Proc EDTA–ERA (1985) Vol 22

INTERACTION BETWEEN DIETARY SODIUM AND CALCIUM IN BLOOD PRESSURE CONTROL IN ESSENTIAL HYPERTENSION

C Zoccali, D Iellamo, S Parlongo, Q Maggiore (with the technical assistance of S Crucitti and D Postorino)

Divisione di Nefrologia and CNR Centro de Fisiologia Clinica, Reggio Calabria, Italy

Summary

Marked changes in calcium metabolism occurred concurrently with the expected blood pressure responses to sodium in seven 'salt sensitive' patients with essential hypertension: calcium excretion decreased markedly with sodium restriction and rose with sodium load while serum total and plasma ionized calcium showed reciprocal variations. Overall mean arterial pressure was inversely related to ionized calcium. Calcium supplementation (1g/day) had no influence on mean arterial pressure at normal and high sodium intake, however, it reduced the hypotensive effect of sodium restriction. The results suggest that short-term calcium supplementation does not influence blood pressure at free sodium intake in 'salt sensitive' essential hypertensive patients, but it may adversely affect their hypotensive response to low sodium diets.

Introduction

The impact of calcium intake on blood pressure was appreciated in the 1970s when a reduced incidence of arterial hypertension was found in areas with a high water calcium content [1]. Recent evidence of an altered calcium metabolism [2] and of a reduced calcium intake in patients with essential hypertension [3] has renewed interest in this subject.

Sodium is another dietary constituent that has caused major concern as a possible hypertensive factor. Although the debate on the relationship between sodium intake and blood pressure is still ongoing, there is firm evidence that some patients are particularly sensitive to changes in sodium intake (salt sensitive essential hypertensive patients) [4]. Since calcium and sodium have mutual metabolic influences, both at the cellular level and on their external balance, they may also interact in blood pressure control. The present study was designed to find out whether calcium supplements alter the blood pressure response to changes in sodium intake in a group of 'salt sensitive' essential hypertensive patients.

Methods

Seven 'salt sensitive' [4] essential hypertensive patients (6 males and 1 female, age 27–50 years) selected from our outpatient clinic were studied. Five patients had never received antihypertensive drugs and two had been treated with α-methyldopa and two with chlorthalidone plus atenolol respectively, which were stopped one month prior to the study. Patients were given a diet containing about 10mEq/day of sodium, and 25mEq of calcium for three weeks. During the second and the third week the diet was supplemented with 140 and 290mEq/day of NaCl respectively. After an interval of one to two weeks, during which they reverted to their customary diet, patients were asked to adhere again for three weeks to the experimental diet and NaCl was stepwisely increased exactly as before. In addition, on both study periods the experimental diet was supplemented with 1g of elemental calcium/day (calcium Sandoz) or with a placebo in a single blind, randomized, crossover and balanced fashion.

On the seventh, fourteenth and twenty-first day of each study period, between 8.00 and 9.00a.m., patients rested in supine position for 30 minutes and their blood pressure was measured at five minute intervals with an automatic blood pressure recorder (Dinamap, Criticon, Tampa USA). The mean value of the last three readings was considered for the analysis. A blood sample for ionized and total calcium and serum phosphate, sodium, potassium, plasma renin activity and aldosterone measurements was then taken. On the same days, 24 hour urine calcium, phosphate, sodium and potassium excretions were also measured.

Results

As expected, during the control period, mean arterial pressure was significantly lower ($p<0.01$) at low than at normal and high sodium intake. Urinary calcium changed concurrently with sodium intake, being lowest during sodium restriction and highest during sodium load while serum total and ionized calcium showed reciprocal changes (Figure 1). Although much less markedly, serum and urinary phosphate varied in parallel with serum and urinary calcium (Table I). Overall, mean arterial pressure was inversely related to ionized calcium ($r=-0.53$, $p<0.02$). Total calcium showed a similar tendency but the relationship did not achive statistical significance ($r=-0.37$).

During the calcium supplemented period, at normal and high sodium intake, mean arterial pressure was similar to that of the corresponding control periods. However, at low sodium, mean arterial pressure was higher ($p<0.05$) during calcium supplemention (Figure 1). As shown in Figure 1 and in Table I, apart from urinary calcium which was consistently ($p<0.01$) higher throughout the calcium supplemented period, no significant differences were found between the two study periods as for total and ionized calcium, and for serum and urinary sodium, potassium and phosphate. Plasma renin activity and aldosterone showed the expected variations when dietary sodium was changed and were not influenced by calcium supplementation (Table I).

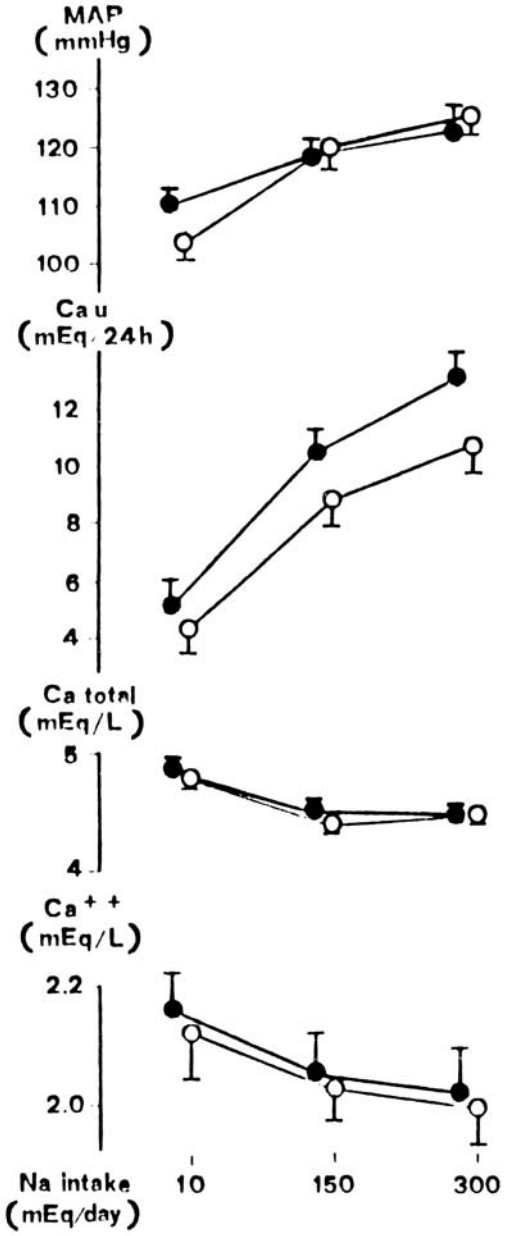

Figure 1. Effects of changes in sodium intake on mean arterial pressure, 24 hour urinary calcium excretion, serum total and plasma ionized calcium in the two study periods. Bars represent SEM. ○ Placebo: ● Calcium

TABLE I. Metabolic effects of changes in sodium intake in the two study periods. Data are expressed as Mean±SEM

	Control Period Na intake (mEq/day)			Calcium Supplemented Period Na intake (mEq/day)		
	10	150	300	10	150	300
Serum sodium (mEq/L)	139.0 ± 1.2	141.0 ± 1.4	139.0 ± 0.8	140.0 ± 1.2	142.0 ± 1.1	140.0 ± 1.3
Serum potassium (mEq/L)	4.1 ± 0.2	4.1 ± 0.2	3.9 ± 0.1	3.9 ± 0.1	4.0 ± 0.1	3.9 ± 0.1
Serum phosphate (mg/dl)	3.5 ± 0.1	3.2 ± 0.2	3.3 ± 0.2	3.5 ± 0.1	3.4 ± 0.1	3.3 ± 0.1
Urine sodium (mEq/24h)	16.0 ± 3.0	176.0 ±13.0	316.0 ±24.0	20.0 ± 4.0	159.0 ±13.0	301.0 ± 9.0
Urine potassium (mEq/24h)	47.0 ± 3.0	56.0 ± 5.0	56.0 ± 7.0	49.0 ± 3.0	49.0 ± 6.0	55.0 ± 4.0
Urine phosphate (mg/24h)	611.0 ±37.0	632.0 ±40.0	657.0 ±38.0	599.0 ±13.0	696.0 ±33.0	667.0 ±26.0
PRA (ng/ml/h)	3.2 ± 0.6	1.1 ± 0.2	0.9 ± 0.2	3.4 ± 0.6	0.9 ± 0.1	0.8 ± 0.1
Plasma Aldosterone (pg/ml)	193.0 ±15.0	91.0 ±14.0	70.0 ±14.0	186.0 ±15.0	93.0 ±11.0	77.0 ±16.0

Discussion

Marked changes in calcium metabolism occurred concurrently with the expected blood pressure responses to sodium in 'salt sensitive' essential hypertensive patients: calcium excretion decreased markedly with sodium restriction and rose with sodium load, while serum total and ionized calcium showed reciprocal variations.

The changes in calcium excretion we have observed appear much greater than previously reported in normal subjects [5]. Renal handling of calcium is related to that of sodium, therefore the increased rate of calcium excretion may be the consequence of the same renal tubular derangements which cause the "exaggerated natriuresis' in essential hypertensive patients. In this respect, both the exaggerated calciuresis and natriuresis may represent the renal response to the putative natriuretic hormone, which, according to De Wardener [6], has a key role in the pathogenesis of essential hypertension. That calcium may be involved in the blood pressure response to dietary sodium changes in 'salt sensitive' hypertensive patients is suggested by the inverse relationship we found between mean arterial pressure and ionized calcium. If changes in calcium metabolism are instrumental to the blood pressure response promoted by variations in sodium intake, then calcium supplementation might alter the blood pressure response to sodium. The fact that, in the short-term of this experiment, we did not observe any influence of calcium supplementation on blood pressure at

normal and high sodium intake would speak against such a possibility. However, calcium has been found to reduce blood pressure in young hypertensive patients when given for considerably longer periods [7].

Perhaps the most intriguing finding of our study is that calcium supplementation prevented in part the hypotensive effect of sodium restriction. Renin and aldosterone secretions are known to be calcium dependent, but we did not find any measurable effect of calcium supplementation on the renin-aldosterone axis at low as well as at normal and high sodium intake. Although unexplained by the present study, the interference of calcium with the hypotensive response to sodium deprivation has a counterpart in animal experiments: indeed, blood pressure does not fall in spontaneous hypertensive rats given a low salt-high calcium diet [8].

References

1 Stitt FW, Clayton DJ, Crawford MD et al. *Lancet 1973; i:* 122
2 McCarron DA, Pingree PA, Rubin RJ et al. *Hypertension 1980; 2:* 162
3 McCarron DA, Morris CD, Henry HJ et al. *Science 1984; 224:* 1392
4 Kawasaki T, Delea CS, Bartter F et al. *Am J Med 1978; 64:* 193
5 Lemann J, Adams ND, Gray RW. *N Engl J Med 1979; 301:* 535
6 DeWardener HE, McGregor GA. *Kidney Int 1980; 18:* 1
7 Belizan JM, Villar J, Pineda O et al. *JAMA 1983; 249:* 1161
8 Hann SA, Schneidman RJ, McCarron DA. *Clin Res 1984; 32:* 36A