Equilibrium Intakes of Calcium and Magnesium within an Adequate and Limited Range of Sodium Intake in Human

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Summary In the previous analysis of our human mineral balance studies, we demonstrated positive correlations between the balances of calcium (Ca) and magnesium (Mg) and sodium (Na) intake in the range of 3.06 and 4.06 g/d or 43.71 and 96.40 mg/kg body weight (BW)/d, but there was no correlation between Na intake and Na balance. This suggested that the balances of Ca and Mg are affected by Na intake. Therefore, in the current study, we recalculated equilibrium intakes for Ca and Mg when balances of their intakes and outputs were equal to zero within the above Na range to reduce the effects of Na intake. From 1986 to 2000, 90 volunteers (10 male, 80 female; age 18 to 28 y) took part in 9 mineral balance studies. The balance periods ranged from 8 to 12 d, with adaptation periods of 2 to 4 d. The dietary intakes of Ca and Mg ranged from 294 to 719 and 154 to 334 mg/d, or from 4.83 to 15.07 and 2.44 to 6.42 mg/kg BW/d, respectively. Intake of Ca significantly correlated with Ca balance ($r^2=0.268$, $p<0.0001$). When the balance was equal to zero, the mean value and upper limit of the 95% confidence interval for the regression equation between intake vs. balance were 10.072 and 10.660 mg/kg BW/d, respectively. Mg intake correlated significantly with Mg balance ($r^2=0.141$, $p=0.003$). When the balance was equal to zero, the mean value and upper limit of the 95% confidence interval for the regression equation between intake and balance were 4.078 and 4.287 mg/kg BW/d, respectively.

Key Words equilibrium intakes of Ca, equilibrium intakes of Mg, adequate Na intake, human balance study

It is generally believed that there are three levels of dietary intake of a nutrient: excess, adequate and deficit. The border between excess and adequate is recognized as the upper limit, while the other border between adequate and deficit is termed the requirement.

To determine an upper limit and a requirement for a nutrient, it is necessary to understand the scientific evidence indicating quantitative information about the dietary intake and the signs and symptoms of excess or deficit of the nutrient.

For the minerals (sodium [Na], potassium [K], calcium [Ca], magnesium [Mg] and phosphorus [P]), whose signs and symptoms of deficit or excess are poor, the determination of the requirement and the upper limit is difficult because of the absence of evidence.

In such cases, the equilibrium intakes (EI) to keep balances of nutrients zero as results of balance studies, are the sole sources of information available to determine the dietary reference intakes (DRIs). However, this value is not equal to the estimated average intake (EAR) in DRIs, but a value in adequate intakes.

In order to estimate the equilibrium intakes (EI) of the above-mentioned minerals, we conducted 11 human mineral balance studies (1–9). In the previous analysis for Ca, Mg and P, we demonstrated positive correlations between the intake and balance for Ca and P, but failed to do so for Mg (5, 6). We demonstrated, however, positive correlations between Mg intake and balance of both Ca and P, which gave the equilibrium intakes (EI) for Mg (7).

On the other hand, in the previous analysis for Na and K, we also demonstrated positive correlations between the intake and balance for Na and K. However, correlation between the intake and balance for Na turned to be not significant when omitting data of two experiments whose Na intake were 2.21 g/d (the lowest Na intake and negative Na balance study) (1) and 6.87 g/d (the highest Na intake and the positive Na balance study) (2). So, we considered the range of Na intakes in the remaining nine experiments to be adequate or within the range between the requirement and the upper limit.

In addition, we already noticed that a relatively low Na intake induced bone absorption to compensate for...
the Na deficit because bone is the sole physiological pool of Na, which was inevitably coupled with loss of Ca and Mg from the bone (1, 10). So, we compared the relationship between intake of Na and balances of Ca and Mg, and found positive correlation between them. These findings suggested that balances of Ca and Mg are affected by Na intake. Therefore, in this study, to reduce the effects of Na intake, we recalculated the equilibrium intakes for Ca and Mg within the adequate Na intake range (3.06 and 4.06 g Na/d) using the same data but omitting the highest (6.87 g Na/d) and lowest (2.21 g Na/d) Na intake studies (6). Na intakes of omitted data are not common in Japan, and this analysis may be better for determining the dietary reference intakes for Japanese.

SUBJECTS AND METHODS

The data analysed in this study included nine previously reported mineral balance studies (1–9), but we omitted the highest and lowest Na intake studies (Table 1). Between 1986 and 2000, 90 volunteers (10 male, 80 female; age 18 to 28 y) took part in 9 mineral balance studies. All subjects provided written, informed consent. The studies were approved by the ethics committee established by the National Institute of Health and Nutrition in 1990, and they were carried out in a metabolic unit.

Table 1 shows the clinical details of the subjects, including the duration of the balance studies; the calculated daily intakes of energy, protein, and fat; and the measured dietary intakes of minerals (Na, K, Ca, and Mg).

| Exp. No. | Sex | Subjects | Duration | Energy | Protein | Fat | Intake of minerals |
|---------|-----|----------|----------|--------|---------|-----|--------------------|
|         |     | n | (d) | (kcal/d) | (g/d) | (% of energy) | Na | K | Ca | Mg |
| 1       | f   | 12 | 8   | 1,850   | 64    | 33  | 3.45 | 1.83 | 294 | 188$ |
| 2       | f   | 11 | 8   | 1,900   | 66    | 35  | 3.40 | 1.86 | 347 | 186$ |
| 3       | f   | 12 | 10  | 1,650   | 65    | 35  | 3.27 | 2.06 | 495 | 194 |
| 4       | f   | 8  | 12  | 1,950   | 87    | 27  | 4.06 | 2.68 | 629 | 261$ |
| 5       | f   | 7  | 8   | 1,800   | 76    | 26  | 3.06 | 2.20 | 653 | 216$ |
| 6       | f   | 7  | 8   | 1,700   | 69    | 25  | 3.08 | 2.20 | 671 | 243$ |
| 7       | f   | 12 | 8   | 1,550   | 75    | 38  | 3.90 | 2.55 | 672 | 261$ |
| 8       | m   | 5  | 10  | 2,150   | 71    | 24  | 3.20 | 1.96 | 676 | 154 |
| 9       | f   | 8  | 12  | 1,750   | 78    | 25  | 3.69 | 2.47 | 719 | 279$ |

Total: 90

Omitted experiments
| f | 6 | 10 | 1,950 | 89 | 25 | 2.21 | 2.71 | 802 | 283 |
| m | 13 | 5 | 3,250 | 136 | 28 | 6.87 | 3.61 | 1,131 | 379 |

Energy, protein and fat are calculated values, while minerals are measured ones.
$Mg$ (180 mg/d) was added to the diet as magnesium oxide (MgO).
$Low calcium study.$
$Mineral lost during exercise was estimated (n=43).
The dietary intake of Ca was 294–719 mg/d (4.83–15.07 mg/kg BW), and the intake of Mg was 154–334 mg/d (2.44–6.42 mg/kg BW/d) (Table 1). The relationship between dietary intake, apparent absorption, urine output, and balances for Ca and Mg are shown in Figs. 1 and 2.

The dietary intake of Na was 3.54–8.67 g/d (0.57–1.34 g/kg BW), and the intake of K was 2.94–6.78 g/d (0.47–1.07 g/kg BW) (Table 1). The relationship between dietary intake, apparent absorption, and balances for Na and K are shown in Figs. 3 and 4.

RESULTS

The dietary intake of Ca was 294–719 mg/d (4.83–15.07 mg/kg BW), and the intake of Mg was 154–334 mg/d (2.44–6.42 mg/kg BW/d) (Table 1). The relationship between dietary intake, apparent absorption, urine output, and balances for Ca and Mg are shown in Figs. 1 and 2.

Dietary intake (Intake) of Ca positively correlated with the apparent absorption (AA) \( r^2 = 0.446 \), which also correlated with both urine output (Urine) and balance (Balance).
(r²=0.309) and balance (Balance) (r²=0.571). Intake of Ca significantly correlated with Balance (r²=0.268; p<0.0001). The mean value and upper limit of the 95% confidence interval for the regression equation between Intake and Balance when the balance was equal to zero were 10.072 and 10.660 mg/kg BW/d, respectively.

The intake of Mg positively correlated with AA (r²=0.471), which also correlated with both Urine (r²=0.470) and Balance (r²=0.470). In addition, Mg Intake significantly correlated with Bal (r²=0.141, p=0.003). The mean value and upper limit of the 95% confidence interval for the regression equation between Intake and Balance when the balance was equal to zero were 4.078 and 4.287 mg/kg BW/d, respectively.

The relationships between Intake and AA rate (%) of Ca and Mg are shown in Fig. 3. There was not a significant correlation between these values. The AA rate (%) for Ca and Mg were (mean±SD) 29.289±10.135% (range: 5–53%) and 44.189±8.700% (range: 27–63%), respectively.

**DISCUSSION**

We found that the intake of Na is one of the factors that affects the metabolism of Ca and Mg (9). Therefore, we recalculated the equilibrium intakes (EI) for Ca and Mg using the same data but omitted the highest and lowest Na intake studies. Consequently, in the relationship between the intake and the balance of Ca, we obtained higher correlation coefficients and lower EI values. Specifically, the previously determined values were r²=0.036 (p=0.048) and 11.752 mg/kg BW/d (n=109) (6), whereas we calculated r²=0.268 (p<0.001) and 10.113 mg/kg BW/d (n=90). In addition, we calculated a stronger correlation and lower EI for the relationship between the intake and the balance of Mg. The previous values were r²=0.018 (not significant) and 4.395 mg/kg BW/d (n=109) (6), whereas we calculated r²=0.141 (p=0.003) and 4.078 mg/kg BW/d (n=90).

These results confirm that the level of Na intake is one of the factors that affects the requirements of Ca and Mg and that under an adequate Na status, the EIs of Ca and Mg are lower than those determined when Na deficit and excess are included.

This may because Na is stored in the bone physiologically as well as Ca and Mg. When Na is short in the blood stream, Na in the bone will be resorbed together with Ca and Mg by macrophage (13), which inevitably increases serum and urine Ca and Mg and decreases intestinal absorption of the two minerals. Omitted data is located above the equation lines between the intake and the apparent absorption in Figs. 1 and 2. When Na intake is excess, renal excretion of Ca and Mg might be increased with that of Na (14), although there is not enough evidence. Omitted data is located within the equation lines between the apparent absorption and the urine excretion in Figs. 1 and 2. So, under the adequate intake of Na, the EIs of Ca and Mg are lower than those determined when Na deficit and excess are included.

Salt intake in Japanese females (20–29 y) was reported to be 9.8±3.8 g/d (mean±SD) (15) and new EIs may be more appropriate to determine DRIs in Japan. DRIs of Ca and Mg for other countries and areas where people consume less salt should be considered when studying the effects of Na intake on the absorption of Ca and Mg.

The apparent absorption (AA) rate (%) for Ca and Mg were (mean±SD) 29.289±10.135% (range: 5–53%) and 44.189±8.700% (range: 27–63%), respectively. There was not a significant correlation between these values. This means that AAs (%) for Ca and Mg were affected by a lot of factors other than the intake. The relationship between the intake and apparent absorption and between the apparent absorption and urine for Ca and Mg are significant but far weaker, compared with those for Na, K and P (6, 8). These data also showed the absorption and urine excretion of Ca and Mg were affected by a lot of factors. Among these factors we already demonstrated that risk factors for chronic degenerative diseases such as physical exercise (16–18), overeating (19, 20) and stress (20, 21) as well as Na intake (1, 8, 9) modified the metabolism of Ca and Mg.

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**REFERENCES**

1) Kodama N, Nishimuta M, Suzuki K. 2003. Negative balance of calcium and magnesium under a relatively low sodium intake in human. J Nutr Sci Vitaminol 49: 201–209.

2) Nishimuta M, Kodama N, Hitachi Y, Otsawa M, Ahmed SM, Oomori T. 1991. A mineral balance study in male long distance runners. J Jap Soc Mg Res (JJSMgR) 10: 243–253 (in Japanese).

3) Nishimuta M, Kodama N. 1993. Magnesium balances studies in young Japanese. J Jap Soc Mg Res (JJSMgR) 12: 29–37 (in Japanese).

4) Takeyama H, Kodama N, Fuchi T, Nishimuta M. 1997. Magnesium, calcium and phosphorus balances in young males at low dietary magnesium levels with or without magnesium supplementation. In: Advances in Magnesium Research: 1 (Smetana R, ed), p 355–363. John Libbey & Co Ltd, London.

5) Nishimuta M, Kodama N, Yoshioka YH, Morikuni E. 2001. Magnesium intake and balance in the Japanese population. In: Advances in Magnesium Research: Nutrition and Health (Rayssiguier Y, Mazur A, Durlach J, eds), p 197–200. John Libbey & Co Ltd, London.

6) Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Takeyama H, Yamada H, Kitajima H, Suzuki K. 2004. Balance of calcium, magnesium and phosphorus in Japanese young adults. J Nutr Sci Vitaminol 50: 19–25.
7) Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Yamada H, Kitajima H, Takeyama H, Suzuki K. 2004. Balance of magnesium positively correlates with that of calcium. *J Am Coll Nutr* 23: 768S–770S.

8) Kodama N, Morikuni E, Matsuzaki N, Yoshioka YH, Takeyama H, Yamada H, Kitajima H, Nishimuta M. 2005. Sodium and potassium balances in Japanese young adults. *J Nutr Sci Vitaminol* 51: 161–168.

9) Nishimuta M, Kodama N, Morikuni E, Yoshioka YH, Takeyama H, Yamada H, Kitajima H. 2004. Positive correlation between dietary intake of sodium and balances of calcium and magnesium in young Japanese adults—Low sodium intake is a risk factor for loss of calcium and magnesium—. *J Nutr Sci Vitaminol* 51: 265–270.

10) Nishimuta M, Kodama N, Ono K, Kobayashi S, Suzuki K. 1985. Mineral contents in arm sweat at a low mineral diet with special reference to the onset of physical exercise. *J Jap Soc Mg Res* (JJSMgR) 4: 13–21 (in Japanese).

11) Resources Council, Science and Technology Agency, Japan. 1982. Standard Tables of Food Composition in Japan. 4th revised ed. Oookurashou Insatukyoku, Tokyo (in Japanese).

12) Ministry of Health and Welfare of Japan. Dietary Allowances for the Japanese. 3rd (1984), 4th (1989), 5th (1994), and 6th (1999) revised ed. Daiichi Shuppan, Tokyo (in Japanese).

13) Kumezawa M. 1993. Formation and function of osteoclast. *Molecular Medicine* 30: 1240–1247 (in Japanese).

14) Itoh R, Suyama Y. 1996. Sodium excretion in relation to calcium and hydroxyproline excretion in a healthy Japanese population. *Am J Clin Nutr* 63: 735–740.

15) Ministry of Health, Labour and Welfare of Japan. 2006. Report of the National Health and Nutrition Survey in Japan, 2003. Daiichishuppan, Tokyo (in Japanese).

16) Nishimuta M, Kodama N, Takeyama H, Toyooka F. 1997. Magnesium metabolism and physical exercise in human. In: Magnesium: Current Status and New Development (Theophanides T, Anastassopoulou J, eds). p 109–113. Kluwer Academic Publishers, Dordrecht.

17) Nishimuta M, Kodama N, Takeyama H, Suzuki K. 1996. Uresis of calcium and magnesium after diets followed by physical exercise—Increased intestinal absorption after physical exercise—. *J Jap Soc Mg Res* (JJSMgR) 15: 133–139 (in Japanese).

18) Meludu SC, Nishimuta M, Yoshiike Y, Toyooka F, Kodama N, Kim CS, Maekawa Y, Fukuoka H. 2001. Magnesium homeostasis before and after high intensity (anaerobic) exercise. In: Advances in Magnesium Research: Nutrition and Health (Rayssiguier Y, Mazur A, Durlach J, eds), p 443–446. John Libbey & Co Ltd, London.

19) Nishimuta M, Tsuji E, Kodama N, Ono K, Kobayashi S. 1988. Magnesiuresis after butter and egg rich diet in young Japanese females. *J Jap Soc Mg Res* (JJSMgR) 5: 53–60 (in Japanese).

20) Nishimuta M, Kodama N, Ono K. 1989. Magnesium uresis by risk factors for chronic degenerative diseases. In: Magnesium in Health and Disease (Itozawa Y, Durlach J, eds). p 279–284. John Libbey & Co Ltd, London.

21) Nishimuta M, Kodama N, Ono K, Matsumoto Y, Tera T, Yamada H, Kobayashi S. 1988. Stress induced magnesiuresis in human. *J Jap Soc Mg Res* (JJSMgR) 7: 123–132 (in Japanese).