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Potassium-Induced Vascular Relaxation in Two Kidney-One Clip, Renal Hypertensive Rats

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Abstract. This study was designed to characterize potassium-induced relaxation in vascular smooth muscle in two kidney-one clip (2K-1C), renal hypertensive rats. Potassium-induced relaxation was evaluated in the isolated tail artery and in the isolated pump perfused renal vasculature. Both preparations relaxed in response to potassium after contraction induced by norepinephrine in potassium-free solution. Arterial preparations from hypertensive rats showed greater relaxation than did those from normotensive rats. Potassium-induced relaxation in tail arteries from hypertensive rats was more sensitive to ouabain inhibition than those from normotensive rats; the renal vasculature of hypertensive rats did not differ from controls with respect to ouabain sensitivity. Relaxation in response to potassium in isolated tail artery segments varied with the: 1. length of incubation in potassium-free solution; 2. concentration of added potassium; and 3. concentration of norepinephrine added during the potassium-free interval. The amplitude of potassium relaxation is believed to be a functional measure of the electrogenic sodium pump. These experiments support the hypothesis that vascular smooth muscle from 2K-1C renal hypertensive rats has increased electrogenic sodium pump activity, in vitro.

Key words: Electrogenic pump – Ouabain – Sodium – Renal vasculature – Tail artery

Introduction

In vascular smooth muscle, the electrogenic sodium pump contributes to the resting membrane potential by causing a net excess of positive charge outside the cell; and it has been suggested that the pump plays an important role in controlling the contractile activity of the smooth muscle cells (see Webb et al. 1981, for review).

Several observations suggest that altered function of the electrogenic sodium pump may contribute to altered vascular responsiveness in various forms of renal hypertension (Haddy et al. 1980; Webb and Bohr 1980). The techniques used to evaluate electrogenic transport include: 1. potassium-induced vasodilatation in intact vascular beds (Overbeck 1972; Overbeck and Clark 1975); and 2. ouabain-sensitive uptake of radioactive rubidium in isolated vascular segments (Brock and Overbeck 1982; Overbeck and Grissette 1982; Overbeck et al. 1976; Pamnani et al. 1981). The observations of these studies have yielded conflicting views concerning the activity of the electrogenic sodium pump in blood vessels from renal hypertensive animals. The current study was intended to add evidence that will assist in the resolution of these conflicts. It was also intended to further characterize vascular changes in two kidney-one clip (2K-1C), renal hypertension (Goldblatt hypertension).

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Methods

Animal Preparation

All studies were performed on male, Sprague-Dawley rats (325–375 g). The animals were anesthetized with ether, and the left kidney was exposed through a flank incision. A silver block (0.22 mm slit) was placed on the left renal artery. In half of the rats, the silver block was tied in place with surgical suture; the remaining rats served as sham controls (the silver block was removed). All rats were maintained on standard laboratory chow (Purina) and tap water *ad libitum*. Systolic blood pressures were determined in the conscious state by means of indirect tail cuff measurements. Experiments were performed at 4–8 weeks after surgery.

Tissue Preparation

Tail Artery Strips. Helical strips (0.8 × 10.0 mm) were cut from tail arteries isolated from 2K-1C, renal hypertensive and sham, normotensive rats. The strips were mounted vertically on a glass holder in a tissue bath containing 50 ml of physiological salt solution (PSS). The upper end of each strip was connected to a force transducer (Grass FT.03) and the resting force placed on each strip was adjusted so that the strip produced maximum active force in response to a standard dose of norepinephrine (10^{-7} g/ml). Before the start of experiments, the strips were allowed to equilibrate for 90 min in PSS. The bathing medium was maintained at 37° C and aerated with a mixture of 95% O_2 and 5% CO_2. The pH of the PSS was 7.4 and the composition (mmol/l) was as follows: NaCl, 130; KCl, 4.7; KH_2PO_4, 1.18; $MgSO_4 \cdot 7H_2O$, 1.17; $CaCl_2 \cdot 2H_2O$, 1.6; $NaHCO_3$, 14.9; dextrose, 5.5; and $CaNa_2$ EDTA, 0.03. Potassium-free solution was of the same composition except that KCl was omitted and 1.2 mM KH_2PO_4 was substituted with 1.2 mM NaH_2PO_4.

In some experiments, helical strips of tail artery from hypertensive and control rats were acutely denervated with

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6-hydroxydopamine according to the method of Aprigliano and Hermsmeyer (1976). The strips were placed in a bicarbonate-free PSS containing 300 µg/ml 6-hydroxydopamine for 10 min. The pH of this unbuffered PSS was adjusted to 4.0 by the addition of 20 µM glutathione. The O_2-CO_2 mixture to the muscle bath was turned off during the denervation procedure. Following denervation, the strips were allowed to recover in normal PSS (95% O_2; 5% CO_2) for 3 h.

Renal Vascular Perfusion. The procedure used to study the effects of potassium on renal vascular resistance was modified from Collis and Vanhoutte (1977). The right renal pedicle was exposed through a midline abdominal incision in rats anesthetized with sodium pentobarbital (50 mg/kg, i.p.). The right renal artery was cannulated via the aorta, and the kidney was perfused at constant flow by means of a peristaltic pump (Harvard Apparatus Co., Model 1202). The animal was terminated by pneumothorax, the renal vein and ureter were cut and the kidney vasculature was perfused with PSS in situ. The PSS was maintained at 37° C and aerated with 95% O_2 and 5% CO_2. Renal perfusion pressure was monitored through a T-tube placed between the pump and kidney. Flow through the pump, and hence the renal vasculature, was gradually increased to establish a minimal renal perfusion pressure which gave maximal vasoconstrictor responses to a standard dose of norepinephrine (10^{-7} g/ml). Changes in the composition of the perfusate were made by switching premixed preoxygenated solutions (potassium-free PSS, potassium-free PSS plus norepinephrine, PSS containing both potassium and norepinephrine and normal PSS) at the inflow side of the pump through a stopcock. The preparation was stable throughout the experimental period (2–3 h).

Statistical Analysis

The results of these experiments were analyzed by a variety of statistical procedures. Dose-response curves were calculated as geometrical means. Paired and unpaired "*t*" tests and curve fitting analyses (logit transformation) were performed. A *P* value less than 0.05 was considered to be statistically significant.

Drugs

Drugs used were: norepinephrine bitartrate (Breon Laboratories, Inc.), ouabain octahydrate (Sigma Chemical Co., St. Louis, MO, USA), 6-hydroxydopamine hydrobromide (Sigma Chemical Co., St. Louis, MO, USA), glutathione (Calbiochem. San Diego, CA, USA) and sodium pentobarbital (generic brand supplied by University of Michigan Hospital Pharmacy).

Results

The systolic blood pressures of rats used in this study were: 2K-1C, renal hypertensive = 181 ± 3 mmHg and sham, normotensive = 118 ± 3 mmHg ($P < 0.05$).

Potassium-Induced Relaxation in Tail Arteries

The tracings in Fig. 1 illustrate the procedure used to evaluate potassium-induced relaxation in tail artery strips from

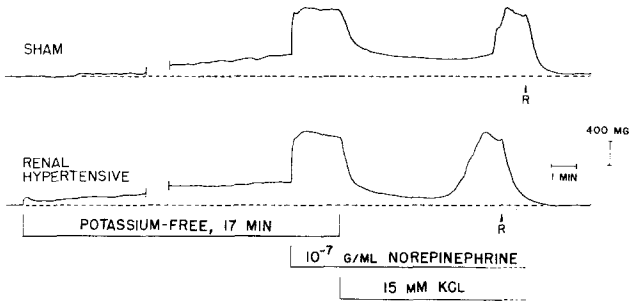

Fig. 1. Relaxation induced by potassium in tail arteries. Helical strips of tail arteries from 2K-1C, renal hypertensive and sham, normotensive rats relaxed in response to potassium after contraction induced by norepinephrine (10^{-7} g/ml) in potassium-free solution. Tail artery strips from hypertensive rats showed greater relaxation in response to potassium than those from normotensive rats. Following the increase in mechanical response which occurred after several minutes of relaxation, normal PSS was rinsed into the bath (*R* = rinse)

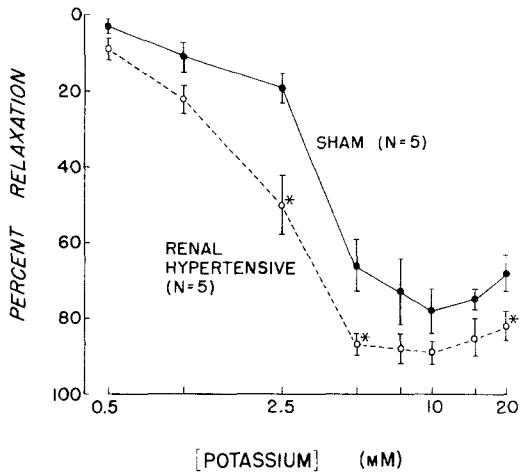

Fig. 2. Dose-response to potassium in tail arteries. Potassium-induced relaxation in tail artery strips was performed as described in Fig. 1, except that the concentration of potassium was varied. The magnitude of the relaxation was related to the concentration of added potassium. Values are the mean ± SEM. The values in parentheses are the number of rats. The asterisks indicate a statistically significant difference between hypertensive rats and normotensive rats ($P < 0.05$)

2K-1C, renal hypertensive rats and sham, normotensive rats. The rat tail artery, placed in a potassium-free solution, undergoes a gradual contraction in response to endogenous norepinephrine released from adrenergic nerve endings in the vessel wall (Bonaccorsi et al. 1977b). Fifteen min into this interval, norepinephrine (10^{-7} g/ml) was added to the muscle bath. Two min later, when the contractile response to exogenous norepinphrine had reached a plateau, the bath concentration of potassium was increased to 15.0 mM and an abrupt relaxation occurred. The magnitude of the relaxation was quantified as a percentage of the total contraction that existed just before the potassium was added. Tail artery strips from 2K-1C, renal hypertensive rats relaxed to a greater percentage of their norepinephrine contraction than those from normotensive rats. Following several min of relaxation, a spontaneous and abrupt increase in mechanical response was observed in tail arteries from both groups of rats.

The magnitude of the relaxation induced by potassium increased as the concentration of added potassium increased over a range of 0.5–20.0 mM (Fig. 2). Arterial strips from

Table 1. Concentrations of norepinephrine, ouabain and potassium to produce half-maximal response

Treatment	ED_{50}			
	Tail artery		Renal Vasculature	
	Normotensive	Hypertensive	Normotensive	Hypertensive
Potassium concentration at which there was half-maximal relaxation (Fig. 2 and 7)	2.9 mM ($N = 5$)	1.7 mM* ($N = 5$)	2.1 mM ($N = 5$)	0.8 mM* ($N = 5$)
Norepinephrine concentration at which there was half maximal contraction (Fig. 4A)	14.8×10^{-9} g/ml ($N = 5$)	4.5×10^{-9} g/ml* ($N = 5$)	–	–
Ouabain concentration at which there was half maximal inhibition of relaxation (Fig. 5 and 8)	17.6×10^{-5} M ($N = 6$)	2.5×10^{-5} M* ($N = 6$)	1.4×10^{-5} M ($N = 5$)	1.0×10^{-5} M ($N = 5$)

The asterisks indicate a significant difference between hypertensive and normotensive rats. The values in parentheses are the number of rats

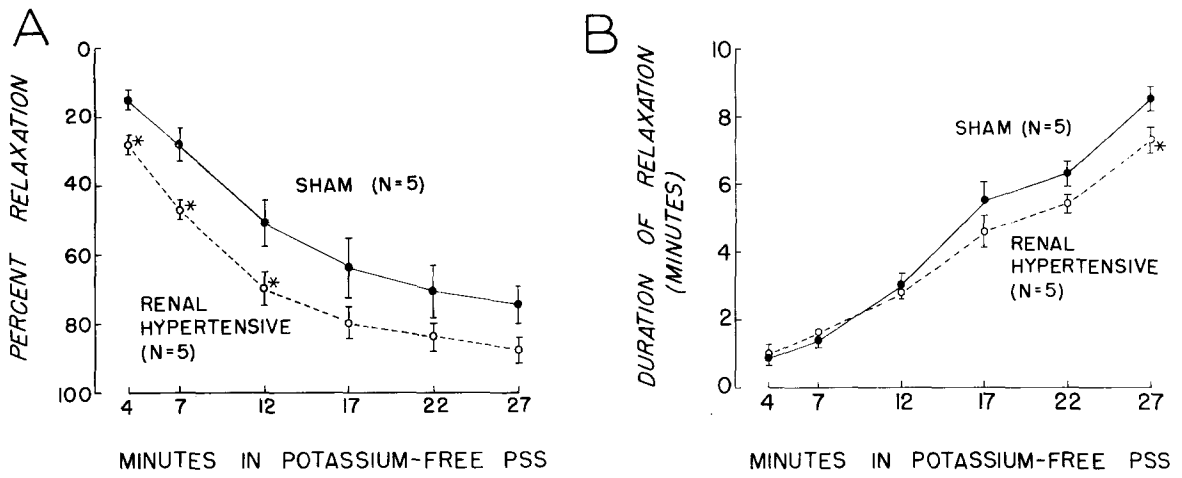

Fig. 3. Potassium-induced relaxation and the interval in potassium-free PSS. Potassium-induced relaxation of tail artery strips was performed as described in Fig. 1 except that the period of time the arterial strips were exposed to potassium-free solution was varied. The magnitude (Fig. 3A) and the duration (Fig. 3B) of the relaxation varied with the time of exposure to potassium-free solution. Values are the mean ± SEM. The asterisks indicate a statistically significant difference between 2K-1C, renal hypertensive rats and normotensive rats ($P < 0.05$). The values in parentheses are the number of rats

2K-1C, renal hypertensive rats relaxed to a greater extent than those from normotensive rats at all concentrations of potassium tested. In order to determine if there was a change in the sensitivity of the relaxation to potassium in arteries from 2K-1C, renal hypertensive rats, the data presented in Fig. 2 were transformed to percent maximal relaxation and the concentration at which half maximal relaxation (ED_{50}) occurred was calculated (Table 1). The ED_{50} for tail artery strips from hypertensive rats was significantly lower than that for artery strips from normotensive rats.

The magnitude and duration of the relaxation induced by 15.0 mM potassium varied with the time of exposure to potassium-free solution (Fig. 3). When the interval of time that the arterial strips were exposed to potassium-free solution was short, the magnitude of the relaxation was small (Fig. 3A) and the duration of the relaxation was short (Fig. 3B). Increasing the interval in potassium-free solution caused the potassium-induced relaxation to be greater in magnitude and in duration. Tail artery strips from 2K-1C, renal hypertensive rats showed greater relaxation than did those from normotensive rats at all incubation intervals. The duration of the relaxation was similar in the two groups of rats at all intervals except the 27-min incubation, where the duration of potassium relaxation was shorter in arteries from 2K-1C, renal hypertensive rats than in those from normotensive rats.

To determine whether the magnitude of the norepinephrine response was responsible for the difference in relaxation between hypertensive and normotensive rats, norepinephrine concentrations of 10^{-9} g/ml to 10^{-5} g/ml were used to produce variations in the magnitude of contraction (Fig. 4A). These experiments were performed on acutely denervated strips of tail artery to eliminate the contraction caused by norepinephrine released from nerve endings in potassium-free PSS. Tail artery strips from 2K-1C, renal hypertensive rats relaxed to a greater percentage of their norepinephrine contraction at all concentrations of norepinephrine as compared to those from normotensive rats (Fig. 4B). The concentration of norepinephrine at which there was a half maximal contraction (ED_{50}) was lower in tail arteries from hypertensive rats (Table 1). The maximal contractile responses of tail artery strips from hypertensive rats (1,887

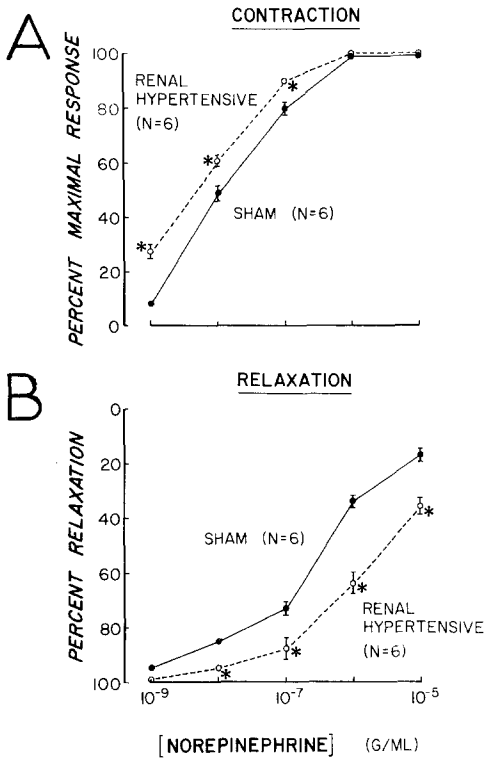

Fig. 4 A and B. Influence of contractile magnitude on potassium-induced relaxation. Potassium-induced relaxation of tail artery strips was performed as described in Fig. 1 except that the contractile state of the strips was altered by changing the concentration of norepinephrine added during the potassium-free cycle. The magnitude of the relaxation (Fig. 4B) varied inversely with the magnitude of the norepinephrine contraction (Fig. 4A). Values are the mean ± SEM. The asterisks indicate a statistically significant difference between 2K-1C, renal hypertensive rats and sham, normotensive rats ($P < 0.05$). The numbers in parentheses are the number of rats

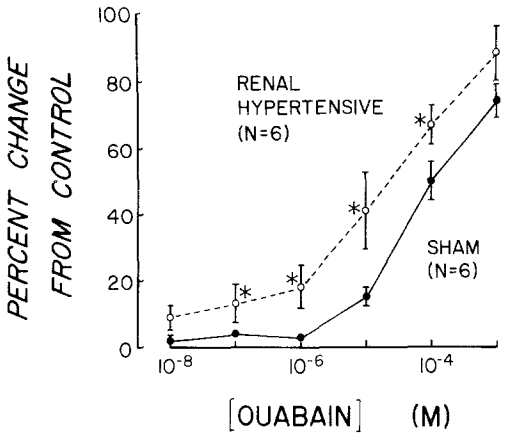

Fig. 5. Inhibition by ouabain. Potassium-induced relaxation in tail artery strips was performed as described in Fig. 1. Ouabain was added 5 min after the beginning of exposure to potassium-free solution (12 min prior to the addition of potassium). The responses of tail artery strips from hypertensive rats were more sensitive to inhibition by ouabain than those from normotensive rats. Values are the mean ± SEM. The asterisks indicate a statistically significant difference between hypertensive rats and normotensive rats ($P < 0.05$). The values in parentheses are the number of rats

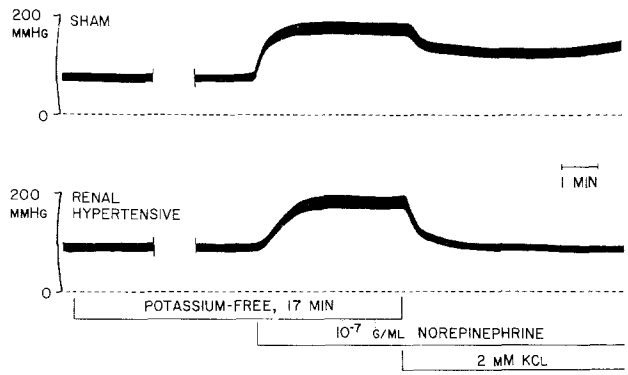

Fig. 6. Potassium-induced vasodilatation in the renal vasculature. The renal vasculature of 2K-1C, renal hypertensive and sham, normotensive rats were perfused at constant flow with potassium-free PSS. Following 15 min of perfusion, 10^{-7} g/ml norepinephrine was added to the perfusate and perfusion pressure increased. Two minutes later, 2.0 mM potassium was added to the perfusate and a decrease in perfusion pressure occurred. The decrease in perfusion pressure was greater in the renal vasculatures of hypertensive rats than in those of normotensive rats

± 170 mg) were similar to those from normotensive rats (1,913 ± 89 mg).

Ouabain, an inhibitor of the electrogenic sodium pump (Schwartz et al. 1975), decreased potassium-induced relaxation in tail arteries from both groups of rats (Fig. 5). Tail arteries from 2K-1C, renal hypertensive rats were more sensitive (lower ED_{50}) to inhibition by ouabain than those from normotensive rats (Table 1). The magnitudes of relaxation prior to ouabain treatment were: 1. 2K-1C, renal hypertensive = 88 ± 2%; and 2. normotensive = 75 ± 3%.

Potassium-Induced Vasodilatation in the Renal Vasculature

The kidney weights of animals used in these experiments were: hypertensive, right kidney (perfused) = 1.65 ± 0.03 g, left kidney (clipped) = 1.20 ± 0.04 g; normotensive, right kidney = 1.35 ± 0.04 g (perfused), left kidney (sham clipped) = 1.37 ± 0.02 g. The right and left kidneys of the hypertensive rats ($N = 5$) were significantly larger and smaller, respectively, than those from the normotensive rats ($N = 5$). Renal perfusion pressure was significantly higher in the hypertensive rats (78 ± 2 mm Hg) than in the normotensive rats (72 ± 1 mm Hg); whereas the perfusate flow was significantly lower in the kidneys of hypertensive rats (6.07 ± 0.01 ml/g/min) compared to that in the kidneys of normotensive rats (6.56 ± 0.01 ml/g/min). The calculated vascular resistance was higher in the kidneys from hypertensive rats (12.83 ± 0.35 mm Hg/ml/g/min vs. 10.67 ± 0.32 mm Hg/ml/g/min, $P < 0.05$).

The format of the procedure used to evaluate potassium-induced vasodilatation in the renal vascular bed is shown in Fig. 6. The renal vasculature of hypertensive and normotensive rats was perfused with potassium-free PSS for 17 min. Thirteen min into this interval, the perfusate was changed to a potassium-free perfusate containing norepinephrine (10^{-7} g/ml) and an increase in perfusion pressure was observed. This concentration of norepinephrine produced comparable increases in renal perfusion pressure in both groups of animals (percent increase in perfusion pressure; hypertensive = 137 ± 5%; normotensive = 147 ± 4%). Four minutes later, when the response to norepinephrine had reached a plateau, the perfusate was changed to one containing 2.0 mM pot-

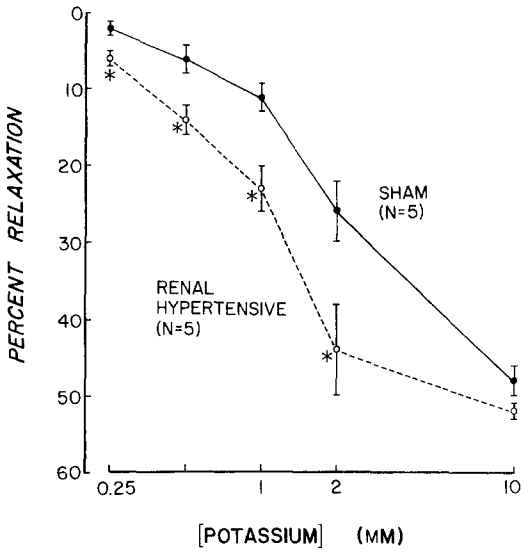

Fig. 7. Dose-response to potassium in the renal vasculature. Potassium-induced vasodilatation was performed as described in Fig. 6, except that the concentration of potassium was varied. The magnitude of the decrease in perfusion pressure was related to the concentration of added potassium. Values are the mean ± SEM. The asterisks indicate a statistically significant difference between hypertensive rats and normotensive rats ($P < 0.05$). The values in parentheses are the number of rats

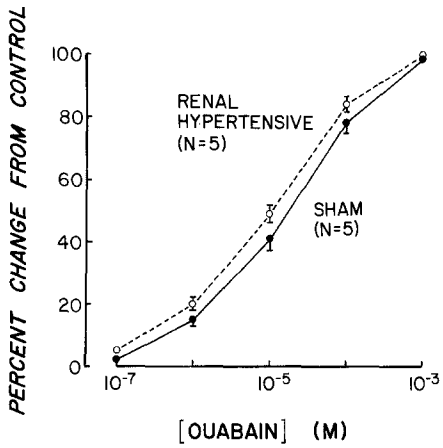

Fig. 8. Inhibition by ouabain. Potassium-induced vasodilatation was performed as described in Fig. 6. Ouabain was added to the perfusate 5 min after the beginning of the perfusion with potassium-free solution (12 min prior to the addition of potassium). The renal vasculatures of the two groups of rats were not different with respect to ouabain sensitivity. Values are the mean ± SEM. The values in parentheses are the number of rats

assium (norepinephrine still present in the perfusate) and a decrease in perfusion pressure occurred indicating vasodilatation. After the vasodilatation had reached a maximum, the perfusate was changed to normal PSS. The magnitude of the vasodilatation was quantified as a percentage of the increase in perfusion pressure in response to norepinephrine. The renal vasculature of hypertensive rats showed a greater decrease in perfusion pressure in response to potassium than did those of normotensive rats.

The sensitivity of the vasodilatation to potassium (Fig. 7) and to ouabain (Fig. 8) was examined. The renal vasculature of hypertensive rats was more sensitive to potassium than that of normotensive rats, whereas the ouabain sensitivity of the vasodilatation was similar in the two groups of rats (Table 1).

Discussion

The cellular process responsibile for potassium-induced relaxation is the electrogenic pumping of sodium and potassium by sodium-potassium ATPase (see Webb et al. 1981 for review). This mechanism has been documented in perfused organs and in isolated blood vessel segments. Bonaccorsi et al. (1977a) observed that isolated rat tail artery segments depolarized when placed in a potassium-free solution. Readmission of potassium resulted in membrane hyperpolarization; and this hyperpolarizing event was blocked by ouabain. Furthermore, these investigators demonstrated that the membrane hyperpolarization in response to potassium was coincident with a decrease in contractile force (relaxation) which was also inhibited by ouabain. They interpreted these observations as resulting from the inhibition of the sodium pump during the incubation in potassium-free solution, and therefore sodium accumulates intracellularly. When potassium is returned to the bathing medium, the sodium pump is activated due to the high intracellular concentration of sodium. Since more sodium is pumped out of the cell than potassium into the cell, this results in hyperpolarization which decreases membrane excitability and causes relaxation. Other investigators also suggested this mechanism for potassium-induced relaxation of vascular smooth muscle (see Webb et al. 1981).

The current study demonstrates that relaxation in response to potassium is exaggerated in the vasculature of 2K-1C, renal hypertensive rats. This observation is consistent with the hypothesis that vascular smooth muscle from these hypertensive animals has increased electronic sodium pump activity. These results contrast with an earlier study (Overbeck and Clark 1975) in which the vasodilator response to intra-arterial infusion of potassium was attenuated in 2K-1C, renal hypertensive rats. However, there are many differences between our study and that of Overbeck and Clark (1975). The preparation used by Overbeck and Clark was an isolated, blood-perfused hindlimb vascular bed, whereas our experiments were performed on isolated tail artery segments and isolated, PSS-perfused renal vascular beds. Recent observations by Pamnani et al. (1981) have provided evidence suggesting that this difference in reponsiveness to potassium may be due to the presence of a humoral factor present in the blood of renal and mineralcorticoid hypertensive animals which suppresses the electrogenic sodium pump. These investigators observed that ouabain-sensitive, rubidium uptake is depressed in tail artery segments from mineralocorticoid hypertensive rats when the measurements were made on arteries immediately removed from the animals. Interposition of an incubation period of 4.5 h between the time of removal of the artery and the measurement of rubidium uptake indicated increased electrogenic pump activity. These findings suggest the washout of a humoral factor which may suppress pump activity (and therefore potassium-induced relaxation) in blood perfused organs of hypertensive animals. Other differences which may contribute to the

disparate observations of our study and that of Overbeck and Clark include: 1. we used a potassium-free incubation period prior to the test for potassium-induced relaxation, whereas Overbeck and Clark infused potassium directly into the blood; and 2. since our preparations are atonic, we used norepinephrine to cause contraction of the tail artery segments and to increase perfusion pressure in the renal vasculature, whereas Overbeck and Clark examined responses in a preparation which had vascular tone.

An interresting observation of this study is that tail arteries from 2K-1C, renal hypertensive rats were more sensitive to the inhibitory effects of ouabain than those from normotensive rats; whereas the renal vasculature of the hypertensitive rats did not differ in its sensitivity to the glycoside compared to the control animals. The reason for this difference is not apparent but suggests that there are differences in the sodium pump of vascular smooth muscle cells of the resistance vessels of the kidney and the pump in cells of the larger conduit arteries such as the tail artery. Other investigators have observed an increased sensitivity to ouabain in vascular smooth muscle from spontaneously hypertensitive rats (Gothberg et al. 1980; Webb and Bohr 1979, 1980) and pigs made hypertensive by mineralocorticoid treatment (Webb 1982).

Both the tail artery and the renal vasculature of 2K-1C, renal hypertensive rats were more sensitive (lower ED_{50}) to the relaxant effect of potassium than those from normotensive rats. Similar increased sensitivity to the cation has been observed in isolated arteries from SHR (Webb and Bohr 1979) and those from mineralocorticoid hypertensive pigs (Webb 1982). The reason for an increased sensitivity to potassium in hypertension is unknown but may partly explain the antihypertensive property of the cation. Suzuki et al. (1981) observed that potassium loading attenuated the development of 2K-1C, renal hypertension in rats. Furthermore, potassium loading abated the hypertension in rats which had already developed an increased blood pressure. The main action of potassium to reduce blood pressure in these studies was accredited to diuresis and natriuresis and to suppression of plasma renin activity caused by potassium loading. Another possibility is that the loading process caused relaxation of the resistance vessels.

The magnitude of potassium-induced relaxation in tail artery strips was influenced by the duration of the exposure to potassium-free solution and by the concentration of norepinephrine added during the potassium-free cycle. The latter observation demonstrates that the comparison of potassium-induced relaxation in arteries from 2K-1C, renal hypertensive rats and those from normotensive rats may be an oversimplified measure of the electrogenic sodium pump since the level of the contractile response depends on a number of interacting variables (sensitivity to the agonist, intracellular calcium concentration, coupling between membrane potential and mechanical response, cyclic nucleotides, etc.; see Webb and Bohr 1981 for review). However, the magnitude of potassium-induced relaxation was greater in arteries of hypertensive rats than in those of normotensive rats, regardless of norepinephrine concentration, suggesting that altered vasoconstrictor sensitivity does not mask the increased responsiveness to potassium in hypertensive arteries under these experimental conditions. The observation that relaxation varies with incubation interval in potassium-free solution is probably due to differences in intracellular sodium concentration at the end of the incubation period. Intracellular sodium accumulates under potassium-free conditions (Friedman and Friedman 1976) and longer exposures would therefore lead to a greater sodium accumulation producing an increased magnitude of relaxation following readmission of potassium. Friedman and Friedman (1976) observed that the intracellular sodium concentration, measured in normal PSS, is less in tail arteries from mineralocorticoid hypertensive rats and SHR as compared to their respective controls. Potassium-free conditions resulted in an increase in intracellular sodium, and the amount gained was greater in the arteries from the hypertensive rats. An increased cellular sodium in hypertensive arteries, under these conditions is probably due to a greater membrane permeability to the cation (Friedman and Friedman 1976; Jones and Hart 1975; Jones and Miller 1978).

The current observations demonstrate both structural and functional changes in the vasculature of rats with 2K-1C hypertension. There was an increase in renal vascular resistance under conditions of complete relaxation of the vascular smooth muscle. This observation is interpreted as indicating that there is a fixed or structural resistance basis for the greater vascular resistance in the untouched, hypertrophied kidney of the hypertensive rat. There was a shift to the left of the concentration response curve to norepinephrine of the tail artery of the hypertensive rat. Since these observations were made on artery strips that had been acutely denervated with 6-hydroxydopamine, this shift must be interpreted as being caused by an increase in vascular smooth muscle sensitivity and not by a change in neuronal uptake of norepinephrine. Both this functional change and the structural change demonstrated by the increase in renovascular resistance would be expected to contribute to the increase in total peripheral resistance in hypertension.

On the contrary, the observed increased potassium relaxation in vascular smooth muscle of both the tail artery and the renal resistance vessel would not contribute to the increased total peripheral resistance. This observation adds to the evidence supporting the conclusion that there is a greater activity of the electrogenic pump in vascular smooth muscle in 2K-1C, renal hypertension. The possibility that contrary observations may be caused by a humoral pump inhibitor in the intact animal that would mask this increased pump activity and thereby increase vascular resistance (Pamnani et al. 1981) has not been dealt with in the current study. However, because of the similarity of the observed increase in potassium relaxation in this model of hypertension in both the isolated tail artery and the perfused kidney, it is unlikely that the disparate observations in the literature could be due to a difference in the effect of the hypertensive process on large arteries and on small resistance vessels.

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