elevated over ranges which might occur naturally. Associated with this is a rise in urine flow rate which probably is related to the dilatation. When the potassium concentration is elevated further, the dilatation is replaced by active constriction. Arguments for these statements follow.

The observed changes of resistance likely were caused by active changes of the caliber of vessels. There is little reason to suspect that the resistance changes were initiated by dynamic changes of the viscosity of the blood. Resistance commenced to change with the rate of blood flow and hence linear velocity held constant. There is also little reason to suspect that the changes of calibers were caused by passive mechanisms. Resistance decreased in the presence of falling intraluminal pressures and increased while intraluminal pressures were rising. Extraluminal pressures probably did not change significantly. There were no discernible changes in the tenueness of the kidneys.

The dilatation resulted from a direct effect of potassium upon renal vessels. The dilatation was apparent before serum potassium levels changed generally within the animal. The constriction also probably resulted from a direct effect of the potassium. A sympathetic-adrenal discharge resulting from elevated potassium levels generally within the animal is an unlikely explanation because the constriction was not prevented by an adrenergic blocking agent. Further, the constriction disappeared immediately upon stopping the infusion of potassium. The chloride ion and hypertonicity of the solution were likely not involved in the caliber changes. Hypertonic potassium chloride and potassium phosphate produce identical resistance changes in the dog foreleg. Hypertonic calcium chloride, calcium gluconate and calcium lactate produce changes which are directionally opposite to those produced by potassium chloride and potassium phosphate (22, 24).

The rise in urine flow rate likely is related to the dilatation. Urine flow rate increased most regularly when potassium was infused at a rate which produced a maximum decrease of resistance. Since aortic pressure was unaffected, a decrease in resistance implies an increase in blood flow rate. When blood flow rate was held constant, urine flow rate did not change.

Potassium has a similar effect upon blood vessels in the dog foreleg. Total resistance to blood flow through the dog foreleg decreases as a function of infusion rate
over the range 0.0 to 0.6 mEq K+/min. It increases as a function of infusion rate over the range 0.6–3.0 mEq K+/min. Segmental resistances were also measured in the dog foreleg. In small vessels (less than 0.5 mm diameter) resistance decreases as a function of infusion rate over the entire range. In large arteries (greater than 0.5 mm diameter) resistance remains constant over the range 0.0–0.6 mEq K+/min. and then increases over the range 0.6–3.0 mEq K+/min. In large veins (greater than 0.5 mm diameter) resistance does not change. The coronary vessels may respond in the same way. Katz and Lindner (9) noted in fibrillating Langendorff preparations of dog hearts that potassium in dilute concentrations produced a dilatation and in stronger concentrations a constriction.

Renal vascular resistance increases as the hydrogen ion concentration is lowered by hyperventilation (27). This may be related to changes in potassium concentration. A number of investigators have reported changes in the level of the serum potassium during acidosis and alkalosis.

REFERENCES