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—

Mamoru NISHIMUTA¹, Naoko KODAMA^{1,2}, Eiko MORIKUNI¹, Yayoi H. YOSHIOKA¹,
Nobue MATSUZAKI¹, Hidemaro TAKEYAMA^{1,3}, Hideaki YAMADA^{1,4} and Hideaki KITAJIMA^{1,5}

¹Laboratory of Mineral Nutrition, Division of Human Nutrition, The Incorporated Administrative Agency of Health and Nutrition, 1-23-1 Toyama, Shinjuku-ku, Tokyo 162-8636, Japan

²Medical University of Yamanashi, 1110 Shimokato, Tamaho-machi, Nakakoma-gun, Yamanashi 409-3898, Japan

³Nagoya City University Graduate School of Medical Science, 1 Kawasumi, Mizuho-machi, Mizuho-ku, Nagoya, Aichi 467-8601, Japan

⁴Mimasaka Women's University, 32 Kamikawara, Tsuyama, Okayama 708-0002, Japan

⁵Taisho Pharmaceutical Co. Ltd., 3-24-1 Takata, Toshima-ku, Tokyo 170-8633, Japan

(Received March 2, 2004)

Summary The content of calcium (Ca) and magnesium (Mg) in sweat during exercise is considerably higher during a relatively low intake of sodium (Na) of 100 mmol/d than with an intake of 170 mmol/d. For this reason and also because Ca and Mg have a negative balance with a Na intake of 100 mmol/d, we analyzed the relationship between Na intake and balances of Ca and Mg in data from 11 balance studies. From 1986 to 2000, 109 volunteers (23 males, 86 females) with an age range of 18 to 28 y took part in mineral balance studies. The balance periods ranged from 5 to 12 d. In a given experiment, the diet of each subject contained the same quantity of food, although this varied between experiments, and was supplied during the balance period without consideration of body weight. In the data of all the studies ($n=109$), the balances of Ca and Mg did not correlate positively with Na intake. However, when the data of the highest Na study were excluded, the balances of Ca and Mg correlated positively with Na Intake. The mean value for the regression equation between Na intake and Ca and Mg balances when the respective balance was equal to zero were, 63.308 mg Na/kg BW/d (Ca: $n=96$, $r^2=0.134$) and 60.977 mg Na/kg BW/d (Mg: $n=96$, $r^2=0.268$), respectively. These values are considerably higher than Na requirements estimated by inevitable Na loss. Low dietary Na may therefore be a risk factor for maintaining positive balances of Ca and Mg.

Key Words sodium intake, calcium balance, magnesium balance, estimated average sodium requirement, human

In our previous study (1), we demonstrated unexpected results in the sodium (Na), calcium (Ca), and magnesium (Mg) content of arm sweat of young Japanese females during relatively heavy bicycle ergometer exercise (1.5 kp, 50 rpm, 66 min, twice a day). This exercise was undertaken during a period in which the study participants were consuming a relatively low mineral diet containing dietary Na of 100 mmol/d (or sodium chloride 6 g/d). The Na content was lower and Ca and Mg content markedly higher in the sweat during this experiment compared to identical experiments in which dietary Na intake was 170 mmol/d (or sodium chloride 10 g/d) (2).

Although no reasonable hypothesis has yet been made to explain these results, one assumption has been proposed (3). With regard to nutritional aspects, these three minerals are all stored in bone (4), and therefore

when any of these minerals reaches a critically low level in the body it is eluted from the bone, thereby compensating for any shortage. The mechanism of elution of these minerals from the bone has been shown to occur through non-mineral selective osteolysis by macrophages (5). If such a mechanism occurs during Na restriction, it is possible that excess Ca and Mg may also be eluted in association with Na and enter the blood stream, leading to an inevitable reduction in intestinal absorption and increase in urine excretion of these minerals. Recently, we reported evidence of such changes with a negative balance of Ca and Mg occurring under relatively low Na intake (ca. 100 mmol/d) in humans (6).

With the assumption that there is a correlation between Na intake and the balances of Ca and Mg, it may be suggested that Na intake will be a factor that may have major effects on the metabolism of these minerals. If this is the case, two estimations of the average

requirements of Na may be used for calculating the regression equations of Na intake and balances of Ca and Mg. The present study involved further analysis of the data of balance studies conducted in our laboratory to investigate these relationships.

SUBJECTS AND METHODS

The data analysed are the same as those reported previously (6–13). From 1986 to 2000, 109 volunteers (23 males, 86 females), age ranging from 18 to 28 y, took part in 11 mineral balance studies after having provided written, informed consent. The ethics committee, established by the National Institute of Health and Nutrition in 1990, approved the studies, which were carried out in a metabolic unit. The clinical details of the subjects, duration of the balance studies, calculated daily intakes of energy, protein and fat, and measured dietary intakes of minerals (Na, K, Ca and Mg) are shown in Table 1.

The balance periods ranged from 5 to 12 d, with adaptation periods of 2–4 d. In a given experiment, the diet of each subject contained the same quantity of food, although this varied between experiments and was supplied during the balance period without consideration of body weight. However, small changes to the diet were carried out during the adaptation period in order to ensure that all the food supplied had been consumed.

The subjects ingested an indigestible fecal marker (Carmine 0.3 g: Merck KGaA, Germany) just before breakfast in the morning, at the beginning and end of the balance period.

In one study (No. 4, Table 1), magnesium oxide (180

mg as Mg) was added to the low Mg diet, which had no adverse or favourable effects on balance of Mg (9). In six studies (Nos. 1–3, 8–10, *n*=49, Table 1), sweat from the arm was collected during exercise on a bicycle ergometer in order to estimate loss of the elements from sweating. The foodstuffs used in each study were selected from those commercially available, with the dietary menus designed by a registered dietician so that they met the dietary allowances in Japan (14), with the exception of the low calcium studies (Nos. 6 and 7, Table 1) in which food composition tables were used (15). The minerals present in the diet [Na, potassium (K), Ca and Mg], feces, urine and sweat (Na, Ca, Mg) were measured by the use of an atomic absorption spectrophotometer (Varian AA-5, Australia). Details of these methods have been described previously (6, 11, 13). Statistical analyses were carried out using StatView-J5.0.

The indicators used in this paper are defined as follows:

Apparent absorption=[(Intake)–(Fecal output)] (mg/kg BW/d)

Apparent absorption (%)=[(Intake)–(Fecal output)]/(Intake)×100 (%)

Balance=(Intake)–[(Fecal output)+(Urine output)+(Sweat loss)*] (mg/kg BW/d)

*Only when sweat loss during exercise was estimated.

RESULTS

The results of the study in which Na intake was the highest of all the studies (Na intake 6.87 g/d, ca. 300 mmol/d) showed an apparent positive Na balance (7). In contrast, the results from the study in which Na

Table 1. Subjects and dietary intake of energy and minerals.

Exp. No.	Sex	Subjects (n)	Duration (d)	Energy (kcal/d)	Protein (g/d)	Fat (% of energy)	Intake of minerals			
							Na	K	Ca	Mg
							(g/d)	(g/d)	(mg/d)	(mg/d)
1	f	6	10	1,950	89	25	2.21	2.71	802	283 [#]
2	f	7	8	1,800	76	26	3.06	2.20	653	216 [#]
2	f	2	8	1,800	76	26	3.06	2.20	653	216
3	f	8	8	1,700	69	25	3.08	2.20	671	243 [#]
4	m	5	10	2,150	71	24	3.20	1.96	676	334 [*]
4	m	5	10	2,150	71	24	3.20	1.96	676	154
5	f	12	10	1,650	65	35	3.27	2.06	495	194
6	f	11	8	1,900	66	35	3.40	1.86	347	186 ^s
7	f	12	8	1,850	64	33	3.45	1.83	294	188 ^s
8	f	8	12	1,750	78	25	3.69	2.47	719	279 [#]
9	f	12	8	1,550	75	38	3.90	2.55	672	261 [#]
10	f	8	12	1,950	87	27	4.06	2.68	629	261 [#]
11	m	13	5	3,250	136	28	6.87	3.61	1,131	379
Total		109								

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).

^sLow calcium study.

[#]Mineral lost during exercise was estimated (*n*=49).

Table 2. Correlation coefficients (*r*²) between Na intakes and metabolic indicators (lines) of Ca and Mg.

	Sample (number)	Na intake (range) (mg/kg BW/d)	Ca intake (range) (mg/kg BW/d)		Ca				
					Intake	AA	AA (%)	Urine	Balance
Na intake	<i>n</i> =109	38.56–142.23	4.83–23.58	<i>r</i> ²	0.416***	0.213***	0.000 NS	0.169***	0.025 NS
	<i>n</i> =96	38.56–96.40	4.83–16.90		0.015 NS	0.111***	0.069**	0.000 NS	0.134***
	<i>n</i> =90	43.71–96.40	4.83–15.07		0.143***	0.163***	0.038 NS	0.109**	0.047*
	Sample (number)	Na intake (range) (mg/kg BW/d)	Mg intake (range) (mg/kg BW/d)		Mg				
					Intake	AA	AA (%)	Urine	Balance
Na intake	<i>n</i> =109	38.56–142.23	2.44–7.83	<i>r</i> ²	0.489***	0.274***	0.020 NS	0.242***	0.029 NS
	<i>n</i> =96	38.56–96.40	2.44–6.42		0.124***	0.239***	0.032 NS	0.015 NS	0.268***
	<i>n</i> =90	43.71–96.40	2.44–6.42		0.373***	0.316***	0.003 NS	0.104**	0.199***

AA: apparent absorption.
p*<0.05, *p*<0.01, ****p*<0.001. NS: not significant.

Fig. 1. Relations between Na intake and metabolic indicators (intake, apparent absorption, urine and balance) of Ca in Japanese young adults (*n*=96 or 90). Data of the highest Na intake study (No. 11, Table 1) were omitted in these figures. Data of the lowest Na intake study are shown as open circles. Regression lines were obtained without the lowest Na intake study (*n*=90).

intake was the lowest of all the studies (2.21 g/d, ca. 100 mmol/d) showed an apparent negative Na balance (6). These data appeared to be different from the remainder of the studies and therefore the regression equations were calculated in the following three ways: all 11 studies (*n*=109); the 10 studies that did not include the highest Na study (*n*=96); and the 9 studies that did not include the highest and lowest Na studies (*n*=90).

The correlation coefficients (*r*²) between the dietary intakes of Na and metabolic indicators of Ca and Mg [intake, apparent absorption (AA), urinary excretion (urine) and balance] are shown in Table 2, grouped according to data used in the analyses as described above. In the data of the combined studies (*n*=109), the balances of Ca and Mg were not correlated positively with Na intake, whereas in the data that excluded the highest Na study (*n*=96) or the highest and lowest Na studies (*n*=90), the balances of Ca and Mg were correlated positively with Na intake.

Relationship between Na intake and indicators of Ca and Mg metabolism

In the data with the highest Na study excluded (*n*=96), there was no correlation between Na intake and intake or urine of Ca, whereas significant correlations existed between Na intake and AA and AA (%) of Ca. The same data showed a correlation between Na intake and intake and AA of Mg but not with AA (%) or urine of Mg. Analysis of the data with the highest and lowest Na studies excluded (*n*=90) showed that all four indicators for both Ca and Mg with the exception of AAs (%) correlated positively with Na intake (Figs. 1 to 3).

Estimated average requirement (EAR) of Na calculated from the relationships between Na intake and Ca and Mg balances

No significant correlation between Na intake and either Ca or Mg balance was found in the analysis of the data from all 11 studies (*n*=109). However, the degree of correlation became significant when the data of the highest Na intake study was excluded (*n*=96 and

Fig. 2. Relations between Na intake and metabolic indicators (intake, apparent absorption, urine and balance) of Mg in Japanese young adults ($n=96$ or 90). Data of the highest Na intake study (No. 11, Table 1) were omitted in these figures. Data of the lowest Na intake study are shown as open circles. Regression lines were obtained without the lowest Na intake study ($n=90$).

Fig. 3. Relations between apparent absorptions (%) (AA%) of Ca and Mg and intakes of Na and respective elements in Japanese young adults ($n=96$ or 90). Data of the highest Na intake study (No. 11, Table 1) were omitted in these figures. Data of the lowest Na intake study are shown as open circles when compared with Na intake and shown as closed circles when compared with the intakes of the respective minerals. Regression lines between Na intake and AAs (%) were obtained with 90 data while those between the intakes and AAs (%) of the respective minerals were from 96 data. Na intake is positively correlated to AA% of Ca when the data of the lowest Na study are included in the analysis. Ca intake is not correlated to its AA%. AA% of Mg is not correlated to Na intake but to Mg intake.

$n=90$) as shown in Figs. 1 and 2. The mean value and upper and lower limits of the 95% confidence interval for the regression equation between Na intake and Ca and Mg balances when the respective balance was equal to zero were, 64.861, 62.784, 66.973 mg Na/kg BW/d (Ca: $n=90$, $r^2=0.047$), 63.308, 61.172, 65.444 mg Na/kg BW/d (Ca: $n=96$, $r^2=0.134$), 62.766, 60.578, 64.953 mg Na/kg BW/d (Mg: $n=90$, $r^2=0.199$) and 60.977, 58.783, 63.170 (Mg: $n=96$, $r^2=0.268$) mg Na/kg BW/d, respectively.

DISCUSSION

This study on mineral balance data of 109 subjects is the first report on the relationship between dietary Na intake and Ca and Mg balances in young Japanese adults.

Positive correlation between Na intake and Ca and Mg balances

Several studies have reported that high intake of Na increases not only urinary Na but also urinary Ca excretion (16). However, these data did not take into account the changes in apparent absorption of Ca caused by the increase in Na intake. As a consequence of this omission high Na intake was regarded as a factor in the loss of body Ca. In contrast, the present study demonstrated positive correlations between Na intake and Ca and Mg balances within limited ranges of Na intake. This indicates that low Na intake decreases the absorption of both Ca and Mg, leading to a reduction in the urine excretions of both minerals. This effect was not apparent in our study of the lowest Na intake with this data showing increases in urine excretion of Ca and

Mg despite apparent absorption of these minerals being decreased (6). When Na status reaches a critically low level in the body, Na is eluted from the bone in order to compensate for any shortage. Under these conditions Ca and Mg may also be eluted from bone leading to an increase in urine excretion of both minerals.

As there was a strong correlation between apparent absorption and urinary excretion of both Ca and Mg (11), low dietary Na intake may therefore be a risk factor for maintaining positive balances of Ca and Mg.

In a previous study we found that Na intake correlated positively with Na balance only when the data of the study with the highest Na intake was included in the analysis (13). Na intake of 300 mmol/d may be excessive and require an alternative mechanism for excretion of Na into the urine. The estimated average requirement (EAR) of Na can be determined based on the relationship between Na intake and Ca and Mg balances, as within the range where Na intake is not correlated with Na balance, Na intake is correlated positively with both Ca and Mg balances.

Estimated average requirement of Na

The mean values for the regression equation between Na intake and Ca and Mg balances when the respective balance was equal to zero were, 64.861 mg Na/kg BW/d (Ca: $n=90$, $r^2=0.047$), 63.308 mg Na/kg BW/d (Ca: $n=96$, $r^2=0.134$), 62.766 mg Na/kg BW/d (Mg: $n=90$, $r^2=0.199$) and 60.977 mg Na/kg BW/d (Mg: $n=96$, $r^2=0.268$), respectively. These values are equivalent to the estimated average requirements (EARs) of Na.

In a previous analysis we reported a significant correlation between Na intake and Na balance in the data of all 11 studies ($n=109$). The mean value and upper and lower limits of the 95% confidence interval for the regression equation between intake and balance for Na, when Na balance was equal to zero, were 55.824, 60.787 and 50.862 mg Na/kg BW/d, respectively ($r^2=0.361$) (13). These values are considerably higher than the Na requirement estimated by inevitable Na loss (16). However, this correlation was not significant when the data of the highest Na intake study was excluded ($n=96$ and $n=90$) (13). Thus, the EAR of Na, as the value for maintaining a positive Na balance should not be considered as the definitive value.

In this study, there was a positive correlation between Na intake and the balances of both Ca and Mg when the data of the highest Na intake study was excluded ($n=96$ and $n=90$). The EARs calculated in the present study are higher than those obtained in our Na study (13). However, the data used in this analysis showed there was no correlation between Na intake and Na balance.

If the EARs of Na are used as the values for maintaining a positive balance of Ca and Mg, this equates to 60–63 mg Na/kg BW/d. Therefore EAR for adult Japanese aged 30–49 y are 4.08–4.28 g Na/d (10.4–10.9 g NaCl/d or 178–186 mmol/d) for males (height 170.0 cm, weight 68.0 kg) and 3.16–3.32 g Na/d (8.0–8.4 g NaCl/d or 137–144 mmol/d) for females (height 156.8 cm, weight 52.7 kg) (17).

In this paper, we reported the upper and lower limits of the 95% confidence interval for the regression equations between Na intake and Ca and Mg balances when the balances of Ca and Mg were equal to zero. However, these values are not the same as those used in the United States of America to determine the recommended dietary allowance for Na (18). The statistical value of Na intake that resulted in 97.5% of population maintaining positive balances of Ca and Mg ($\pm 2SD$) may be difficult to find experimentally and may not even exist. Instead of this value, upper limits of the 95% confidence interval for the regression equation between Na intake and Ca and Mg balances when the respective balance was equal to zero will be proposed for recommended dietary allowance for Na as scientific values.

Although excess salt (NaCl) intake is an important etiological factor in salt sensitive hypertension, it has not been determined how much is excessive or whether short intakes of Na results in increases in blood pressure. In our previous study (13) as well as in this study, we showed Na intake affected the balances of Na, K, Ca and Mg with an intake of about 55–65 mg of Na per kg of body weight each day being required to maintain a positive balance of these minerals. This value represents the average Na requirement and corresponds to the borderline between short and adequate but is beyond the borderline between adequate and excess for the dietary reference intakes (DRIs) of Na (17, 18). Our results may therefore explain the higher incidence of ischemic heart diseases and bone fracture in Western countries compared to those in Japan. Further studies and discussion will, however, be needed to establish the DRIs for Na and to clarify the relation between Na status and etiology of diseases.

In conclusion, we found positive correlations between Na intake and Ca and Mg balances in humans. Using the mean values for the regression equation between Na intake and balances of Ca and Mg we calculated a preliminary estimated average requirement for Na of 60–63 mg Na/kg BW/d.

Acknowledgments

We thank the volunteers who graciously gave their time and effort to these studies.

MN and NK designed the studies. MN, NK, EM, YHY, NM, HT, HY and HK conducted the human metabolic studies and analyzed data. MN wrote the manuscript. MN received grant funding from the Environmental Agency, Health Science Foundation, Uehara Memorial Foundation, the Salt Science Research Foundation (Japan) and the Ministry of Health, Labor and Welfare. None of the authors had a conflict of interest.

REFERENCES

- 1) 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 (JJSMDR)* 4: 13–21 (in Japanese).
- 2) 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.
- 3) Nishimuta M. 1990. The concept (intra and extra cellular minerals). *In: Metal Ions in Biology and Medicine* (Collery P, Poirier LA, Manfait M, Etienne J-C, eds), p 69–74. John Libbey Eurotext, Paris.
- 4) Ishizaki A. 1974. Mineral metabolism. *In: Handbook in Nutrition*, p 605–657. Gihoudou, Tokyo (in Japanese).
- 5) Kumegawa M. 1993. Formation and function of osteoclast. *Molec Med* **30**: 1240–1247 (in Japanese).
- 6) 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.
- 7) Nishimuta M, Kodama N, Hitachi Y, Ozawa M, Ahmed SM, Oomori T. 1991. A mineral balance study in male long distance runners. *J Jap Soc Mg Res (JJS MgR)* **10**: 243–253 (in Japanese).
- 8) Nishimuta M, Kodama N. 1993. Magnesium balances studies in young Japanese. *J Jap Soc Mg Res (JJS MgR)* **12**: 29–37 (in Japanese).
- 9) 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.
- 10) 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.
- 11) 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.
- 12) 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—Estimated average requirement of Mg—. *J Am Coll Nutr* **23**: 768S–770S.
- 13) 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.
- 14) Ministry of Health and Welfare. Dietary Allowances for the Japanese, Third (1984), Fourth (1989), Fifth (1994) and Sixth (1999) revised edition. Daichi Shuppan, Tokyo (in Japanese).
- 15) Resources Council, Science and Technology Agency, Japan. 1982. Standard Tables of Food Composition in Japan, Fourth revised edition. Oookurashou Insatukyoku, Tokyo (in Japanese).
- 16) Cirillo M, Ciacci C, Laurenzi M, Mellone M, Mazzacca G, De Santo NG. 1997. Salt intake, urinary sodium, and hypercalciuria. *Miner Electrolyte Metab* **23**: 265–268.
- 17) Ministry of Health, Labour and Welfare. 2005. Dietary Reference Intakes (DRIs) for the Japanese. (Draft)
- 18) Food and Nutrition Board, Institute of Medicine. 2004. Sodium and chloride. *In: Dietary Reference Intakes for Water, Potassium, Sodium, Chloride, and Sulfate* (2004), p 247–349. Internet: <http://books.nap.edu/books/0309091691/html/247.htm> (accessed 14 February 2005).