Effect of Dietary Calcium Supplementation at Recommended Doses on Calcium Excretion in Japanese Postmenopausal Women

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Context: Japanese people have low intakes of milk and dairy products, and there is a high risk of fractures in postmenopausal women due to calcium deficiency; hence, effective calcium supplementation is required.

Objective: To determine the relationship between dietary calcium intake and calcium accumulation rate in postmenopausal women by comparing the amount of calcium absorbed when ingesting milk, which is a calcium-containing food, and a commercially available calcium food.

Subjects: A crossover study of milk and a highly absorbable calcium supplement (UNICAL™) as calcium-containing foods was conducted on 38 postmenopausal women (mean age and standard deviation: 58 ± 3.8 years) using calcium carbonate as a common comparative food. Calcium intake was set at 700 mg/day, and in addition to the basal diet (which was designed to have a calcium content of 250 mg/day), participants received 450 mg/day of calcium from milk or calcium carbonate in Study 1 (n = 19) and from UNICAL™ or calcium carbonate in Study 2 (n = 19). There was a period of no calcium supplement intake (washout period) between the two interventions. The amount of calcium in urine, feces, and meals was measured, and the calcium accumulation rate ((intake − excretion)/intake) was compared.

Results: The Ca-supplemented diet accumulated −216 to −246 mg during the intervention period, and calcium loss was observed in all subjects. On the other hand, the amount of calcium accumulated during the washout period ranged from −346 to −356 mg/day, with greater losses than during the intervention, and the addition of calcium to the diet reduced calcium loss in the body. The difference between the mean accumulation rates of milk and calcium carbonate in Test 1 was −0.2% (95% CI; −52.2% to 51.8%, p = 0.99), and the difference between the accumulation rates of UNICAL™ and calcium carbonate in Test 2 was +6.1% (95% CI; −36.1% to 48.3%, p = 0.77), neither of which was significant.

Conclusion: UNICAL™, a highly absorbable calcium supplement, was as effective as milk in reducing calcium loss in postmenopausal Japanese women. However, neither milk nor calcium supplements adequately controlled calcium loss in postmenopausal Japanese women at the traditional recommended intake of 650 mg/day.

Keywords: Calcium supplement, Postmenopausal women, Osteoporosis, Crossover study

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1. Introduction

The number of patients with osteoporosis is rapidly increasing in Japan with the growing aging society, and it is estimated to reach 12.8 million (3 million men and 9.8 million women) [(1)]. Osteoporosis is characterized by a decrease in bone strength due to a decrease in calcium content in bone tissue, and it is defined as a disease with an increased probability of risk of fractures [(1)].

As fractures comprise one of the major causes of the need for long-term care among elderly people, their prevention has become a major health issue. In particular, estrogen deficiency in postmenopausal women activates osteoclasts to elute calcium from bone tissue, a problem that is well established to lead to the progression of osteoporosis by decreasing bone tissue strength and hardness [(1–3)].

Furthermore, the average daily calcium intake of Japanese women aged ≥20 years in 2019 was only 500 mg/day, which is 24% less than the recommended daily amount of 650 mg/day [(4,5)]. In the aging Japanese society, there is a concern that the number of patients with osteoporosis due to calcium deficiency will increase further if the conventional dietary habits are maintained, and hence an effective calcium intake method is required.

Calcium is also involved in the regulation of various physiological functions in the body, and when calcium intake is insufficient, the living body demineralizes bones to maintain normal blood calcium levels [(6,7)]. Thus, appropriate dietary calcium intake is essential for the maintenance of healthy bone tissue. However, the relationship between calcium intake and accumulation in the body has not been completely elucidated in early postmenopausal women, who have significant body calcium loss despite a low calcium intake, is not fully understood. Therefore, it is desirable to conduct a detailed investigation of the effects of calcium supplements, which have been in increasing demand in recent years, on the accumulation effect of the body, especially in postmenopausal women.

Milk and dairy products are commonly used as a convenient method of compensating for insufficient calcium intake. Nevertheless, Japanese elderly people primarily prefer conventional foods without milk or dairy products, which is the major reason why calcium intake does not increase.

Despite the increasing rate of calcium deficiency, several Japanese people do not drink much milk. In addition to the traditional Japanese food culture that does not require milk, milk intake has decreased due to the recent diversification of eating habits such as eating out and delivery foods. The milk intake of Japanese people decreased by approximately 30% compared with the peak amount in 1996 [(8)]. The recent annual per capita consumption in Japan is 30.8 kg, which is significantly lower than 128.5 kg in Finland, 108.4 kg in the United Kingdom, 71.6 kg in the United States, and 52.6 kg in France [(9)]. Therefore, there is a continuous need for effective methods to enhance the intake of calcium in the Japanese population.

Previous studies have demonstrated that calcium supplements reduce the risk of fractures in people with such low milk intake [(10, 11)]. It has been reported that calcium supplement challenge tests for older and younger women have an effect of increasing bone mineral density [(12)], however, supplement absorption tests for postmenopausal women with markedly reduced bone mineral density have not yet been implemented in Japan.

Therefore, we attempted to evaluate the supplementation effect of calcium supplements in postmenopausal women by comparing them with a normal diet, such as milk. Commercially available UNICAL™, which has been demonstrated to have a higher ionization rate in gastric juice [(13)] and higher intestinal absorption than calcium carbonate, calcium phosphate and calcium hydroxide [(14,15)], was used as a calcium supplement.

The purpose of this study was to compare the effects of high-absorption calcium supplements with those of milk intake to determine whether they have the effect of not accelerating the decline in bone mineral density in Japanese postmenopausal women with low-calcium intake.

To explore the calcium supplementation effect under the condition of eating a low-calcium diet, the calcium absorption effect of milk and the UNICAL™ intake effect were evaluated by the weight accumulated in the body using calcium carbonate as a comparative control. We also examined the relationship between changes in bone metabolism markers and calcium absorption.

2. Materials and Methods

2.1 Calcium supplement foods

Milk and UNICAL™ (Universal Calcium Food Co. Ltd, Tokyo) were used as calcium-containing foods, and the amount of calcium absorbed was measured using calcium carbonate as a comparative agent.

2.2 Postmenopausal subjects

A total of 38 postmenopausal women were enrolled as study subjects from medical institution workers. They were aged 53–64 years and could consume calcium test foods for 12 days. Those with constipation were excluded. The subjects participated in the calcium absorption test in parallel with their normal work from July to August 2019. To compare the two types of calcium-added foods according to each subject, a 12-day crossover study was conducted twice, with an absorption test conducted for 4 days before and after a 4-day washout (WO) period [16].

2.3 Calcium absorption test

The schedule of food intake and analytical sampling in a crossover study of calcium absorption by milk and calcium absorption by calcium-supplemented foods is shown in **Table 1.** In Test 1, 19 subjects were divided into two groups, with group A taking milk as the first intervention calcium source for 4 days, followed by 4 days of WO period, and then calcium carbonate for 4 days. Subjects in group B took calcium carbonate as the first intervention food for 4 days, followed by 4 days of WO period, and then milk for 4 days. Similarly, in Test 2, 19 subjects were divided into groups C and D, and the crossover study of UNICAL™ and calcium carbonate was performed.

Calcium-containing foods with a calcium content of 450 mg/day were provided. Milk was provided with 2 packs of 225 mg Ca-containing products, and UNICAL™ and calcium carbonate were provided with 150 mg/bag 3 times.

Subjects were asked to consume the full amount of the basic diet and the calcium-containing foods provided, and the calcium-containing foods were ingested with the diet. The basic diet (low-calcium diet) was set to contain 250 mg of calcium, approximately 1500 kcal of energy, 45 g of protein, 12 g of dietary fiber, and ≤8 g of salt/day. The energy of the snack was set to 400 kcal, and the amount of calcium was set to ≤20 mg/day.

During the WO period, subjects were provided with the basic diet, light meals, and water. Snacks were freely consumed by the subjects within the range provided and were excluded from the calculation of calcium intake.

During the test periods, subjects were prohibited from the consumption of alcohol, tobacco, coffee, and other luxury items that affect calcium absorption. They were instructed to maintain their daily activities, except for stool and urine collection during the test period. The daily excretion status was also recorded to ensure that there was no constipation.

Table 1 Schedule of food intake and analytical sampling in a crossover study of calcium absorption by milk and calcium supplements.

Day	0	1	2	3	4	5	6	7	8	9	10	11	12
Test 1: group A		milk				washout				calcium carbonate			
Test 1: group B		calcium carbonate				washout				milk			
Test 2: group C		UNICAL™				washout				calcium carbonate			
Test 2: group D		calcium carbonate				washout				UNICAL™			
Feces collection				**X**	**X**			**X**	**X**			**X**	**X**
Urine collection				**X**	**X**			**X**	**X**			**X**	**X**
Blood collection	**X**												

X: implementation

2.4 Calcium intake and excretion

Calcium intake was determined by measuring the total amount of calcium in the basic diet and calcium-supplemented foods. The amount of calcium in the basic diet was measured using the duplicate diet method after cryopreservation of the basic diet. For measuring the calcium intake, we calculated the average value for each period of 1–4, 5–8, and 9–12 days.

To measure calcium excretion, the subjects collected fecal and urine samples on days 3 and 4 of each period. The collected fecal samples were cryopreserved, the urine samples were stored at room temperature, the weight was measured, and then the amount of calcium in the sample was measured. The calcium content of the basic diet, urine, and feces was measured using ICP luminescence analysis at SRL Inc. (Sakai City, Osaka Prefecture).

2.5 Blood tests and related tests

Blood tests were performed at enrollment. Age, body mass index (BMI), gait, and serum calcium and phosphorus levels were measured as factors that may be associated with calcium absorption. For the bone metabolism-related factors, the concentrations of estradiol E2 (E2), osteocalcin (OC), 1,25-dihydroxyvitamin D_3 (1,25-$(OH)_2D_3$), type I collagen cross-linked N-telopeptide (NTX), and bone-type alkaline phosphatase (BAP) were measured.

2.6 Calcium accumulation rate

To evaluate the absorption of calcium derived from the calcium-added food, the following calculation was performed as described by Kanematsu [16]. The "calcium accumulation amount ($Ac = In - Ex$)" was calculated by subtracting the "calcium excretion amount (Ex)", which is the sum of the amount of calcium in feces and the amount of calcium in urine, from the "calcium intake (In)". Next, the "added calcium intake (ΔIn)" and the "added calcium accumulation (ΔAc)" were calculated by subtracting each amount of the WO period from the addition period. The "added calcium accumulation rate (ΔP)" was determined by dividing ΔAc by ΔIn.

2.7 Statistical analysis

Descriptive statistics are expressed as n (%) or mean ± standard deviation (SD). To compare the absorption between calcium foods in the crossover study, a paired t-test was conducted using the calcium accumulation rate as an evaluation index, and the significance level was set to 5% on both sides. The magnitude of the difference between the two groups is expressed by the point estimate and the 95% confidence interval. The correlation between the calcium accumulation rate and each measurement item was evaluated using the Pearson correlation coefficient. The statistical analysis was performed using Stata 14 (Lightstone Co., Ltd., Tokyo).

2.8 Ethical considerations

This study was conducted according to the ethical guidelines for human medical research. Subjects were informed of the content of the study and voluntarily provided a written consent. This study has been preregistered in the public database (UMIN-CTR) of the clinical trial registration system (UMIN000037219) of the University Hospital Medical Information Network Research Center (UMIN) and approved by the ethical review committee of the medical institution Nisshinkai Hospital (February 26, 2019).

3. Results

3.1 Characteristics of subjects

Table 2 shows the average height, weight, exercise habits, number of steps/day, and blood test results of the study subjects. Factors that may be associated with calcium absorption, including age, BMI, gait, serum calcium and phosphorus, and the bone metabolism-related hormones estradiol E2 (E2), osteocalcin (OC), 1,25-dihydroxyvitamin D_3 (1,25-$(OH)_2D_3$), type I collagen cross-linked N-telopeptide (NTX), and BAP, were measured in advance. The subjects had average physique and exercise habits, and their blood test results were in the normal range.

3.2 Calcium intake and excretion

There was no leftover meal of the basic meal during the test period, and the amount of snack intake was also within the range provided. **Table 3** shows the calcium intake and excretion during each test period.

Throughout Tests 1 and 2, calcium intake (*In*) was 664–668 mg/day during the calcium addition period and 241 mg/day during the WO period. However, the amount of calcium accumulated (*Ac*) ranged from −216 to −246 mg/day during the calcium addition period and from −346 to −356 mg/day during the WO period. In both cases, *Ac* was negative, but the amount of calcium loss was suppressed during the addition period compared to that during the WO period.

Table 2 Height, weight, exercise habits, and blood test results (mean ± SD) at subject enrollment.

		Test 1	Test 2
Number of subjects	(n)	19	19
Age		58.2 ± 3.8	57.8 ± 3.7
Height	(cm)	156.0 ± 5.5	155.9 ± 5.6
Weight	(kg)	55.6 ± 7.8	56.6 ± 7.4
BMI		22.8 ± 2.8	23.3 ± 2.8
Exercise habits		11 (57.9%)	11 (57.9%)
Number of steps	(/day)	9992 ± 2902	9909 ± 2407
Blood component			
Ca	(mg/dL)	9.3 ± 0.3	9.4 ± 0.3
P	(mg/dL)	3.8 ± 0.4	3.8 ± 0.5
Estradiol E2	(pg/mL)	8.7 ± 11.9	8.7 ± 11.9
Osteocalcin	(ng/mL)	26.9 ± 9.3	26.6 ± 9.7
1,25-$(OH)_2D_3$	(pg/mL)	66.0 ± 14.5	65.4 ± 13.4
NTX	(nmol BCE/L)	23.5 ± 5.7	23.0 ± 5.8
BAP	(μg/L)	15.8 ± 4.9	15.8 ± 4.3

Table 3 Calcium intake and excretion amounts (mean ± SD) in the crossover study of calcium absorption.

	Test 1		Test 2	
	test period	Ca (mg/day)	test period	Ca (mg/day)
Ca intake (*In*)	milk	668 ± 5	UNICAL™	665 ± 5
	calcium carbonate	664 ± 5	calcium carbonate	664 ± 5
	WO	241 ± 0	WO	241 ± 0
Ca excretion urine (*Ex*1)	milk	164 ± 56	UNICAL™	161 ± 44
	calcium carbonate	166 ± 48	calcium carbonate	176 ± 41
	WO	123 ± 41	WO	122 ± 30
Ca excretion feces (*Ex*2)	milk	726 ± 393	UNICAL™	720 ± 304
	calcium carbonate	722 ± 394	calcium carbonate	734 ± 351
	WO	474 ± 240	WO	464 ± 460
Ca excretion total ($Ex = Ex1 + Ex2$)	milk	891 ± 403	UNICAL™	881 ± 295
	calcium carbonate	888 ± 402	calcium carbonate	910 ± 357
	WO	597 ± 244	WO	587 ± 460
Ca accumulation ($Ac = In - Ex$)	milk	−223 ± 404	UNICAL™	−216 ± 298
	calcium carbonate	−224 ± 402	calcium carbonate	−246 ± 357
	WO	−356 ± 244	WO	−346 ± 460

Table 4 Accumulation rate of the added calcium by subtracting each amount of the WO period from the intake period.

	Ca intake *ΔIn* (mg/day)	Ca accumulation *ΔAc* (mg/day)	Accumulation rate *ΔP* = *ΔAc* /*ΔIn*
Test 1			
milk	427 ± 5	134 ± 396	31.0% ± 93.1%
calcium carbonate	424 ± 5	132 ± 411	31.2% ± 96.7%
Test 2			
UNICAL™	424 ± 5	130 ± 559	29.9% ± 130.7%
calcium carbonate	424 ± 5	100 ± 542	23.9% ± 129.3%

Table 4 shows the results of the analysis of changes in the accumulation rate with and without the addition of calcium. In all cases of Tests 1 and 2, the addition of calcium enhanced the accumulated amount (*ΔAc*) compared to that without calcium addition. The mean accumulation rate (*ΔP*) of added calcium was 31.0% for milk and 31.2% for calcium carbonate in Test 1, whereas it was 29.9% for UNICAL™ and 23.9% for calcium carbonate in Test 2. Although there was no significant difference in the effect of additives in each study, the average accumulation rate of calcium carbonate in Test 2 was lower than that of UNICAL™, suggesting that differences in solubility had an effect [(13)]. The difference in the accumulation rate of added calcium to calcium carbonate as a comparison standard was −0.2% for milk (95% CI, −52.2% to 51.8%, p = 0.99) and +6.1% for UNICAL™ (95% CI, −36.1% to 48.3%, p = 0.77), and no statistically significant difference was found in either case.

3.3 Correlation of factors related to calcium absorption in calcium-containing foods

Figure 1 shows the relationship between the amount of calcium accumulated during the intake period of UNICAL™ and the age and BAP of the subjects. Young subjects showed an increasing trend of calcium accumulation. Furthermore, the high accumulation of calcium suggests that subjects with high blood BAP levels had increased calcium absorption with UNICAL™ ingestion. Therefore, we analyzed the correlation coefficient between blood test results and the calcium accumulation rates by the intake of various calcium-supplemented foods, and the size and exercise habits of the subjects. The results were summarized in **Table 5**.

Assuming that the absolute value of the correlation coefficient is 0.2 ~ 0.4 for a weak but non-negligible correlation, 0.4 ~ 0.7 for the medium correlation, and over 0.7 for the strong correlation, the following trends were suggested in the correlation between calcium accumulation and each factor.

For UNICAL™, age and calcium accumulation showed a negative medium correlation of −0.58, indicating that younger age was associated with calcium accumulation. Calcium carbonate, on the other hand, showed a weak positive correlation of 0.35 in Test 1 when alternating with milk, but a fairly weak negative correlation of −0.24 in Test 2 when alternating with UNICAL™.

The relationship between BMI and calcium accumulation was a weakly correlated at 0.28 for UNICAL™ intake, but not for other Ca-supplemented diets.

Step count as a motor indicator showed a weak negative correlation with calcium carbonate at −0.39 in Test 1 and UNICAL™ at −0.21 in Test 2. The results suggest that postmenopausal people who exercise more may accumulate less calcium.

Subjects with low serum Ca and P ion levels tended to accumulate more calcium in Test 1 with milk and calcium carbonate, but no correlation was found in Test 2.

Estradiol E2 showed a weak negative correlation with calcium carbonate in Test 2, but no other correlations. In addition, 1,25-$(OH)_2D_3$ showed a weak negative correlation with milk in Test 1 and with UNICAL™ in Test 2, but no correlations to calcium carbonate. Therefore, the relationship between these components and the calcium accumulation rates was not clear.

On the other hand, OC and NTX showed positive weak correlations for both UNICAL™ and calcium carbonate in Test 2, but no correlation for either milk or calcium carbonate in Test 1. BAP also showed a positive medium correlation for UNICAL™ and a weak correlation for calcium carbonate.

Thus, the rate of calcium accumulation in the subjects varied widely among individuals, but correlated with several factors. In particular, Test 2 suggested that younger postmenopausal women with higher OC, NTX, and BAP levels accumulated more calcium. That is, when calcium supplements were taken instead of milk, these factors were suggested to be involved in the calcium accumulation rates.

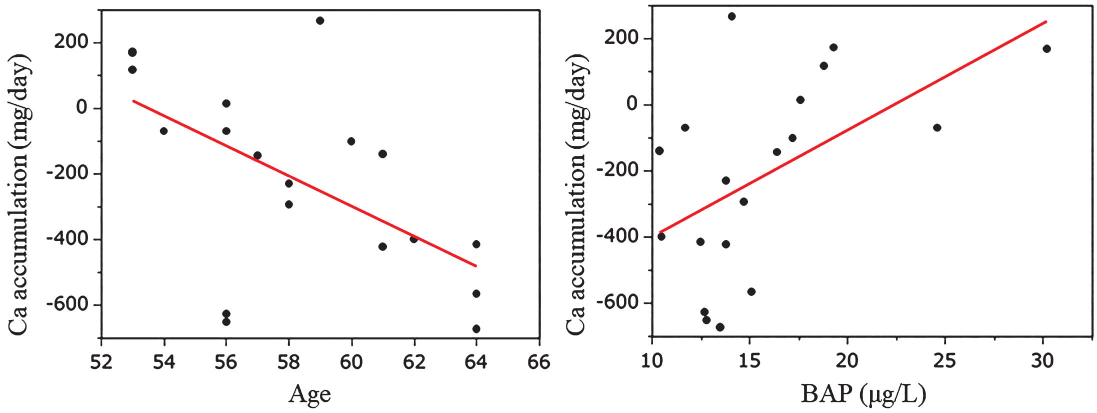

Figure 1 Relationships between calcium accumulation by UNICAL™ intake and age and BAP.

Table 5 Correlation coefficients (R) between milk, calcium carbonate and the rate of calcium accumulation by UNICAL™ and various factors.

		Test 1		Test 2	
		milk	calcium carbonate	UNICAL™	calcium carbonate
		R	R	R	R
Age		0.15	0.35	−0.58	−0.24
BMI		0.04	−0.08	0.28	0.04
Walking steps		0.03	−0.39	−0.21	−0.15
Ca	(mg/dL)	−0.44	−0.38	0.03	−0.02
P	(mg/dL)	−0.31	−0.63	−0.17	0.08
Estradiol E2	(pg/mL)	−0.15	0.15	0.19	−0.43
1,25-$(OH)_2D_3$	(pg/mL)	−0.21	0.07	−0.33	−0.07
Osteocalcin	(ng/mL)	−0.15	−0.07	0.40	0.38
NTX	(nmol BCE/L)	−0.05	0.07	0.27	0.38
BAP	(μg/L)	−0.01	0.04	0.54	0.42

4. Discussion

We compared the calcium accumulation rates of milk and UNICAL™ with calcium carbonate in healthy postmenopausal Japanese women. We found no significant difference in calcium accumulation in either comparison, and UNICAL™ showed the same accumulation rate as that of milk.

Most participants in the study took calcium powder at the end of the meal because there was no detailed explanation of how to take calcium supplements with the meal. Therefore, gastric juice was diluted in the diet, and in Test 2, highly soluble UNICAL™ at neutral pH probably resulted in higher average calcium accumulation than calcium carbonate [13].

Results from Test 2 using UNICAL™ suggested that younger people have a higher rate of calcium accumulation than older people and that bone metabolic components such as OC, NTX and BAP were involved in calcium accumulation due to calcium supplements. In contrast, the results of Test 1, in which milk was alternated, showed no correlation between these.

It has been suggested that less induction of bone metabolic activity is required for calcium accumulation from milk intake [17]. Milk contains casein phosphopeptide, which promotes calcium absorption [18,19], and protein and vitamin D, which are involved in bone metabolism [20–22]. Therefore, it is not considered necessary to specifically increase bone metabolic activity. However, calcium carbonate and UNICAL™ do not contain these components, so they need to increase the activity of bone metabolism-related enzymes. Therefore, it is likely that the younger, the more calcium they accumulated in Test 2.

The average calcium loss with the same calcium intake was −223 mg/day for milk and −224 mg/day for calcium carbonate in Test 1, whereas it was −216 mg/day for UNICAL™ and −246 mg/day for calcium carbonate in Test 2. The lower calcium accumulation from calcium carbonate intake in Test 2 than in other cases suggested that the lower solubility in diet-neutralized gastric fluids compared to the more soluble UNICAL™ was the cause.

To date, four calcium balance tests have been reported in Japanese women. In a study conducted in elderly subjects, Okuda *et al* reported that elderly participants with an average age of 72 years who ingested 537 mg/day of calcium had an average calcium accumulation rate of −91 mg/day of calcium [22]. DeSauza *et al* reported that participants with an average age of 70 years who ingested 1474 mg/day of calcium had an average calcium accumulation rate of +339 mg/day [6]. Uenishi *et al* reported that participants with an average age of 67 years who ingested 850 mg/day of calcium had an average calcium accumulation rate of +5 mg/day [7]. On the other hand, among young people with a mean age of 19 years who consumed 900 mg/day of calcium, the mean calcium accumulation was +120 mg/day [23]. In contrast, the average rate of calcium accumulation in this study, which ingested 660 mg, was −230 mg/day, and calcium loss was greater than in these four reports.

Because the study subjects were postmenopausal women with an average age of 58 years, it is considered that the normal recommended amount of calcium intake was insufficient to suppress calcium loss in these individuals with a high calcium loss rate. However, ingestion of calcium-added foods leads to an increased amount of calcium accumulation compared to that with nonadditive foods, and the fact that intake of calcium-added foods suppressed calcium loss is consistent with previous reports.

According to the recent Japanese Dietary Reference Intakes [4], the recommended amount of calcium is 650 mg/day, which is considered to be effective in maintaining calcium loss in adults, including the elderly, at 0 mg/day. However, the results of this study indicate that if healthy postmenopausal women ingested 660 mg of calcium per day, their calcium accumulation rate was −230 mg per day, indicating significant calcium loss. Based on this information, it was concluded that postmenopausal women need more calcium intake.

In postmenopausal women, calcium excretion from the body increases the risk of osteoporosis, whereas an overdose of calcium supplements may increase the risk of cardiovascular disease, researchers have reported [24,25]. Some studies have also suggested that calcium supplementation has no effect on the maintenance of bone mineral density [26,27]. However, these studies included different age groups, genders, and diets, making it difficult to definitively rule out the effects of calcium supplements in maintaining bone density. Several reports have shown that calcium supplements reduced the rate of loss of bone density in postmenopausal women, suggesting that the solubility of the supplements has different effects [28].

Regarding the effect of calcium-added food supplementation in early postmenopausal Japanese women investigated in this study, it was found that calcium intake at 650 mg/day, which is the recommended calcium balance for Japanese people, was insufficient to maintain the calcium content in the body. In Japan, there is a shortage of milk and dairy products among all age groups [4], hence, it is obvious that high absorbable calcium supplementation is required to maintain the amount of calcium in the body.

During the crossover tests, all individuals were provided the same diet and their calcium intake and excretion were measured. As the subjects were medical professionals, they understood the research well and appeared to adhere to the plan. Moreover, as the calcium intake was set to a value close to the current recommended amount in Japan, it can be mentioned that it can be directly reflected in the lifestyle guidance in Japan. In particular, among Test 2 subjects who did not consume milk, younger women after menopause may be able to improve their bone metabolism function by actively ingesting calcium.

In contrast, UNICAL™ intake showed a weak correlation between calcium accumulation and BMI. According to Kajita *et al*, a significant positive correlation exists between BMI and bone mineral density after menopause and being underweight has been reported to be a risk factor for osteoporosis and fracture [(29,30)]. That means postmenopausal women tend to lose weight and have a lower BMI as their bone density decreases. On the other hand, it was suggested that UNICAL™ is effective in preventing a decrease in BMI because of its high bone resorption. In other words, maintaining BMI by calcium supplementation may help prevent bone loss and prevent osteoporosis in postmenopausal women.

As the trend in the milk intake of the Japanese [(8,9)] shows, it is not easy to switch to a diet that increases milk intake even if one is aware of calcium deficiency. Therefore, it is important to establish a lifestyle that activates bone metabolism, maintains calcium accumulation, and suppresses osteoporosis progression by taking supplements that exert the same calcium accumulation effect as that of milk with meals.

In Japan, where the number of elderly people continues to grow, the hope is to reduce the risk of fractures caused by osteoporosis by increasing intake of high-absorption calcium supplements, which have the same calcium-replenishing properties as milk. In particular, there is a strong need for effective calcium supplementation to reduce the number of elderly patients who are bedridden due to fractures.

5. Conclusion

A comparative calcium absorption study was conducted using calcium-containing foods. The difference in calcium accumulation when calcium carbonate was used as a control was −0.2% for milk and 6.1% for UNICAL™, but it was not statistically significant.

Calcium loss in early postmenopausal women was significant. Addition of calcium to foods suppressed the loss of calcium in the body, but it was clearly demonstrated for the first time that postmenopausal Japanese women require more calcium intake than the conventional recommended amount of 650 mg/day.

UNICAL™, a highly absorbable calcium supplement, was found to be as effective as milk in reducing the progression of calcium loss in postmenopausal Japanese women.

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和文抄録

日本人閉経後女性のカルシウム排泄に対する推奨用量のカルシウム補給食の効果

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日本人は牛乳や乳製品の摂取量が少なく慢性的にカルシウム不足のため，閉経後に骨粗鬆症を発症し骨折する女性の割合が高い。骨折は，寝たきりとなる要介護高齢者の主要因であり，骨粗鬆症を防ぐために効果的なカルシウム補給方法が求められている。そこで，牛乳と市販のカルシウム補給食品を摂取した際のカルシウム吸収量を比較することにより，閉経後女性におけるカルシウム摂取量とカルシウム蓄積率の関係を明らかにすることを試みた。閉経後女性 38 名（平均年齢:58 歳）を対象に炭酸カルシウムを比較食品として，牛乳と高吸収性カルシウムサプリメント（UNICAL™）のクロスオーバー試験を行った。カルシウム摂取量は 700 mg/日に設定され，基礎食 （カルシウム含有量 250 mg/日） に加えて，試験 1 （19 人） では牛乳または炭酸カルシウムから，試験 2 （19 人） では UNICAL™ または炭酸カルシウムから，それぞれ 450 mg/日のカルシウムを摂取した。尿・便中のカルシウム排出量を測定し，摂取量に対するカルシウム蓄積率を比較した。その結果，炭酸カルシウムと比較したカルシウム蓄積率の差は，試験 1 における牛乳が−0.2%，試験 2 では UNICAL™ が 6.1%といずれも大差なく，統計的に有意な差ではなかった。したがって，UNICAL™ は閉経後の日本人女性のカルシウム損失を減らす効果が牛乳と同等であることが明らかとなった。しかし，牛乳，UNICAL™，炭酸カルシウムのいずれの場合も，一日あたりの摂取量（700 mg/日）を上回るカルシウムが尿と便に排出されており, 従来の一般的な推奨摂取量である 650 mg/日では，閉経後女性のカルシウム損失による骨粗鬆症の進行を防ぐことが困難であることが判明した。

Keywords: カルシウムサプリメント，閉経後女性，骨粗鬆症，クロスオーバー試験

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