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Calcium supplementation amongst postmenopausal women: Effect on serum calcium, phosphorus and magnesium level

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Abstract

This study assessed the effect of calcium supplementation towards the change in serum calcium, phosphorus and magnesium level. We carried out a randomized controlled trial of calcium supplementation in 113 postmenopausal women for 24 months period study. Subjects were randomly assigned into two groups. Subjects in Calcium Supplemented Group (CSG) were to take calcium supplement (1200 mg/day) while the Control Group were not given any placebo and advised to continue with their regular diet. The study showed that calcium supplementation helps to increased daily intake of calcium amongst the subject which in results helping to maintain the serum calcium level within normal range. The serum magnesium and phosphorus level in this study were kept at a normal range although there is a slight decrease in serum phosphorus levels may be due to a reduction in the daily intake of the mineral.

Introduction

The use of calcium supplements from pills, chewable tablets and other formulation has increased because the community has become concerned about calcium deficiency in their bone health. In Malaysia, consumption of calcium supplements is gaining popularity as there were 35.7% (Foo and Zaitun, 2000) and 78% (Chee *et al*., 1998) postmenopausal women in the study who took calcium supplement on a regular basis. During the next decade, the increasing awareness of the importance of calcium supplementation in preventing osteoporosis will further expand the market.

The role of nutritional factors in the etiology of osteoporosis is controversial. However adequate nutrition does influence all aspects of bone health throughout human life cycle. Calcium is particularly important in elderly women because low dietary intake have been associated with reduced bone mineral density (BMD) (Dawson-Hudges *et al*., 1990; Prince *et al*., 1995; Reid *et al*., 1995). Postmenopausal women need to obtain sufficient amounts of calcium to maintain bone health and suppress parathyroid hormone (PTH) (Mc Kane *et al*., 1996). In addition to its function in building and maintaining bones and teeth, calcium also has numerous metabolic roles in cells and in other tissues (Nordin, 1997). Even though only small amounts of calcium required for these roles, it is good to remember that it also gives a big impact to the calcium homeostasis.

Phosphorus and magnesium are among minerals that have been proposed as having an important role in bone metabolisms. Phosphorus, as phosphates combine with calcium ions to form hydroxyapatite, the major inorganic molecule in teeth and bones. Magnesium (Mg) is an essential intracellular cation, a cofactor of many basic cellular processes, particularly those involving energy metabolisms (Heaney, 2001). Individuals with low calcium to phosphorus serum (Ca:P serum) ratio would benefit from increasing their calcium intake from foods or supplements.

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Epidemiologic studies have demonstrated a positive correlation between dietary Mg intake and bone density and/or an increased rate of bone loss with low dietary intake suggesting that dietary Mg deficiency may be a risk factor for osteoporosis. In vivo study for calcium bioavailability however, has shown tendencies towards lowering serum phosphorus and magnesium level. Though there has been study on beneficial effect of calcium towards BMD, there are few data in regard to the biochemical status. The objective of this study was to assess the effect of long term calcium carbonate supplementation on serum calcium, phosphorus and magnesium level.

Materials and Methods

Subjects

This randomized controlled trial of calcium supplementation was a preplanned sub-study of a larger trial that assessed the effects of calcium supplementation on bone health. The entry criteria for the main study required that subjects be postmenopausal for more than 5 years and aged between 50 to 65 years old. Women with history of bone disease and receiving therapy for osteoporosis were ineligible, as were those with any other medical conditions that affect bone metabolism, including hypothyroidism or hyperthyroidism, liver disease, malignancy or metabolic bone disease. None of the subjects had been regular users of calcium supplements, hormone replacement therapy (bisphosphonate, estrogen, tamoxifen or testosterone), anabolic steroids, glucocorticoids, anticonvulsants or any other drugs known to affect calcium or bone metabolism within the past year.

Women were recruited by health screening test done in the selected area. Of the 236 post menopausal women assessed for eligibility for the study, only 173 meet the entry criteria but 60 were elected not to proceed. Thus, 113 women entered the study and randomly assigned to calcium supplementation group (CSG) and control group (CG). Subjects in CSG received 1200 mg of elemental calcium daily as the carbonate, $CaCO_3$ (Caltrate, WhiteHall USA) while CG were not given any placebo and advised to continue with their regular diet and lifestyle. The supplemented subjects were asked to take 600-mg tablets twice a day after meal in the morning and in the evening.

Data Collection

Subjects' demographic background and lifestyle were assessed using validated questionnaire. Dietary intakes were assessed using the Three-Day Food Record and analyzed using Nutrionist IV Diet Analysis Version 4.1 (First Data Bank 1995 The Hearst Corp., USA). Compliance was assessed by tablet counts. Serum levels of calcium, magnesium and phosphorus were measured using Dimension Clinical Chemistry System (Dade International Inc., Deerfield, IL, USA) autoanalyzer. Intact PTH (hPTH 1-84), PTHi level were determined using DiaSorin N-tact PTH SP IRMA kit (DiaSorin Inc., MN, USA) which is based on immunoradiometric assay (IRMA). All data were collected during baseline, at 12 months and 24 months. Statistical analyses were performed using The Statistical Package for the Social Sciences (Windows version 10.05 SPSS).

Results

Clinical characteristics of the study subjects are shown in Table 1. Mean age of the subjects at baseline was 60$\pm$4 years and with a mean of 11$\pm$5 years post menopause. Physical characteristic of subjects were similar in both groups. There was no significant difference between group in calcium, phosphorus and magnesium intake at baseline. Mean intake for calcium among subjects were low when compared to Recommended Nutrient Intake (RNI) for Malaysian (NCCFN, 2005) which recommend intake of 1000 mg/day for elderly aged 50 to 65 years old. Almost 78% had calcium intake less than 2/3 of recommended value.

Calcium supplementation had been found to help increase daily calcium level intake among subjects in CSG (Table 2). This situation had increased calcium to phosphorus ratio from 0.5 to 2.1 for the group. However, subject in both groups had decreased their phosphorus intake (significantly difference ($p<0.05$) from baseline) at 12 and 24 months. There was no significant change in magnesium intake among subjects in both groups.

The serum levels determined in this study were within normal range in both groups. Changes in biochemical measurements are shown in Table 1. Serum calcium in CSG had been significantly higher compared to CG at the end of this study. There was a decrement of -1.4% (at 24 months) in calcium serum level among subject CG. The calcium level in CSG however, had been similar to baseline level though there was a slight decrement during 12 months. PTH_i level had been decreased in both group, which is significantly higher in CSG compared to CG.

Dietary intake of calcium and Ca:P ratio had been found positively correlated with serum calcium level. Dietary phosphorus also had been shown to influence the Ca:P serum ratio, while increment in magnesium

Table 1. Clinical characteristics of the study subjects, by randomized group assignment

Characteristic	Control	Calcium
Age (years)	59.3 ± 3.7	60.0 ± 3.4
Duration of menopause (years)	10.7 ± 4.8	11 ± 4.8
Weight (kg)	62.9 ± 11.8	60.9 ± 9.9
Height (m)	1.51 ± 0.04	1.53 ± 0.06
BMI (kg/m^2)	27.6 ± 5.3	26.1 ± 4.3
Compliance (%)	-	91.7%

Table 2 . Calcium, phosphorus and magnesium intake and serum level among subject

Measurements (unit)	Group	Mean ± S.D			
		Baseline (n=113)	12 months (n=92)	24 months (n=87)	% change Baseline to 24 months
Dietary calcium (mg)	Control	545 ± 295	492 ± 293[a]	467 ± 221[a]	1.4 ± 67.6
	Calcium	496 ± 239	1602 ± 263	1600 ± 134	295 ± 163
Dietary phosphorus (mg)	Control	1055 ± 455	910 ± 344	903 ± 321	-10.9 ± 40.1
	Calcium	1012 ± 363	834 ± 280	800 ± 226	-7.8 ± 41.0
Dietary magnesium (mg)	Control	176 ± 78	167 ± 59	178 ± 79	8.0 ± 47.2
	Calcium	175 ± 71	159 ± 63	168 ± 46	6.5 ± 48.1
Dietary calcium : phosphorus ratio	Control	0.5 ± 0.3	0.6 ± 0.3	0.5 ± 0.2	-
	Calcium	0.5 ± 0.3	2.1 ± 0.6	2.1 ± 0.5	-
Serum calcium (mmol/L)	Control	2.30 ± 0.11	2.26 ± 0.09	2.27 ± 0.08[a]	-1.4 ± 4.9
	Calcium	2.32 ± 0.09	2.29 ± 0.09	2.32 ± 0.11	0.0 ± 4.4
Serum phosphorus (mmol/L)	Control	1.16 ± 0.11	1.20 ± 0.13	1.14 ± 0.12	-0.9 ± 11.2
	Calcium	1.18 ± 0.14	1.16 ± 0.12	1.15 ± 0.15	-1.5 ± 15.2
Serum magnesium (mmol/L)	Control	0.74 ± 0.09	0.76 ± 0.08	0.78 ± 0.10	5.9 ± 10.4
	Calcium	0.71 ± 0.08	0.74 ± 0.09	0.77 ± 0.08	8.1 ± 12.1
Serum calcium : phosphorus ratio	Control	2.0 ± 0.2	1.9 ± 0.2	2.0 ± 0.2	-
	Calcium	1.9 ± 0.3	2.0 ± 0.2	2.0 ± 0.3	-
PTH_i (pmol/L)	Control	2.64 ± 0.95	2.78 ± 1.10	2.09 ± 0.97	-9.0 ± 45.2
	Calcium	2.74 ± 1.15	2.47 ± 0.93	1.88 ± 0.80	-26.0 ± 29.9[a]

[a] Significant difference between group at time determined p<0.01

intake had been statistically found to reduce PTH_i level (Table 3).

Discussion

This study identified a low dietary calcium intake situation among the subjects. A low calcium intake is universally reported in Asian countries (Tan, 2002). The result of this study should be cited as a reason for encouraging the Malaysians to increase their calcium intake. The key to bone health lies in the body's calcium balance. Calcium's vital role in intracellular communications and other body processes require that the concentration of ionized calcium in plasma be regulated within narrow limits (Gurr, 1999). The skeleton serves as a bank from which the blood can borrow and return calcium as needed. If the 'saving account' is not sufficient, then it will develop the fragile bones of osteoporosis. Maintaining serum calcium level through sufficient dietary intake could prevent this from happening or at least would slow down one of the consequences of aging which is bone loss (Reid *et al*., 1993). This study proved that the use of calcium carbonate supplements in a daily dose containing 1200 mg of elemental calcium is sufficient in helping to maintain constant serum calcium level. The suppression of PTHi occurs significantly higher in calcium group, likely in respond to the increased concentration of calcium ions in plasma as a result of increased intake. This "negative feedback" mechanism would keep the serum calcium within normal range (Nordin, 1997b).

Table 3. Correlation between dietary and serum level

	Dietary calcium	Dietary phosphorus	Dietary Ca:P	Dietary magnesium
Calcium serum	0.321[b]	0.160	0.282[b]	-0.026
Phosphorus serum	-0.057	-0.208	0.021	0.066
Ca:P serum	0.148	0.278[a]	0.052	-0.059
Magnesium serum	0.077	0.085	0.054	-0.033
PTH_i	-0.098	-0.166	0.129	-0.241[a]

[a] Significant correlation at p<0.05 , b Significant correlation at p<0.01

It was good to find that subject's magnesium serum level had been increased throughout the time study. An *in vivo* assessment by (Patwardhan *et al*. (2001) had shown a tendency of hypomagnesemic, however this was only happened in competitive environment created by the presence of extra calcium in the normocalcemic animals. Magnesium is needed for the normal function of parathyroid glands, and its deficiency markedly disturbs calcium homeostasis leading to hypocalcemia (Rude *et al*., 2005), which explained the negative correlation between the mineral and PTH found (Table 3). Postmenopausal women with osteoporosis have also been reported to have a low serum magnesium concentration (Martini and Meyer, 1999).

Serum phosphorus showed a tendency to reduce might be caused by decreased intake by the subjects. Though the change was not significant, the situation should not be encouraged. Study by (Chapuy *et al*., 1992), found elderly women given calcium and vitamin D supplements, with or without anti-osteoporosis drugs developed a risk for hypophosphatemia which would prevent bone recovery process. However in this study it is likely that phosphorus intake is, in fact sufficiently high for most subjects. It is calcium that is mainly deficient in their diets. However, supplementing calcium with

phosphate should be encouraged especially in elderly who tend to have a low food phosphorus intake.

Conclusion

Calcium supplementation amongst postmenopausal women benefits them by increasing the subject daily intake of calcium. Sufficient intake of calcium maintains serum calcium level, and suppresses PTH secretion.

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