J. Pharm. Pharmacol. 1997, 49: 912–918
Received February 7, 1997
Accepted June 2, 1997

Influence of Age on Cardiovascular Effects of Increased Dietary Sodium and Angiotensin-converting Enzyme Inhibiton in Normotensive Wistar Rats

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Abstract

Recent studies have shown that increased intake of dietary sodium chloride produces blood pressure-independent increase in cardiac and renal mass even in young normotensive rats. With advancing age the harmful cardiovascular effects of increased dietary sodium are not so well known. In the present study the influence of advancing age on the cardiovascular effects of increased intake of sodium (control diet, 0·3% and high-sodium diet, 2·6% sodium in the chow) were examined in young and aged (3 and 18 months old, respectively, at the beginning of the experiment) male normotensive Wistar rats in a six-week study. Moreover, the potential role of renin-angiotensin system in ageing during normal and a high-sodium intake was studied using a pharmacological tool, angiotensin converting enzyme (ACE) inhibitor ramipril.

Ageing did not significantly modify basal systolic blood pressure measured by the tail cuff method. A high intake of sodium chloride increased blood pressure significantly only in aged rats, while in young rats it increased renal weight. Left ventricular weight was not affected by high-sodium diet in either age group. The ACE inhibition during control diet lowered blood pressure and decreased left ventricular weight in young rats only and these effects were completely blocked by a high-sodium diet. The maximal vascular contraction force of mesenteric arterial rings to noradrenaline was decreased with ageing while endothelium-dependent and -independent relaxation responses were unaltered with ageing. The sensitivity to sodium nitroprusside was impaired by the high-sodium diet in young rats. In both age groups the urinary excretion of calcium was increased during the high-sodium diet.

In conclusion, the increased intake of sodium produced different changes in cardiovascular function in normotensive rats depending on age. With advancing age, the sensitivity to sodium-induced increase in blood pressure was increased. In aged rats a high intake of dietary sodium elevated blood pressure, while in young rats it increased renal mass without increase in blood pressure. In both age groups sodium did not affect left ventricular hypertrophy. Both high-sodium intake and ageing attenuated or even abolished the cardiovascular effects of ACE inhibition.

The cardiovascular alterations induced by hypertension are very similar to those observed during normal ageing in normotension (Lakatta 1987, 1993). Therefore, it is difficult to clearly attribute the observed functional and structural changes of the cardiovascular system to ageing itself or to increased blood pressure associated with ageing. Recent investigations have demonstrated an important role of a high intake of sodium chloride (regular salt) in arterial hypertension (Frost et al 1991; Law et al 1991a, b). Older subjects are more sensitive than younger ones to the arterial pressure increasing effect of dietary sodium, due to age-related renal functional and structural deterioration (Anderson & Brenner 1986; Mimran et al 1992). Moreover, a high intake of sodium is able to induce cardiac hypertrophy by a pressure-independent mechanism in young normotensive and hypertensive rats (Kihara et al 1985; Yuan & Leenen 1991; Mervaala et al 1992, 1994a, b, c), and may be an independent risk factor for cardiac hypertophy also in humans (Schmieder et al 1988; du Cailar et al 1989). A high sodium intake also increases kidney weight both in the presence and in the absence of a rise in blood pressure (Wilson et al 1973; McCormick et al 1989; Mervaala et al 1994a).

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The aim of the present study was to examine whether advancing age would modify the sodium-induced pressure-independent organ damage differently in young and aged normotensive rats. The possible role of the renin-angiotensin system/kallikrein-kinin system was also examined by the use of the angiotensin-converting enzyme (ACE) inhibitor, ramipril.

Materials and Methods

Experimental animals, diets and sample preparations

Two age groups of male Wistar rats from our breeding colony were studied. Young rats (n = 39) were three months old, and aged rats (n = 37) were eighteen months old at the beginning of the experiment. The rats were housed, three to four animals per cage, in an animal laboratory in 12 h light/dark cycles (artificially illuminated 0600–1830 h), room temperature 22–24°C. At the beginning of the study, body weight- and blood pressure-matched rats in both age groups were divided into four subgroups to receive different diet and drug regimens for six weeks. The rats received either a moderately low-sodium

control diet (R3, Finnewos Aqua, Helsinki, Finland), containing Na^+ 0·3%, K^+ 0·8%, Mg^{2+} 0·2%, Ca^{2+} 1·1%, P 0·8% of the dry weight of the chow or a high-sodium diet (Na 2·6%) which was produced by adding 6·0 g of NaCl to 94·0 g of the control rat diet. Ramipril was added to the diet (35 mg ramipril per kg dry weight of the chow) to produce an approximate daily dose of 3 mg kg^{-1} body weight. During the experiment the rats had free access to the chow and tap water.

Systolic blood pressure and heart rate of the pretrained rats were measured weekly using a tail-cuff blood pressure analyser (Apollo-2AB Blood Pressure Analyzer, Model 179-2AB, IITC Life Science, Woodland Hills, CA). The digital values for systolic blood pressure and heart rate were evaluated automatically from the analogue data by a microprocessor. Before the measurements the rats were warmed for 5–10 min at 28°C to make the pulsations of the tail artery detectable. Values for systolic blood pressure and heart rate were obtained by averaging readings from three to five measurements. To minimize stress-induced fluctuations in blood pressure all measurements were taken by the same experienced technician.

On the sixth week of the experiment the rats were placed individually in metabolic cages. Food intake was recorded and urine was collected over 24-h periods. The urine collections were used for determinations of electrolytes and protein and stored at −70°C until assayed. After the six-week experimental period the rats were weighed, then decapitated. The heart was excised, great vessels, atria and the free wall of the right ventricle were dissected and the left ventricular mass was measured. The left ventricular wet weight-to-body weight was calculated as left ventricular hypertrophy (LVH) index. The kidneys were washed with ice-cold saline and weighed. The combined weight of the right and the left kidneys-to-body weight ratio was calculated as renal hypertrophy (RH) index. The procedures and protocols of the study were in accordance with our institutional guidelines and were approved by the Animal Experimentation Committee of the University of Helsinki, Finland.

Mesenteric arterial responses in-vitro

A modification of the method described by Pörsti et al (1990) was applied. Briefly, the superior mesenteric artery was excised and cleaned of connective tissue. A section (3 mm in length) of the vessel, 3 mm distally from the mesenteric artery–aorta junction, was cut. The ring was placed between stainless steel hooks and mounted in an organ bath chamber in physiological salt solution (PSS, pH 7·4) of the following composition (mM): NaCl 119·0, $NaHCO_3$ 25·0, glucose 11·1, $CaCl_2$ 1·6, KCl 4·7, KH_2PO_4 1·2, $MgSO_4$ 1·2, and aerated with 95% O_2 and 5% CO_2. The rings were equilibrated for 20 min at 37°C with a resting tension of 1·5 g. The force of contraction was measured with an isometric force-displacement transducer and registered on a polygraph (FTO3C transducer, Model 7C8 Polygraph; Grass Instrument Co., Quincy, MA).

The presence of intact endothelium on vascular preparations was confirmed by a relaxation response to 1 μM acetylcholine (ACh) in rings precontracted by 1 μM noradrenaline (NA). The contractile concentration curves to NA and to potassium chloride (KCl), and the relaxation concentration curves to cumulative doses of ACh and sodium nitroprusside (SNP) were determined. The NA- and KCl-induced contractile responses were expressed in g and as percentage of the maximal response. The EC50 values for NA and KCl in each ring were calculated as percentage of maximal response, and for ACh and SNP as percentage of 1 μM NA-induced precontraction. The relaxations in response to ACh and SNP were calculated as percentage of pre-existing contractile force. All EC50 values were calculated with a computer program and presented as the negative logarithm (pD_{50}), which values were also used in statistical analyses.

Biochemical determinations

The concentrations of sodium, potassium, magnesium, calcium and phosphorus were determined with a Baird PS-4 inductively-coupled plasma emission spectrometer (Baird Co., Bedford, MA) as described in detail previously (Laakso et al 1991). Total urine protein concentration was measured by the method of Lowry et al (1951) after precipitation with 10% trichloroacetic acid.

Drugs

The following drugs were used: ramipril (Astra Hässle AB, Mölndal, Sweden), acetylcholine chloride, noradrenaline bitartrate (Sigma Chemical Co., St. Louis, MO), and sodium nitroprusside (F. Hoffman-La Roche AG, Basel, Switzerland). The stock solutions of the compounds used in in-vitro studies were dissolved in distilled water. All solutions were freshly prepared before daily use and protected from light.

Statistical analysis

Statistical analysis was carried out by one-way analysis of variance followed by the Tukey's test for pairwise comparisons between the study groups. Data for multiple observations over time were analysed by two-way analysis of variance with repeated measures for overall treatment effect, and the Tukey's test was used for multiple pairwise comparisons of treatment groups at different times. To test differences between the two age-groups unpaired *t*-test was used. Differences between means that had $P < 0.05$ were considered statistically significant. The data were analysed using SYSTAT statistic software (SYSTAT Inc., Evanston, IL). The results are expressed as means ± s.e.m.

Results

Blood pressure, left ventricular and renal hypertrophy and heart rate

No age-related difference in blood pressure (Fig. 1) or in heart rate was observed in this strain. The absolute left ventricular and renal weight was significantly increased with age. However, the organ weight-to-body weight ratio was not increased due to heavier body weight of aged rats (Table 1). Increased intake of dietary sodium significantly increased blood pressure in aged rats only. On the contrary, a high-sodium diet caused an increase in renal weight in young rats only but did not affect left ventricular weight in either age group. The blood-pressure-lowering effect of ramipril during the control diet was significant as compared with all other groups in young rats, but in aged rats the effect was significant only as compared with the high-sodium group. Ramipril during the control diet decreased left ventricular weight as compared with all other groups in

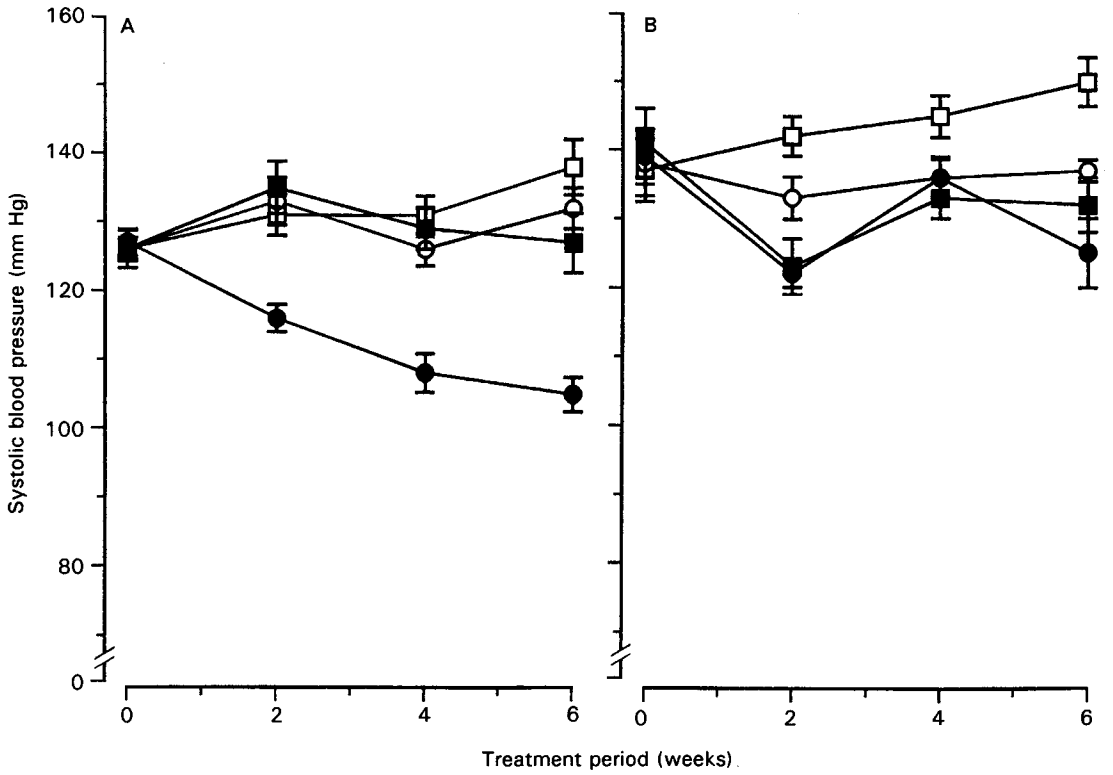

FIG. 1. Line plots show blood pressure in young (A; n = 9–10 in each group) and aged (B; n = 8–10 in each group) Wistar rats during different diet and drug regimens. ○ Control group; □ high-sodium diet; ● ramipril during control diet; ■ ramipril during high-sodium diet. In young Wistar rats, repeated analysis of variance between-subjects effects, $P < 0.0001$; within-subject effects $P < 0.0001$; time-group interaction, $P < 0.0001$. Ramipril therapy during control diet decreased blood pressure ($P < 0.001$ vs all other groups). In aged Wistar rats, repeated analysis of variance between-subjects effects, $P < 0.001$; within-subject effects, $P < 0.001$; time-group interaction, $P < 0.001$. Ramipril during both the control and high-sodium diet decreased blood pressure as compared with the high-sodium group ($P < 0.01$). The results are expressed as means ± s.e.m.

young rats but in aged rats the decrease was significant only when compared to high-sodium groups. Ramipril did not affect renal weight in either age group. The high-sodium diet blocked the blood-pressure-lowering and left-ventricular-weight-decreasing effect of ramipril in both age groups (Table 1, Fig. 1). There were no significant differences in the heart rate between various treatment groups in either age group (Table 1).

Body weight gain

There was no difference in body weight gain in either age group during the experimental period as shown by repeated measurements of analysis of variance (in young $F = 1.65$, $P = 0.20$ and in aged $F = 1.60$, $P = 0.21$). However, at the end of the experiment, the body weight of ramipril-treated young rats was smaller than in the control group, while no difference was observed in aged rats (Table 1).

Mesenteric arterial responses in-vitro

An age-related decrease in NA-induced maximal contractile force (g) in isolated arterial rings was observed, while the sensitivity to NA was the same in the two age groups (Table 2). No age-related difference was found in contractile responses to KCl or relaxation responses to ACh (data not shown) or SNP (Table 2).

In young rats ramipril therapy tended to improve the vascular relaxation to SNP. Young rats on high-sodium diet showed impaired sensitivity to SNP (ie. higher pD_{50} value) as compared with low-sodium groups with or without ramipril. However, the maximal values were comparable between the groups studied (Table 2). On the contrary, in aged rats no significant differences were observed in relaxation responses to SNP (Table 2).

ACh induced endothelium-dependent relaxations, and both NA and KCl evoked concentration-dependent contractions of artery rings in all groups studied. Neither age nor different treatments significantly affected relaxation or contraction responses induced by ACh or KCl (data not shown).

Metabolic variables

The average daily dose of ramipril calculated on the basis of the food intake, was 2·5 ± 0·1 in young rats on the control diet, 2·1 ± 0·1 in young rats on the high sodium diet, 0·9 ± 0·1 in aged rats on the control diet and 1·0 ± 0·1 mg kg^{-1} in aged rats on the high sodium diet (analysis of variance $P < 0.001$).

Table 1. Blood pressure, heart rate, body weight, left ventricular weight and kidney weight of young and aged Wistar rats after six weeks on different diet and drug regimens.

	Age group	Control	High-sodium	Control + ramipril	High-sodium + ramipril
Blood pressure (mm Hg)	Young	132 ± 4	138 ± 4	105 ± 3	126 ± 4
	Aged	137 ± 2	150 ± 4	125 ± 5	132 ± 4
Heart rate (beats min^{-1})	Young	339 ± 6	335 ± 5	344 ± 6	327 ± 6
	Aged	358 ± 16	342 ± 17	329 ± 4	343 ± 13
Left ventricle weight (mg)	Young	714 ± 18	724 ± 25‡	530 ± 13†	685 ± 28‡
	Aged	866 ± 34*	921 ± 36‡	798 ± 46	953 ± 31†‡
Left ventricle hypertrophy index (mg g^{-1})	Young	1·8 ± 0·1‡	1·9 ± 0·1‡	1·5 ± 0·1	1·8 ± 0·1‡
	Aged	1·4 ± 0·1*	1·6 ± 0·1‡	1·3 ± 0·1	1·5 ± 0·1‡
Left and right kidney weight (mg)	Young	2308 ± 70	2570 ± 99‡	2107 ± 78	2478 ± 103‡
	Aged	2919 ± 142*	3005 ± 126	2971 ± 167	3082 ± 104
Renal hypertrophy index (mg g^{-1})	Young	5·80 ± 0·02	6·63 ± 0·17†‡	6·11 ± 0·08	6·53 ± 0.10†
	Aged	4·85 ± 0·11*	5·14 ± 0·18	4·96 ± 0·16	5·19 ± 0·18
Body weight (g)	Young (week 1)	251 ± 5	250 ± 9	244 ± 5	254 ± 9
	Young (week 6)	386 ± 12	380 ± 10	340 ± 11†	373 ± 12
	Aged (week 1)	586 ± 22	599 ± 26	603 ± 32	603 ± 28
	Aged (week 6)	605 ± 20*	591 ± 22	603 ± 33	603 ± 26

Values are means ± s.e.m., n = 8–10 in each group. *$P < 0·05$ compared with the corresponding group of young rats (unpaired t-test); †$P < 0·05$ vs control group; ‡$P < 0·05$ vs control + ramipril group (Tukey's test); $P < 0·05$ vs high-sodium group; $P < 0·05$ vs high-sodium + ramipril group.

Table 2. Contractile and relaxation responses of isolated mesenteric arterial rings of young and aged Wistar rats after six weeks on different diet and drug regimens.

		Control	High-sodium	Control + ramipril	High-sodium + ramipril
Noradrenaline					
pD_{50}	Young	6·78 ± 0·14	6·98 ± 0·10‡	6·45 ± 0·07	6·68 ± 0·13
	Aged	6·72 ± 0·09	6·78 ± 0·06	6·62 ± 0·11	6·52 ± 0·09
Maximal force (g)	Young	2·64 ± 0·24	2·75 ± 0·34	2·00 ± 0·44	2·09 ± 0·23‡
	Aged	3·46 ± 0·21*	3·08 ± 0·19	3·29 ± 0·24	2·75 ± 0·25
Sodium nitroprusside					
pD_{50}	Young	7·92 ± 0·08	8·12 ± 0·08†‡	7·64 ± 0·05	7·82 ± 0·08‡
	Aged	7·80 ± 0·01	7·92 ± 0·01	7·58 ± 0·11	7·77 ± 0·01
Maximal relaxation					
(% of 1 μM NA-induced precontraction)	Young	100 ± 0	100 ± 0	100 ± 0	99 ± 1
	Aged	100 ± 0	100 ± 0	99 ± 1	100 ± 0

Values are means ± s.e.m., n = 8–10 in each group. NA, noradrenaline. pD_{50} is the negative logarithm of the concentration of agonist producing 50% of maximal response. *$P < 0·05$ compared with the corresponding group of young rats (unpaired t-test); †$P < 0·05$ vs control + ramipril group (Tukey's test).

The food consumption was significantly less in aged than in young rats on the control diet. Neither dietary sodium nor ramipril caused any significant changes in the food intake in either age group (Table 3). In both age groups the high sodium diets both in the presence and in the absence of ramipril increased the water intake and diuresis when compared with the control diet groups (Table 3). Urinary excretion of sodium, magnesium and potassium was decreased in aged animals as compared with the young ones, while no difference in the excretion of calcium, phosphorus or protein was found between young and aged rats receiving the control diet (Table 4). In both age groups the high-sodium diet increased the urinary excretion of sodium and calcium, and in young rats ramipril partially blocked the sodium-induced increase. The excretion of magnesium and phosphorus was increased in young rats only (Table 4). There were no significant differences between different treatment groups in the urinary excretion of potassium or protein in either age group (Table 4).

Discussion

The present study was performed in Wistar rats, a strain reported to maintain normal blood pressure to an old age and to have a very low incidence of chronic progressive nephropathy (Anderson et al 1994; Heudes et al 1994; Michel et al 1994). Thus, our finding of the absence of age-related development of hypertension are consistent with previous studies on this particular strain. However, differences were found in the vascular studies. With advancing age the NA-induced maximal contractile force generation in isolated arterial rings was decreased, although the sensitivity remained unaltered. The contractile responses to KCl and

Table 3. Daily (24-h) food and water intakes and urinary output of young and aged Wistar rats after six weeks on different diet and drug regimens.

		Control	High-sodium	Control + ramipril	High-sodium + ramipril
Food intake (g)	Young	5·7 ± 0·6	5·8 ± 0·2	7·0 ± 0·3	6·1 ± 0·3
	Aged	2·7 ± 0·2*	2·6 ± 0·2	2·8 ± 0·3	2·8 ± 0·2
Water intake (mL)	Young	6·5 ± 1·3	14·6 ± 0·9†‡	9·3 ± 0·7	10·2 ± 0·4†#
	Aged	2·7 ± 0·5*	4·0 ± 0·5†	7·5 ± 1·4	6·7 ± 1·0†
Urinary volume (mL)	Young	6·9 ± 1·1	15·1 ± 0·7†‡	8·8 ± 0·6	10·8 ± 0·3†#
	Aged	3·3 ± 0·5*	5·5 ± 0·6†	7·7 ± 1·5	7·7 ± 1·0†

Values are means ± s.e.m. per 100 g of body weight; n = 8–10 in each group. *$P < 0.05$ compared with corresponding group of young rats (unpaired t-test); †$P < 0.05$ vs control group; ‡$P < 0.05$ vs control + ramipril group; #$P < 0.05$ vs high sodium group (Tukey's test).

Table 4. Daily (24-h) urinary electrolyte and protein excretion in young and aged Wistar rats after six weeks on different diet and drug regimens.

		Control	High-sodium	Control + ramipril	High-sodium + ramipril
Sodium (mmol)	Young	0·41 ± 0·04	3·44 ± 0·60†‡#	0·52 ± 0·05	1·93 ± 0·33†‡
	Aged	0·14 ± 0·02*	1·52 ± 0·31†‡	0·15 ± 0·02	1·56 ± 0·25†‡
Calcium (μmol)	Young	8·0 ± 1·3	53 ± 12†‡#	14 ± 2	27 ± 2†
	Aged	6 ± 1	27 ± 6†‡	8 ± 2	26 ± 4†‡
Magnesium (μmol)	Young	53 ± 10	171 ± 43†	99 ± 18	85 ± 19
	Aged	17 ± 6*	31 ± 9	20 ± 9	34 ± 7
Potassium (mmol)	Young	0·81 ± 0·04	1·22 ± 0·31	0·92 ± 0·10	0·86 ± 0·10
	Aged	0·33 ± 0·02*	0·25 ± 0·05	0·37 ± 0·03	0·37 ± 0·03
Phosphorus (mmol)	Young	0·13 ± 0·02	0·25 ± 0·05†‡#	0·07 ± 0·02	0·13 ± 0·01
	Aged	0·08 ± 0·01*	0·08 ± 0·01	0·09 ± 0·02	0·08 ± 0·01
Protein (mg)	Young	4·3 ± 0·3	7·2 ± 1·9	5·6 ± 1·3	6·0 ± 1·0
	Aged	4·5 ± 1·1	5·0 ± 1·6	3·2 ± 0·8	6·1 ± 1·8

Values are means ± s.e.m. per 100 g of body weight; n = 7–10 in each group. *$P < 0.05$ compared with corresponding group of young rats (unpaired t-test); †$P < 0.05$ vs control group; ‡$P < 0.05$ vs control + ramipril group; #$P < 0.05$ vs high-sodium + ramipril group (Tukey's test).

relaxation responses to endothelium-dependent (ACh) and endothelium-independent (SNP) agents were similar in the two age groups.

The effects of an increased sodium intake are age-dependent in various experimental animals (Zicha et al 1986; Soltis & Newman 1991; Yuan & Leenen 1991; Dobešová et al 1995). In the present study, increased intake of dietary sodium induced blood pressure elevation in aged rats only and did not increase left ventricular weight in either age group. On the other hand, young rats showed higher sensitivity of kidneys to the detrimental effects of sodium as indicated by increased renal mass and elevated urinary excretion of protein. Moreover, in young rats the vascular sensitivity to endothelium-independent relaxation induced by sodium nitroprusside was impaired by a high intake of sodium. Previous findings have demonstrated that increased dietary sodium intake increases renal and left ventricular weight in 10-week-old Wistar rats without a concomitant rise in blood pressure (Mervaala et al 1994b), while in more mature rats these trophic responses to sodium were diminished (Yuan & Leenen 1991). The sodium-induced blood pressure increase in aged rats is in agreement with human studies where it has been demonstrated that sodium sensitivity of blood pressure increased significantly with increasing age (Weinberger & Fineberg 1991). It has been suggested that alterations in renal tubular function might be the sensitizing factor for the sodium- and age-related blood pressure increase (Umeda et al 1988; Weinberger & Fineberg 1991). Moreover, the detrimental effects of increased intake of sodium has been postulated to be mainly mediated by an increased volume load and by the activation of the sympathetic nervous system (Meggs et al 1988; Oparil et al 1988; Wyss et al 1990; Tobian 1991).

In accordance with earlier studies made with ACE inhibitors in young normotensive rats during a low sodium diet (Michel et al 1988, 1994; Mooser et al 1991; Mervaala et al 1994b), ramipril therapy effectively lowered blood pressure and reduced left ventricular mass without having effects on renal mass in young rats. Unlike in young rats, the capability of ramipril to lower blood pressure and reduce left ventricular weight was diminished in aged animals. The calculated daily dose of ramipril based on food consumption was lower in aged rats (approximately 1 mg kg^{-1}) than in young rats (approximately 2·3 mg kg^{-1}). The dose may not in fact have been as low as estimated based on food consumption. Aged rats should have lost body weight during the six-week experimental period which was not the case. However, it has been extensively demonstrated that a dose of 1 mg of ramipril has maximal antihypertensive effect (for review, see Linz et al 1995). Moreover, it has been shown that in contrast with 10-month-old rats, the acute administration of an ACE inhibitor did not affect arterial pressure and renal plasma flow in 30-month-old Wistar rats (Corman & Michel 1986). Such results may indicate that the progressive reduction in circulating renin with age is associated with a decline in the participation of the system in the maintenance of arterial pressure and and renal vascular tone.

The high-sodium diet totally blocked the blood-pressure- and left-ventricular-weight-decreasing effect of ramipril in young rats and also diminished the minor changes observed in aged rats. This finding of sodium-induced antagonism of the effects of ACE inhibitors is consistent with earlier reports (Mervaala et al 1994a, c), although enalapril has been shown to lower blood pressure during a high-sodium diet in young Wistar rats (Mervaala et al 1994b). ACE inhibitors can lower blood pressure and decrease cardiac hypertrophy by reducing angiotensin II production and by decreasing bradykinin degradation, the former being more important (for review, see Linz et al 1995). Leenen & Toal (1989) have shown that even a moderately increased intake of sodium chloride suppresses the renin-angiotensin system of both normotensive and hypertensive rats. The sodium-induced suppression of the renin-angiotensin system could thus explain, at least in part, the lack of the effect of ramipril on blood pressure and left ventricular weight during the high-sodium diet. In agreement with previous studies both in man and animals (Shortt & Flynn 1990), increased intake of dietary sodium elevated the urinary excretion of calcium in both age groups. In young rats the urinary excretion of magnesium and phosphorus was also increased. An important connection between the excretion of sodium and calcium is shown by the finding that a high intake of calcium increases the excretion of sodium (Pörsti et al 1990), and that calcium supplementation decreases the blood pressure of salt-sensitive spontaneously hypertensive rats (Wuorela et al 1992). The calciuretic effect of dietary sodium in both young and aged animals lends further support to the concept that dietary salt is an important factor in the pathogenesis of osteoporosis (MacGregor & Cappuccio 1993).

In conclusion, increased intake of sodium chloride induced elevation of blood pressure in aged normotensive rats only, but increased renal weight in young rats without having effect on left ventricular weight in either age groups. Both a high intake of dietary sodium and ageing attenuated or even abolished the lowering effects of ACE inhibitor on blood pressure and left ventricular hypertrophy in normotensive young rats.

Acknowledgements

This study was part of the Biomed-2 project n:o BMH4-CT96-0979 and was supported by the grants from the Academy of Finland, Sigrid Juselius Foundation and the Ida Montin Foundation (T.-L. T). The gift of ramipril from Astra Hässle AB, Mölndal, Sweden is gratefully acknowledged. We thank Ms Anneli von Behr, Ms Remi Hakama, Ms Valma Karlsson, Miss Mia Pekkanen and Ms Toini Siiskonen for providing excellent technical assistance.

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