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The Effect of Dietary Calcium Intake on Plasma Renin Activity and Parathormon in Deoxycorticosteron Salt Hypertension*

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Abstract: The effects of diets containing 2% and 4% calcium (Ca) on deoxycorticosteron (DOC) salt hypertension were studied in 29 male rats weighting 210–260 g. Rats were categorized into four groups: Group I: control rats (6), group II: DOC hypertensive group (n=8), group III: DOC–low Ca diet (2% $CaCl_2$) (8) and group IV: DOC–high Ca diet (4% $CaCl_2$) (n=7). During the six weeks follow up period, indirect systolic blood pressure (SBP) was highest in group II while it was found to be less increased in group III and IV. Weight increase was lowest in group IV ($P<0.005$ versus 3 other groups). There was no relationship between blood pressure (BP) and plasma renin activity (PRA), parathormon (PTH), angiotensin II (AII), serum Ca, serum phosphorus, urine Ca and final body weight. Serum Ca level was lower in group II as compared to group III ($P<0.006$). PTH was lower in group III and IV than other groups but the differences were statistically nonsignificant. PRA was found supressed in group IV and group II compared to control and group III (Control vs group II p=0.014, control vs group IV p=0.006, group III vs group IV p=0.01). However, the decrease in PRA was more important in group IV than group III. Left heart weight was greater in group IV than group II ($p = 0.033$) while right heart weight was not different among the groups. Kidney weight showed an increase in group II and group III, when compared with controls (p=0.009, p=0.045 respectively).

As a result, at uninephrectomized DOC–salt treated hypertension model in rats, the increase in BP was less prominent in Ca supplemented diet and this effect continued during the study period. In this hypertension model with suppressed PRA, we can state that a decrease in PTH which suggests the suppression of parathyroid gland, may affect BP.

Key Words: Calcium, hypertension, parathormon.

Introduction

In human hypertension, Ca supplementation has been suggested to decrease blood pressure (1, 2). Ca supplementation is especially effective in sodium volume–dependent hypertension in various experimental models (3, 4). Antihypertensive effects of increased dietary Ca intake have not been fully understood. In this study, we evaluated the effects of Ca supplementation on blood pressure and the levels of PRA, PTH, SCa, SP in DOC–salt treated rats.

Material and Methods

All studies were carried out in male wistar rats with documented normotension. The experiments adhered to legal standards and protocol was approved in advance by the appropriate committee at TIBDAM, Adana, Turkey. The rats (130–140 g) were purchased from TIBDAM and received standart laboratory rat chow (containing 0.5% NaCl and 22% protein) and tap water ad libitum. The animals were housed in a humidity and temperature controlled room with a 12 hour light–dark cycle. One week after receiving the animals, systolic blood pressure was recorded by tail plethysmography (rat tail BP monitor, Harvard Apparatus Ltd., Kent, England) in conscious state. This was repeated at weekly intervals until reached 210–260 g body weight. Rats (210–260 g) were anaesthetized with ketamine (130 mg/kg body weight {bw} im.) and chlorpromazine (1.3 mg/kg bw im). Through a midline abdominal incision the right kidney

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was removed. One week after nephrectomy, the rats were divided into 4 groups; group I; control group (6 rats) which were injected olive oil subcutaneously and given tap water. Other three groups were injected DOC dissolved in olive oil (12.5 mg at first and then 6.5 mg weekly for 6 weeks). Ten miligrams of DOC was dissolved in 0.4 ml olive oil). DOC injected rats were given 1% NaCl as drinking water. In Group II (DOC hypertensive group). 8 rats were given normal rat chow containing 1% Ca. Diet supplemented 2 and 4% $CaCl_2$ were given to 8 rats and 7 rats, respectively, in group III (DOC–low Ca group) and group IV (DOC–high Ca group).

SBP were measured daily with tail cuff method except DOC injection days. Rats were followed up 6 weeks. At the end of the study, blood and urine samples were taken for serum Ca, P, AII, PTH, PRA, urinary Ca, Na, K.

Repeated measures of analysis of variance technique was used for between and within group. To determine the group(s) that are different than other (s), simultaneous multiple comparison techniques of Bonferroni was used. The p value less than 0.05 was assumed to be significant. All results were expressed as mean and standard deviations.

Results

In uninephrectomized DOCA salt treated rats, increase in BP is shown in Figure 1. The increase in BP was less prominent in group IV during the study period. Body weight increased at the end of follow up period. However, the increase in body weight in group IV was lower than other groups (Table). Final day measurements of serum Ca, P, PTH, PRA and urine Ca, Na, K and comparison of the groups are shown in Table. There was negative correlation between serum Ca and P (p=0.001). There was no correlation between PRA, AII, PTH and urine Ca and pulse, final weight, serum Ca, P, PRA, PTH, urine Ca in all rats and within each group.

During the study period, the changes of body weight and PRA and PTH levels are shown in Figure 2 and 3.

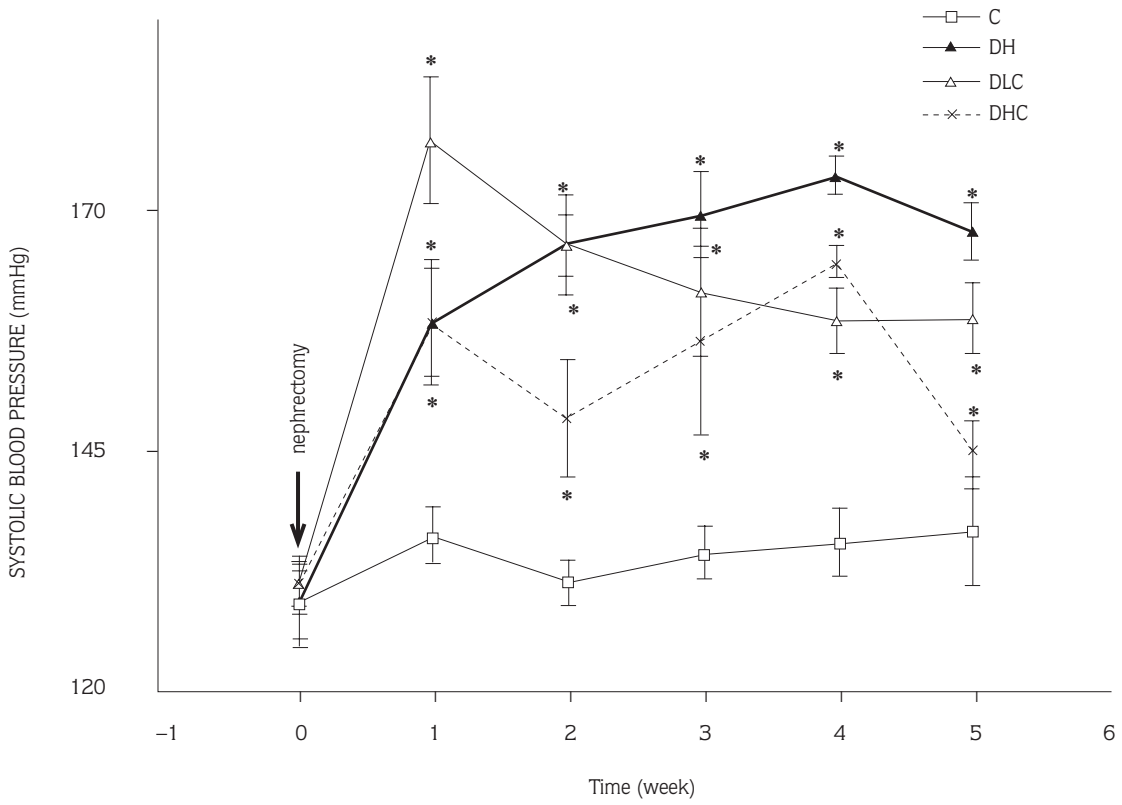

Figure 1. Effect of DOC and dietary–calcium on indirect systolic blood pressures in uninepectomized rats. C: Control (n=6), DH: DOC + standard diet (n=8), DLC: DOC + Low calcium diet (n=8), DHC: DOC + High calcium diet (n=7). Values are mean + SEM. *P<0.05 vs the prenephrectomy values.

Table. The Characteristics of the Rats, and Serum and Urine Levels of Some Biochemical Parameters.

	Group I Control	Group II Doc–hypertension	Group III Doc Low–Ca	Group IV Doc High–Ca	P value
Number	6	8	8	7	
Body weight basal (g)	225.83±4.91	228.12±9.23	240.00±16.03	226.42±12.15	
Body weight final (g)	305.83±16.89	306.25±14.07	326.25±17.67	270.00±19.14	0.4[b], 0.004[e], 0.01[c], 0.001[f], 0.02[d]
Righ heart weight (mg)	149.16±34.70	150.50±24.40	149.37±20.04	142.05±13.80	> 0.05
Left heart weight (mg)	533.83±30.98	557.25±27.97	562.75±49.83	567.1±28.11	0.03[e]
Kidney weight (mg)	1191.7±91.1	1385.0±130.2	1395.0±103.4	1304.3±112.7	0.009[a] 0.0045[b]
Pulse (basal)	425.0±35.07	435.0±27.77	427.50±31.05	424.28±32.07	> 0.05
Pulse (final)	425.00±12.24	427.50±21.21	431.25±7.89	420.00±24.49	> 0.05
ISBP (basal) mmHg	128.83±10.77	129.37±9.79	130.62±6.23	130.85±7.88	> 0.05[a,b,c,d,e]
ISBP (final) mmHg	135.83±13.93	166.87±8.42	157.87±10.23	144.28±9.32	
SCa mg/dl	10.16±0.50	9.70±0.41	10.88±0.99	10.05±0.57	0.006[d]
SP mg/dl	6.31±1.19	5.92±1.21	6.95±1.53	5.77±1.03	> 0.05
PTH ng/ml	42.53±37.16	42.33±33.18	28.61±28.74	15.71±15.63	> 0.05
PRA ng/ml	14.89±9.59	6.23±3.77	9.00±3.21	3.88±3.44	0.014[a], 0.01[f] 0.09[b], 0.006[c]
AII	122.48±162.1	222.23±146.0	70.16±136.03	428.34±531.7	
Urine Na mEq/L	–	–	320.00±56.56	209.00±128.2	> 0.05
Urine K	81.50±12.02	71.50±3.53	62.50±30.67	72.33±30.42	> 0.05
Urine Ca	34.13±10.43	39.75±15.93	34.40±10.83	33.484.44	> 0.05

a : Control vs group II
b : Control vs group III
c : Control vs group IV
d : Group II vs group III
e : Group II vs group IV
f : Group III vs group IV

ISBP : Indirect systolic blood pressure
SCa : Serum calcium
SP : Serum phosphorus
PRA : Plasma renin activity
AII : Angiotensin II

Discussion

The effect of Ca supplemented diet on blood pressure was evaluated in uninephrectomized DOC–salt treated rats. Blood pressure was markedly attenuated in the rats on Ca supplemented diet. Ca supplemantation had long–term antihypertensive effect during the study period. Serum Ca level did not rise in these rats, especially in high–Ca diet group. Serum PTH level was not different significantly between these groups but the level of PTH decreased on high Ca diet. In salt sensitive low renin hypertension, there are some paradoxical features (5). Such hypertensive individuals are often beneficially responsive both to a Ca antagonist (6) and to high Ca diet (7). These observations are rather paradoxical. In addition many such individuals have a higher circulating

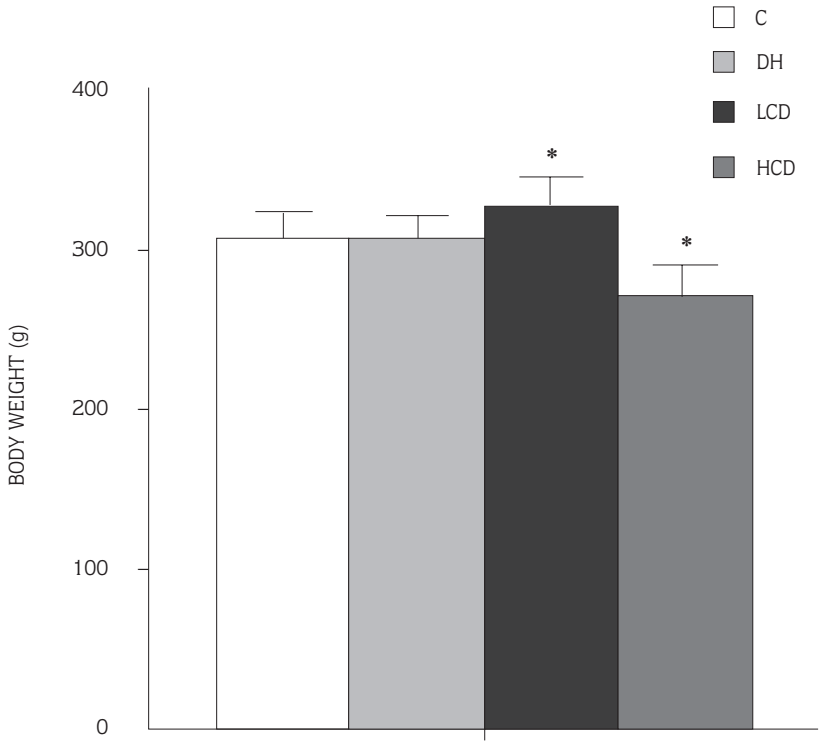

Figure 2. Effect of DOC and dietary–calcium on body weight in uninephrectomized rats. C: Control (n=6), DH: DOC + standard diet (n=8), DLC: DOC + Low calcium diet (n=8), DHC: DOC + High calcium diet (n=7). Values are mean ± SD.* P<0.05 vs C.

PTH level (8). In our study, in addition to decreased blood pressure, high Ca diet caused lower serum PTH. If parathyroid hypertensive factor (PHF) is the major contributing or causative factor of low–renin salt–sensitive hypertension, it should be able to elicit this paradoxical observations. The parathyroid gland is one of the few glands which are stimulated by a negative calcium balance in the human body. Therefore, high dietary–Ca should inhibit the parathyroid gland function and the production of PHF, hence alleviating hypertension (9). Some authors showed that a high Ca diet reduced the blood pressure and PHF in hypertensive patients (5). In other studies, a high–Ca diet reduced blood pressure and PHF level in spontanous hypertansive rats compared with those in animals fed a low–Ca diet (9). Since the parathyroid gland is stimulated by low–Ca, it is understandable that hypocalcemia can lead to the increased activity of the parathyroid gland producing PHF as well as PTH. The effect of PHF can explain the rather paradoxical features of low renin salt–sensitive hypertension. In group IV, the lowest PRA was found. Group II was not different significantly from group IV for PRA but control group was different from group II and IV with regard to PRA. In rats on low–Ca diet, PRA was decreased, however PRA was not different between other groups except group IV. The similarities in decreases of PRA in group IV and II were interesting. In mineralocorticoid salt sensitive hypertensive rats, Ca supplementation for 8 weeks attenuated the increase in blood pressure and cardiac hypertrophy and prevented DOC–salt induced sodium volume retention (10). But we did not find a decrease in left ventricular weight in rats that were fed with calcium supplemented diet. This finding was paradoxical with the measurement of blood pressure, PRA and PTH. As in our study, in hypertensive men on Ca supplemented diet; serum ionized Ca did not change but PTH decreased (11).

AII levels were widely variable. Aldosteron levels were not measured. Excretions of urinary Na, K and Ca were not changed with high–Ca diet or low–Ca diet. We did not find any correlation between body weight and blood pressure in each group and all rats. Increase in body weight in rats that were fed with high Ca diet was less than other groups.

As a result, in uninephrectomized DOC –salt hypertension, Ca supplemented diet (4% more prominent) attenuated the increase in blood pressure and this effect continued throughout the study. In the rats on 4% Ca diet, PRA was importantly supressed. However, body weight in this group did not increase as much as in others. PTH levels also decreased in group IV, but the difference was not significant , statistically. Attenuation of increase in blood pressure may be due to suppression of parathyroid gland.

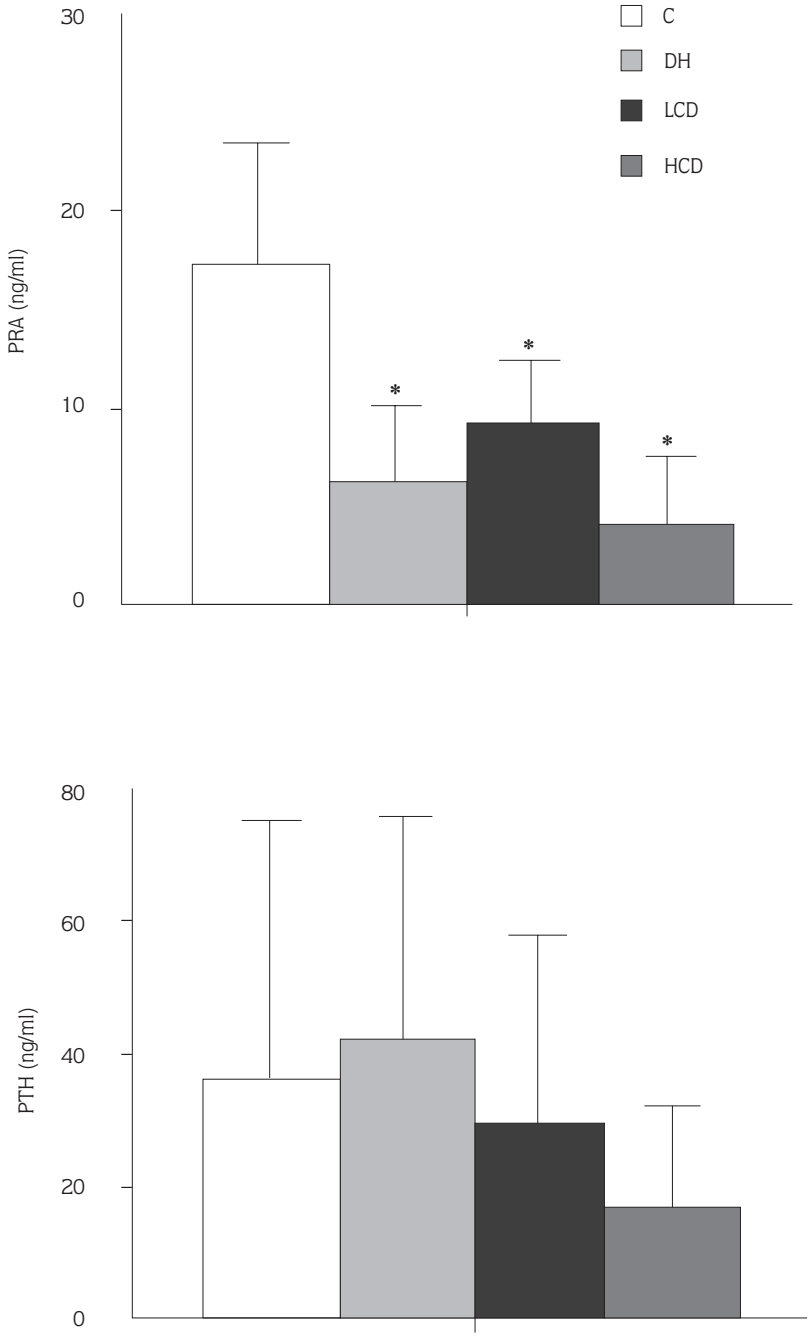

Figure 3. Effect of DOC and dietary–calcium on plasma renin activity (PRA) and plasma parathormon levels (PTH) in unineprectomized rats. C: Control (n=6), DH: DOC + standard diet (n=8), DLC: DOC + Low calcium diet (n=8), DHC: DOC + High calcium diet (n=7). Values are mean ± SD.* P<0.05 vs C.

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