Abstract

Calcium intake may play an important role on bone health. The recent national nutritional survey in Japan revealed the gradual decrease in calcium intake to around 480 mg/day. In addition, the patients with low level of vitamin D become too large in proportion. The present perspective proposes to increase calcium intake in Asian population.

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Keywords: Calcium; Vitamin D; Bone; Fracture

1. Introduction

Osteoporotic fractures continue to be a major health problem worldwide. Among osteoporotic fractures, hip fracture is the most serious morbid state and the secular trend in the incidence of hip fracture has been stabilized in Western countries. However, the incidence of hip fracture is rising in Asian countries [1]. Although the estimated number of hip fractures is recently decreasing in women in their seventies and eighties in Japan, the annual number of hip fractures among all age groups is still increasing [2]. In addition, the prevalence of vertebral fractures in Asian people has been reported to be higher than that in Caucasians [3]. Therefore, efforts to reduce fracture incidence should be concentrated in Asian countries.

Sufficient calcium intake and adequate serum vitamin D level have been considered to be essential factors in maintaining optimal function of body organs and systems. However, recent reports from the national nutritional survey of Japan in 2013 [4] raised concerns about calcium nutrition (Fig. 1). Furthermore, we have investigated the level of serum vitamin D (25(OH)D) in patients with osteoporosis [5] and in postmenopausal women [6]. Those results suggested that a considerable number of subjects had an insufficient serum 25(OH)D level.

The low calcium intake and low serum 25(OH)D level are undoubtedly associated with the desire for weight reduction and for avoidance of skin darkening. Because the low calcium intake was associated with low energy intake leading to reduction of body weight (Fig. 2), that may be a reflection of national promotion against metabolic syndrome. In addition, recent sales of cosmetics for sun protection have markedly increased, suggesting the desire for protection against skin darkening. However, the trends of low calcium intake and vitamin D insufficiency seen in recent years may have a potential risk for future fractures or frailty, especially in women. Therefore, the aim of the present study is to drive the revision of calcium and vitamin D nutrition in not only Japan, but also in East Asian countries.

2. History of calcium intake in Japan (Fig. 1)

Calcium intake from food in Japan increased from the end of World War II to the 1990s. The extremely low calcium
intake of 250 mg/day just after the war ended, was due to inadequate food supply and this turned to increase to approximately 600 mg/day during the post-war economic boom. In the subsequent era (2000~), recognized as an economic recession, the calcium intake reached to its nadir of approximately 550 mg/day. However, this trend ended at 2007 when national promotion against metabolic syndrome has been started and the national nutrition survey indicated the reduction in calcium intake to 500 mg/day or less in 2008, especially in women (Fig. 1) [4]. This trend was accompanied with a significant decline of body weight in women (Fig. 2), suggesting that the trend in decreasing calcium intake may be due to the women’s desire to reduce their weight.

3. Calcium requirement in Asian people

Previously, we reported the calcium requirement in women by a calcium balance study [7]. The calcium requirements in young and old Japanese women were calculated as 543 and 788 mg/day, respectively. On the other hand, the recommended intakes of calcium for the young and old generations of women were 652 and 946 mg/day, respectively. Therefore, the calcium intake never exceeded the levels of calcium requirement or recommendation until now.

Joo N-S et al. [8] reported that the mean calcium intake and serum 25(OH)D level were 485 mg/day and 48.1 nmol/L, respectively in Korean people who participated in the KNHANES. The authors concluded that a calcium intake of at least 668 mg/day and serum 25(OH)D level of at least 50 nmol/L may be needed to prevent secondary hyperparathyroidism [8]. This estimated calcium intake obtained from the Korean population is very close to our proposal for the recommended daily calcium intake in the young generation based on the calcium balance study. As the recent mean calcium intake in Japan was almost the same as that in Korean people, the calcium deficiency in both populations was approximately 200 mg/day. The traditional dietary habit in Asian countries may be one of the barriers to increase in calcium intake, and therefore, calcium supplementation may be required to improve the calcium imbalance. According to the data from NHANES 2009–2010, the US females aged over 60 year-old took 842 mg/day of calcium from foods and supplementation. Around 40% of calcium originated from milk and dairy products in the US [9]. On the other hand, Japanese women aged sixties took 525 mg/day of calcium from foods. Around 30% of calcium was taken from milk [4]. Therefore, Japanese women took less total amount of calcium and also less proportion of calcium from relatively high bioavailable source comparing to those in the US.
4. Effects of calcium nutrition on PTH secretion and bone mineral density

As shown in the Korean population, calcium deficiency results in secondary hyperparathyroidism and low BMD. Calcium supplementation induced reduction in the levels of PTH and bone resorption markers [10]. Tai et al. reported that increased calcium intake by both dietary intake and supplementation increased BMD in meta-analysis [11]. Senior high school students were reported to have a lower calcium intake from food [12] and calcium or milk consumption is weakly correlated with BMD, suggesting that poor juvenile calcium nutrition may connect to inadequate formation of peak bone mass. The community-based nutrition education of calcium intake was effective to increase bone mass and reduced secondary hyperparathyroidism in postmenopausal Vietnamese women. In this prospective study, the postmenopausal women with low calcium intake (<400 mg/day) was educated to increase calcium intake to around 600 mg/day for 18 months. This study indicated that parathyroid hormone secretion was decreased by the increased calcium intake. The bone status measured by quantitative ultra-sound conduction in calcaneal bone was improved by the increase in calcium intake [13].

5. Calcium intake from foods or supplementation on fracture prevention

Although the increase in calcium intake certainly connects to improve bone and calcium metabolism in women, there were many controversies regarding whether increase in calcium intake achieve the prevention of fractures or not. Two positive effects of high calcium intake on fracture prevention have been reported in a prospective cohort study and RCT [14,15]. One systematic review reported that higher dietary intake of calcium did not reduce the risk of fracture, but calcium supplementation significantly achieved the fracture risk reduction. However, the effects of calcium supplementation on fracture risk were weak and inconsistent [16]. The most recent prospective cohort study in Australia [14] reported that the highest quartile of calcium intake reduced the self-reported risk of fractures including hip, wrist and shoulder (OR for fracture was 0.75 (0.54–0.92 for 95% CI) after adjustment for confounding factors). The subgroup analysis revealed that the group with higher calcium intake of approximately 1000–1300 mg/day, resulted in various health benefits other than fracture prevention such as decrease in all causes of death, non-fatal cardiovascular disease and stroke [14].
The increase in calcium intake from food may have beneficial effects on bone in specified subpopulations having low calcium absorption from gut [14]. The ability of calcium absorption in the intestine was adapted to habitual calcium intake. Namely, active transcellular calcium transport in the duodenum is up-regulated by vitamin D-dependent processes in the subjects with low calcium intake [17]. On the other hand, calcium in people with high calcium intake was mainly absorbed in jejunum or ileum via passive transport [17].

A 12-year prospective cohort study evaluating the effects of calcium intake on fracture incidence did not support the hypothesis that higher consumption of milk or other food sources of calcium protects against fractures [18]. A total of 3 RCTs and one prospective observational cohort study examined the effects of calcium intake on fracture incidence. All these reports showed negative results, namely calcium supplementation did not reduce fractures [19–22]. However, those reports were mainly evaluating in Caucasian populations, where the calcium intake from food was estimated to be higher than that in the Asian population. In the Japan Public Health Centre-based Prospective Study [23], two different cohort studies evaluated the dairy calcium intake and observed 10-year incidence of self-reported vertebral fracture. The mean calcium intakes in the women of Cohorts I and II was 512 and 334 mg/day, respectively. The RR of vertebral fracture incidence in the lowest calcium intake (<350 mg/day) versus the highest group (>700 mg/day) was 2.10 (95% CI 1.25, 3.55). If the results obtained from Japanese study were extrapolated to entire Asian countries, the ideal daily calcium intake should be increased to around 700 mg/day. However, this target calcium intake might be hard to achieve because of the dietary customs in Asia. Therefore, a strategy to resolve fracture issues related to calcium insufficiency should focus on the reduction in the proportion of people who are taking extremely low calcium intake but not focused on the efforts to improve the mean calcium intake in entire population. For example, promoting another cup of milk or calcium tablet to increase another 200 mg/day of calcium in the people whose calcium intake of 400 mg/day or less on average. Further study is required to evaluate what level of calcium intake should be recommended in order to increase the minimum calcium intake or to change food customs leading to extreme calcium deficiency. Finally, the effects of increased calcium nutrition on bone health in the Asian population need to be further assessed. One limitation of the previous RCT using calcium supplementation on fracture prevention was the short observation period. Almost all studies observed the participants for less than 15 years. The calcium effects on bone may require a longer time to be concluded.

6. Calcium biology in other systems

Although calcium supplementation or increased intake of calcium had little effect on bone health, especially in Caucasian populations, other benefits of calcium intake for health problems have been reported. African Americans are known to have higher bone mass despite a lower calcium intake. The relative resistance of bone to secondary hyperparathyroidism may be a cause of this black paradox [24]. However, African Americans have higher several other risks for chronic diseases such as cardiovascular diseases, stroke, obesity and insulin resistance syndrome [24] comparing to those in Caucasians.

We have reported that calcium intake was negatively associated with the serum homocysteine level, which is a known factor to promote atherosclerosis [25]. Calcium supplementation or dairy product modulated lipid utilization and energy expenditure [26]. However, intervention studies using calcium supplementation or dairy products in obese women were controversial, namely one was positive [27] and the other was negative [28]. Dietary intake of calcium had been reported to correlate with hypertension [29]. The most recent meta-analysis revealed that the intake of dairy products might improve blood pressure and decrease in hypertension risk [30]. On the other hand, Bolland et al. reported the harm of calcium supplementation on cardiovascular events in healthy older women [31]. Thus, the health benefits of calcium intake or supplementation are currently controversial in Caucasian populations who took higher calcium intake comparing to Asian population.

7. Vitamin D nutrition and survival

Serum level of vitamin D is associated with increase in all cause of mortality in Asian population [32]. Although the exact mechanism(s) of vitamin D on mortality has not been fully elucidated, many association studies between vitamin D insufficiency and wide range of health related outcomes such as malignancies, cardiovascular diseases, autoimmune diseases, infections and metabolic diseases, had been carried out and the results indicated that vitamin D nutrition associated with those health related outcomes [33]. Vitamin D level also associated with fractures [6,34]. The attempts to reduce the fractures and other health problems related to vitamin D nutrition, have been carried out extensively. High-dose vitamin D supplementation (>800IU daily) was somewhat favorable in the prevention of hip fracture and any non-vertebral fracture in elderly people [35]. However, the other meta-analysis revealed that vitamin D supplementation with or without calcium does not reduce skeletal or non-skeletal outcomes [36]. Those discrepancies may result in the differences in vitamin dose or in the subjects. In fact, Bischoff-Ferrari et al. reported that relatively high dose of vitamin D was shown to prevent fractures [35]. Murad et al. reported vitamin D use was associated with statistically significant reduction of falls (Odds 0.86: 95% CI 0.77–0.96) and the effect of vitamin D on fall was more prominent in the patients with vitamin D deficiency at baseline [37]. Therefore, we have to clarify what kind of subgroups will require pharmacological intervention with vitamin D.

In this context, we have to define the level of vitamin D deficiency. The reported definitions were varied from 50 nmol/L to 75 nmol/L. Those variations were due to the differences in outcomes. Because the level of PTH was taken for the evidence of vitamin D deficiency, the level of cut-off of serum 25(OH)D level was defined to 50 nmol/L [8,38]. On the other hand, when vitamin D related fracture occurrence was used as
an outcome of vitamin D deficiency, the cut-off value was 75 nmol/L [6]. The inverse relationship between serum 25(OH)D and PTH may be influenced by age, calcium intake, physical activity, renal function and even ethnicity [39]. Nakamura et al. reported that serum 25(OH)D levels less than 50 nmol/L indicated higher PTH level and that less than 70 nmol/L showed lower femoral neck BMD [40]. We have reported the significant relationship between serum 25(OH)D and incident non-vertebral fracture [6] and the cut-off value to reduce the incident long bone fractures was 62.5 nmol/L. Okazaki et al. demonstrated that the serum 25(OH)D level above which PTH reached a plateau was 70 nmol/L [41]. Dawson-Hughes proposed that the optimal levels of 25(OH)D could not be determined and it will be changed from 50 to 70 nmol/L depending on what type of outcome is expected.

8. Calcium and vitamin D interaction

It is well known that vitamin D resistance induces bone abnormalities such as large osteoid with lower mineralization, also known as osteomalacia or rickets. However, calcium infusion reversed bone and mineral abnormalities in a patient with vitamin D-resistant rickets [43]. In addition, bone phenotypes of VDR knockout mice were normalized by high calcium and phosphate dietary modifications [44]. Calcium absorption in the gut depends on two pathways: active transport via vitamin D action in the duodenum and the passive transport system in the jejunum and ileum [17]. Thus, the sufficient calcium supply may prevent the loss of vitamin D action via passive transport at ileum or jejunum [14,17]. Therefore, calcium intake is preferentially important to keep bone health.

9. Conclusion

In conclusion, Asian populations are evidently under calcium deficient. The mean calcium intakes in Japan and Korea were approximately 500 mg/day or less. This nutritional background is associated with secondary hyperparathyroidism, increased bone resorption and low bone mineral density. Although increased calcium intake from food or supplementation did not improve fracture incidence in Caucasian populations, fracture occurrence in Japanese women after the intervention of calcium nutrition had achieved to decrease in incident fracture. Thus, the calcium intake should be increased to 600 mg/day in populations with a low calcium level (<400 mg/day). When the calcium intake can be increased properly, it is expected that bone abnormalities of vitamin D deficiency may be compensated.

Conflicts of interest

The authors declare that we have no conflict of interest and the authors did not receive any support from the third party.

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