The effect of dietary calcium supplementation on serum calcium, phosphorus, and alkaline phosphatase concentrations in a rural black population\textsuperscript{1-3}

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ABSTRACT In a rural community, where low calcium intakes and a high prevalence of hypocalcemia elevated alkaline phosphatase values and hypocalciuria had previously been documented, two groups of 30 black school children were supplemented with calcium (500 mg/day) or a placebo for a period of 3 months. No change in serum calcium or alkaline phosphatase values occurred in the placebo group, while a significant rise in mean serum calcium and fall in mean alkaline phosphatase concentrations was found in the calcium-supplemented group over the 3-month trial. No difference in growth velocities in the two groups of children was noted over the period. These results suggest that the prevalence of biochemical abnormalities in the rural population is related to a low dietary calcium intake which can be corrected by a supplement of oral calcium only. \textit{Am. J. Clin. Nutr.} 34: 2187-2191, 1981.

KEY WORDS Dietary calcium, hypocalcemia, alkaline phosphatase, calcium supplementation

Dietary calcium requirements of children are difficult to define (1), thus recommended calcium intakes vary considerably from 400 to 800 mg/day. Even so, there has until recently been little evidence that low calcium diets are disadvantageous to children (2). However, in the past decade two infants suffering from calcium deficiency rickets have been reported (3, 4) and we have recently suggested that bone deformities and biochemical abnormalities (hypocalcemia, elevated alkaline phosphatase concentrations, and hypocalciuria) in rural black children might be due to low dietary intakes (5, 6). Calcium supplementation of children on low calcium diets is generally considered to have no effect on growth velocity (7, 8) although reports to the contrary have appeared (9, 10). Little or no information is available on the effects of calcium supplementation on biochemical variables in children. We report here the effect of calcium supplementation (500 mg/day) on serum calcium, phosphorus, and alkaline phosphatase concentrations and on the urinary excretion of these variables in children on low calcium diets who were supplemented for 3 months.

Methods

Two groups of 30 children each were randomly selected from two classes in the lower primary school in Driefontein. The ages of the two groups of children ranged from 9 to 12 yr. The school children from Driefontein, a rural farming community in the southeastern areas of the Transvaal, South Africa, had previously been shown to have a high prevalence of hypocalcemia.

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and high alkaline phosphatase values and to have a low dietary calcium intake (those with biochemical abnormalities having a mean intake of 125 mg/day, and those with normal biochemistry having a mean intake of 337 mg/day (6). Mean dietary phosphorus intakes were estimated to be 816 and 914 mg/day, respectively. Dietary vitamin D intakes were very low as the diets were largely vegetable in origin, however circulating 25-hydroxyvitamin D concentrations (28.9 ± 8.7 ng/ml) were well within the normal range (12 to 50 ng/ml), as skin coverage was minimal and sunlight exposure high. One group of children received a calcium supplement of 300 mg/day for 3 months, while the other group received a placebo of identical size, shape, and packing. The calcium was provided in the form of one tablet of Calcium Sandoz Forte daily (Table 1). The placebo and calcium tablets were handed out daily to the children in the trial by the teachers in each of the classes. On Fridays two extra tablets were given to the children to be taken over the weekend. The trial was only continued for 3 months as this was the longest period the children had at school between vacations. No dietary advice was given during the study, but the diets of rural Black children are rather monotonous with very little variation occurring from day to day.

Anthropometric data, blood and random urine samples were obtained at the start of the trial and then at monthly intervals throughout the study. On the day that the samples were collected, the tablets were withheld until after the specimens had been obtained. The urine and blood samples were collected at least 3 to 4 h after breakfast, as it was not possible to ensure an overnight fast before venesection. Serum and urine calcium were measured by atomic absorption spectrophotometry, and serum alkaline phosphatase, serum and urine phosphorus, and creatinine were measured on a Technicon Auto Analyser II by standard methods.

Results

The mean ages, heights, and weights of the two groups are shown in Table 2. The two groups of children were similar in age and anthropometric measurements at the start of the trial, and the male to female ratios were the same in both groups (14 boys and 16 girls).

At the start of the trial serum calcium, phosphorus, and alkaline phosphatase concentrations were similar in the two groups (Table 3). Three children in each group were hypocalcemic (< 9.0 mg/dl), while six and seven children in the placebo and calcium-supplemented groups, respectively, had elevated alkaline phosphatase values (> 300 IU/l). Two children in the placebo group and one in the calcium supplemented group were hypophosphatemic (< 3.6 mg/dl) at the start of the trial.

The mean urinary calcium excretion was similar in the two groups (urinary calcium excretion was assessed by the urinary calcium creatinine ratio in random urine samples). Both groups had a number of children whose urinary calcium excretion was low (< 0.03) (11), 13 and 20 children being hypocalciuric in the placebo and calcium supplemented groups, respectively. Urinary phosphate excretion, as assessed by the phosphorus/creatinine clearance ratio was normal in all children in both groups (Table 4).

Over the 3-month period of calcium supplementation, no difference in growth velocity was found between the two groups; however, the placebo group was significantly

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**TABLE 1**

<table>
<thead>
<tr>
<th>Constituents</th>
<th>Calcium Sandoz Forte</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calcium carbonate</td>
<td>0.300</td>
<td></td>
</tr>
<tr>
<td>Calcium lactate-glucose</td>
<td>2.940</td>
<td></td>
</tr>
<tr>
<td>Citrus flavor</td>
<td>0.020</td>
<td>0.020</td>
</tr>
<tr>
<td>Saccharine sodium</td>
<td>0.022</td>
<td>0.022</td>
</tr>
<tr>
<td>Polyethylene glycol</td>
<td>0.200</td>
<td>0.200</td>
</tr>
<tr>
<td>Sucrose</td>
<td>0.868</td>
<td>0.868</td>
</tr>
<tr>
<td>Sodium bicarbonate</td>
<td>1.000</td>
<td>2.220</td>
</tr>
<tr>
<td>Citric acid</td>
<td>1.650</td>
<td>3.570</td>
</tr>
</tbody>
</table>

**TABLE 2**

Mean age, height, and mass of the two groups

<table>
<thead>
<tr>
<th>Height (cm) (mean ± SD)</th>
<th>Mass (kg) (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age years</td>
<td></td>
</tr>
<tr>
<td>Placebo group</td>
<td></td>
</tr>
<tr>
<td>10.4 ± 0.86</td>
<td>131.9 ± 5.80</td>
</tr>
<tr>
<td>Calcium group</td>
<td></td>
</tr>
<tr>
<td>9.8 ± 0.85</td>
<td>130.2 ± 6.46</td>
</tr>
<tr>
<td>Difference between</td>
<td></td>
</tr>
<tr>
<td>groups</td>
<td>t = 1.41</td>
</tr>
<tr>
<td></td>
<td>t = 0.90</td>
</tr>
<tr>
<td></td>
<td>p &gt; 0.05</td>
</tr>
<tr>
<td></td>
<td>t = 1.25</td>
</tr>
<tr>
<td></td>
<td>t = 1.87</td>
</tr>
<tr>
<td></td>
<td>p &gt; 0.15</td>
</tr>
<tr>
<td></td>
<td>p &gt; 0.10</td>
</tr>
<tr>
<td></td>
<td>p &lt; 0.05</td>
</tr>
</tbody>
</table>
TABLE 3
Mean serum calcium, phosphorus, and alkaline phosphatase values in the two groups of children

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Calcium (mg/dl)</th>
<th>Phosphorus (mg/dl)</th>
<th>Alkaline phosphatase (IU/l*)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group</td>
<td>Mean ± SD</td>
<td>Group</td>
</tr>
<tr>
<td>Placebo</td>
<td></td>
<td>9.48 ± 0.59</td>
<td>Placebo</td>
</tr>
<tr>
<td></td>
<td>9.43 ± 0.59</td>
<td>9.39 ± 0.42</td>
<td>4.56 ± 0.67</td>
</tr>
<tr>
<td></td>
<td>9.51 ± 0.49</td>
<td>10.02 ± 0.40</td>
<td>4.70 ± 0.55</td>
</tr>
<tr>
<td></td>
<td>0-1: t = 1.20; p &gt; 0.1</td>
<td>0-2: t = 1.60; p &gt; 0.05</td>
<td>0-1: t = 2.03; p &lt; 0.05</td>
</tr>
<tr>
<td></td>
<td></td>
<td>0-3: t = 0.71; p &gt; 0.45</td>
<td></td>
</tr>
</tbody>
</table>

* Geometric mean and range.

TABLE 4
Mean urinary calcium and phosphorus excretion in the two groups of children

<table>
<thead>
<tr>
<th>Table 4</th>
<th>Uca*/Ucr</th>
<th>Calcium/Cer</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group</td>
<td>Mean ± SD</td>
</tr>
<tr>
<td>Placebo</td>
<td>0.033</td>
<td>± 0.014</td>
</tr>
<tr>
<td></td>
<td>0.014-0.077</td>
<td>0.013-0.037</td>
</tr>
<tr>
<td></td>
<td>0.058-0.037</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.01-0.045</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.009-0.027</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.00-0.05</td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.0005</td>
<td></td>
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<tr>
<td></td>
<td>0.0005</td>
<td></td>
</tr>
</tbody>
</table>

* Geometric mean and range. Uca/Ucr: (urinary calcium/creatinine ratio); Cp/Cer: (urinary phosphate clearance/urinary creatinine clearance ratio).

heavier than the calcium supplemented group at the end of the trial. Striking changes in serum calcium concentrations were noted 1 month after the start of the trial, and the differences between the two groups continued to increase throughout the study. The mean serum calcium concentration of the placebo group did not alter significantly during the 3-month period. However, in the calcium supplemented group, the mean serum calcium was significantly greater after one month (9.88 mg/dl compared to 9.53 mg/dl, p < 0.0005) and continued to rise throughout the study, reaching a mean of 10.02 mg/dl at the end of 3 months. Mean serum phosphorus concentration in the placebo group rose during the study from 4.44 to 4.70 mg/dl, while in the calcium supplemented group it remained constant except for an unexplained drop 1 month after the start of the trial. The mean alkaline phosphatase concentration in the calcium supple-
mented group fell significantly over the trial period from 265 to 247 IU/l (p < 0.005),
while values remained constant in the placebo group. The mean percentage change in
alkaline phosphatase values over the 3-month period was −6.90 and +2.16% in the calcium-
supplemented and placebo groups, respectively.

During the trial, urinary calcium excretion decreased significantly in the placebo group
(p < 0.0005), while it remained constant in the calcium-supplemented group (p > 0.10).
Urinary phosphate excretion did not change in the placebo group over the 3-month trial;
however, there was a significant fall in phosphate excretion in the calcium supplemented
group (p < 0.0005) (Table 4).

Discussion

In a previous study (6), we found that school children in Driefontein had a high
prevalence of hypocalcemia (13.2%), elevated alkaline phosphatase concentrations (41.5%)
and hypocalciuria (76.2%), while dietary calcium intakes ranged from a mean of 125 to
337 mg/day in biochemically abnormal and biochemically normal children, respectively.
It was postulated that the biochemical abnormalities were related to the low calcium con-
tent of the rural diet, which consisted mainly of semirefined corn with almost a total ab-
sence of milk and milk-related products. In order to substantiate this hypothesis, a daily
calcium supplement (500 mg/day) was given to school children in their rural environment
over a 3-month period. A supplement of 500 mg/day was chosen to increase the mean
calcium intake to that approaching the recommended daily allowance of 800 mg (12).
This supplement resulted in a significant rise in the mean serum calcium concentration and
fall in the mean serum alkaline phosphatase value, while there was no change in these
variables in the placebo group. These observations indicate that an increase in the dietary
calcium intake alone to approximately the Recommended Daily Allowance corrected
the low mean serum calcium concentration. Thus an impairment of calcium absorption
(e.g., due to a high phytate content of the diet) is unlikely to be the etiology of the high
prevalence of biochemical abnormalities in

the children in Driefontein. The persistently
low urinary calcium excretion throughout the
study despite the rapid correction of serum
calcium concentrations would suggest that
calcium is being taken up avidly by bone.

Phosphate excretion by the kidney did not
change significantly in the placebo group
over the study period, while in the calcium-
supplemented group excretion decreased sig-
nificantly suggesting that parathyroid hor-
more secretion decreased in association with
the rise in serum calcium. Unfortunately nei-
ther parathyroid hormone concentrations nor
urinary cyclic AMP excretion were measured
during the study, and thus the presumed fall
in parathyroid hormone activity could not be
confirmed.

Calcium supplementation had no effect on
height gain over the 3-month period, thus
confirming the findings of the majority of
previous workers (7, 8, 13, 14). It is, however,
realized that the duration of supplementation
may have been insufficient to have allowed
differences in growth velocity to have becom
manifest. Further studies over a prolonged
period to assess the effect of calcium supple-
mentation on growth and bone mineral den-
sity are at present being planned.

Walker et al. (15) had previously noted
that serum calcium values in both black chil-
dren and adults in South Africa tended to be
lower than those in whites, but they did not
consider this to be a reflection of low body
stores. Rather they believed that it was due
to decreased input into the serum from the
gastrointestinal tract because of decreased di-
etary calcium intake. This argument is unten-
able for several reasons. First, because in the
present study the last calcium supplement
before the blood determination being per-
formed had been 24 h previously. Thus any
transient rise in serum calcium due to in-
increased absorption from the supplement
would have returned to basal levels by the
time of the determination (16, 17). Second, if
there were no alteration in bone metabolism
due to low calcium intakes as has been sug-
gested (15), the slight but significant decrease
in alkaline phosphatase values during cal-
cium supplementation in the present study is
difficult to explain.

These findings are strong evidence for the
hypothesis that the high prevalence of abnor-
mal biochemical variables in the children of Driefontein is due to dietary calcium deficiency. As far as the authors are aware, this is the first report of alterations in serum alkaline phosphatase values due to calcium supplementation, and may account for the reported higher normal values of alkaline phosphatase in children from developing countries (18), where calcium intakes are often low.

The authors thank the teachers and students of the Cabangani Primary School for their cooperation, Professor J. D. L. Hansen for his encouragement, and Sandoz (Pty) Ltd. for their supply of Calcium Sandoz and the placebo.

References