Dietary salt influences postprandial plasma sodium concentration and systolic blood pressure

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The plasma sodium concentration has a direct effect on blood pressure in addition to its effects on extracellular volume regulated through changes in the endothelium. The mechanism for elevated blood pressure seen with habitually increased salt intake is unclear, especially the effect of salt in a single meal on plasma sodium concentration and blood pressure. To resolve this we compared the effect of soup with or without 6 g of salt (an amount similar to that in a single meal) on the plasma sodium concentration and blood pressure in 10 normotensive volunteers using a randomized, crossover design. The plasma sodium concentration was significantly increased by 3.13 ± 0.75 mmol/l with salted compared with unsalted soup. Blood pressure increased in volunteers ingesting soup with added salt, and there was a significant positive correlation between plasma sodium concentration and systolic blood pressure. A 1-mmol/l increase in plasma sodium was associated with a 1.91-mm Hg increase in systolic blood pressure by linear regression. Thus, changes in plasma sodium concentration occur each time a meal containing salt is consumed. A potential mechanism for the changes in blood pressure seen with salt intake may be through its effects on plasma sodium concentration.


KEYWORDS: blood pressure; dietary salt; plasma sodium

There is increasing evidence that high salt intake has a direct effect on the cardiovascular system independent and additive to its effects on blood pressure (BP).1 Despite this, the mechanisms whereby salt increases BP remain unclear. The prevailing hypothesis suggests that habitual salt intake increases extracellular volume (ECV) and this leads to high BP. Until recently the direct role of plasma sodium had been ignored, although it is the major component of plasma osmolality and is therefore important in stimulating thirst, as well as controlling ECV.2

Salt intake could influence BP through its direct effects on plasma sodium concentration.3 This is supported through several lines of evidence. In two out of three large cohort studies there is a positive association between the level of plasma sodium and BP, with a 1-mmol/l increase in plasma sodium concentration being associated with 1-mm Hg increase in systolic BP in hypertensive and normotensive individuals.4,5 A third study in 2,172 normotensive individuals found no association between plasma sodium concentration and BP, although the timing of the samples in relation to meals is not clear.6 In intervention trials, large changes in salt intake have been found to change plasma sodium concentration by 3.0 ± 0.3 mmol/l and more modest reductions of dietary salt have been found to lower plasma sodium concentration by 0.4 ± 0.2 mmol/l, with these changes significantly correlating with falls in BP.2 In experimental studies, small increases in plasma sodium concentration were seen to increase the BP rapidly, despite reducing ECV.7

As yet the effect of acute consumption of salt, as is present in an average meal in the Western world, on plasma sodium is unclear. In this study the effects of 6 g salt in a single meal in normotensive volunteers on plasma sodium and BP are described. This is compared with changes caused by an identical meal with no added salt.

RESULTS

The effect of added salt on plasma sodium concentration
Soup with added salt increased the plasma sodium concentration by 2.12 ± 0.46 mmol/l, from 138.94 ± 0.55 to 141.06 ± 0.49 mmol/l, whereas soup with no added salt lowered the plasma sodium concentration by 1.22 ± 0.62 mmol/l, from 139.72 ± 0.66 to 138.49 ± 0.79 mmol/l at 120 min. For added
salt, the area under the curve (AUC) was significantly greater (added salt 400.35 ± 78.59 (mmol/l) min; no added salt 38.03 ± 18.01 (mmol/l) min; mean difference 362.32 ± 79.72 (mmol/l) min; P < 0.01). Changes in plasma sodium concentration from baseline are illustrated in Figure 1.

The effect of added salt on osmolality
Soup with added salt increased the plasma osmolality by 3.80 ± 0.58 mosmol/l from 278.28 ± 1.30 to 282.07 ± 1.23 mosmol/l at 60 min (Figure 2). Soup with no added salt lowered the plasma osmolality by 4.37 ± 1.02 mosmol/l from 279.30 ± 1.63 to 274.93 ± 1.49 mosmol/l at 120 min. For added salt, the AUC was significantly greater (606.00 ± 122.60 (mosmol/l) min) compared with no added salt (32.25 ± 24.23 (mosmol/l) min); mean difference 573.75 ± 78.01 (mosmol/l) min; P < 0.01.

The effect of added salt on chloride concentration
Soup with added salt increased the plasma chloride concentration by 2.87 ± 0.40 mmol/l from 105.76 ± 0.56 to 108.63 ± 0.83 mmol/l at 120 min and soup with no added salt lowered the plasma chloride concentration by 1.18 ± 0.47 mmol/l from 105.91 ± 0.90 to 104.73 ± 0.83 mmol/l (Figure 3). For added salt the AUC was significantly greater (469.65 ± 78.63 (mosmol/l) min) compared with the soup with no added salt (14.93 ± 9.79 (mmol/l) min); mean difference 454.73 ± 78.01 (mmol/l) min, P < 0.01.

The effects of salt on BP
There was an increase in BP following intake of both the soup with added salt and that with no added salt. This increase in BP was greater following intake of the soup with added salt compared with the soup with no added salt. For systolic BP, the AUC was 2499.00 ± 560 (mm Hg) min with added salt, and 1488.00 ± 453.59 (mm Hg) min with no added salt; mean difference 1011.00 ± 420.36 (mm Hg) min, P < 0.05. For diastolic BP, the AUC was 1665.00 ± 499.22 (mm Hg) min with added salt and 1059.00 ± 271.40 (mm Hg) min with no added salt; mean difference 606.00 ± 416.84 (mm Hg) min. This difference was not statistically significant, P = 0.180 (Figure 4).

Although baseline BP was higher before intake of the soup with no added salt (108/70 ± 6/2 mm Hg no added salt; 101/66 ± 4/2 mm Hg added salt), there was no difference in pulse rate (70 ± 5 b.p.m. added salt; 67 ± 3 b.p.m. no added salt), 24-h urinary sodium (105 ± 18 mmol per 24 h added salt; 106 ± 16 mmol per 24 h no added salt) or other demographic or biochemical markers to explain for this difference.

The relationship between plasma sodium concentration and BP
To examine the relationship between plasma sodium concentration and BP, we calculated the regression coefficient...
using linear regression analysis and the Pearson correlation coefficient between the change in plasma sodium concentration from baseline and the change in BP from baseline at each time point. This analysis was performed for each participant separately. Following Fisher $r$ to $z$ transformation, we then calculated the pooled regression coefficient and correlation coefficient using the random-effects model. Linear regression demonstrated a significant relationship between the change in plasma sodium concentration from baseline and the change in systolic BP following intake of soup with added salt (effect size 1.91 mm Hg per mmol/l, 95% CI: 0.16 to 3.66, $P<0.05$). This suggests that the greater the change in plasma sodium concentration, the greater the change in BP, with an increase in plasma sodium concentration of 1 mmol/l being associated with an increase in systolic BP of 1.91 mm Hg (Figure 5). The pooled correlation coefficient was 0.42 (CI: 0.01-0.71). The relationship between change in plasma sodium concentration and change in systolic BP following intake of soup with no added salt was not significant (effect size 2.16 mm Hg per mmol/l ($-1.07$ to 5.40); $r=0.29$, CI: $-0.13$ to 0.63). There was no significant relationship between the change in plasma sodium and the change in diastolic BP (added salt: effect size 1.58 mm Hg per mmol/l (CI: $-1.67$ to 4.83); $r=0.10$, CI: $-0.33$ to 0.49; no added salt: effect size 0.83 mm Hg per mmol/l ($-1.18$ to 2.83); $r=0.23$, CI: $-0.21$ to 0.58).

**DISCUSSION**

In this study, a soup containing 6 g salt, a similar amount of salt that may be found in a single meal, was shown to immediately increase plasma sodium concentration and BP. An identical soup with no added salt had the contrasting effect of reducing plasma sodium concentration. The change in plasma sodium concentration stimulates compensatory mechanisms to reduce the level of plasma sodium back to baseline levels. The raised plasma sodium concentration, and therefore osmolality, results in fluid movement from the intracellular to the extracellular space, stimulates thirst, and increases vasopressin secretion to reduce water excretion.

Our study demonstrated that an increase in plasma sodium concentration was associated with an increase in BP. It is difficult to increase plasma sodium concentration without there being an associated expansion in ECV. However, experimental studies in animals have demonstrated a direct effect of plasma sodium concentration and ECV have an independent effect of BP. When plasma sodium concentration was increased by 10–15 mmol/l in rats using peritoneal dialysis and ECV was reduced, BP rapidly increased. BP fell when plasma sodium concentration was lowered by the same amount and extracellular volume was increased. This could suggest that small increases in plasma sodium may independently regulate BP.
It has been suggested that plasma sodium concentration may alter vascular function.\(^2\,^3\,^\text{10}\) In cultured human endothelial cells, cell stiffness increased by 20% within minutes of raising plasma sodium concentration from 135 to 145 mmol/l. This was associated with a reduction in nitric oxide formation and endothelial nitric oxide synthase activity, suggesting a functional link between nitric oxide metabolism and plasma sodium concentration.\(^\text{10}\,^\text{12}\,^\text{13}\) These findings are supported by studies in cultured bovine endothelial cells, where an increase in sodium bath concentration from 135 to 142 mmol/l reduced endothelial nitric oxide synthase activity by 25%.\(^\text{12}\) Salt loading reduced endothelial vasodilation in hypertensives and healthy volunteers,\(^\text{13}\,^\text{14}\) and modest salt reduction increased endothelial vasodilation in obese normotensive women.\(^\text{15}\) Elevated plasma sodium concentration may have direct effects on vascular smooth muscle by way of increasing the vascular smooth muscle cell hypertrophy\(^\text{16}\) and through the direct effects of raised intracellular sodium concentration on vascular smooth muscle tension.\(^\text{17}\)

In our study, there was also a significant increase in plasma chloride concentration with salt loading. It is unclear as to how far plasma chloride concentration affects BP, although it is the effect of the combination of sodium and chloride that has the greatest effect on BP when compared with other sodium salts, for example, phosphate and bicarbonate.\(^\text{18}\) The relationship between plasma chloride concentration and BP is not consistent, and a strong relationship was seen between BP and plasma sodium concentration.\(^\text{18}\,^\text{21}\)

Our study had several limitations. We did not measure atrial natriuretic peptide (ANP), renin and aldosterone, or vasopressin. However, this has been explored in similar experiments. When plasma sodium concentration was increased using hypertonic saline, ANP levels were not affected by the loading procedures.\(^\text{22}\) In a study using a similar protocol, in individuals on a very-low-salt diet, plasma ANP levels were not affected by oral salt loading.\(^\text{23}\) Salt loading led to an immediate fall in plasma concentration of angiotensin II, with suppression of plasma–renin activity and plasma aldosterone in both studies. Oral salt loading increases plasma vasopressin concentration.\(^\text{24}\)

In conclusion, we have demonstrated that an increase in salt intake, which could occur with a single meal, rapidly increases plasma sodium concentration and BP. The significant positive relationship between plasma sodium concentration and BP levels is in agreement with previous studies.\(^\text{2}\) A potential mechanism whereby dietary salt could increase BP is through its effects on plasma sodium concentration.

**MATERIALS AND METHODS**

Ten healthy volunteers, six men and four women with a mean age of 39 ± 4 years, provided written informed consent (see Table 1). The protocol was approved by the Local Research Ethics Committee and followed local institutional guidelines (LREC Approval Number 06/Q0803/323). Volunteers were advised to achieve a modest salt intake of 6 g/day for a run-in period of 2 weeks and throughout the study. Dietary compliance was assessed with 24-h urinary sodium measurement. Volunteers were studied in fasting condition for 10 h and were studied at 0800 hours. They were randomized to receive 400 ml vegetable soup, which either contained 6 g of salt or did not contain any salt. They were then crossed over to receive the other soup on the following visit. Soup was consumed over 20 min and no other liquid was consumed during the study.

Two 18-G intravenous cannulae were used to draw blood samples without stasis or a cuff at 15-min intervals for the first 90 min, after which they were drawn half hourly. BP was measured using Omron HEM-705CP (Omron, Kyoto, Japan), and the mean of the second and third readings obtained at 1 to 2-min intervals was used for analysis. Plasma and urine sodium and chloride concentration were measured with an autoanalyzer with a coefficient of variation of 0.65% (ADVIA 2400 Chemistry System, Deerfield, IL). Osmolality was measured by freezing point depression with a coefficient of variation of 0.55% (Advanced Micro Osmometer Model 3300, Advanced Instruments, Norwood, MA).

**Statistical analysis**

Results are reported as mean ± s.e.m. We calculated the area under the curve above baseline for each analyte for each participant separately and compared the mean area under the curve between the no salt and salt visits using paired Student’s t-tests. To study the relationship between plasma sodium concentration and BP, we calculated the regression coefficient using linear regression analysis and the Pearson correlation coefficient between change in plasma sodium concentration and change in BP for each participant separately. Correlation coefficients were transformed using Fisher r to z transformation. We then calculated the pooled regression coefficient and correlation coefficient using the random-effects model. The null hypothesis was rejected at P values of <0.05. Data were analyzed using SPSS for Windows, Rel. 15.0.0 (SPSS, Chicago, IL).

**DISCLOSURE**

All the authors declared no competing interests.

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**Table 1 | Baseline demographic and clinical characteristics of all study participants**

<table>
<thead>
<tr>
<th>Salt</th>
<th>No salt</th>
<th>Diff</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>80.4 ± 4.5</td>
<td>80.5 ± 4.5</td>
<td>0.2 ± 0.2</td>
</tr>
<tr>
<td>Sitting BP (mm Hg)</td>
<td>101/66 ± 4/2</td>
<td>108/70 ± 6/2</td>
<td>7/4 ± 3/2</td>
</tr>
<tr>
<td>Sitting pulse (min(^{-1}))</td>
<td>70 ± 5</td>
<td>67 ± 3</td>
<td>3 ± 4</td>
</tr>
<tr>
<td>Sodium (mmol/l)</td>
<td>138.9 ± 0.6</td>
<td>139.7 ± 0.7</td>
<td>0.8 ± 0.7</td>
</tr>
<tr>
<td>Chloride (mmol/l)</td>
<td>105.8 ± 0.5</td>
<td>105.9 ± 0.9</td>
<td>0.2 ± 0.7</td>
</tr>
<tr>
<td>Osmolality (mosmol)</td>
<td>278.2 ± 1.4</td>
<td>279.3 ± 1.8</td>
<td>1.0 ± 1.5</td>
</tr>
<tr>
<td>Urine 24-h sodium (mmol/24h)</td>
<td>105 ± 18</td>
<td>106 ± 16</td>
<td>0.3 ± 18.8</td>
</tr>
</tbody>
</table>

Abbreviation: BP, blood pressure.

Age (years), 39.4 ± 4.5 years; body mass index (kg/m\(^2\)), 26.6 ± 1.1; male/female (n), 6/4.

Data presented as mean ± s.e.m. (n=10).

\(P \leq 0.05\).
REFERENCES


