Dietary Sodium Effects on Responses of Atrial Natriuretic Peptide, Aldosterone and Renin Release to Acute Volume Expansion in SHR†

Ae Ra Kim, Won Jung Lee, Young Eun Choo, Suhn Hee Kim* and Kyung Woo Cho*

*Department of Physiology, School of Medicine, Kyungpook University and Jeonbug University**

(Received 17, October 1989)

= Abstract =

Responses of atrial natriuretic peptide (ANP), aldosterone and renin release to acute volume expansion were compared in normotensive Wistar and spontaneously hypertensive rat (SHR) fed low- or high-sodium diet (2 or 25 mmol Na/100 g diet). Experimental diets were fed for 6 weeks from 7-week-old and the growth rate was similar in all groups. In the morning of the experiment, catheters were inserted under ether anesthesia in femoral artery for pressure recording and blood collection, femoral vein for saline infusion, and bladder for urine collection. Then, the rats were placed in restraining cages. When the rats were recovered from anesthesia and the arterial pressure became stabilized, control urine and blood samples were collected. Then, 0.9% saline was infused for 30 min for volume expansion (3% BW).

Arterial pressure was significantly higher in the high-sodium SHR but there was no difference between the two groups of Wistar rats. Control plasma levels of Na, K, ANP, renin activity, and hematocrit were not different among the 4 groups. However, plasma aldosterone level was significantly higher in the low-sodium groups. Wistar low-sodium rats showed approximately two times higher plasma aldosterone level than the SHR counterpart. Volume expansion produced a marked increase in plasma ANP level, especially in the high-sodium groups. The low-sodium groups of both strains showed approximately two-fold increase in plasma ANP level. Following a volume expansion plasma aldosterone level and renin activity decreased in all groups. There was a significant logarithmic positive correlation between plasma renin activity and aldosterone concentration. The low-sodium rats produced a greater increase in aldosterone release by small increase in plasma renin than did the high-sodium rats. The low- and high-sodium rats produced a similar degree of diuresis and natriuresis after volume expansion. However, SHR produced a greater natriuresis than did the Wistar rats.

The above results indicate that regulatory mechanisms of ANP, aldosterone and renin release are different between the normotensive and hypertensive rats, and between the low- and high-sodium groups.

Key Words: volume expansion, ANP, aldosterone, renin, salt diet, SHR

INTRODUCTION

Homeostatic regulation of sodium balance and body fluid volumes are under the influence of a variety of hormonal control systems such as the renin-angiotensin system (Hall et al, 1980; Laragh & Sealey, 1973) and aldosterone (de Wardener, 1973). Recently, it has been shown that cardiac atria from a

†본 연구는 한국과학재단 및 계명의대 동산의료원 특수과제 연구비로 이루어 졌음.

variety of mammalian species contain a peptide hormone which may play a role in the regulation of sodium balance and extracellular fluid volume (de Bold, 1979; Burnett et al, 1984; Needleman et al, 1985). This hormone, atrial natriuretic peptide (ANP, atriopeptin, auriculin, cardionatrin), is released from the atrial myocytes in response to stimuli such as acute volume expansion (Lang et al, 1985; Sagnella et al, 1985) or increased heart rate (Tikkanen, 1985). Mechanical stretching of the atria induces release of ANP in animals (Dietz, 1984).

In human, plasma ANP level is higher than normal in states of volume overloading such as renal failure and congestive heart failure (Hasegawa et al, 1986; Shenker et al, 1985). Specific renal, vascular and adrenal receptors for ANP have been identified (Needleman et al, 1985; Maak et al, 1985). ANP injection produces very prompt and potent diuretic and natriuretic effects both in animals and man (de Bold 1985; Freeman et al, 1985). ANP has also been shown to reduce blood pressure, and inhibit synthesis and release of renin and aldosterone (Maak et al, 1985; Burnett et al, 1984).

These observations have led to the suggestion that ANP may be an important humoral mechanism in the regulation of sodium balance and extracellular fluid volume by linking a pressure-sensitive mechanism in the atria with the control of body fluid volume by the kidney (de Bold, 1985; Maak et al, 1985; Needleman et al, 1985).

Some evidences suggest differences between normotensive and hypertensive rats in circulating levels of hormones (renin, aldosterone and ANP) regulating sodium balance and body fluid volume (Koletsky et al, 1970; Kim et al, 1988).

However, it is poorly understood on the role of these hormones in short-term and long-term regulation of sodium balance in normotensve and hypertensive rats. The present study was designed to compare the responses of ANP, aldosterone and renin releases to acute volume expansion in normotensive and hypertensive rats fed low- or high-sodium diet for 6 weeks. In addition, diuretic and natriuretic responses to chronic and acute changes in sodium loading were compared in the same rats.

METHODS

Male Wistar and spontaneously hypertensive (SH) rats at 7 weeks of age were randomly placed in the low or high Na diet (2, 25 mmol Na/100 g diet, respectively). Rats had free access to food and water. Body weight and food intakes were measured every week.

After 6 weeks on the low or high Na diet, rats were anesthetized with ether and catheters (pulled PE 50, Clay Adams) were placed in left femoral artery for blood pressure measurement and femoral vein for saline infusion. The free ends of the catheters filled with heparinized saline (50 U/ml) were exteriorized at the back and secured. Then the urinary bladder was exposed via a median abdominal incision and cannulated (PE 100 with a flared tip) for urine collection. The rats were placed in restraining cages and arterial catheters were connected to a Statham P50 transducer for the recording of the blood pressure (Narco, MK-IV-P).

When arterial pressure had been stabilized, the venous catheter was connected to a infusion pump (Sage, 341-A) and 0.9% saline was infused at a rate of 1.0 ml/hr for 90 min and control urine was collected for the last 30 min. Then 2.5 ml of control blood were taken slowly into a plastic syringe containing 50 μl aprotinin (1 mg/ml) and 50 μl EDTA (50 mg/ml) with soybean trypsin inhibitor (3 mg/ml). The same volume of donor blood was given simultaneously through the venous catheter during the arterial blood sampling period of approximately one min. Donor blood was obtained just prior to the experiment from the trunk of rats after decapitation under light ether anesthesia (Lee-Kwon et al, 1984).

Donor blood was divided into 2.5 ml aliquots in plastic syringes and kept at room temperature. The blood was warmed to 37 ℃ right before use.

For acute volume expansion, 0.9% saline was infused over a period of 30 min (3% body weight), starting at the end of the control sample collections. Arterial blood sample was collected immediately after the saline infusion by the same method as described.

Hematocrit was measured by a microhematocrit procedure and plasma was separated by centrifugation at 2000 rpm for 20 min at 4 ℃. One ml of plasma was extracted freshly on C_{18} Sep-Pak cartridge (Waters Inc.) for ANP measurement with the method of radioimmunoassay (RIA) described by Kim et al. (1988). Rest of the plasma was stored at −20 ℃ for measurement of aldosterone by using RIA kit (Diagnostic Inc.), and renin with RIA method described by Kim and Cho (1986). Plasma and urinary Na and K were measured with flame photometer (Beckman). Osmolality was measured with osmometer (Advanced, 3dII).

RESULTS

Growth rate was similar in Wistar and SHR fed low- or high-salt diet for 6 weeks. Plasma levels of hormones and electrolytes are shown in Table 1. Control plasma Na and K concentrations and hematocrit were not different among 4 groups. Acute volume expansion produced approximately 10% decrease in hematocrit.

Plasma ANP level was not different between the low and high salt groups of Wistar and SH rats (Fig. 1). Acute volume expansion produced a marked increase in plasma ANP level. Low salt groups of both Wistar and SHR showed approximately 2-fold increase in ANP level. High salt groups showed a greater increase in ANP than the low salt groups: 300% increase in Wistar rats and 160% increase in SHR. Wistar rats showed a greater ANP response to volume expansion than SHR.

Plasma aldosterone level was significantly higher in low salt groups than in high salt groups (Fig. 1).

Table 1. Control values for mean arterial blood pressure (MABP), plasma levels of atrial natriuretic peptide (ANP), aldosterone, renin, sodium and potassium, and hematocrit obtained before volume expansion in conscious Wistar and SHR fed low- or high-sodium diet for 6 weeks

	Wistar		SHR	
	Low-Na	High-Na	Low-Na	High-Na
MABP, mmHg	113.2± 3.3	110.0±1.7	141.6± 1.7##	148.9± 2.3##
ANP, pg/ml	47.0±12.5	41.6±7.7	37.1± 8.1	50.4±14.3
Aldosterone, ng/dl	207.3±19.0	59.4±7.2*	117.1 ±13.3#	53.6± 4.9*
Renin, ng AI/ml. hr	23.5± 4.7	27.4±5.7	13.0± 2.5#	16.7± 2.7
Na, mEq/L	141.0± 1.2	143.5±1.0	142.5± 0.5	144.5± 3.7
K, mEq/L	4.7± 0.3	4.8±0.2	4.5± 0.2	4.4± 0.2
Hematocrit, %	45.5± 0.7	43.8±2.8	44.1± 0.7	45.5± 0.6
n	6	7	9	11

Values are means±SEM.

*$p<0.01$, low-Na vs. high-Na rats.

#$p<0.05$, ##$p<0.01$, Wistar vs. SHR.

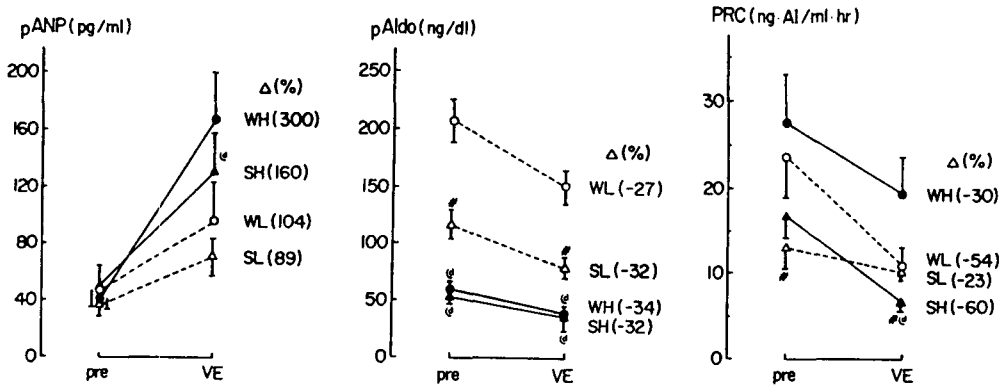

Fig. 1. Changes in plasma atrial natriuretic peptide (ANP), aldosterone, renin concentration (PRC) following acute volume expansion (VE: 3% BW) in Wistar (W) and SHR (S) fed low (L) or high (H) sodium diet for 6 weeks. Numbers in the parenthesis are % changes from the pre values. @$p<0.01$, low-sodium vs. high-soldium rats, *$p<0.05$, Wistar vs. SHR.

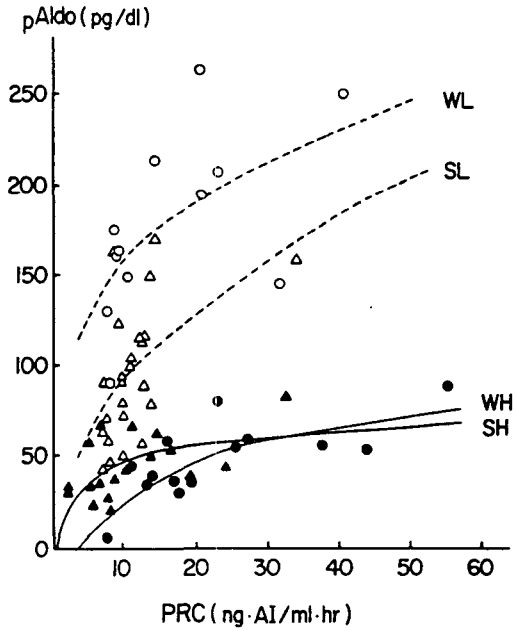

Fig. 2. Relationship between plasma renin concentration and aldosterone Wister (W) and SHR (S) fed low (L) or high (H) sodium diet for 6 weeks (WL --○--, WH —●—, SL --△--, SH —▲—).

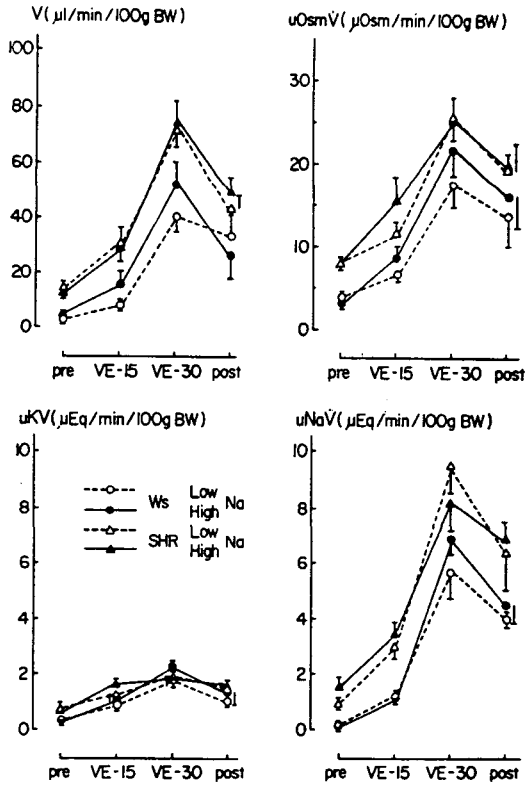

Fig. 3. Effects of volume expansion (VE) on urine flow and urinary solute excretion in Wistar and SHR fed low or high sodium diet for 6 weeks. VE-15: the first 15 min of VE, VE-30: the second 15 min of VE, post: 15 min after VE.

Wistar low salt rats showed about 2 times higher plasma aldosterone levels than SH low salt rats. Volume expansion produced approximately 30% decrease in plasma aldosterone levels in all groups.

Control plasma renin concentration (PRC) was slightly lower in low salt rats than in high salt rats (Fig. 1). SHR showed significantly lower control PRC than Wistar rats. Volume expansion produced a significant decrease in PRC in all groups. When all hormone data were analyzed, only aldosterone and renin showed a significant logarithmic correlation (Fig. 2). The relationship between PRC (X) and aldosterone (Y) can be described:

Wistar :

low salt $Y=54.8 \ln X+31.6$ ($r=0.64$, $p<0.05$)

high salt $Y=29.5 \ln X-41.6$ ($r=0.75$, $p<0.01$)

SHR :

low salt $Y=56.8 \ln X-36.0$ ($r=0.51$, $p<0.05$)

high salt $Y=12.8 \ln X+17.2$ ($r=0.52$, $p<0.05$)

Acute volume expansion produced a marked diuresis and natriuresis (Fig. 3). The low and high salt rats showed no difference in urine flow or urinary excretion rates of Na and K. However, SHR produced a greater diuresis and natriuresis after volume expansion than the Wistar rats.

DISCUSSION

The development and maintenance of hypertension in SHR can be influenced by the level of dietary sodium intake (Pettinger et al, 1982; Winternitz & Oparil, 1982). The present study also shows that young SHR given a high sodium diet developed a higher blood pressure than SHR maintained on a low sodium diet. This exacerbating effect of high salt intake on hypertension may be related to an increased sympathetic activity, because young SHR maintained on a high-sodium diet from 7 to 10 weeks had elevated plasma and urinary norepinephrine concentrations associated with elevated pressure (Winternitz & Oparil, 1982).

ANP has been suggested to play an important role in the acute and chronic regulation of sodium excretion and extracellular fluid volume (Needleman et al, 1985). A variety of experimental maneuvers that lead to acute central volume expansion, such as acute saline loading, water immersion, and postural change, result in significant increases in circulating levels of ANP (Hall et al, 1980; Sagnella et al, 1985; Salazar et al, 1986). In the present study, acute saline loading resulted in marked elevation in circulating levels of ANP. However, chronic high sodium intake did not result in any significant increase in circulating level of ANP.

Results from recent human and animal studies examined the effects of chronic changes in dietary sodium intake on plasma ANP are contradictory. Shenker et al (1985) and Sagnella et al (1985) reported that increases in dietary sodium intake were associated with increase in circulating levels of ANP. In contrast, other studies reported no significant changes in plasma levels of ANP during changes in dietary sodium intake (Raine et al, 1985; Salazar et al, 1986). The reason for these discrepancies are not clear but may be related to experimental protocol such as duration of dietary regimen and sampling time. Ogihara et al (1988) observed in patients with essential hypertension that during 2 weeks of high salt intake, the circulating ANP level increased gradually, reached a maximum on the day 7 and decreased thereafter. The same pattern of changes in plasma ANP level during long-term sodium loading was observed in rats. During high-sodium diet in rats, circulating ANP level was elevated after 1 week, but returned to the control level after 3 weeks (Luft et al, 1986; Lattion et al, 1988). This phasic change in circulating ANP level during chronic high-sodium intake in man and animal suggests that the ANP system is activated primarily during short-term adaptation to high solium intake. In the present study, plasma ANP levels after 6 weeks on the low- or high-sodium diet were not different. This is in accord with the above result of the lack of sustained effect of the high-sodium diet on ANP release (Raine et al, 1985; Salazar et al, 1986). Taken together, ANP does not seem to be responsible for the long-term regula-

tion of sodium and volume homeostasis.

Although chronic sodium intake had no sustained effect on ANP release, chronic elevation of sodium intake continuously altered the activity of the renin-angiotensin system and aldosterone (Hall et al, 1980; Laragh & Sealey, 1973; Salazar et al, 1986; Ogihara et al, 1988). These marked changes in the activity of the renin-angiotensin-aldosterone system suggest that these systems are probably more important in the maintenance of sodium balance during chronic changes in sodium intake than ANP. The present study also showed that the circulating aldosterone level was markedly suppressed by the high sodium intake. However, on the contrary to the other reports, the plasma renin level of the high sodium groups was rather higher than that of the low sodium groups. The reasons for the discrepancy are not clear, but the method of blood sampling might affect the renin level.

There were strain differences in the circulating levels of aldosterone and renin: SHR showed lower levels than Wistar rats. This result is in accord with other reports (Koletsky et al, 1970; Freeman et al, 1975; Kim et al, 1988). However, it is not clear whether these differences in hormonal levels between normotensive and hypertensive rats result in differences in regulating salt and body fluid balance.

As shown in the present study, volume expansion induces an elevation of ANP release and a reduction in release of renin and aldosterone. Although the plasma levels of aldosterone and renin before the saline loading were significantly different among the low- and high-sodium groups of Wistar and SHR (Fig. 1), percent decrease in hormonal levels after volume expansion were similar. Further studies are required to understand the relative importance of the increased levels of ANP in relation to the reduction in renin and aldosterone in controlling the sodium excretion in different physiological conditions of normotensive and hypertensive subjects.

In our study we found out that response of ANP release to acute volume expansion is different not only between the low- and high-salt groups, but also between SHR and Wistar rats. The rise in plasma ANP during acute volume expansion was smaller in the SHR than in Wistar rats. Other investigators also observed the blunted ANP response to acute volume expansion in the SHR (Gradin et al, 1987; Pettersson et al, 1988; Jin et al, 1988). During the 10% and 20% volume load, central venous pressure, central blood volume and cardiac output increased relatively more in the SHR compared with the WKY rats (Pettersson et al, 1988). Despite of the increased centralization of the volume load in SHR, ANP release was blunted in SHR. Furthermore, there is an evidence that the responses of natriuresis and diuresis to ANP infusion are lower in SHR than in WKY (Marsh et al, 1985). These dysfunction of ANP system in SHR might be related to the development or maintenance of high blood pressure. However, pathophysiological significances of the ANP system in SHR remains to be resolved.

The present result shows that about 15-week-old SHR tends to excrete a sodium load more quickly than do normotensive rats. Even with the low sodium intake, SHR showed the enhanced diuresis and natriuresis during the acute volume expansion. This is in agreement with other reports on hypertensive animals (Willis et al, 1976; DiBona & Rios, 1978; Ledinghan & Simpson, 1984) and men (Baldwin et al, 1958; Buckalew et al, 1969). However, some investigators have failed to confirm this (Farman & Bonvalet, 1975; Beierwaltes & Arendshorst, 1978; Kim et al, 1988). The reasons for these conflicting results are not clear, but they might be related to many factors such as the age of rats tested, heterogeneity of renal function in SHR strain and experimental procedures like anesthesia, restraint or extensive surgical cannulation. Mullins & Banks (1976) evaluated the renal function of SHR of different age groups to excrete an acutely administered isotonic saline load. SHR from two different colonies were

also compared. The fraction of administered sodium load excreted by SHR was lower than normotensive rats at age 6 week, but was similar at age 12 week. However, at age 16 week, one colony of SHR excreted significantly more sodium than the other colony of SHR and normotensive rats. Therefore, when we compare renal function, we have to be cautious about the age and colony of SHR.

Mechanisms of enhanced diuresis and natriuresis in hypertensive disorders are not clear. Some studies indicate that diminished reabsorption in the loop of Henle results in the exaggerated diuresis and natriuresis of the SHR (Stumpe et al, 1970; DiBona & Rios, 1978). Some investigators have suggested that exaggerated natriures is a blood pressure-related event (pressure diuresis) (Hall et al, 1986). However, elevated pressure, per se, cannot be the sole factor. Additional experiments will be required to determine the factors involved in the e ıhanced natriuresis observed in hypertensives.

REFERENCES

Baldwin DS, Biggs AW, Goldring W, Hulet WH & Chasis H (1958). Exaggerated natriuresis in essential hypertension. *Am J Med* 24, 893-902

Beierwaltes WH & Arendshorst WJ (1978). Renal function of conscious spontaneously hypertensive rats. *Circ Res* 42, 721-726

Buckalew VM Jr, Puschett JB, Kintzel JE & Goldberg M (1969). Mechanism of exaggerated natriuresis in hypertensive man: Impaired sodium transport in the loop of Henle. J Clin Invest 48, 1007-1016

Burnett JC Jr, Granger JP & Opgenorth TJ (1984). Effects of synthetic atrial natriuretic factor on renal function and renin release. *Am J Physiol* 247, F863-F866

DeBold AJ (1979). Heart atria granularity effects of changes in water and electrolyte balance. *Proc Soc Exp Biol Med* 161,508-511

DeBold AJ (1985). Atrial natriuretic factor: a hormone produced by the heart. *Science* 230, 767-770

Dibona GF & Rios LL (1978). Mechanism of exaggerated diuresis in spontaneously hypertensive rats. *Am J Physiol* 235, F409-F416

Dietz JR (1984). Release of natriuretic factor from rat heart-lung preparation by atrial distension. *Am J Physiol* 247, R1093-R1096

Farman N & Bonvalet JP (1975). Abnormal relationship between sodium excretion and hypertension in spontaneously hypertensive rats. *Pflugers Arch* 354, 39-53

Freeman RH, Davis JO, Vari RC (1985) Renal response to ANF in conscious dogs with caval constriction. *Am J Physiol* 248, R495-R500

Gradin K, Hedner J, Hedner T & Persson B (1987). Plasma atrial natriuretic peptide and blood pressure during chronic salt loading in spontaneously hypertensive rats with right atrial appendectomy. *J Neural Transm* 69, 255-264

Hall JE, Guyton AC, Smith MJ Jr & Coleman TG (1980). Blood pressure and renal function during chronic changes in sodium intake: role of angiotensin. *Am J Physiol* 239, F271-F280

Hall JE, Gramger JP, Hester RL & Montani JP (1986). Mechanisms of sodium balance in hypertension: role of pressure natriuresis. *J Hypertens* 4(Suppl 4), S57-S65

Hasegawa K, Matsushita K, Inoue T, Morii H, Ishibashi M & Yamaji T (1986). Plasma levels of immunoreactive atrial natriuretic factor in healthy subjects and in patients with chronic renal failure. *J Clin Endocrinol Metab* 63, 819-822

Jin H, Chen YF, Yanf RH, Meng QC & Oparail S (1988). Impaired release of atrial natriuretic factor in NaCl-loaded spontaneously hypertensive rats. *Hypertension* 11, 739-744

Kato J, Kida O & Nakamura S, et al. Dissociation between plasma and atrial content of atrial natriuretic polypeptide (ANP) following sodium load in rats. *Life Sci* 18, 2623-2627

Khraibi AA, Granger JP, Burnett JC, Walker KR & Knox FG (1987). Role of atrial natriuretic factor in the natriuresis of acute volume expansion. *Am J Physiol* 252, R921-R924

Kim HJ & Cho KW (1986). On the negative feedback control mechanism of the renin release in kidney slices. *Kor J Physiol* 20, 236-248 (in Korean)

Kim SH, Kim SH, Seul KH & Cho KW (1988). Effects of atrial natriuretic peptide on renal and endocrine functions in spontaneously hypertensive rats. *Kor J Physiol* 22, 41-53 (in Korean)

Kobrin I, Kardon MB, Trippodo NC, Pegram BL & Frohlich D (1985). Renal response to acute volume overload in conscious rat with atrial appendectomy. *J Hypertens* 3, 145-148

Koepke JP & DiBona GF (1987). Blunted natriuresis to atrial natriuretic peptide in chronic sodium-retaining disorder. *Am J Physiol* 252, F865-F871

Lang RE, Tholken H, Ganten D, Luft FC, Ruskoaho H & Unger T (1985). Atrial natriuretic factor—a circulating hormone stimulated by volume loading. *Nature* 314, 264-266

Laragh JH & Sealey JF (1973). The renin-angiotensin-aldosterone hormonal system and regulation of sodium, potassium, and blood pressure homeostasis, In: Handbook of Physiology. Renal Physiology, Washington, D.C. *Am Physiol Soc Chapt* 26, 831-908

Lattion AL, Aubert JF, Fluckiger JP, Nussberger J, Waeber B & Brunner HR (1988). Effect of sodium intake on gene expression and plasma levels of ANF in rats. *Am J Phsiol* 255, H245-H249

Lee-Kwon WJ, Share L, Crofton JT & Brooks DP (1984). Effect of angiotensin II on vasopressin in plasma and platelets in SH and WKY rats. Clin Exp Hypertension A6, 1653-1672

Luft FC, Sterzei B, Lang RE, Trabold EM & Veelken R, et al (1986). Atrial natriuretic factor determinations and chronic sodium homeostasis. *Kidney Int* 29, 1004-1010

Maak T, Camargo MJF, Kleinert HD, Laragh JH & Atlas SA (1985). Atrial natriuretic factor: structure and functional properties. *Kidney Int* 27, 607-615

Marie JP, Guillemot H & Hatt PY (1976). Le degre de granulation des cardiocytes auriculaires. *Path Biol* 24, 549-554

Marsh E, Seymour AA, Haley AB, Whinnery MA, et al (1985). Renal and blood pressure responses to synthetic atrial natriuretic factor in spontaneously hypertensive rats. *Hypertension* 7, 386-391

Mullins MM & Banks RO (1976). Age-related changes in Na^+ excretion in saline-loaded spontaneously hypertensive rats. *Am J Physiol* 231, 1364

Nagaoka A, Kakihana M, Shibota M, Fujiwara K & Shimakawa K (1982). Reduced sodium excretory ability in young spontaneously hypertensive rats. *Jpn J Pharmacol* 32, 839-844

Needleman P, Adams SP, Cole BR, Currie MG, Gellers DM, Michener ML, Saper CB, Schwartz D & Standaert DG (1985). Atriopeptins as cardiac hormones. *Hypertension* 7, 469-482

Ogihara T, Hara H, Shima J, Iinuma K & Kumahara Y (1988). Changes in the plasma ANP level during long-term salt loading in patients with essential hypertension. *Clin Exper Hypertension* 10(1), 105-117

Pettersson A, Ricksten SE, Towle AC, Hedner J & Hedner T (1988). Haemodynamics and plasma ANP (atrial natriuretic peptide) after acute blood volume expansion in normotensive and spontaneously hypertensive rats. *Acta Physiol Scand* 133 (Suppl 571), 513-518

Raine AEG, Muller FB, Brouwer RML, Burgisser E, Belli P, Buhler FR (1985). Plasma atrial natriuretic factor in man: parallel changes with renin, noradrenaline and salt balance (Abstract). *Hypertension* 7, 88

Saganella GA, Markandu ND, Short AC & MacGregor GA (1985). Effects of changes in dietary sodium intake and saline infusion on immunoreactive atrial natriuretic peptide in human plasma. *Lancet* 2, 1208-1212

Salazar FJ, Romero JC, Burnett JC Jr, Schryvers Granger JP (1986). Atrial natriuretic peptide levels during acute and chronic saline loading in conscious dogs. *Am J Physiol* 251, R499-R503

Shenker Y, Sider RS, Ostafin EA & Grekin RJ (1985). Plasma levels of immunoreactive atrial natriuretic factor in healthy subjects and in patients with edema. *J Clin Invest* 76, 1684-1687

Schwab TR, Edwards BS, Heublein DM & Burnett JC Jr (1986). Role of atrial natriuretic peptide in volume-expansion natriuresis. *Am J Physiol* 251, R310-R313

Tikkanen I, Metsarinne K & Fyhrquist F (1985). Atrial natriuretic peptide in paroxysmal supraventricular tachycarida. *Lancet* 2, 40-41

Toal CB & Leenen FHH (1983). Dietary sodium restriction and development of hypertension in spontaneously hypertensive rats. *Am J Physiol* 245, H1081-H1084

Willis LR, McCallum PW & Higgins JT Jr (1976). Exaggerated natriuresis in the conscious spontaneously hypertensive rat. *J Lab Clin Med* 87, 265-272

Winternitz SR & Oparil S (1982). Sodium-neural interaction in the development of spontaneous hypertension. *Clin Exp Hypertension* A4, 751-760

= 국문초록 =

장기간 고염 섭취한 SHR 고혈압 쥐에서, 급성 혈장량 증가에 대한 Atrial Natriuretic Peptide, Aldosterone 및 Renin 분비 반응의 비교

경북대학교 의과대학 생리학교실 및 전북대학교 의과대학 생리학교실*

김애라 · 이원정 · 주영은 · 김선희* · 조경우*

장기적으로 소금량을 다르게 섭취시킴에 따라서, 체내의 Na 대사에 관여하는 호르몬인 aldosterone, atrial natriuretic peptide (ANP) 및 renin 분비와 신장의 배설 반응에 나타나는 변화를 정상 혈압쥐 Wistar와 spontaneously hypertensive rat (SHR)에서 비교하고자 실험하였다. 생후 7주의 숫쥐인 Wistar와 SHR에게 저염과 고염 식이(각각 2, 25 mmol Na/100 g diet)를 6주간 먹였다. 그 후 ether 마취하에서 대퇴 동맥과 정맥 및 방광에 관을 삽입한 후, restraining cage에 넣었다. 수술회복 후 안정시 뇨와 혈액을 채취한 후, 0.9% saline을 30분동안 체중의 3%되게 정맥주입(혈장량 증가)하고 뇨와 혈액을 채취하였다. 혈장의 호르몬을 방사면역법으로 측정하였다.

Wistar와 SHR의 저염, 고염 식이군의 성장률에는 유의한 차이가 없었다. Wistar 저염과 고염군의 평균 동맥혈압은 각각 113과 110 mmHg로 차이가 없었으며, SHR의 동맥압은 141과 149 mmHg로 고염군이 높았다. 저염식이군에서 혈장 aldosterone농도는 고염군보다 월등히 높았고, ANP 농도는 차이가 없었으며, renin은 고염군보다 낮았다. 혈장량 증가 이후 혈장 aldosterone은 모든 군에서 30~40%정도 감소하였고, renin은 30~60%정도 감소하였다. 혈장량 증가 이후 ANP는 증가하였는데 고염군에서의 증가도가 저염군에서보다 월등히 높았다. 혈장량 증가 이전의 Wistar군의 혈장 aldosterone과 renin의 대조치 값은 SHR보다 유의하게 높았고, ANP 농도는 차이가 없었다. 그러나 혈장량 증가 이후의 Wistar와 SHR의 aldosterone과 renin의 감소정도는 유의한 차이가 없었으나, ANP의 증가도는 Wistar가 SHR보다 높은 경향을 보였다. 호르몬들 중에서 혈장 aldosterone과 renin사이에는 양의 대수함수 관계가 있으며, 기울기는 고염군이 저염군보다 유의하게 높았다. 혈장량 증가 이후에 나타나는 뇨량과 소금 배설률의 증가 정도는 고염군과 저염군 사이에 차이가 없었다. 그러나 SHR이 Wistar보다 더 심한 이뇨와 Na 배설항진 반응을 보였다. 이상의 결과는 소금 섭취량에 따라서 aldosterone, ANP 및 renin의 분비 조절이 다르며, 정상 혈압과 고혈압쥐 사이에서도 차이가 있음을 시사해 주고 있다.