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Role of Calcium in Function of Isolated Perfused Rabbit Kidney

Kweon-Haeng Lee*, Eun-Eui Chun, Kyoung-Ja Hong and Kyu-Chul Cho

Department of Pharmacology, Catholic Medical College, Seoul 135, Korea

ABSTRACT

This study was designed to investigate the role of calcium in the function of an isolated perfused rabbit kidney and its effect on the diuretic action of furosemide. The administrations of hydralazine and verapamil produced remarkable diuretic actions mainly by decreasing renal resistance. The administration of furosemide in combination with hydralazine or verapamil produced remarkable diuretic action and there was no difference between the two groups. The administration of quinidine produced a diuretic action in spite of vasoconstriction and potentiated the diuretic action of furosemide.

In the calcium-free perfusion medium, the administration of calcium produced a marked diuretic action in spite of vasoconstriction and potentiated significantly the diuretic action of furosemide. The administration of quinidine did not alter renal function and the diuretic action of furosemide, but the combined administration of quinidine and calcium showed antidiuretic effect due to excessive vasoconstriction in the calcium-free perfusion medium. Although the administration of verapamil produced a slight diuretic action in the calcium-free perfusion medium, verapamil did not alter the diuretic action of calcium as well as the diuretic actions of furosemide alone and in combination with calcium.

The results of this experiment show that calcium, verapamil and quinidine produced diuretic actions and calcium potentiates the diuretic action of furosemide.

Key Words: isolated perfused rabbit kidney, calcium, furosemide, quinidine, verapamil

INTRODUCTION

It is well known that changes in cytosolic calcium concentration can influence transcellular ion and water transport in toad bladder and mammalian renal tubular epithelium (Gardos, 1958; Marty, 1981; Meech, 1978; Yau *et al.*, 1981). Quinidine and calcium ionophore (A 23187) to increase the level of cytosolic free calcium ions (Balzer, 1972; Batra, 1974; Fuchs *et al.*, 1968; Isaacson and Sandow, 1967) were found to inhibit sodium absorption in proximal convoluted tubule of the rabbit kidney (Friedman *et al.*, 1981) and toad urinary bladder (Taylor, 1975; Wiesmann *et al.*, 1977).

The plasma membrane of absorptive epithelial cells is composed of a passive apical membrane and an active basolateral membrane which has sodium pump in accordance with double-membrane model of Koefoed-Johnson and Ussing (1958). The hypothesis that elevated intracellular free calcium levels inhibit sodium absorption by diminishing the sodium permeability of the apical membrane has been formed in studies on isolated toad bladder and on isolated membrane vesicles prepared from apical membranes of toad bladder epithelium (Chase and Al-Awqati, 1981), but the molecular mechanism by which calcium influences sodium ion permeability is still unknown.

This study was designed to investigate the role of calcium on the function of an isolated perfused rabbit kidney excluding from hormonal, neuronal and biochemical influences and its effect on the diuretic action of furosemide to inhibit sodium and chloride reabsorptions in the thick ascending limb of Henle.

* To whom reprint requests should be addressed.

MATERIALS AND METHODS

Animals

Male rabbits weighing 1.8-2.3 kg were used. Experimental groups were divided into three groups as follows:

a) **Constant perfusion flow rate:** Control, hydralazine, verapamil, furosemide + verapamil, furosemide + hydralazine.

b) **Constant perfusion pressure:** Control, hydralazine, verapamil, furosemide, quinidine, furosemide + verapamil, furosemide + hydralazine, furosemide + quinidine.

c) **Calcium-free perfusion medium:** Control, calcium, verapamil, furosemide, quinidine, calcium + verapamil, calcium + quinidine, furosemide + quinidine, furosemide + verapamil, furosemide + calcium, furosemide + verapamil + calcium.

The concentration of drugs administered were as follows: hydralazine 5×10^{-5}M, veapamil 10^{-5}M, furosemide 5×10^{-4}M, quinidine 10^{-4}M, calcium 2×10^{-3}M.

Operative technique

The rabbits were anesthetized with 25% urethane (5 ml/kg body weight, i.p.) and laparotomized. The left kidney was exposed and the left ureter was cannulated with a polyethylene tubing (22G). Then, 1 mg/kg body weight of 25% mannitol and 500 U/kg body weight of heparin were injected intravenously to ear vein. The left renal artery was cannulated with a arterial cannula (polyethylene tubing, 18 G) and immediately flow of oxygenated perfusate through the arterial cannula was started.

Through operation, 0.9% normal saline (0.5 ml/kg/min) continuously was injected to ear vein. The kidney with cannulas was isolated and transferred to a temperature-controlled chamber and immersed in the kidney bath containing perfusate. Renal venous effluent was discarded during the initial period, thereafter perfusate was recirculated through the perfusion period. Urine and perfusate samples were collected in 5-min intervals.

Perfusion medium

The base solution of the medium was Tyrode's solution. Bovine serum albumin (Cohn fraction V)

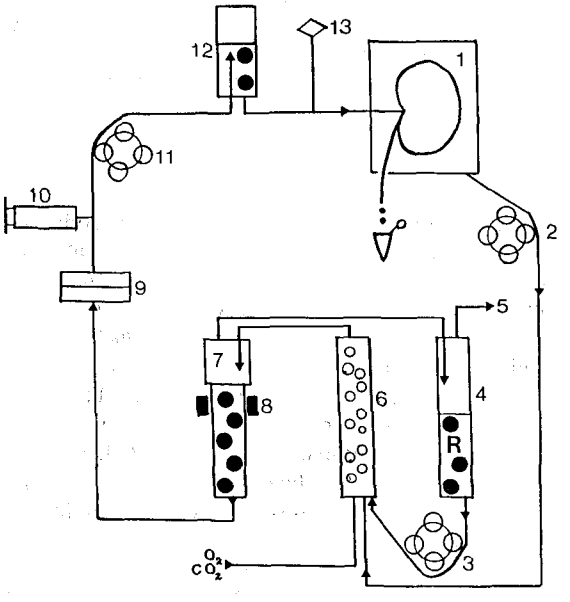

Fig. 1. Schematic diagram of the kidney perfusion system. 1, kidney chamber; 2, venous pump; 3, reservoir pump; 4, reservoir; 5, gas out; 6, oxygenator; 7, arterial reservoir; 8, level detector; 9, in-line filter; 10, drug injector; 11, arterial pump; 12, bubble trap; 13, pressure transducer.

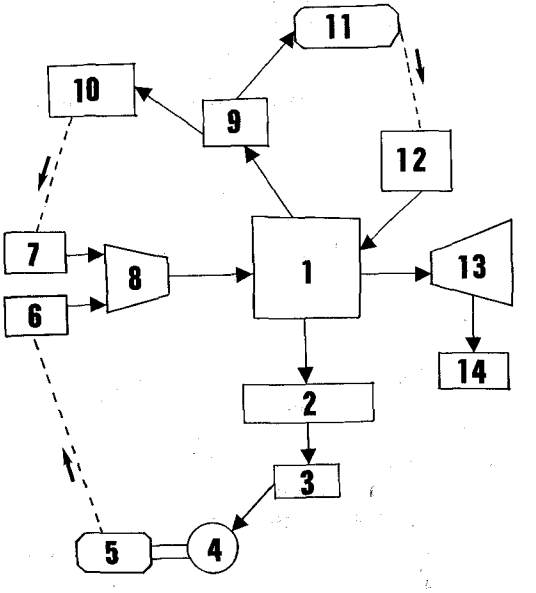

Fig. 2. Schematic diagram of computer controlled system. 1, computer Apple II + ; 2, pulse generator; 3, step motor driver; 4, step motor; 5, arterial pump; 6, pressure transducer: 7, thermistor; 8, analog digital converter; 9, switch controller; 10, heater; 11, reservoir pump; 12, level detector; 13, digital analog converter; 14, recorder.

was dissolved in Tyrode's solution and then it was dialyzed for 24 hours againt protein-free Tyrode's solution. Calcium-free perfusion medium was obtained by dialyzing against Tyrode's solution except calcium and sodium ethylene diaminetetraacetic acid (Na_2EDTA, 0.5 mM), calcium chelator, was added to it.

The substrates added to the perfusate dialyzed were as follows:

Dextrose 1 mg/ml, methionine 0.5 mM, alanine 2 mM, serine 2 mM, glycine 2 mM, arginine 1 mM, proline 2 mM, isoleucine 1 mM and aspartic acid 3 mM.

The perfusate pH was adjusted to 7.45 and perfusate was filtered once through a 1.2 μm membrane filter (Gelman Company, U.S.A.) immediately prior to the experiment.

Apparatus

The design of the apparatus is illustrated in Fig. 1. Perfusate from the kidney bath was passed through the bubble oxygenator by a venous pump (P1, Jin-Ahn Company, Korea) to a arterial reservoir. For oxygenation, a prewarmed and moistened gas mixture (95% O_2, 5% CO_2) was used.

The level of arterial reservoir was maintained constantly by feedback regulation of level detector and reservoir pump (P1, Jin-Ahn Company, Korea). The oxygenated perfusate from arterial reservoir was filtered by in-line filter (10 μm polypropylene filter, Gelman Company, U.S.A.) and was passed through bubble trapper by arterial pump (HP4, Gilson, France) to the renal artery. The pressure signal, monitored by a pressure transducer (5108, San-Ei Instrument, Japan) linked to the arterial cannula, was used in feedback regulation of the arterial pump in order to achieve constant pressure perfusion and was transferred through a physiograph (MK-IV, Nacro-Biosystem, U.S.A.) to the computer (Apple II+) (Fig. 2).

The temperature of the chamber was continuously monitored with a thermistor probe (Yellow Springs Instrument, U.S.A.) and maintained at 37.5 C by heater attached to the floor. The perfusion apparatus except computer was enclosed in a thermoregulated acrylbox.

Access to the kidney during perfusion was provided by a small door in the front of the box. The components were connected by Tygon and silicone tubings.

After the experiments, the glass ware and tubings were washed with water and detergent, then rinsed with distilled water and autoclaved.

Materials

Bovine serum albumin, amino acids, quinidine sulfate, hydralazine HCl, electrolytes, Na_2 EDTA and dextrose were purchased from Sigma (U.S.A.). Furosemide was obtained from Young-Jin pharmaceutical Company (Korea). Verapamil as Isoptin was obtained from Knoll Pharmaceutical Company (F.R.G.).

Analytical methods

Sodium and potassium were analyzed by flame photometry (443, Instrumentation Laboratory, U.S.A.). Chloride and osmolarity were analyzed by chloridometer (Buchler-Cotlove Instrument Incorporation, U.S.A.) and osmometer (5002, Precision systems Incorporation, U.S.A.) respectively. Urine volume was measured gravimetrically in preweighed tubes. Renal resistance was calculated from PP/RPF (perfusion pressure/renal perfusion flow rate).

All results were expressed as mean $\pm$ S.D. Statistical analyses were performed with Student's paired t-test.

RESULTS

Constant perfusion flow rate

There were no significant changes of urine volume, perfusion pressure, osmolar clearance and the excretion rates of sodium, potassium and chloride in control group.

The administrations of hydralazine and verapamil decreased urine volume, the excretion rates of electrolytes and osmolar clearance significantly in comparison with control group. Also, remarkable decreases of perfusion pressure appeared immediately after the administrations of hydralazine and verapamil and maintained during experimental period.

The administration of furosemide in combination with hydralazine or verapamil increased urine volume, the excretion rates of electrolytes, osmolar clearance and decreased perfusion pressure significantly and there was no difference between the two groups (Fig. 3).

Constant perfusion pressure

There were no significant changes of urine volume and the excretion rates of sodium, potassium and chloride in control group.

The administrations of hydralazine and verapamil

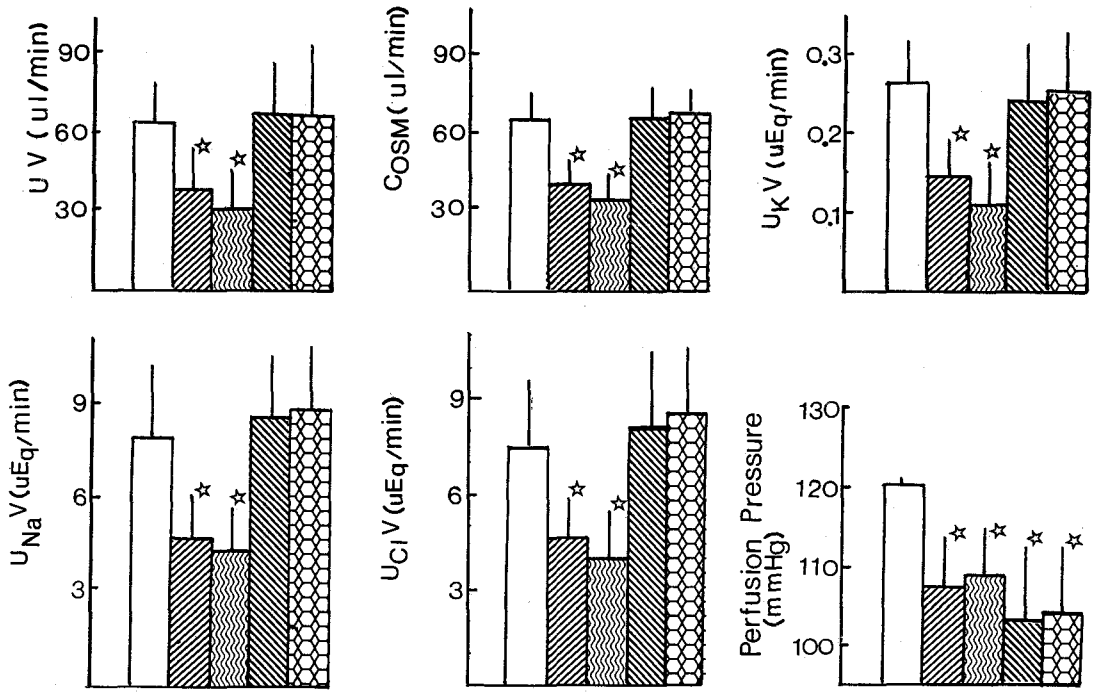

Fig. 3. Effects of hydralazine and verapamil on the diuretic action of furosemide in isolated perfused rabbit kidney at a constant perfusion flow rate. Results are presented as mean values ± S.D. UV; urine volume, $U_{Na}V$; urinary sodium excretion rate, U_KV; urinary potassium excretion rate, $U_{Cl}V$; urinary chloride excretion rate, C_{osm}; osmolar clearance. □; control, ▨; hydralazine (5×10^{-5}M), ▩; verapamil (10^{-5}M), ▩; furosemide (5×10^{-4}M) + hydralazine (5×10^{-5}M), ▩; furosemide (5×10^{-4}M) + verapamil (5×10^{-5}M). Significant difference as compared with control is denoted by ☆ $p<0.05$

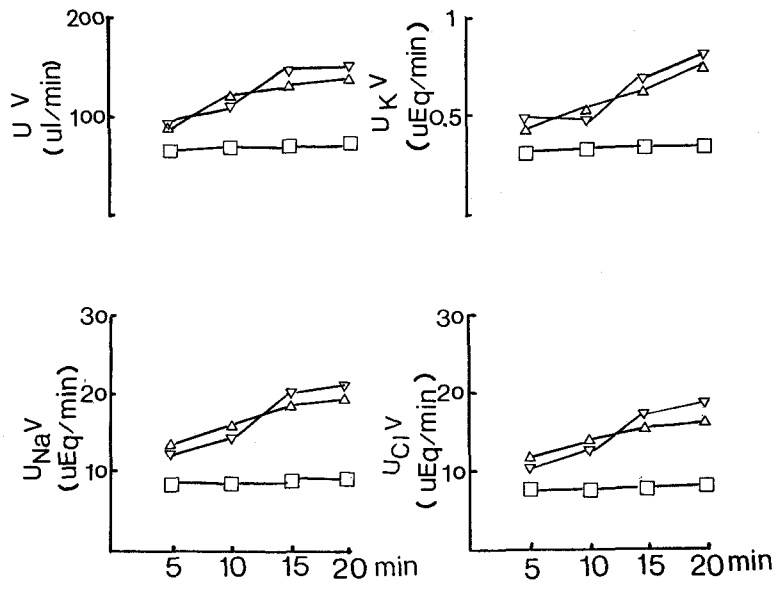

Fig. 4. Effects of hydralazine and verapamil on functions of isolated perfused rabbit kidney at a constant perfusion pressure of 120 mmHg. □; control, △; hydralazine (5×10^{-5}M), ▽: verapamil (10^{-5}M).

increased urine volume, the excretion rates of electrolytes and significantly in comparison with control group (Fig. 4). The administration of quinidine increased renal resistance gradually with time course and its peak value was shown in the fourth period (15-20 min) as 2.339 ±0.168 mmHg ml^{-1} min. Urine volume and the excretion rates of sodium, potassium and chloride in the third period (10-15 min) were increased significantly to 80.2 ± 13.7 μl/min, 10.85 ± 2.63 μEq/min, 0.335 ± 0.071 μEq/min and 10.59 ± 2.16 μEq/min respectively by quinidine compared with control group (Fig. 5).

The administration of furosemide in combination with hyralazine or verapamil produced remarkable diuretic action. Urine volume and the excretion rates of electrolytes were increased markedly by the combined administration of quinidine and furosemide compared with furosemide alone (Table 1).

Calcium-free perfusion medium

There were no significant changes of urine volume and the excretion rates of electrolytes in control group.

The administration of calcium increased urine volume and the excretion rates of electrolytes in control group.
significantly compared with control group. The renal resistance in the first, the second and the third periods were 2.534 ± 0.236 mmHg ml^{-1} min, 2.324 ± 0.215 mmHg ml^{-1} min, and 2.337 ± 0.204 mmHg ml^{-1} min. respectively after the administration of calcium (Fig. 6). In spite of vasoconstriction, calcium showed remarkable diuretic action.

There were no differences of renal functions between quinidine and control group.

The combined administration of quinidine and calcium increased renal resistance markedly, but decreased urine volume and the excretion rates of electrolytes. The renal resistances in the first, the second and the third periods were 2.495 ± 0.265 mmHg ml^{-1} min, 2.566 ± 0.247 mmHg ml^{-1} min, and 2.590 ± 0.321 mmHg ml^{-1} min, respectively (Fig. 6). This meant that antidiuretic effect after the combined administration of quinidine and calcium might be excessive vasoconstriction.

The administration of verapamil increased urine volume and the excretion rates of electrolytes slightly and did not inhibit the diuretic action of calcium (Table 2).

The administation of furosemide increased urine volume and the excretion rates of sodium, potassium

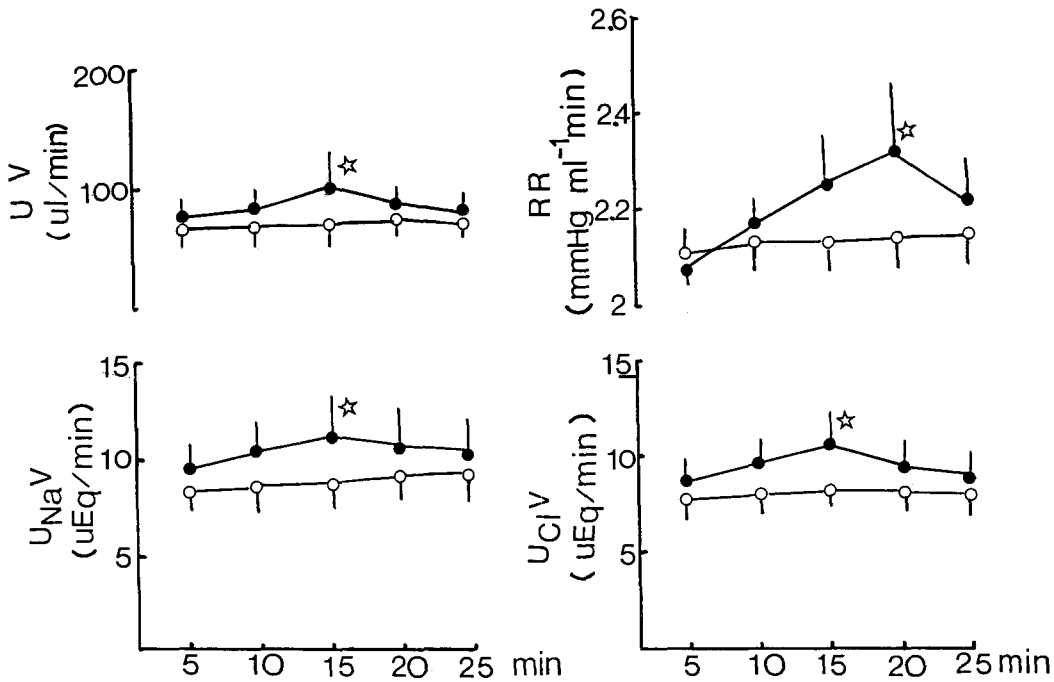

Fig. 5. Effect of quinidine on functions of isolated perfused rabbit kidney at a constant perfusion pressure of 120 mmHg. Results are presented as mean values ± S.D.
○; control, ●; quinidine(10^{-4} M), RR; renal resistance.
Significant difference as compared with control is denoted by $p<0.05$

Table 1. Effects of hydralazine (5×10^{-5} M), verapamil (10^{-5} M) and quinidine (10^{-4} M) on the diuretic action of furosemide (10^{-4} M) at a constant perfusion pressure of 120 mmHg

Time (min)	Group	U.V (μl/min)	$U_{Na}.V$ (μEq/min)	$U_K.V$ (μEq/min)	$U_{Cl}.V$ (μEq/min)
0-5	F (7)	96.3 ± 17.5	13.25 ± 4.19	0.375 ± 0.089	13.12 ± 3.85
	F + H (9)	142.1 ± 49.8[b]	21.09 ± 6.21[b]	0.700 ± 0.154[b]	20.10 ± 4.96[b]
	F + V (8)	189.3 ± 49.3[c]	26.54 ± 7.01[c]	0.817 ± 0.164[c]	24.99 ± 5.31[c]
	F + Q (9)	105.4 ± 34.5	14.31 ± 3.96	0.389 ± 0.091	13.69 ± 4.05
6-10	F	123.1 ± 27.8	17.25 ± 3.97	0.495 ± 0.095	16.95 ± 4.03
	F + H	190.1 ± 58.5[b]	25.35 ± 6.59[b]	0.842 ± 0.139[b]	24.95 ± 6.04[b]
	F + V	217.3 ± 65.4[c]	28.59 ± 7.58[c]	0.925 ± 0.232[c]	25.84 ± 6.23[c]
	F + Q	135.4 ± 39.1	19.05 ± 4.01	0.525 ± 0.090	18.41 ± 4.31
11-15	F	149.9 ± 40.2	20.83 ± 6.99	0.714 ± 0.183	19.04 ± 6.65
	F + H	205.9 ± 61.3[a]	29.01 ± 8.98[a]	0.931 ± 0.204[a]	28.09 ± 8.85[a]
	F + V	210.8 ± 71.9[a]	30.11 ± 9.02[a]	0.909 ± 0.210[a]	29.85 ± 10.97[a]
	F + Q	195.9 ± 41.3[a]	27.05 ± 6.98[a]	0.874 ± 0.152[a]	26.98 ± 6.98[a]

Mean ± S.D. Number in parenthesis; number of experimental animals
F; furosemide F + H; furosemide + hydralazine
F + V; furosemide + verapamil F + Q; furosemide + quinidine
a: $p<0.05$, b: $p<0.01$, c: $p<0.001$

Table 2. Effects of calcium (2×10^{-3} M), verapamil (10^{-5} M) and quinidine (10^{-4} M) on functions of isolated perfused rabbit kidney in calcium-free perfusion medium at a constant perfusion pressure of 120 mmHg

Time (min)	Group	U.V (μl/min)	$U_{Na}.V$ (μEq/min)	$U_K.V$ (μEq/min)	$U_{Cl}.V$ (μEq/min)
0-5	C (8)	67.9 ± 16.2	9.38 ± 2.81	0.321 ± 0.086	9.29 ± 2.57
	Ca (9)	61.5 ± 16.9	9.03 ± 2.96	0.287 ± 0.070	8.94 ± 2.85
	V (7)	78.7 ± 20.3	10.51 ± 3.05	0.375 ± 0.085	10.05 ± 3.14
	Q (9)	69.8 ± 14.9	9.46 ± 2.87	0.342 ± 0.081	8.92 ± 2.90
	Q + Ca (7)	62.0 ± 15.3	8.75 ± 2.90	0.314 ± 0.081	8.97 ± 2.90
	V + Ca (8)	62.9 ± 17.0	9.12 ± 2.94	0.310 ± 0.084	8.95 ± 1.95
6-10	C	68.4 ± 13.8	9.47 ± 2.85	0.329 ± 0.091	9.31 ± 2.67
	Ca	98.9 ± 23.2[a]	13.95 ± 3.87[a]	0.436 ± 0.089[a]	13.74 ± 3.54[a]
	V	87.4 ± 22.9	11.35 ± 3.21	0.405 ± 0.085	11.31 ± 3.32
	Q	70.3 ± 15.3	9.52 ± 2.14	0.339 ± 0.073	9.39 ± 2.95
	Q + Ca	53.2 ± 23.0[a]	7.54 ± 1.99[a]	0.237 ± 0.054[a]	7.10 ± 2.24[a]
	V + Ca	101.8 ± 20.5[a]	14.10 ± 3.95[a]	0.451 ± 0.090[a]	13.84 ± 3.61[a]
11-15	C	71.5 ± 17.3	9.80 ± 2.74	0.319 ± 0.084	9.64 ± 2.84
	Ca	97.4 ± 21.3[a]	13.24 ± 3.31[a]	0.465 ± 0.095[a]	13.05 ± 2.95[a]
	V	85.3 ± 23.5	11.05 ± 3.35	0.397 ± 0.109	10.95 ± 3.26
	Q	72.9 ± 12.9	10.19 ± 2.84	0.358 ± 0.097	9.67 ± 2.94
	Q + Ca	48.7 ± 17.3[a]	6.95 ± 2.56[a]	0.210 ± 0.104[a]	6.84 ± 3.01[a]
	V + Ca	99.5 ± 21.6[a]	13.57 ± 3.64[a]	0.484 ± 0.129[a]	13.19 ± 3.09[a]

Mean ± S.D. Number in parenthesis; number of experimental animals
C; control, Ca; calcium, V; verapamil, Q; quinidine
Q + Ca; quinidine + calcium, V + Ca; verapamil + calcium
a: $p<0.05$

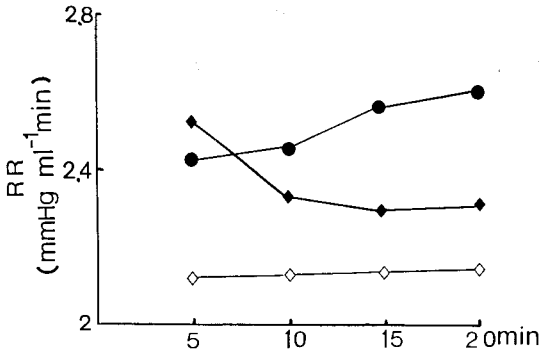

Fig. 6. Effects of calcium alone or in combination with quinidine on renal resistance in isolated perfused rabbit kidney at a constant perfusion pressure of 120 mmHg in calcium-free perfusion medium. □; control, ■; calcium (2×10^{-3}M), ●; calcium (2×10^{-3}M) + quinidine (10^{-4}M).

and chloride markedly. Verapamil and quinidine did not alter the diuretic action of furosemide. Calcium potentiated the diuretic action of furosemide significantly. Verapamil did not inhibit the effect of calcium on the diuretic action of furosemide (Table 3).

DISCUSSION

The maintenance of low cytosolic free calcium-ion levels is dependent on the extrusion of calcium out of cell by Ca ATPase and Na-Ca exchange (Gmaj *et al.*, 1979; Schwartz *et al.*, 1974) and on the intracellular sequestration by mitochondria (Borle, 1975; Murphy and Mandel, 1982), calcium-binding protein (Roth *et al.*, 1982) and smooth cytoplasmic reticulum (Moore *et al.*, 1974) in epithelial cells.

Quinidine has been used as a tool of selectively increasing cytosolic free calcium ion levels in mammalia epithelia (Friedman *et al.*, 1981). Although the precise mode of action of quinidine on epithelial cells is unknown, quinidine inhibits calcium uptake by isolated muscle mitochondria and sarcoplasmic reticulum and may induce the release of calcium from these intracellular organelles (Carvalho, 1968).

The administration of quinidine is isolated perfused proximal tubules of the rabbit resulted in not only a decreased in unidirectional Na efflux (lumen-to-bath) from 10.4 to 7.5×10^{-5}cm sec^{-1} but also the reduction in fluid absorption (an index of sodium net reabsorption) from 1.05 to 0.66 nl min^{-1} mm^{-1}

Table 3. Effects of calcium (2×10^{-3} M), verapamil (10^{-4} M) and quinidine (10^{-4} M) on the diuretic action of furosemide (5×10^{-4} M) in calcium-free perfusion medium at a constant perfusion pressure of 120 mmHg

Time (min)	Group	U.V (μl/min)	U_{Na}.V (μEq/min)	U_K.V (μEq/min)	U_{Cl}.V (μEq/min)
0-5	F (9)	100.7 ± 26.3	14.30 ± 4.67	0.414 ± 0.114	13.05 ± 3.87
	F + V (7)	118.4 ± 35.3	16.59 ± 5.54	0.496 ± 0.195	15.95 ± 5.20
	F + Ca (8)	149.2 ± 47.4	18.57 ± 7.48	0.517 ± 0.254	18.14 ± 6.36
	F + Q (7)	92.0 ± 22.3	13.70 ± 5.01	0.410 ± 0.094	12.94 ± 3.59
	F + V + Ca (9)	143.4 ± 59.3	18.05 ± 7.91	0.562 ± 0.271	17.39 ± 7.52
6-10	F	128.4 ± 29.5	18.25 ± 6.45	0.527 ± 0.191	17.64 ± 5.74
	F + V	138.7 ± 33.9	19.47 ± 6.50	0.548 ± 0.179	18.47 ± 6.01
	F + Ca	205.4 ± 65.3[a]	28.30 ± 8.95[a]	0.797 ± 0.201[a]	26.31 ± 8.92[a]
	F + Q	110.3 ± 25.4	16.37 ± 6.91	0.484 ± 0.195	16.36 ± 6.4
	F + V + Ca	198.4 ± 58.9[a]	27.98 ± 9.05[a]	0.854 ± 0.295[a]	27.04 ± 8.97[a]
11-15	F	158.4 ± 39.8	22.31 ± 7.94	0.684 ± 0.205	21.45 ± 8.95
	F + V	152.3 ± 40.5	21.94 ± 8.01	0.696 ± 0.214	20.57 ± 9.51
	F + Ca	226.3 ± 62.9[a]	33.47 ± 8.90[a]	1.211 ± 0.413[a]	32.05 ± 9.20[a]
	F + Q	160.3 ± 35.6	21.95 ± 8.14	0.693 ± 0.216	20.11 ± 9.05
	F + V + Ca	215.2 ± 56.9[a]	30.37 ± 8.21[a]	1.150 ± 0.398[a]	29.34 ± 8.56[a]

Mean ± S.D. Number in parenthesis; number of experimental animals
F; furosemide, F + V; furosemide + verapamil, F + Ca; furosemide + calcium
F + Q; furosemide + quinidine, F + V + Ca; furosemide + verapamil + calcium
a: $p<0.05$

by increasing cytoplasmic calcium ion activity (Friedman *et al.*, 1981).

In this experiment quinidine produced diuretic action and vasoconstriction only in the presence of calcium (Table 5, Table 6). But there were transient and slight decreases of renal resistance in the first period following administration of quinidine unconcerned in the presence of calcium although exact reason was unknown.

In this experiment extracellular calcium ion was essential for expressing the action of quinidine, but this did not correspond with the other report that quinidine inhibit sodium transport by urinary bladder of freshwater turtles and this inhibitory effect was dose-dependent, independent of extracellular calcium concentration (Arruda and Sabatini, 1980). However, quinidine decreased sodium reabsorption by increasing intracellular calcium ion concentration.

Verapamil, an inhibitor of calcium entry into several tissues, was administered in order to decrease intracellular calcium ion concentration in this experiment and produced diuretic effect mainly by renal vasodilation similar to hydralazine. Verapamil in the calcium-free perfusion medium showed a slight diuretic effect with no significant change of renal resistance. This meant that other factor, rather than calcium, related to the diuretic action of verapami. There were several reports to be related. Yamaguchi *et al.*, (1974) suggested that diltiazem produced a natriuretic effect without alteration in renal hemodynamics and its effect is partly due to direct suppression of sodium reasorption in renal tubules. Furthermore, it has been proposed that renal kinins at least in part play a role in diltiazem-induced natriuresis (Seino *et al.*, 1986).

In this study, verapamil did not inhibit the diuretic action of calcium. These results suggest that calcium may not enter into cell through voltage-operated calcium channel or do influence directly the permeability of ion transport through membrane in paracellular passway (Barry *et al.*, 1971).

Calcium in this study produced a prominent increase of renal resistance in the first period and renal resistance in the second period decreased significantly and thereafter was maintained in same level more than 30 min (data are not shown). It is necessary to investigate the mechanism about decrease of renal resistance by calcium in the second period.

It is generally accepted that the diuretic action of furosemide has something to do with prostaglandin, especially prostaglandin E (Frolich *et al.*, 1975; Patak *et al.*, 1975; Weber *et al.*, 1977). In this study calcium produced a diuretic action and potentiated the diuretic action of furosemide.

A possibility that prostaglandin may be related to the effect of calcium in this study is supported by other reports that prostagland in E synthesis in response to several stimuli in rat renal cortical tubular cell is a calcium dependent process, acting via phospholipase (Wuthrich and Valloton, 1986) and calcium in frog skin inhibit ion reabsorption by increasing prostaglandin E (Erlij *et al.*, 1981).

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=국문초록=

적출관류 토끼 신장기능에서 칼슘의 역할

가톨릭대학 의학부 약리학교실

이권행*, 전은의, 홍경자, 조규철

저자는 적출관류 토끼 신장기능에서 칼슘의 역할과 furosemide의 이뇨작용에 미치는 영향을 관찰하여 다음과 같은 결과를 얻었다.

hydralazine과 verapamil은 주로 신혈관 저항의 감소로 이뇨작용을 나타냈다. furosemide를 hydralazine 또는 verapamil 병합투여시 뚜렷한 이뇨작용이 나타났으며 두군 사이에 차이는 없었다. quinidine은 신혈관 수축을 일으켰으나 이뇨작용이 나타났으며 furosemide의 이뇨작용을 항진시켰다.

칼슘제외된 관류액으로 관류시 칼슘은 신혈관 수축에도 불구하고 이뇨작용이 나타났으며 furosemide의 이뇨작용을 항진시켰다. quinidine은 칼슘이 제외된 상태에서 신장기능 및 furosemide의 이뇨작용에 영향을 미치지 못하였으나 calcium 병합투여시 과도한 신혈관 수축으로 항이뇨작용을 보였다. verapamil은 칼슘이 제외된 상태에서 약간의 이뇨작용을 보였지만 칼슘 및 furosemide의 이뇨작용을 변화시키지 못하였다.

이상의 성적은 적출관류 토끼 신장에서 칼슘, verapamil 및 quinidine이 이뇨작용이 있으며 칼슘은 furosemide의 이뇨작용을 항진시킨다.