

# Dietary Calcium Supplementation As A Treatment For Mild Hypertension

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**Abstract:** The blood pressure responses of 19 mildly hypertensive (diastolic blood pressure 90–104 mmHg) individuals to treatment with either 1200 mg of elemental calcium supplementation or placebo were assessed weekly in a 6-month randomized, double-blind, placebo-controlled crossover study. Both groups showed a decrease in blood pressure (calcium treated:  $6 \pm 12$  mmHg systolic,  $7 \pm 7$  mmHg diastolic; and placebo controlled:  $9 \pm 14$  mmHg systolic,  $9 \pm 8$  mmHg diastolic). Differences between the two groups were not significant ( $P > 0.1$ ). There were no adverse effects to either treatment. This study does not support the hypothesis that dietary calcium supplementation is more effective than placebo in reducing blood pressure in mildly hypertensive individuals. (J Am Board Fam Pract 1991; 4:145-50.)

Approximately 58 million Americans, or nearly 25 percent of the adult population in the United States, have the diagnosis of hypertension.<sup>1</sup> It is clearly recognized that individuals with even mild hypertension (diastolic blood pressure 90–104 mmHg) are at an increased risk for coronary artery disease.<sup>2</sup> Yet, the Multiple Risk Factor Intervention Trial showed that persons treated for mild hypertension had a higher morbidity and mortality than those who were left untreated.<sup>3</sup> As one result of this finding, the 1988 Report of the Joint National Committee on the Detection, Evaluation, and Treatment of High Blood Pressure emphasized the importance of nonpharmacologic methods for the treatment of mild hypertension.<sup>2</sup>

The concept that dietary changes could affect blood pressure became attractive in light of this background. A hypothesis that dietary calcium deficiency was associated with hypertension was presented.<sup>4-6</sup> Epidemiologic evidence<sup>5-10</sup> suggested an association between a low dietary calcium intake and the presence of elevated blood pressure. Other epidemiologic studies asserted that low dietary calcium played a contributory role in association with magnesium,<sup>11</sup> alcohol,<sup>12,13</sup>

lead,<sup>14</sup> and the ratio of sodium to potassium.<sup>15</sup> Animal studies on spontaneously hypertensive rats supported the calcium-hypertension relation,<sup>16-18</sup> whereas others disagreed entirely with the hypothesis.<sup>19-21</sup> Several human experimental studies using dietary calcium supplementation in normotensive subjects<sup>22-24</sup> showed a significant decrease in blood pressure. More recent studies<sup>25-28</sup> using a randomized, placebo-controlled, crossover methodology have reported a decrease in blood pressure with dietary calcium supplementation, while several other studies<sup>29-31</sup> showed no difference.

Because of the finding in published studies that the response of blood pressure to dietary calcium supplementation was so variable, a need for more studies was identified.<sup>19</sup> To address this need, we examined for a 6-month period the efficacy of dietary calcium supplementation as a treatment for mild hypertension using a randomized, double-blind, placebo-controlled crossover design.

## Methods

Patients between the ages of 30 and 65 years previously given the diagnosis of mild hypertension were identified by a computer search at the Family Practice Center, University of California, Davis Medical Center, Sacramento. Mild hypertension was defined as a diastolic blood pressure in the range of 90–104 mmHg.<sup>32</sup> Enrollment in the study was offered through recruitment of the study population from that list. A recruitment process through provider selection was also made

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at the Family Care Center, Shasta-Cascade General Hospital, Redding, California. Informed consent through each institutional review board was obtained. Criteria for exclusion from the study were the following: myocardial infarction within 6 months, unstable angina, stable angina treated with a calcium channel blocker, third-degree heart block, serum creatinine levels greater than 354  $\mu\text{mol/L}$  (4.0 mg/dL), serious hematologic or hepatic disease, unstable hypertensive end-organ damage, or any condition resulting in an abnormal calcium metabolism (e.g., hyperparathyroidism, parathyroidectomy).

We performed a complete history, physical examination, and review of the medical records for each person upon entry into the study. Patients receiving antihypertensive medications were asked to discontinue their medication for the duration of the study beginning 2 weeks before study entry. Blood pressures for all subjects were measured every week for 2 weeks to insure that the blood pressure measurements did not rise dramatically. A baseline assessment of compliance was measured by instructing the subject to take one tablet of placebo daily during this 2-week period. Bottles were brought to each visit, and a pill count was the method for validating compliance. Subjects were accepted into the study if their average diastolic blood pressure measurements were in the range of 90–104 mmHg and if 75 to 100 percent of the placebo tablets were taken during the 2-week period.

Laboratory tests included a complete blood count and chemistry panel, which included serum glucose, potassium, sodium, calcium, and blood urea nitrogen (BUN). Magnesium, phosphate, and plasma renin levels were also drawn. Values for the complete blood count and the chemistry panel were determined using an autoanalyzer technique. Renin values were determined by radioimmune assay. Each subject's baseline di-

**Table 1. Mean Blood Pressure Values for Patients Receiving Calcium versus Placebo.\***

	Blood Pressure (mmHg)		
	All Patients Entry	Calcium Group (1200 mg/day)	Placebo Group
Systolic	146 $\pm$ 13	140 $\pm$ 15	140 $\pm$ 19
Diastolic	95 $\pm$ 4	88 $\pm$ 7	87 $\pm$ 8

\*No significant difference between groups ( $P > 0.1$ )

**Table 2. Mean Systolic Blood Pressure Values (mmHg) for Patients Receiving Calcium versus Placebo.\***

Week	Calcium Group	Placebo Group
Entry	146 $\pm$ 13	145 $\pm$ 14
1	143 $\pm$ 12	144 $\pm$ 12
2	142 $\pm$ 14	142 $\pm$ 14
3	140 $\pm$ 12	140 $\pm$ 16
4	138 $\pm$ 15	141 $\pm$ 18
5	141 $\pm$ 11	140 $\pm$ 16
6	140 $\pm$ 16	138 $\pm$ 22
7	137 $\pm$ 17	140 $\pm$ 16
8	139 $\pm$ 12	138 $\pm$ 17
9	141 $\pm$ 14	139 $\pm$ 19
10	140 $\pm$ 12	141 $\pm$ 18
11	139 $\pm$ 13	140 $\pm$ 22
12	138 $\pm$ 12	140 $\pm$ 15
13	138 $\pm$ 14	138 $\pm$ 22

\*No significant difference between groups ( $P > 0.1$ )

etary intake of sodium, potassium, calcium, phosphate, and magnesium was measured by a 1-week prospective dietary survey and was analyzed by hand using Bowe and Church's *Food Values of Portions Commonly Used*<sup>33</sup> as the reference.

Twenty-eight subjects were then randomly assigned to either the placebo or treatment group, and they were required to return to the clinic every week during the study. Those in the treatment group received 1200 mg of elemental calcium per day in the form of calcium carbonate. Those in the control group received a placebo made of lactate. After a 3-month period, the groups switched in a crossover fashion. There was a 1-week washout phase between the crossover periods. Subjects were then followed weekly for 3 additional months. Complete chemistry panels including serum glucose, potassium, sodium, calcium, BUN, magnesium, and phosphate were obtained at the crossover period and at the end of the study to assess changes in these values.

During the weekly clinic visits, systolic and diastolic blood pressure readings were taken three times (to the 5th Korotkoff sound) on the right arm of each patient using a standard aneroid sphygmomanometer while the patient was seated.<sup>32</sup> Patients brought their medication, which was counted on randomly selected days, to determine their degree of compliance. An open-ended question regarding side effects was also asked at each visit. The frequency, duration, se-

**Table 3. Mean Diastolic Blood Pressure Values (mmHg) for Patients Receiving Calcium versus Placebo.\***

Week	Calcium Group	Placebo Group
Entry	95 ± 5	94 ± 6
1	92 ± 7	91 ± 7
2	92 ± 6	93 ± 8
3	90 ± 9	91 ± 9
4	87 ± 8	89 ± 11
5	86 ± 8	87 ± 8
6	87 ± 9	88 ± 7
7	88 ± 5	91 ± 4
8	87 ± 6	90 ± 6
9	86 ± 5	89 ± 7
10	85 ± 7	87 ± 8
11	87 ± 8	88 ± 9
12	88 ± 7	87 ± 6
13	88 ± 8	87 ± 8

\*No significant difference between groups ( $P > 0.1$ )

verity, and treatment of any side effect were noted in the chart.

Patients whose diastolic blood pressure exceeded 105 mmHg on two successive visits were removed from the study. Patients who failed to keep more than two weekly visits in a given month or who developed symptomatic hypertension, other systemic diseases, or serious complications of hypertension were also removed from the study. Five patients completed more than one-

half of the study and were included for the purposes of data collection. We used the following rationale for their inclusion: 3 subjects were two visits short of completing the calcium phase, after fully completing the placebo phase, and they met the criteria for all other phases of the study; 2 subjects missed three and four visits, respectively, in the placebo phase, having fully completed the calcium phase.

The blood pressure data were analyzed using analysis of variance (ANOVA) for the 19 subjects who fully completed the study.<sup>34</sup> A second analysis was performed using the 5 additional subjects who completed more than one-half the study to insure that their inclusion would not alter the findings of the 19. Descriptive data were analyzed using Student's paired t-test and presented as mean plus or minus standard deviation. To determine sample size for the group, the  $P$  value was 0.5 and the power value was 0.5.

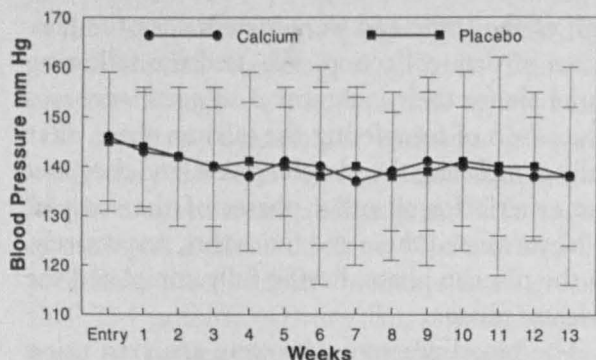
### Results

Twenty-eight patients initially enrolled in the study, 21 from Sacramento and 7 from Redding. Nineteen fully completed the study, an additional 5 completed more than one-half, and 4 dropped out in the early stages. The reasons for dropping out were geographic movement (2 patients), the development of headache without elevation in

**Table 4. Mean Serum Laboratory Values for Patients at Baseline and after Calcium and Placebo (n = 24).\***

	Baseline	After Calcium	After Placebo
Calcium, mmol/L (mg/dL)	2.40 ± 0.12 (9.6 ± 0.5)	2.35 ± 0.12 (9.4 ± 0.5)	2.32 ± 0.12 (9.3 ± 0.5)
Total protein, g/L (g/dL)	75 ± 11 (7.5 ± 1.1)	75 ± 10 (7.5 ± 1.0)	76 ± 11 (7.6 ± 1.1)
Albumin, g/L (g/dL)	44 ± 6 (4.4 ± 0.6)	45 ± 7 (4.5 ± 0.7)	44 ± 6 (4.4 ± 0.6)
Sodium, mmol/L (mEq/L)	143 ± 4 (142.7 ± 4.2)	144 ± 5 (144.2 ± 4.5)	143 ± 5 (143.4 ± 4.7)
Phosphate, mmol/L (mg/dL)	1.05 ± 0.20 (3.2 ± 0.7)	1.05 ± 0.15 (3.2 ± 0.5)	1.05 ± 0.20 (3.2 ± 0.7)
Potassium, mmol/L (mEq/L)	4.3 ± 0.6 (4.3 ± 0.6)	4.2 ± 0.4 (4.2 ± 0.4)	4.3 ± 0.5 (4.3 ± 0.5)
Glucose, mmol/L (mg/dL)	5.3 ± 1.1 (96.2 ± 19.1)	5.2 ± 1.2 (94.3 ± 21.1)	5.3 ± 1.0 (95.7 ± 18.4)
BUN, mmol/L (mg/dL)	4.6 ± 1.0 (12.8 ± 2.9)	4.6 ± 1.0 (13.1 ± 2.6)	4.6 ± 1.0 (12.9 ± 2.8)
Creatine, μmol/L (mg/dL)	100 ± 2 (1.1 ± 0.02)	90 ± 3 (1.0 ± 0.03)	100 ± 2 (1.1 ± 0.02)
Renin, ng/(L · s) (ng/mL/h)	0.70 ± 1.20 (2.5 ± 4.3)	0.75 ± 1.42 (2.7 ± 5.1)	0.78 ± 1.56 (2.8 ± 5.6)

\*No significant difference ( $P > 0.1$ ).



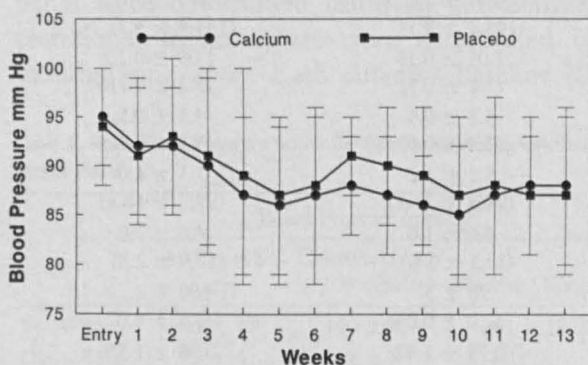
**Figure 1.** Mean systolic blood pressure values of patients while receiving calcium versus placebo.

blood pressure in the prestudy evaluation stage (1), and the lack of consent from the patient's primary care physician (1). The reasons 5 patients did not complete the entire phase were geographic movement (3 subjects) and change in work schedule (2). For the purposes of the study, the 19 who fully completed and the 5 who completed more than one-half of the study were analyzed.

The mean age of subjects ( $n = 24$ ) was  $47.5 \pm 12.4$  years. There were 16 women and 8 men in the group. The ethnic distribution was 16 whites (67 percent), 5 blacks (21 percent), 2 Hispanics (8 percent), and 1 Asian (4 percent).

The mean blood pressure measurement of all patients upon entry to the study was  $146 \pm 13$  mmHg systolic and  $95 \pm 4$  mmHg diastolic. For the group, mean baseline dietary intake values were elemental calcium,  $551.6 \pm 236.8$  mg/d; sodium,  $1907.6 \pm 603.7$  mg/d; phosphate,  $909.8 \pm 291.9$  mg/d; potassium  $1768.7 \pm 566.8$  mg/d; and magnesium,  $175 \pm 128.9$  mg/d.

Mean serum baseline laboratory values were calcium,  $2.4 \pm 0.12$  mmol/L ( $9.6 \pm 0.5$  mg/dL);



**Figure 2.** Mean diastolic blood pressure values of patients while receiving calcium versus placebo.

serum sodium,  $143 \pm 4$  mmol/L ( $142.7 \pm 4.2$  mEq/L); serum phosphate,  $1.05 \pm 0.20$  mmol/L ( $3.2 \pm 0.7$  mg/dL); serum potassium,  $4.3 \pm 0.6$  mmol/L ( $4.3 \pm 0.6$  mEq/L); and serum magnesium,  $0.90 \pm 0.20$  mmol/L ( $1.8 \pm 0.4$  mg/dL). Other baseline values were plasma renin,  $0.70 \pm 1.20$  ng/(L·s) ( $2.5 \pm 4.3$  ng/mL/h); serum creatinine,  $100 \pm 2$   $\mu$ mol/L ( $1.1 \pm 0.02$  mg/dL); serum BUN,  $4.5 \pm 1.0$  mmol/L ( $12.8 \pm 2.9$  mg/dL).

Mean blood pressure values of subjects measured weekly while receiving calcium supplementation for a 3-month period were  $140 \pm 15$  mmHg systolic and  $88 \pm 7$  mmHg diastolic. For patients receiving the placebo, the mean blood pressure values for the 3-month period were  $140 \pm 19$  mmHg systolic and  $87 \pm 8$  mmHg diastolic. There was no significant difference between these groups ( $P > 0.1$ ) (Table 1). For their weekly blood pressure values, both groups showed decreases in systolic and diastolic blood pressure measurements that were not significantly different (Figures 1 and 2, Tables 2 and 3).

The laboratory value for serum calcium after 3 months of dietary calcium supplementation was  $2.35 \pm 0.12$  mmol/L ( $9.4 \pm 0.5$  mg/dL) and did not differ significantly from serum calcium levels after 3 months of placebo ( $2.32 \pm 0.12$  mmol/L [ $9.3 \pm 0.5$  mg/dL]). Similarly, the laboratory values for serum sodium, phosphate, potassium, and magnesium did not differ significantly among baseline values after 3 months of calcium supplementation or after 3 months of placebo (Table 4).

## Discussion

It is debateable whether dietary calcium supplementation is an effective treatment for patients with mild hypertension.<sup>19</sup> On the one hand, there is evidence that nutritionally the lack of dietary calcium is most closely associated with hypertension.<sup>5</sup> Double-blind, placebo-controlled crossover studies have affirmed the efficacy of dietary calcium supplementation as a treatment for adults with mild hypertension.<sup>25-28</sup> On the other hand, similar studies,<sup>29-31</sup> including this one, report no differences between calcium and placebo groups.

The strengths of this study included the design: a randomized, double-blind, placebo-controlled crossover protocol. The study time of 6 months (each subject spending 3 months in the treatment

group and 3 months in a control group) with blood pressures followed weekly was an additional strength. Assessing each patient's dietary intake using a 1-week prospective diary was advantageous compared with using a 24-hour dietary recall. Having the study done at two centers had both advantages and disadvantages. An advantage was a more heterogeneous population, which represented both an urban and suburban distribution. A disadvantage was the variability in the measurement of blood pressures between the Sacramento and Redding examiners. Other weaknesses in the study included the possibility of selection bias. Eighty percent of the population at the Family Practice Clinic was on public assistance. We did not use a random-zero blood pressure measurement device, so examiner bias in blood pressure measurements was a possible weakness. This weakness, however, was minimized by the use of a double-blind protocol in the study design.

Studies that have reported the efficacy of dietary calcium as a treatment for mild hypertension have also showed individual variability in blood pressure response to calcium.<sup>25-28,35</sup> Further studies are needed to clarify which factors predict a lowering of blood pressure in response to calcium. Until that time, we agree with Kaplan and Meese<sup>19</sup> that routine supplementation with dietary calcium should not be advocated for patients with mild hypertension.

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