Influence of Intracerebroventricular Yohimbine on the Renal Function of the Rabbit

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ABSTRACT

The renal function is under regulatory influence of the central nervous system, mainly through activation of sympathetic nerve to the kidney, and it was recently reported that clonidine, an agonist to α_2-adrenoceptors, induces diuresis and natriuresis when injected directly into a lateral ventricle of the rabbit brain (i.c.v.). This study was undertaken, therefore, to obtain further information as to the role of the central α_2-adrenoceptors in regulating renal function, by observing the effects of i.c.v. yohimbine, a specific antagonist of adrenoceptors of α_2-type, on the rabbit renal function, and to elucidate the mechanism involved in it.

With 10 μg/kg i.c.v. of yohimbine sodium excretion transiently increased along with increasing tendency of urine flow, renal plasma flow and glomerular filtration rate. These responses decreased with increasing doses. With 100 and 300 μg/kg i.c.v. marked antidiuresis and antinatriuresis as well as profound decreases of renal perfusion and glomerular filtration were noted. Systemic blood pressure transiently increased.

In reserpinized rabbits, 100 μg/kg yohimbine i.c.v. did not produce any significant changes in urine flow, sodium excretion as well as in renal hemodynamics. The pressor response was also abolished.

In preparations in which one kidney was denervated and the other left intact as control, i.c.v. yohimbine elicited typical antidiuretic antinatriuretic response in the innervated control kidney, whereas the denervated experimental kidney responded with marked diuresis and increases in excretory rates of sodium and potassium and in osmolar clearance in spite of absence of increased filtration and perfusion. Systemic blood pressure responded as in the normal rabbits.

These observations indicate that i.c.v. yohimbine affects renal function in dual ways in opposite directions, the first being the antidiuretic antinatriuretic effects which results from decreased renal perfusion and glomerular filtration due to sympathetic activation and which is predominantly expressed in the normal rabbits, and the second less apparent effect being the diuretic and natriuretic action which is not mediated by nerve pathway but brought about by some humoral mechanism and which is effected by decreased sodium reabsorption in the tubules, possibly of the proximal portion.

Key Words: yohimbine, central adrenergic system, renal function, central regulation of renal function, natriuretic factor

Abbreviations: i.c.v.; intracerebroventricular, cr; creatinine

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INTRODUCTION

The renal function is constantly under regulatory influences from the central nervous system, among which the sympathetic tone to the kidney plays the most prominent role (Anderson, 1969; Gottschalk et al., 1979: Kim et al., 1980). Increased activity of the renal sympathetic nerve produces antidiuresis, either through vasoconstriction causing decrements in renal perfusion and glomerular filtration (Gill & Casper, 1972), or through enhanced tubular reabsorption of sodium (Bello-Reuss et al., 1976). In addition, increased sympathetic activity results in increased renin secretion (Gordon et al., 1967) as well as in systemic hypertension, which then could indirectly affect the renal function in various ways.

In a series of experiments in which attempts were made to modify the sympathetic tone to the kidney, various adrenergic agonists and antagonists were directly administered into lateral ventricle (i.c.v.) of the rabbit brain, and the changes in renal function were investigated.

Lee (1972) observed antidiuresis when norepinephrine was given i.c.v., and Kook et al. (1985) reported diuresis and natriuresis with i.c.v. phenoxybenzamine. Prazocin elicited antidiuresis when given i.c.v. (Choi & Kook, 1983), whereas clonidine, an α_2-adrenoceptor agonist, induced diuresis and natriuresis (Kook et al., 1984). Yohimbine, a specific antagonist for α_2-adrenoceptor, was shown to abolish the clonidine-induced natriuresis. However, it was noted that i.c.v. yohimbine tended to increase sodium excretion, even though renal hemodynamics tended to decrease.

This study was therefore undertaken to ascertain the renal responses to i.c.v. yohimbine and to elucidate the possible mechanism involved in it.

MATERIALS AND METHODS

Adult rabbits of either sex, weighing 1.6-2.4 kg, were anesthetized with 1 g/kg urethane, s.c. Free air passage was secured by inserting a T-tube into the trachea. Into an ear-vein infusion of 0.3 % NaCl + 3 % glucose solution containing 45 mg % of p-aminohippuric acid (PAH) and 250 mg % of creatinine (cr) was given at a rate of 0.5 ml/min. Through a small midline incision on the lower abdomen, both ureters were cannulated with PE 50 tubings for the collection of urine samples. For sampling blood a femoral artery was cannulated with a PE tubing, which was then kept patent by filling with heparin-saline (400 U/ml).

For the intracerebroventricular (i.c.v.) administration of the agents a lateral ventricle of the cerebrum was cannulated. At a point 1.5 cm rostral to the occipital tubercle and 0.5 cm lateral to the midline, a hole was drilled and a cannula made of PE tubing of 1.5 mm O.D. was introduced and kept in place by cementing to the bone. The volume administered did not exceed 0.15 ml. At the end of each experiment the location of the cannula was checked.

When urine flow rate became stable several hours after starting the infusion, collection of clearance samples was begun. After collecting two ten-minute samples of control clearance periods, the agents were given, and then four or five samples of ten- or twenty-minute clearance periods were collected, and the blood samples were immediately centrifuged to separate the plasma.

In denervation experiments the kidney was approached through a paravertebral incision and the renal pedicle was isolated from surrounding tissues, and the renal nerve was removed as thoroughly as possible with aid of a magnifier, and the renal pedicle was wrapped with a cotton swab soaked in 10 % phenol.

For reserpinizing animals, 1 mg/kg reserpine was given intravenously 24 hours prior to the experiment, and in anesthetizing these rabbits half the regular dose of urethane was employed.

Quantitative analyses of creatinine were done by the method of Phillips (1944) and PAH by that of Smith et al. (1945). Na and K concentrations were determined by flamephotometry, and the osmolality with an "Advanced" osmometer. Systemic arterial pressure was recorded from a femoral artery.

Yohimbine hydrochloride was obtained from Sigma Co. and dissolved in 0.9 % saline immediately before the administration. Reserpine was obtained from Fluka. Co. The doses administered were calculated as free base.

Statistical significance was tested with Student's paired t-test for the changes of renal function from the control period, and when comparing two groups of experiments the unpaired t-test was employed (Snedecor & Cochran, 1980).

RESULTS

Effects of i.c.v. yohimbine on renal function

Table 1 shows the changes of renal function brought about by i.c.v. yohimbine in the rabbit. With 10 μg/kg, urine flow rate tended to increase during two ten-minute periods following the administration, and then it declined. Renal perfusion (C_{PAH}) and glomerular filtration rate (C_{cr}) also tended to increase for twenty minutes, by about 24 % and 15 % respectively, and then they decreased below the control levels after 40 min. Excretory rates of both sodium and potassium significantly increased during 10-20 min period after the administration. Reflecting the increase in electrolyte excretion, osmolar clearance tended to increase. Free water reabsorption did not change significantly. Mean arterial pressure tended to increase slightly (7 mmHg) immediately following the administration.

With 30 μg/kg, urine flow and renal hemodynamics tended to decline, with the initial tendency toward increases becoming less apparent. After 40 min, the decreases in urine flow and glomerular filtration became significant. Excretory rate of sodium did not show any consistent change, while potassium excretion significantly decreased. Free water reabsorption also did not change markedly.

With further increase of doses up to 100 μg/kg, the decrements in renal function became significant, as shown in the lower part of Table 1. Urine flow rate as well as renal hemodynamics significantly decreased by 70-80 % for twenty minutes and then they gradually recovered. Filtration fraction tended to increase, with no statistical significance noted. Urinary excretion of both sodium and potassium decreased significantly. Fractional sodium excretion (FE_{Na}) showed a transient tendency toward increase. Free water reabsorption did not change significantly. Mean arterial pressure transiently increased immediately following the administration. Further tripling the doses up to 300 μg/kg did not bring any further increases in the responses.

Fig. 1 depicts the changes from the control values of several parameters of renal function after the i.c.v. administration of yohimbine. As clearly seen here, small doses of yohimbine tend to increase urine flow and sodium excretion along with improvements of renal hemodynamics, whereas this tendency is reversed to a decrease with increasing doses. Maximal response was attained with 100 μg/kg.

Effects of i.c.v. yohimbine in reserpinized rabbits

To remove the influence of sympathetic nerve to the kidney, the effects of i.c.v. yohimbine was observed in the reserpinized rabbits. Table 2 shows the changes of renal function after 100 μg/kg yohimbine. As seen in the control period, reserpinization itself affects the renal function markedly. Renal plasma flow (C_{PAH}) and glomerular filtration rate (C_{cr}) are higher, and excretory rates of electrolytes also tend to be higher in the reserpinized animals compared to the normal rabbits.

In these animals, 100 μg/kg yohimbine i.c.v. produced gradual decrease in renal hemodynamics. However, urine flow rate and electrolyte excretion tended to increase transiently. In Fig. 2 changes of various parameters of renal function of reserpinized rabbits as compared to the normal group are shown. Mean arterial pressure did not change at all. It is thus clear that the antidiuretic, antinatriuretic response as well as decreases in renal hemodynamics elicited by i.c.v. yohimbine in normal rabbits could not

manifest itself in reserpinized rabbits.

Influence of denervation on the yohimbine effects

In order to eliminate all the nervous influence to the kidney, observation were made in animals in which one kidney was denervated and the other was left intact. In Table 3 the data from 6 such experiments are summarized. As seen here, in the pre-administration control periods the denervated kidney has greater perfusion and filtration rate, and urine flow and sodium excretion are far greater in the

Table 1. Effect of i.c.v. yohimbine on renal function

	Control	0'-10'	10'-20'	20'-40'	40'-60'
			10 μg/kg i.c.v. (6)		
Vol	0.21 ± 0.05	0.29 ± 0.07	0.30 ± 0.07	0.20 ± 0.07	0.13 ± 0.03
C_{PAH}	19.8 ± 2.6	24.1 ± 4.6	24.5 ± 3.6	20.0 ± 3.5	15.4 ± 2.6[a]
C_{cr}	9.34 ± 0.83	10.37 ± 1.38	10.72 ± 0.87	8.80 ± 1.09	7.10 ± 1.14[a]
$U_{Na}V$	3.2 ± 1.9	3.9 ± 0.9	6.0 ± 1.9[b]	6.4 ± 3.6	2.8 ± 1.1
FE_{Na}	0.26 ± 0.16	0.27 ± 0.06	0.39 ± 0.11	0.48 ± 0.24	0.34 ± 0.17
$U_K V$	5.6 ± 0.5	7.0 ± 1.1	8.2 ± 0.7[a]	6.0 ± 0.8	3.9 ± 0.6
			30 μg/kg i.c.v. (6)		
Vol	0.33 ± 0.04	0.26 ± 0.04	0.29 ± 0.05	0.21 ± 0.06[a]	0.16 ± 0.04[c]
C_{PAH}	16.8 ± 2.2	14.1 ± 2.5	14.0 ± 1.7	13.2 ± 2.5	12.1 ± 1.4
C_{cr}	6.17 ± 0.44	5.12 ± 0.74	5.21 ± 0.53	4.73 ± 0.61[a]	4.92 ± 0.44
$U_{Na}V$	8.5 ± 2.3	6.4 ± 2.0	9.3 ± 3.0	7.5 ± 3.6	5.0 ± 2.8
$U_K V$	5.9 ± 1.4	4.8 ± 1.2	5.3 ± 1.4	4.2 ± 1.0[a]	3.5 ± 0.6
$T^c H_2O$	0.14 ± 0.04	0.10 ± 0.03	0.11 ± 0.03	0.10 ± 0.02	0.11 ± 0.01
			100 μg/kg i.c.v. (5)		
Vol	0.33 ± 0.06	0.10 ± 0.02[a]	0.08 ± 0.03[a]	0.14 ± 0.02[a]	0.23 ± 0.05
C_{PAH}	16.3 ± 3.9	3.9 ± 1.7[b]	4.5 ± 2.7[b]	9.1 ± 2.3[a]	10.8 ± 2.4
C_{cr}	6.12 ± 1.14	1.74 ± 0.55[b]	1.71 ± 0.86[b]	3.74 ± 0.97[a]	4.39 ± 1.13[a]
FF	39.3 ± 3.4	51.3 ± 6.2	50.0 ± 6.7	40.7 ± 2.0	38.8 ± 3.5
$U_{Na}V$	11.0 ± 2.1	3.6 ± 1.1[a]	2.8 ± 1.2[a]	5.4 ± 1.3[a]	9.7 ± 1.7
FE_{Na}	1.57 ± 0.49	1.85 ± 0.57	1.66 ± 0.45	1.46 ± 0.45	2.24 ± 0.59
$U_K V$	3.7 ± 0.4	1.3 ± 0.4[c]	1.4 ± 0.7[b]	2.7 ± 0.5[a]	3.5 ± 0.8
$T^c H_2O$	0.02 ± 0.06	0.01 ± 0.02	0.02 ± 0.01	0.07 ± 0.02	0.08 ± 0.06
MAP	92 ± 5	125 ± 7[b]	111 ± 8	94 ± 1	89 ± 4
			300 μg/kg i.c.v. (6)		
Vol	0.27 ± 0.08	0.11 ± 0.04[a]	0.09 ± 0.03[a]	0.13 ± 0.04[a]	0.13 ± 0.04[a]
C_{PAH}	17.7 ± 3.4	5.6 ± 2.0[b]	6.1 ± 2.4[b]	10.7 ± 3.0[a]	10.7 ± 2.7[a]
C_{cr}	7.68 ± 1.18	3.05 ± 0.97[b]	3.52 ± 1.36[b]	5.09 ± 1.16[b]	5.41 ± 1.13[a]
$U_{Na}V$	7.6 ± 3.3	2.8 ± 1.3	1.6 ± 0.6	2.3 ± 0.7	2.8 ± 1.2

Mean ± S.E. In parentheses are number of experiments. Vol represents urine flow rate in ml/min; C_{PAH}, C_{cr} and C_{osm} are clearances of p-aminohippuric acid, creatinine and osmolar substances, resp., in ml/min; $U_{Na}V$ and $U_K V$ are excretory rates of sodium and potassium, resp., in μEq/min; FF = filtration fraction in percent; FE_{Na} is fractional excretion of sodium in percent; $T^c H_2O$ = rate of free-water reabsorption in ml/min; MAP is mean arterial pressure in mmHg. Significance of paired difference from control periods were tested with Student's t-test. a: $p<0.05$; b: $p<0.01$; c: $p<0.001$.
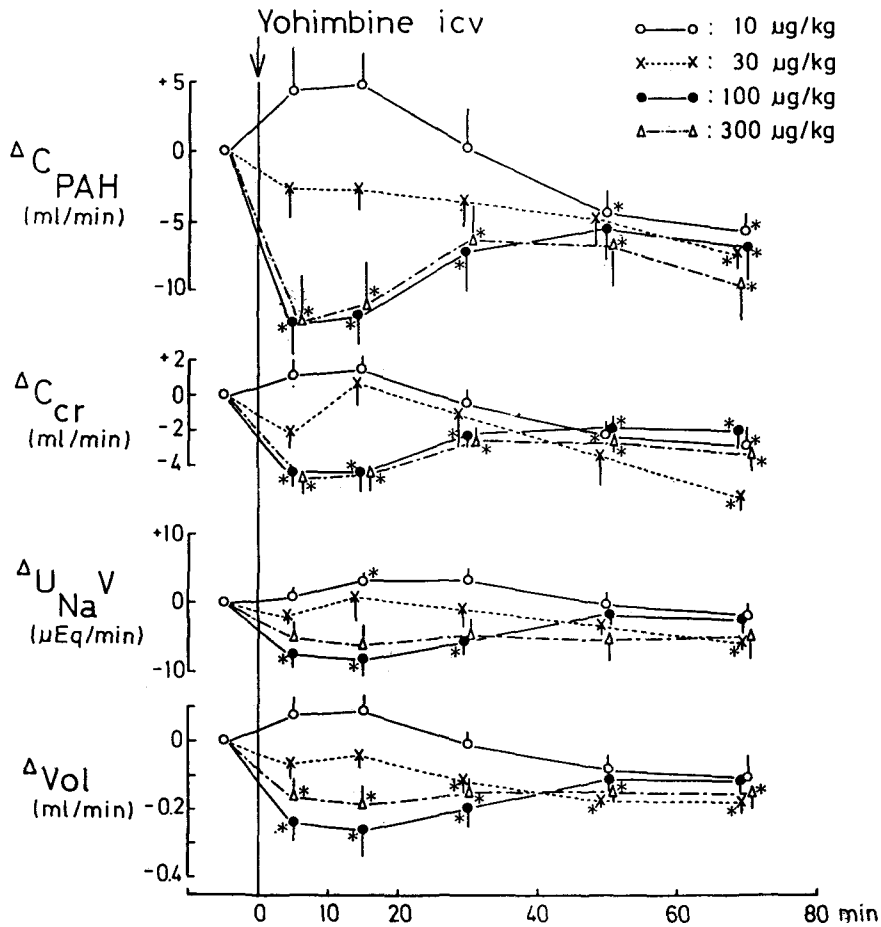
Fig. 1. Effects of i.c.v. yohimbine on renal function of the rabbit. Mean differences from the control values with one standard error are shown. Asterisks indicate significant difference from the control values. Other legends are as in Table 1.

Table 2. Renal effect of 100 μg/kg yohimbine i.c.v. in reserpinized rabbits

	Control	0'-10'	10'-20'	20'-40'	40'-60'
Vol	0.21 ± 0.06	0.18 ± 0.04	0.25 ± 0.07	0.21 ± 0.05	0.12 ± 0.03
C_{PAH}	25.1 ± 2.7	18.8 ± 4.2	21.3 ± 3.7^a	17.7 ± 3.1^b	15.5 ± 3.0^b
C_{cr}	8.32 ± 1.16	7.53 ± 1.99	7.54 ± 1.15^a	6.04 ± 0.79^b	5.70 ± 0.92^b
$U_{Na}V$	10.7 ± 4.9	8.5 ± 2.4	18.1 ± 7.5	13.8 ± 5.4	4.8 ± 2.5
FE_{Na}	1.18 ± 0.56	1.07 ± 0.39	1.73 ± 0.75	1.66 ± 0.66	0.61 ± 0.30
U_KV	6.1 ± 0.7	6.6 ± 1.9	8.2 ± 2.5	5.7 ± 1.1	3.8 ± 0.6^a
T^cH_2O	0.23 ± 0.03	0.23 ± 0.06	0.24 ± 0.04	0.18 ± 0.02	0.16 ± 0.02^a
MAP	62 ± 3	64 ± 7	71 ± 7	62 ± 4	55 ± 3

Mean $\pm$ S.E. from 6 experiments. Reserpine 1 mg/kg was given i.v. 24 hrs prior to the experiment. Other legends are as in Table 1. a: $p<0.05$; b: $p<0.01$.

Yohimbine icv
(100 μg/kg)

●——● : Reserpinized
○┄┄○ : Control

ΔC_{PAH} (ml/min)

ΔC_{cr} (ml/min)

$\Delta U_{Na} V$ (μEq/min)

ΔVol (ml/min)
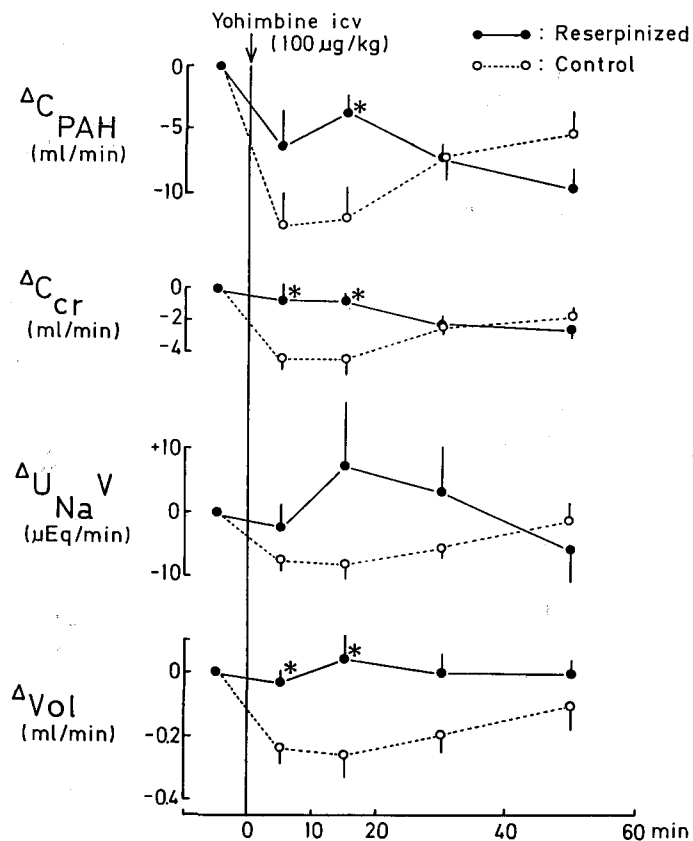
0   10   20   40   60 min

Fig. 2. Influence of reserpine-pretreatment on the renal action of i.c.v. yohimbine. Asterisks indicate significant difference from the corresponding value of the control (non-treated) group.

Table 3. Influence of denervation on the renal effects of 100 μg/kg yohimbine i.c.v.

		Control	0'-10'	10'-20'	20'-40'	40'-60'
Vol	D	0.37 ± 0.06	0.66 ± 0.11^b	0.68 ± 0.13	0.26 ± 0.05	0.17 ± 0.05^a
	I	0.09 ± 0.01	0.04 ± 0.01^b	0.03 ± 0.01^b	0.04 ± 0.01^b	0.04 ± 0.01^b
C_{PAH}	D	10.9 ± 1.4	10.1 ± 1.2	10.8 ± 1.6	6.5 ± 1.1^b	6.8 ± 1.1^a
	I	7.6 ± 1.1	3.0 ± 1.1^b	2.9 ± 1.1^b	3.9 ± 1.0^b	3.7 ± 0.8^b
C_{cr}	D	3.89 ± 0.31	3.71 ± 0.49	4.00 ± 0.35	2.74 ± 0.42^a	2.77 ± 0.34^b
	I	3.27 ± 0.49	1.30 ± 0.51^b	1.20 ± 0.55^a	1.75 ± 0.47^b	1.89 ± 0.49^b
$U_{Na}V$	D	24.2 ± 5.0	47.5 ± 9.7^a	52.8 ± 11.8	17.7 ± 4.7	7.2 ± 3.6^a
	I	1.1 ± 0.3	0.4 ± 0.2^b	0.5 ± 0.3^a	0.4 ± 0.1^a	0.1 ± 0.0^a
FE_{Na}	D	4.62 ± 1.03	9.91 ± 2.40^a	9.76 ± 1.96^a	5.53 ± 1.97	1.72 ± 0.83
	I	0.28 ± 0.07	0.22 ± 0.05	0.25 ± 0.04	0.18 ± 0.04	0.07 ± 0.02^a
$U_K V$	D	4.8 ± 0.5	6.2 ± 0.7^a	6.4 ± 0.5	3.4 ± 0.3^a	2.7 ± 0.3^b
	I	2.5 ± 0.5	1.1 ± 0.6^b	1.1 ± 0.7^b	1.2 ± 0.4^b	1.1 ± 0.3^b

Mean ± S.E. from 6 experiments. "D" represents the denervated, experimental kidney; "I" stands for the innervated, control kidney. Other legends are as in Table 1. a: $p<0.05$; b: $p<0.01$.
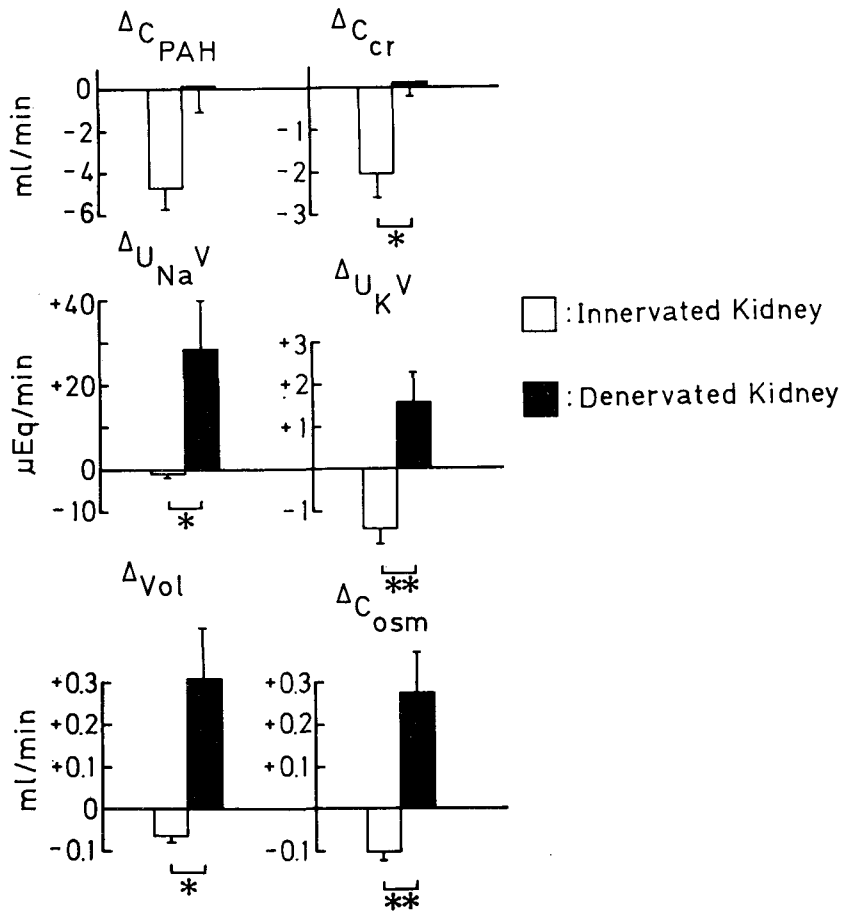
Fig. 3. Comparison of effects of 100 μg/kg yohimbine i.c.v. during the 10-20 min period after administration between the denervated experimental kidney and the control innervated kidney. Mean difference from control value and standard error are shown. Asterisks indicate significant difference between both kidneys.

experimental kidney than in the control kidney, indicating that the denervated kidney is undergoing "denervation diuresis," whereas the contralateral kidney is subjected to a marked antidiuresis.

In this state, i.c.v. yohimbine (100 μg/kg) produced typical antidiuretic, antinatriuretic response in the control kidney, whereas the denervated kidney responded with marked natriuresis and diuresis, with the fractional excretion of sodium more than doubling. Renal hemodynamics did not change in the experimental kidney. Fig. 3 compares both kidneys in the changes of various functional parameters during the 10-20 min period after yohimbine. It is clear that the natriuresis in the denervated kidney results from decreased tubular reabsorption of sodium and that it is not associated with increased filtration.

DISCUSSION

Yohimbine is an indolealkylamine alkaloid obtained from a plant Yohimhébé and is known to produce adrenergic blockade (Bowman & Rand, 1980; Goodman & Gilman, 1985). Recently it has been shown that yohimbine selectively block central α_2-adrenoceptors (Starke et al., 1975; Drew, 1976) and since then it has been employed as a pharmacological tool to block the α_2-adrenoceptors. It can enhance

norepinephrine release from nerve endings in much lower concentrations than those required to block the postsynaptic α_1-adrenoceptors (Starke, 1977). On the renal effects of yohimbine very little is known except that it causes antidiuresis due to release of ADH (Goodman & Gilman, 1985) and that it can abolish the clonidine-induced natriuresis in the rabbit (Kook et al., 1984).

In this study a small dose of yohimbine when given i.c.v. produced transient increase in sodium excretion and exhibited a tendency toward increased renal hemodynamics. However, with increasing doses antidiuresis and antinatriuresis became prominent along with decreased renal perfusion and filtration. It was further shown that reserpine pretreatment abolished those responses, and that denervation of the kidney reversed the antidiuretic response to a marked natriuretic and diuretic one. These results suggest that the renal action of centrally administered yohimbine is dual in nature, i.e., antidiuresis and antinatriuresis on the one hand, and diuretic and natriuretic action on the other, and that the former is mediated by neural pathways, presumably through sympathetic nerve to the kidney, resulting in vasoconstriction and decreased perfusion and filtration. The latter natriuretic effect seems to be of humoral origin and due to decreased tubular reabsorption of sodium, and this can be brought into light only when the former influence is removed. The findings in the denervation experiment further indicate that the renal responses to i.c.v. yohimbine is not related to direct renal action of the agent which might have reached systemic circulation from the site of administration. And it can also preclude the possibility of secondary action which may be related to elevation of systemic blood pressure.

As regards the origin and nature of the humoral natriuretic factor involved in here, no evidence is available so far. Whether it is related to various natriuretic peptides isolated from atrium (Flynn et al., 1983) or a factor released from the brain (Beasley et al., 1983) awaits further studies. Antidiuretic hormone, known to be released by yohimbine, is not related to the natriuresis. Participation of the ADH in the antidiuresis could not be completely ruled out, as all the rabbits in this study were already undergoing urine concentration, possibly because of anesthesia, although the reserpine-experiment speaks against the possibility.

The fact that yohimbine when given i.c.v. influences renal function indicates that central adrenergic system plays an important role in regulating renal function, and the facts that i.c.v. clonidine produces diuresis and natriuresis and that i.c.v. yohimbine elicits antidiuresis suggest that sympathetic tone to the kidney is the major determinant of the adrenergic regulation. It is further suggested that release of some natriuretic humoral factor is associated with alpha-2 adrenoceptors in the center.

REFERENCES

Andersson B, Dallman MF and Olsson K: Evidence for a hypothalamic control of renal sodium excretion. Acta Physiol Scand 7:496-510, 1969

Beasley D, Malvin RN and Mouw DR: CNS-induced natriuresis and renal hemodynamics in conscious. Am J Physiol 245:763-771, 1983

Bello-Reuss E, Trevino DL and Gottschalk CW: Effect of renal sympathetic nerve stimulation on proximal water and sodium reabsorption. J Clin Invest 57:1104-1107, 1976

Bowman WC & Rand MJ: Textbook of Pharmacology (2nd ed.). Blackwell Scientific Publ p 11-45, 1980

Choi BK and Kook YJ: Renal action of prazosin administered into a lateral ventricle of the rabbit brain. Chonnam Med J 20:115-130, 1983

Drew GM: Effects of α-adrenoceptor agonists and antagonists on pre- and postsynaptically located α-adrenoceptors. Eur J Pharmacol 36:313-320, 1976

Flynn TG, DeBold ML and DeBold AJ: The amino acid sequence of an atrial peptide with potent diuretic and natriuretic properties. Biochem Biophys Res Commum 117:859-865, 1983

Gill JR Jr. and Casper AGT: Role of sympathetic nervous system in the renal response to hemorrhage. J Clin Invest 48:915, 1972

Goodman and Gilman: *The Pharmacological Basis of Therapeutics* (7th ed.). MacMillan, p 190, 1985

Gordon RD, Kuchel O, Liddle GW and Island DP: Role of the sympathetic nervous system in regulating renin and aldosterone production in man. J Clin Invest 46:599-605, 1967

Gottschalk CW: Renal nerves and sodium excretion. Ann Rev Physiol 41:229-240, 1979

Kim JK, Linas S and Schrier RW: Catecholamines and sodium transport in the kidney. Pharmacol Rev 31:169-178, 1980

Kook YJ, Choi BK, Yoo KY and Kim KH: Influence of intracerebroventricular phenoxybenzamine on the renal action of intracerebroventricular morphine. Arch int Pharmacodyn 273:289-298, 1985

Kook YJ, Lee YH and Choi BK: Influence of intracerebroventricular clonidine on the rabbit renal function. Kor J Pharmacol 20:59-71, 1984

Lee AS: Renal effects of norepinephrine and acetylcholine administered into a lateral ventricle of the rabbit brain. Chonnam Med J 9:29-31, 1972

Phillips RA: In *Quantitative clinical chemistry* (ed. Peters & van Slyke). Vol 2 Methods, Williams & Wilkins, 1944

Snedecor GW and Cochran WG: Statistical Methods (7th ed.). Lowa, 1980

Smith HW, Finkelstein N, Aliminosa L, Crawford B and Graber B: The renal clearances of substituted hippuric acid derivatives and other aromatic acids in dog and man. J Clin Invest 24:388-404, 1945

Starke K: Regulation of noradrenalin release by presynaptic receptor system. Rev Physiol Biochem Pharmacol 77:1-24, 1977

Starke K, Borowski E and Endo T: Preferential blockade of presynaptic α-adrenoceptors by yohimbine. Eur J Pharmacol 34:385-388, 1975

=국문초록=

가토 신장기능에 미치는 측뇌실내 Yohimbine 의 영향

전남대학교 의과대학 약리학교실

국영종, 김경근, 김세종

신장의 기능은 중추신경계 특히 교감신경계의 큰 영향을 받고 있으므로 α-adrenoceptor의 길항제로 알려진 yohimbine을 가토의 측뇌실내로 (i.c.v.) 투여하여 신장 기능의 변동을 관찰하였다.

Yohimbine 10 μg/kg i.c.v. 로써 일과성인 Na 배설 증가와 함께 뇨량, 신혈류 및 사구체 여과율의 증가 경향을 볼 수 있었으나, 투여량을 증가시키면 그와 같은 작용은 소실되고 100 μg/kg 과 300 μg/kg에있어서는 신혈류 및 사구체 여과율의 심한 감소와 함께 현저한 항이뇨 작용과 Na 배설의 감소가 관찰 되었다. 이때 전신 혈압은 일과성으로 증가를 나타내었다.

Reserpine 전처치 가토에 있어서는 100 μg/kg i.c.v. yohimbine에 의한 항이뇨, Na 배설 감소작용, 신혈류 역학의 감퇴등이 소실되어 유의한 변동을 관찰할 수 없었다. 이때 전신 혈압의 상승도 소실 되었다. 일측 신장 신경을 제거하고 반대측 신장을 대조로 둔 표본에 있어서 yohimbine 100 μg/kg을 측뇌실내로 투여하면 대조신에서는 정상 가토에서와 같은 전형적인 항이뇨 작용이 나타났으나, 제신경(실험)신에 있어서는 신혈류 역학에는 변동이 없으나 Na 및 K 배설과 Cosm 및 뇨량의 유의한 증가를 나타냈다. 이때 신세뇨관에서의 Na 재흡수가 억제되었다. 전신 혈압의 변동은 정상 가토에서와 같이 일과성인 증가를 볼 수 있었다.

이상의 실험으로, 가토 측뇌실내 yohimbine은 신기능에 대하여 두 가지 상반되는 영향을 미치며, 첫째는 교감신경 긴장도의 증가로써 신혈류 및 사구체 여과율을 감소시켜 항이뇨 및 Na 배설 감소를 초래하는 작용과, 둘째는 신경 경로를 통하지 않고, 아마도 humoral factor를 통하여 신세뇨관에서 Na 재흡수를 억제하는 작용이 복합적으로 나타내는 것을 알수 있었다.