Dietary Salt (Sodium Chloride) Requirement and Adverse Effects of Salt Restriction in Humans

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Summary

Inevitable sodium loss under sodium restriction must not be construed as evidence for the estimated average requirement (EAR) for sodium (Na) in humans. We conducted human mineral balance studies to determine the EAR for some minerals (Na, K, Ca, Mg, P, Zn, Fe, Cu and Mn). Na concentration in arm sweat was low while those of calcium (Ca) and magnesium (Mg) were high, during relatively heavy bicycle-ergometer exercise under relatively low Na intake (100 mmol/d). This suggests that Na was released from the bone, the sole pool of Na, with Ca and Mg. Additionally, the negative balances of Ca and Mg was observed under a relatively low sodium intake (100 mmol/d) even with the sufficient supply and intake of Ca and Mg into human body. Finally, we found no correlation between the Na intake and the Na balance, while the Na-intake was correlated significantly to the balances of K, Ca and Mg. The Na intake necessary to keep the balances of Ca and Mg positive was calculated to be 68 mg/kg body weight/d. To learn the signs and symptoms of low sodium intake, we compared the results of a metabolic study in which subjects consumed diets with 6 g and 12 g salt/d respectively. The blood pressure decreased only with the 6 g/d group. Fecal moisture contents of the 6 g/d group were lower than for the 12 g/d group, suggesting the fecal Na was strongly reabsorbed with water when the dietary Na was insufficient. Indiscriminate Na restriction may have adverse effects on health.

Key Words   sodium restriction, potassium, calcium, magnesium

The estimated average requirement (EAR) of a nutrient is the intake level proven to be adequate to maintain the nutrient balance for 50% of the population, according to the definition in the Dietary Reference Intakes for Japanese, 2015 (DRI Japanese 2015) (1). The EAR of sodium (Na), however, was determined as the inevitable Na loss under no sodium intake, with no evidence, whereas the value of inevitable Na loss is the output (i.e., excretion), at which 100% of the subject population suffers from sodium deficiency.

We analyzed, therefore, the data from a series of our human studies of minerals [Na, potassium (K), calcium (Ca), magnesium (Mg), phosphorus (P), iron (Fe), zinc (Zn), copper (Cu), and manganese (Mn)] in order to determine the intakes equivalent to the excretion of those minerals. We do not know of other human mineral balance data measuring multiple elements.

In this review, we focused on the requirement and metabolism of Na based on our original experiment data and the articles based thereon.

All the cited experiments in this review were approved by the ethics committee of the National Institute of Health and Nutrition.

Evidence

1. Bone is the physiological pool for Na as well as Ca and Mg (2)

   In our previous study, unexpected results were demonstrated from the arm-sweat contents of Na, Ca, and Mg of young Japanese females during relatively heavy bicycle ergometer exercise (1.5 kp, 50 rpm, 66 min, twice a day), while taking a relatively low-mineral diet limiting the dietary Na to 100 mmol/d (or NaCl 6 g/d (2).

   Sweat-Na was relatively lower, but sweat-Ca and -Mg were obviously higher than the identical experiments with the only difference being the dietary Na, which was 170 mmol/d (or NaCl 10 g/d) (Fig. 1) (3).

   While no reasonable hypothesis has yet been proposed regarding the nutritional aspects of these three minerals, i.e., Na, Ca, and Mg, the commonality that they are all stored in the bone (4, 5) leads to a series of important facts: first, when any of these minerals reaches the insufficient level in the human body, the depleted mineral is eluted from the bone to compensate for any shortage in the body. The mechanism of elution of these minerals...
from the bone has been reported to occur through non-mineral selective osteolysis by macrophages (6).

When this mechanism functions under Na restriction, then Ca and Mg are collaterally eluted into the blood stream, by the definition of "non-mineral selective osteolysis," only to be in excess, along with Na which is in need of replenishment in the first place. This sequence also causes the unavoidable reduction of sweat Na content, simultaneously with the increase in sweat contents of Ca and Mg. In this experiment, the salt intake of 6 g/d seems to be short, but this value is also the upper limit value for salt according to Dietary Guidelines for Americans, 2010 (7).

2. Na intake, and Ca and Mg balances under a relatively low-Na diet (8)

Whether the salt intake of 6 g/d is insufficient or not became the next question in our series of efforts to determine the requirement of Na for the Japanese. A mineral balance study, therefore, was conducted under the sufficient intake of Ca and Mg.

The balances of minerals (Na, K, Ca, and Mg) were measured under a relatively low Na intake (100 mmol/d or NaCl 6 g/d), with an adequate intake of Ca (20 mmol/d or 800 mg/d) and Mg (12 mmol/d or 280 mg/d) of six female students for 10 d. Plasma renin activity (PRA) and the aldosterone levels were above the reference ranges throughout the experiment. This suggests that all the subjects were in the state of Na insufficiency.

The urinary Na excretion, however, was approximately the same as the ingested amount from the given diet.

On the other hand, the urine Ca and Mg were high, while the apparent absorptions of Ca and Mg were moderate (21±5%, 34±4%, respectively), resulting in the negative balance of these two elements. It is, therefore, scientifically appropriate to conclude that the stored Na in the bones is eluted to compensate for the inadequate dietary Na intake, while the collaterally eluted Ca and Mg unavoidably flow into the blood stream only to be excessive during the bone resorption, causing both the inhibition of the intestinal absorption and the acceleration of the urine excretion of these minerals.

This experiment revealed that even the adequate intake of Ca and Mg did not contribute to a positive balance of these minerals under the low Na intake of 100 mmol/d (NaCl 6 g/d). This study proves, therefore, that there are cases among healthy, young individuals whose Na intake of 100 mmol/d is insufficient, and as a consequence, may cause the negative balance of Ca and Mg (Table 1).

3. The relationship between Na intake and balances of Ca and Mg (9)

In order to confirm the relationship between the Na intake and the balances of Ca and Mg, we analyzed the data accumulated from our series of 11 balance studies.

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**Fig. 1.** Arm sweat contents of sodium (Na), calcium (Ca) and magnesium (Mg) from the female students during the relatively heavy bicycle ergometer exercise (1.5 kp, 50 rpm, 66 min, twice a day) while ingesting a relatively low-mineral diet with a dietary Na of 100 mmol/d (or sodium chloride 6 g/d) (2). All data are individual values of three subjects. The sweat Na was relatively lower, but the sweat Ca and Mg were obviously higher during the experiment as compared to the identical experiments in which the dietary Na was 170 mmol/d (or sodium chloride 10 g/d). (cited from ref. 3).
Table 1. Balance of sodium (Na), potassium (K), calcium (Ca), and magnesium (Mg) under a low Na diet.

<table>
<thead>
<tr>
<th>Sodium (Na)</th>
<th>Potassium (K)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sub.</strong></td>
<td><strong>Intake g/d</strong></td>
</tr>
<tr>
<td>a</td>
<td>2.21</td>
</tr>
<tr>
<td>b</td>
<td>2.21</td>
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<tr>
<td>c</td>
<td>2.21</td>
</tr>
<tr>
<td>d</td>
<td>2.21</td>
</tr>
<tr>
<td>e</td>
<td>2.21</td>
</tr>
<tr>
<td>f</td>
<td>2.21</td>
</tr>
<tr>
<td>Mean</td>
<td>0.02</td>
</tr>
<tr>
<td>SD</td>
<td>0.01</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Calcium (Ca)</th>
<th>Magnesium (Mg)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sub.</strong></td>
<td><strong>Intake mg/d</strong></td>
</tr>
<tr>
<td>a</td>
<td>802</td>
</tr>
<tr>
<td>b</td>
<td>802</td>
</tr>
<tr>
<td>c</td>
<td>802</td>
</tr>
<tr>
<td>d</td>
<td>802</td>
</tr>
<tr>
<td>f</td>
<td>802</td>
</tr>
<tr>
<td>Mean</td>
<td>631</td>
</tr>
<tr>
<td>SD</td>
<td>38</td>
</tr>
</tbody>
</table>

\[^1\] Only half the values of mean sweat loss of 5 physical exercise during 10 d were estimated. (cited from ref. 8)

Fig. 2. Relationship between Na intake and balances of Ca and Mg. Dietary intake of sodium (Na) is not positively correlated to the balance of either calcium (Ca) or magnesium (Mg) when all the data are included (n=109). After excluding the data from the study in which the Na intake was 6.87 g/d (ca. 300 mmol/d), the highest among all the 11 studies, however, and after adopting all the data from the remaining 10 studies (n=96), these sets of correlations emerged to be significant. These sets of correlations are still significant when another set of data from the other extreme study (with the lowest Na intake: 2.21 g/d or ca. 100 mmol/d) was excluded, reducing the number of samples to 90. The mean values and the upper and the lower limits of 95% confidence intervals for the regression equation between the Na intake and the balances of Ca and Mg when each respective balance is equal to zero were: 64.861, 62.784, 66.973/mg Na/kg body weight (BW)/d (Ca: n=90, \(r^2=0.047\)), and 62.766, 60.578, 64.953/mg Na/kg body weight (BW)/d (Mg: n=90, \(r^2=0.199\)), respectively. (modified from ref. 9)

(n=109). The dietary intake of sodium (Na) shows significant correlation to the balances of neither calcium (Ca) nor magnesium (Mg) when all the data (n=109) are subjected to a correlation test. 

By excluding the data from the study in which the Na intake was 6.87 g/d (ca. 300 mmol/d), the highest among all the 11 studies, however, and by adopting all the data from the remaining 10 studies (n=96), the same sets of variables show positively significant correlation. Somewhat weaker but still significant correlation remains in the same combination of variables when another set of data from the study at the other extreme [i.e., the lowest Na intake, 2.21 g/d (ca. 100 mmol/d)] was excluded, reducing the number of samples to 90 (Fig. 2). 

The mean values and the upper and lower limits of 95% confidence intervals for the regression equation
between Na intake and the balances of Ca and Mg when each respective balance is equal to zero were:
64.861, 62.784, 66.973/mg Na/kg body weight (BW)/d (Ca: n = 90, $r^2 = 0.047$), and
62.766, 60.578, 64.953/mg Na/kg body weight (BW)/d (Mg: n = 90, $r^2 = 0.199$),
respectively.

All of these findings confirmed that low Na intake is at least one of the major factors to cause the negative balance of Ca and Mg. The true Na intake necessary to maintain the balance of Ca and Mg must be, therefore, ten times higher than Na requirements estimated from the inevitable Na loss alone (less than 500 mg/d/caput) (1).

4. Proposed dietary Na requirement for Japanese (10)

This series of our study proceeded further to determine the estimated equilibrated dietary intakes (EEDIs) of Na for Japanese. The data from the thirteen studies of young female subjects (total n = 131), consuming a standard diet, were reviewed. Other sets of data from those who were subjected to low sodium intake were excluded from this study. Na balance at the median was positive. Assuming that the unmeasured dermal excretion is most likely causing this gap or offset in reality, we judged that the data might as well be adjusted to shift

Table 2. Equilibrated intake of 9 minerals (n = 131).
Estimated by mg (µg)/kg body weight (BW)/d

<table>
<thead>
<tr>
<th>Element</th>
<th>Units</th>
<th>Intake</th>
<th>Balance</th>
<th>Equilibrated intake</th>
<th>$r^2$</th>
<th>$p$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium (Na)$^3$</td>
<td>mg/kg BW/d</td>
<td>68.0±9.7</td>
<td>67.0</td>
<td>6.07±4.06</td>
<td>6.04 (9.0)</td>
<td>67.9 ±62.0</td>
</tr>
<tr>
<td>Potassium (K)</td>
<td>mg/kg BW/d</td>
<td>40.7±6.8</td>
<td>39.2</td>
<td>4.79±3.47</td>
<td>4.68 (11.9)</td>
<td>40.7 ±38.5</td>
</tr>
<tr>
<td>Calcium (Ca)</td>
<td>mg/kg BW/d</td>
<td>11.0±2.8</td>
<td>11.5</td>
<td>0.04±1.52</td>
<td>0.00 (0.0)</td>
<td>11.0 ±10.5</td>
</tr>
<tr>
<td>Magnesium (Mg)</td>
<td>mg/kg BW/d</td>
<td>4.20±0.82</td>
<td>4.08</td>
<td>0.18±0.39</td>
<td>0.16 (3.9)</td>
<td>4.18 ±4.06</td>
</tr>
<tr>
<td>Phosphorus (P)$^2$</td>
<td></td>
<td>18.6±3.5</td>
<td>17.6</td>
<td>–0.18±1.45</td>
<td>–0.21 (–1.2)</td>
<td>18.7 ±18.1</td>
</tr>
<tr>
<td>Iron (Fe)</td>
<td>µg/kg BW/d</td>
<td>180±49</td>
<td>179</td>
<td>28.9±28.7</td>
<td>28.1 (15.7)</td>
<td>180 ±165</td>
</tr>
<tr>
<td>Zinc (Zn)$^3$</td>
<td>µg/kg BW/d</td>
<td>182±82</td>
<td>160</td>
<td>14.5±24.1</td>
<td>15.4 (9.6)</td>
<td>181 ±162</td>
</tr>
<tr>
<td>Copper (Cu)</td>
<td>µg/kg BW/d</td>
<td>32.8±10.7</td>
<td>28.7</td>
<td>4.78±10.5</td>
<td>4.14 (14.4)</td>
<td>32.3 ±29.6</td>
</tr>
<tr>
<td>Manganese (Mn)$^4$</td>
<td></td>
<td>55.0±8.1</td>
<td>53.6</td>
<td>–0.48±8.11</td>
<td>0.89 (1.7)</td>
<td>55.1 ±5.3</td>
</tr>
</tbody>
</table>

1 Equilibrated intake of Na was obtained from the relationship between Na intake and adjusted K balance.
2 n = 119.
3 Equilibrated intake of Zn was obtained from the relationship between Zn intake and adjusted Fe balance.
4 n = 91
(cited from ref. 10).
the median of the Na balances to zero (or neutral) to cancel the unmeasured dermal excretion.

No significant simple regression equation was obtained from the direct comparison of the intake, against the balance of Na per se. As an alternative, K balances were statistically tested to determine the intercepts for Na intake (Fig. 3). EEDI of Na to maintain the K balance at 0 are 67.9 mg/kg body weight (BW)/d (Table 2).

5. Fecal excretion of Na in humans (11)

Feces are one of the Na excretion sites in humans. Little is known, however, about the nature of fecal Na. We measured, therefore, the fecal moisture and minerals (Na, K, Ca, Mg, P, Fe, Zn, Cu, and Mn) in a balance study.

Na content is strongly related to fecal moisture. Na content in feces was low and stable when the moisture content was below 80%, while it increased when the moisture content exceeded 80%.

On the other hand, the fecal K content increased with the fecal moisture against the dry matter. The K concentration/g moisture base, however, is somewhat complicated, as the fecal K content increased with the moisture when the fecal moisture was below 70%, but decreased in cases with the fecal moisture exceeding 70%.

A significantly negative correlation was found between the fecal Na and K contents with the fecal moisture exceeding 80% (Fig. 4). This relationship indicates that there is an exchange of Na and K through the intestinal membrane when the fecal moisture increased, e.g., in case of diarrhea.
As the exchange rate of Na/K is essentially 1 (Fig. 5), this exchange may increase the moisture content in feces as a consequence of Na entering the intestine accompanied by water. The maximum level of Na concentration measured in feces was as high as the Na levels in serum, a finding consistent with the mechanism described above. Na intake may influence the relationship between the fecal moisture and the contents of minerals.

6. Urine excretion of Na in humans (8, 12)

Urine-Na and -K excretion is known to show daily variations, i.e., high in daytime and low at night (13). In an experiment with a low-Na diet, urine Na showed the same daily variation as the cases with the moderate-Na diet.

At the beginning of the experiment (Pre-period), urine-Na was relatively higher with the moderate dietary Na intake before the experiment, but within the first 14 h. into the experiment, reached lower levels, as the graph shows (Fig. 6). This may be the sign that Na control in kidney is reacting immediately to the Na restriction (8).

On the other hand, after the sodium loading (500 mL, 0.9% saline), urine Na increased immediately following ingestion, and reached the maximum level within 2 h after ingestion. The kidney reacts immediately to both Na loading and restriction (12).

7. Signs and symptoms of sodium restriction (14)

To learn the signs and the symptoms of low sodium intake, as well as the relationship between the fecal moisture and the contents of minerals, the results of a metabolic study, based on diets with a Na intake of 100 mmol/d (NaCl 6 g/d) and 200 mmol/d (NaCl 12 g/d) were compared.

Blood pressure decreased significantly only when the 6 g/d diet was supplied. The fecal moisture contents of the 6 g/d group were lower than those of the 12 g/d group (72.51±7.61%, vs. 80.59±4.65%, p=0.000), suggesting that fecal Na was strongly reabsorbed with water when the dietary Na was insufficient. Salt restriction to 6 g/d in people with normal blood pressure may have disadvantageous effects against health, such as hypotension and constipation.

Consideration

Inevitable Na loss under sodium restriction

In the current estimated average requirement of sodium [EAR (Na)] for the Japanese, the inevitable Na loss under sodium restriction is used in lieu of scientific evidence. The inevitable Na loss under Na restriction, however, is nothing but one of the lowest possible values of the total Na excretion, and lacks the evidence and/or the substantiation to be construed as the true EAR that assures the maintenance of health with the balanced ingestion and excretion of Ca and Mg under diversified conditions. Water and Na loss from the extra-cellular fluid may not be recovered by Na ingestion barely equivalent to the inevitable loss alone. Further, no report, so far, denies with evidence the risk that the stored Na in the bone, the major physiological Na pool in the human body, may not be replenished. Therefore, the inevitable Na loss under Na restriction must not be construed as the EAR (Na). We suspect that some amount of Na is necessary to maintain renal function physiologically, as is the case with water as the “inevitable water loss.”

Estimated Na requirement

No significant correlation emerged between Na intake and Na balance from our data. This means, as a consequence, that it is impossible to determine the estimated Na requirement based only on these two parameters. By comparing the Na intake against the balances of K, Ca and Mg, however, significant sets of correlation emerged (10). It is possible, therefore, to determine the Na requirement based on these sets of correlation. More realistically estimated Na requirement can be obtained that maintains positive balances of K, Ca and Mg. In addition, the median of the Na balance is positive, showing that the systemic dermal Na loss, which was not measured, was not negligible. Therefore, the authors propose to approximate the effect of non-measured dermal loss, (and cancel the displacement caused by the dermal Na loss on the graph) by shifting the median of Na balance to zero arbitrarily. In the cases of P and Mn, whose dermal losses were negligible, the medians of balances were almost zero, and therefore, did not need to be adjusted arbitrarily for the unmeasured dermal losses.

Our final proposal of the Na requirement for the Japanese, based on this study, is 67.9 mg/kg body weight/d, 89.0 mg/kg lean body mass, or 62.5 mg/kg standard body weight [22×(height (m))^2]/d (10).

When this value (67.9 mg/kg body weight) introduces to the reference body weight, (68.5 kg for 30–49 y males, 53.1 kg for 30–49 y females), the salt (NaCl) requirement is 11.8 g/d for males and 9.2 g/d for females, respectively.

On the other hand, recently the National Health and Nutrition Survey in Japan (2016) reported that mean dietary salt intake was 10.8 g/d for men and 9.1 g/d for women, respectively (15).

From our data in this review, we judged mean salt status in Japanese appropriate in these years.

Na insufficiency

In this review, the signs and the symptoms of a low salt intake of 6 g/d (ca. 100 mmol/d), were described based on our experiment. First to be mentioned among the grave symptoms of sodium insufficiency is bone resorption. The abnormal increase in the sweat concentration of Ca and Mg associated with the decrease in that of Na, during relatively heavy physical exercise, is evidence to substantiate the bone resorption to utilize Na from the bone (2).

In addition, the balances of Ca and Mg were negative even with the sufficient intakes of these minerals per se, with a salt intake of 6 g/d (ca. 100 mmol/d) (8).

Na intake is significantly related to the balances of K, Ca and Mg (10). All of these facts indicated that the bone is the physiological reservoir of Na, and when Na is insufficent, bone Na is resorbed to compensate for the Na insufficiency in the body.

The second symptom is the decrease in fecal moisture.
Fecal moisture is related to the concentration of fecal Na. Fecal Na may be reabsorbed more under Na insufficiency compared to the control (11, 14). This decrease in fecal moisture may cause constipation.

The third symptom is the decrease in blood pressure. Usually a low-salt diet is effective for the treatment of essential hypertension to decrease pathologic high blood pressure (BP). Even for the normal BP subjects, however, a low-salt diet has led to BP decrease. Therefore, the low-salt diet may cause hypotension for the normal BP population.

Adding to the results of our studies, low salt intake is known to cause a decrease in extracellular fluid (dehydration), and reduce the resistance against fever. Low sodium intake, therefore, is disagreeable, and may not be recommendable, for maintaining health especially for the elderly.

A tentative dietary goal for preventing life-style related disease (upper limit of NaCl in Dietary Reference Intakes for Japanese (2015) was determined for adult males and females as 8.0 g/d and 7.0 g/d, respectively. These values are less than that we proposed in this review. We strongly expect to reconsider the Na requirement as quickly as possible to avoid salt insufficiency.

**Low sodium intake as a treatment for hypertension**

It is widely established to treat the hypertensive patients by advising them to decrease their salt intake. The demerit of decreasing the salt intake is described in the preceding sections. Sodium restriction seems to be a better treatment than medication for hypertension with some side effects. More evidence is needed to authenticate the application of salt restriction for essential hypertension, including the dose of salt.

**Conclusion**

Our final proposal of the Na requirement for the Japanese, based on this study, is 67.9 mg/kg body weight/d. 89.0 mg/kg lean body mass, or 62.5 mg/kg standard body weight [22×(height(m))²]/(10).

Estimated equilibrated dietary intake of Na derived from this research for adult (30–49 y) men (68.5 kg) and women (53.1 kg) is 11.8 g NaCl (or 4.65 g Na) and 9.2 g NaCl (or 3.61 g Na), respectively (15).

It is possible to determine the Na requirement based on the sets of significantly positive correlations between Na intake and the balances of K, Ca and Mg. The estimated Na requirement can be more reasonably determined to keep all the balances of K, Ca and Mg positive. Furthermore, the median of the Na balance is found to be positive, strongly suggesting that the systemic dermal Na loss, which was not measured, was not negligible.

Significant correlation is found between the Na intake and the balances of K, Ca and Mg, respectively (10).

Strict and regimental Na restriction may have adverse effects on health.

**Acknowledgments**

The authors hereby express our most sincere thanks to all the participants in our human mineral balance studies, especially to the volunteers taking part in our studies as the subjects.

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