Effect of sodium and potassium supplementation on vascular and endothelial function: a randomized controlled trial

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ABSTRACT

Background: It is known that increased potassium and reduced sodium intakes can improve postprandial endothelial function. However, the effect of increasing potassium in the presence of high sodium in the postprandial state is not known.

Objective: We aimed to determine the effect of high potassium and high sodium on postprandial endothelial function as assessed by using flow-mediated dilatation (FMD) and arterial compliance as assessed by using pulse wave velocity (PWV) and central augmentation index (AIX).

Design: Thirty-nine healthy, normotensive volunteers [21 women and 18 men; mean ± SD age: 37 ± 15 y; BMI (in kg/m²): 23.0 ± 2.8] received a meal with 3 mmol K and 65 mmol Na (low-potassium, high-sodium meal [LKHN]), a meal with 38 mmol K and 65 mmol Na [high-potassium, high-sodium meal (HKHN)], and a control meal with 3 mmol K and 6 mmol Na (low-potassium, low-sodium meal) on 3 separate occasions in a randomized crossover trial. Brachial artery FMD, carotid-femoral PWV, central AIX, and blood pressure (BP) were measured while participants were fasting and at 30, 60, 90, and 120 min after meals.

Results: Compared with the LKHN, the addition of potassium (HKHN) significantly attenuated the postmeal decrease in FMD (P<meal by time interaction < 0.05). FMD was significantly lower after the LKHN than after the HKHN at 30 min (P < 0.01). AIX decreased after all meals (P < 0.05). There were no significant differences in AIX, PWV, or BP between treatments over time.

Conclusion: The addition of potassium to a high-sodium meal attenuates the sodium-induced postmeal reduction in endothelial function as assessed by FMD. This trial was registered at http://www.anzctr.org.au/ as ACTRN12613000772741. Am J Clin Nutr 2015;101:939–46.

Keywords: endothelial function, potassium, sodium, vascular function, flow-mediated dilatation

INTRODUCTION

Endothelial dysfunction is a predictor of cardiovascular disease (CVD), and impaired endothelial function has been associated with increased CVD morbidity and mortality in people with and without pre-existing vascular disease (1, 2). Vascular function or arterial stiffness measures, including the pulse wave velocity (PWV) and central augmentation index (AIX), also provide a noninvasive assessment of CVD risk in the general population (3, 4).

Dietary sodium intake is associated with increased risk of stroke and CVD (5, 6). Increased dietary sodium intake is known to impair endothelial function in fasting and postprandial states (7, 8). A reduction of 3-g Na/d intake can improve endothelial function as assessed by using flow-mediated dilatation (FMD) in the fasting state (9). Furthermore, dietary salt loading is known to impair measures of vascular function in hypertensive populations (10). Conversely, high potassium intake is associated with lower CVD risk and lower blood pressure (BP), particularly in hypertensive populations and populations with higher sodium intake (11). Increased dietary potassium improves fasting FMD independent of BP (12), and a high potassium meal can attenuate a postprandial decrease in FMD (13). The effect of high potassium on vascular function measures is unclear (14).

The mechanisms for the effect of sodium and potassium on vascular and endothelial function are currently unknown. However, alterations in sodium and potassium intakes are known to alter biological molecules such as adhesion molecules. Increases in dietary sodium increase endothelin-1 expression (9), and increased dietary potassium reduces E-selectin in the short term (12). Berry et al. (15) also observed a reduction in fasting intercellular adhesion molecule-1 (ICAM-1) after a high-potassium diet.

The ratio of sodium to potassium has been identified as a more useful predictor of CVD than is sodium or potassium intake alone (16). Follow-up studies on the Trials of Hypertension Prevention I and II named the ratio between sodium and potassium as...
a significant predicting factor for CVD (17). Combined sodium and potassium interventions showed a benefit of reducing sodium and increasing potassium on blood pressure and vascular function in some populations (18, 19); however, the effect of modifying the ratio of sodium to potassium on postprandial vascular and endothelial function remains to be determined.

The primary hypothesis tested in this study was that the addition of potassium to a high-sodium meal would mitigate the adverse effects of sodium on postprandial FMD. A low-potassium, low-sodium control meal was included in the study design to confirm the known adverse effect of high sodium on postprandial FMD.

METHODS

Subjects
Men and women aged between 18 and 70 y were recruited through personal contact and an advertisement on community notice boards (Figure 1). Inclusion criteria were BMI (in kg/m²) ≥18 and ≤30, systolic blood pressure (SBP) <130 mmHg, diastolic blood pressure (DBP) <90 mmHg, weight stability in the preceding 6 mo, and no use of an antihypertensive or cholesterol-lowering medication, systemic steroids, nonsteroidal anti-inflammatory drugs, or folate supplementation. Participants were not excluded if they were taking any other vitamin supplements provided that the dose was kept constant for the duration of the study. Exclusion criteria were known metabolic disease such as liver or kidney disease, treated hypertension, known or treated high cholesterol, clinical CVD, and inability to comprehend study protocol.

Study methods
In a randomized, double-blind, crossover design, 39 participants completed the study on 3 mornings separated by a minimum 7-d washout period. Participants consumed 3 test meals that contained 3 mmol K and 6 mmol Na [low-potassium, low-sodium meal (LKLN)], 3 mmol K and 65 mmol Na [high-potassium, low-sodium meal (HKHN)], or 38 mmol K and 65 mmol Na [high-potassium, high-sodium meal (HKNH)]. Meals consisted of tomato soup (Heinz Big Red Condensed Tomato Salt Reduced Soup; Coles) made according to the manufacturer’s instructions. Sodium chloride (SAXA Plain Table Salt; Coles) was added to LKHN and HKHN, and potassium chloride (Paddymelon Gourmet Foods; The Melbourne Food Ingredient Depot) was added to the HKHN. All other macro-nutrients and micronutrients were identical between meals. After screening, participants were assigned to a treatment order by using an online-generated balanced random-number allocation sequence (http://www.randomization.com) by a person independent of the study. Participants were asked to fast (no food; 250 mL H₂O only) from 22:00 the night before each visit and refrain from alcohol, caffeine, and vigorous exercise in the 24 h before each study visit.

Diet analysis
Participants completed an online dietary survey (Dietary Questionnaire for Epidemiologic Studies; Cancer Council Victoria) before commencing dietary interventions to determine habitual dietary intakes of potassium and other nutrients. Volunteers recorded their food intakes on the day before the first study and replicated these intakes before subsequent test days.

Weight and height
On arrival, participants had body height (first visit only) measured to the nearest 0.1 cm with a stadiometer (SECA) while barefoot. Body weight was measured to the nearest 0.05 kg by using calibrated electronic digital scales (SECA) while participants wore light clothing and no footwear.

FMD
As previously described (13), endothelium-dependent FMD of the right brachial artery was measured in the longitudinal plane

![Consolidated Standards of Reporting Trials diagram of the flow of subjects through the study.](https://academic.oup.com/ajcn/article-abstract/101/5/939/4577580)
above the antecubital fossa with an 8.8-MHz linear array transducer (MySono U6; Samsung Medison) according to published guidelines (20, 21). Subjects attended after an overnight fast and lay quietly for 5 min in a quiet, temperature-controlled room before endothelium-dependent FMD measurements were obtained (21). The brachial artery diameter was measured before and after forearm ischemia caused by inflation of a sphygmomanometer cuff applied to the right forearm 2 cm below the olecranon process to 200 mmHg for 5 min. Continuous longitudinal 2-dimensional images of the brachial artery were obtained and digitally recorded during quite rest (1 min) and from 30 s before cuff release and during reactive hyperemia (3 min). All images were stored for offline analysis by a single trained observer who was unaware of the treatments at the time of measurement.

FMD analysis

Ultrasound images were recorded at a rate of 30 frames/s with screen-capture software (Debut Video Capture Software Professional V1.82; NCH Software) without QRS gating because previous studies showed that continuous recording has good agreement with R-wave gated measures when edge-detection software is used (22, 23). FMD video files were analyzed with edge-detection software (Brachial Analyzer for Research V6.1.3; Medical Imaging Application LLC). For both baseline and deflation, a region of interest was defined over a clear section of vessel with care to ensure that the region of interest was the same size and position for both baseline and deflation files. The automated edge-detection feature of the software was used to perform a frame-by-frame analysis to generate artery diameter (mm) values for both baseline and deflation. Baseline was defined as the average of 60-s pre-inflation diameter measures. The peak diameter was determined as the maximum diameter postcuff release. With the use of baseline and peak diameters, the percentage change in diameter during the last 30 s before cuff release and expressed as follows:

\[
4 \times \frac{V}{D} \]

Normalized FMD was calculated by dividing the %FMD by the shear rate (21). The intraobserver CV calculated from baseline measurements \((n = 39)\) was 19.6%. Low flow-mediated constriction (L-FMC) was calculated from the mean arterial diameter during the last 30 s before cuff release and expressed as the percentage change from baseline (25).

Arterial compliance

Carotid-femoral PWV (PWV\(_{c-f}\)) was measured by using a SphygmoCor device (AtCor Medical). Measurements were taken in the supine position by a single operator (CV = 5%) as previously described (26). Central AIx was measured by using the SphygmoCor device. Measurements were taken in the seated position by a single operator.

BP

Brachial BP was measured by using the SphygmoCor device. Measurements were taken in the seated position by a trained laboratory technician after participants were seated for 2 min. A series of measurements were taken, each 1 min apart until 4 consistent measurements were obtained (i.e., SBP within a range of 10 mm Hg and DBP within a range of 5 mm Hg). The first reading was discarded, and 3 consistent measurements were averaged (27).

Laboratory analysis

Blood samples were collected from a cannula inserted into the left brachial vein into tubes with no additive for the measurement of serum sodium and potassium concentrations and ICAM-1, E-selectin, and endothelin-1. Serum was isolated by centrifugation at 2500 \(\times\) g for 10 min, and samples were stored at −80°C until analyzed.

Biochemical assays were performed in a single assay on completion of the study. ICAM-1, E-selectin, and endothelin-1 were measured by using Quantikine human immunoassay kits (R&D Systems; Bioscientific) on the basis of the manufacturer’s protocols. An analysis of serum sodium and potassium concentrations was performed at the Institute of Medical and Veterinary Sciences, Adelaide, South Australia.

Ethics

This study was approved by the University of South Australia’s Human Research Ethics Committee (ethics approval number: 0000031547). All participants gave written informed consent. This trial was registered at http://www.anzctr.org.au/ as ACTRN12613000772741.

Statistical analysis

The primary outcome for the statistical analysis was the effect of HKHN compared with LKHN on FMD. The secondary outcome was the effect of HKHN compared with LKHN on PWV. On the basis of power calculations from our previous study (13) with 80% power and \(P < 0.05\) to detect a minimum change in FMD of 1.3% absolute, 40 people were required in a crossover study. With 80% power and \(P < 0.05\) to detect a 10% (0.6-m/s) change in PWV\(_{c-f}\) and the assumption of a within-patient SD of 0.9 m/s, 20 people were required in a crossover study.

All analyses were performed with SPSS 21 for Windows software (SPSS Inc.). Significance was set at \(P < 0.05\). Data were tested for the normality of distribution and to ensure that residuals had approximately constant SDs by using the Kolmogorov-Smirnov test, Q-Q plots, and histograms. An ANOVA with repeated measures (with diet as the within-subject factor) was used to analyze outcomes (with and without covariates including diet order and BP), and we performed a post hoc analysis to assess primary and secondary comparisons. For FMD only, differences from baseline were calculated before the analysis to make meal comparisons easier to see. The primary comparison was HKHN compared with LKHN as reflected by the hypothesis. A secondary comparison was included to show a difference in LKHN and the LKLN control to show the adverse effect of sodium on postprandial FMD. Age, BMI, sex, and habitual potassium intake were also included as covariates. Preliminary analyses were performed to ensure no violation of assumptions of linearity. Pearson correlation analyses were conducted to assess the association of change.
between variables. Data are expressed as means ± SDs or median (IQRs) as appropriate.

RESULTS

Subjects

Thirty-nine subjects completed the study, and baseline characteristics are outlined in Table 1. DBP before the LKHN was significantly lower than before the LKLN or the HKHN (P = 0.01). There were no significant differences between other fasting variables between treatments.

Brachial artery endothelial function

There was no meal × time interaction (P = 0.06) but a significant effect of meal (P < 0.01) for the comparison of the 3 meals (Table 2). The addition of potassium in the HKHN significantly attenuated the postprandial decrease in FMD after the LKHN (P-meal × time interaction = 0.02). There was no significant meal × time interaction (P = 0.65) or time effect (P = 0.59) for the FMD change from baseline (time 0) between the 3 meals (Figure 2). There was a significant effect of meal (P < 0.01), and FMD decreased by −1.5% from baseline after the LKLN and was further decreased to −2.9% from baseline after the HKHN. When the change in FMD from baseline was compared for the primary hypothesis (LKHN compared with HKHN), there was no meal × time interaction (P = 0.57), but the meal effect was significant (P < 0.01). The maximum difference in FMD after the LKHN compared with the HKHN was at 30 min (−3.58 ± 0.85%; P < 0.01). There was no effect of age, sex, BMI, or habitual potassium intake observed. When FMD was normalized for the shear rate, the meal effect did not change, but meal by time interaction weakened and became nonsignificant (P-meal effect < 0.01; P-meal × time interaction = 0.12 for the LKHN compared with the HKHN).

The low flow constriction observed with the LKHN (Table 2) was completely abolished by the HKHN (P-meal × time interaction < 0.01) with a difference of −4.95 ± 0.87% and P < 0.01 at 60 min. There was no effect of age, BMI, sex, or habitual potassium intake observed.

BP

SBP and DBP increased after all meals (P < 0.01 for both) (Table 2). There were no significant differences in SBP after each of the test meals and a borderline change in DBP (P-meal × time = 0.05). No effect of age, BMI, sex, or habitual potassium intake was observed.

Mean arterial pressure increased after all meals (P = 0.03). There were no significant differences in mean arterial pressure after each of the meals.

Arterial compliance measures

PWVc-f increased after all meals compared with fasting (P-time effect < 0.01). There were no significant differences in PWVc-f after each of the meals (P-meal × time interaction = 0.29 for the HKHN compared with the LKHN). Central AIx and AIx corrected for heart rate at 75 beats/min (n = 34) decreased after each meal (P-time < 0.01 for both). There was no meal × time interaction (HKHN compared with LKHN) for AIx (P = 0.20) or AIx corrected for heart rate at 75 beats/min (P = 0.10). Heart rate decreased after all meals (P-time < 0.01). There were no significant differences in heart rate after each of the meals. Pulse pressure increased after all meals (P-time < 0.01). There were no significant differences in pulse pressure after each of the meals (P-meal × time interaction = 0.53).

Biochemical analysis

Serum sodium increased significantly after the LKHN (maximum change was 1.2 ± 0.9 mmol at 60 min) and the HKHN compared with the LKLN (P-meal × time interaction < 0.01 for both comparisons). There was no difference in serum sodium between the LKHN and the HKHN (P = 0.59). Serum potassium significantly increased after the HKHN (maximum change was 0.6 ± 0.3 mmol at 90 min) compared with the LKHN and the control meal (P-meal × time interaction < 0.01 for both comparisons).

Endothelin-1 decreased after both meals (P-time < 0.01) but was higher after the HKHN than after the LKLN (P-meal × time interaction = 0.03). ICAM-1 decreased after both meals (P-time < 0.01) but decreased less after the HKHN than after the LKHN. There were no changes in serum E-selectin after any of the interventions.

FMD and serum sodium was negatively correlated at 60 min with the LKHN (r = −0.45, P = 0.01). There were no correlations between FMD and serum potassium, adhesion molecules, or maximum flow. There was a weak inverse correlation between FMD and SBP at various time points but only with the LKHN diet.

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### Table 1

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Baseline</th>
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<tbody>
<tr>
<td>Age, y</td>
<td>38 ± 16</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>23.1 ± 2.9</td>
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<tr>
<td>HR, beats/min</td>
<td>57 ± 9</td>
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<tr>
<td>SBP, mm Hg</td>
<td>115 ± 8</td>
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<tr>
<td>DBP, mm Hg</td>
<td>71 ± 6</td>
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<tr>
<td>MAP, mm Hg</td>
<td>83 ± 7</td>
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<td>Brachial artery diameter, mm</td>
<td>3.80 ± 0.66</td>
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<tr>
<td>FMD, %</td>
<td>9.5 ± 3.5</td>
</tr>
<tr>
<td>PWVc-f, m/s</td>
<td>6.7 ± 1.1</td>
</tr>
<tr>
<td>AIx, %</td>
<td>12 ± 15</td>
</tr>
<tr>
<td>AIx@75beats/min, %</td>
<td>7 ± 16</td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>31 ± 4</td>
</tr>
<tr>
<td>Serum sodium, mmol/L</td>
<td>140 ± 1</td>
</tr>
<tr>
<td>Serum potassium, mmol/L</td>
<td>4.2 ± 0.2</td>
</tr>
<tr>
<td>ICAM-1, µg/L</td>
<td>131.5 ± 38.1</td>
</tr>
<tr>
<td>E-selectin, µg/L</td>
<td>38.3 ± 22.1</td>
</tr>
<tr>
<td>Endothelin-1, pg/mL</td>
<td>1.34 ± 0.36</td>
</tr>
</tbody>
</table>

1 All values are means ± SDs. n = 39 (21 women and 18 men). AIx, augmentation index; AIx@75beats/min, augmentation index corrected to heart rate at 75 beats/min; DBP, diastolic blood pressure; FMD, flow-mediated dilatation; HR, heart rate; ICAM-1, intracellular adhesion molecule-1; MAP, mean arterial blood pressure; PP, pulse pressure; PWVc-f, carotid-femoral pulse wave velocity; SBP, systolic blood pressure.

2 n = 34 (18 women and 16 men).
### TABLE 2
All outcome variables for each meal intervention

<table>
<thead>
<tr>
<th></th>
<th>LKLN (min)</th>
<th>LKHN (min)</th>
<th>HKHN (min)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 30 60 90 120</td>
<td>0 30 60 90 120</td>
<td>0 30 60 90 120</td>
<td>Meal × Time effect!</td>
</tr>
<tr>
<td>PMD, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>L-FMC, %</td>
<td>-1.5 ± 0.8</td>
<td>0.11 ± 0.7</td>
<td>0.01 ± 0.8</td>
<td></td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>41.2 ± 2.4</td>
<td>113 ± 5.1</td>
<td>83 ± 3.1</td>
<td></td>
</tr>
<tr>
<td>SBP, mm Hg</td>
<td>70 ± 1</td>
<td>112 ± 1</td>
<td>82 ± 1</td>
<td></td>
</tr>
<tr>
<td>DBP, mm Hg</td>
<td>70 ± 1</td>
<td>112 ± 1</td>
<td>82 ± 1</td>
<td></td>
</tr>
<tr>
<td>MAP, mm Hg</td>
<td>30 ± 1</td>
<td>10 ± 2</td>
<td>6 ± 2</td>
<td></td>
</tr>
<tr>
<td>PWV,&lt;sub&gt;c&lt;/sub&gt; m/s</td>
<td>6.5 ± 0.2</td>
<td>6.6 ± 0.2</td>
<td>6.6 ± 0.2</td>
<td>0.49 &lt; 0.01 0.19</td>
</tr>
<tr>
<td>AxI, %</td>
<td>10 ± 2</td>
<td>11 ± 3</td>
<td>6 ± 3</td>
<td></td>
</tr>
<tr>
<td>AxI@7beats/ mm&lt;sup&gt;3&lt;/sup&gt;</td>
<td>6.2 ± 2.6</td>
<td>-1 ± 3.2</td>
<td>-3 ± 2.9</td>
<td></td>
</tr>
<tr>
<td>PP, mm Hg</td>
<td>30 ± 1</td>
<td>31 ± 1</td>
<td>8 ± 2</td>
<td></td>
</tr>
<tr>
<td>Semn sodium, mmol/L</td>
<td>140 ± 0.2</td>
<td>139 ± 0.2</td>
<td>140 ± 0.2</td>
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<tr>
<td>Semn potassium, mmol/L</td>
<td>4.2 ± 0.4</td>
<td>4.3 ± 0.4</td>
<td>4.3 ± 0.4</td>
<td></td>
</tr>
<tr>
<td>ICAM-1, μg/L</td>
<td>128 ± 5.1</td>
<td>1164 ± 4.8</td>
<td>1185 ± 4.8</td>
<td></td>
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<tr>
<td>E-selectin, μg/L</td>
<td>33.1 ± 4.1</td>
<td>37.5 ± 3.9</td>
<td>36.5 ± 3.9</td>
<td></td>
</tr>
</tbody>
</table>

1 All values are means ± SEMs. n = 39 (21 women and 18 men). AxI, augmentation index; AxI@7beats/min, augmentation index corrected to heart rate at 75 beats/min; DBP, diastolic blood pressure; PMD, flow-mediated dilatation; HKHN, high-potassium, high-sodium meal; HR, heart rate; ICAM-1, intracellular adhesion molecule-1; L-FMC, low-flow mediated constriction; LKHN, low-potassium, high-sodium meal; LKLN, low-potassium, low-sodium meal; MAP, mean arterial blood pressure; PP, pulse pressure; PWV,<sub>c</sub>, carotid-femoral pulse wave velocity; SBP, systolic blood pressure.
2 Repeated-measures ANOVA for 3 meals.
3 Repeated-measures ANOVA for LKHN compared with HKHN.
4 Repeated-measures ANOVA for baseline measurements, P = 0.01.

n = 34 (18 women and 16 men).
The main outcome from this study was that the addition of potassium to a high-sodium meal significantly attenuated a sodium-invoked postmeal reduction in endothelial function as assessed by FMD. To our knowledge, this is the first time that combined sodium and potassium has been examined in the postprandial state. The amount of added sodium used in the meals was equivalent to ~2 rashers of bacon [or 2 thick sausages (80 g each)]. The amount of added potassium was equivalent to 3 large bananas [or 2 large potatoes (340 g cooked weight) or 0.75 cups dried apricots).

Dickinson et al. (7) reported that a high-sodium meal impaired brachial artery FMD in the postprandial state, which was a finding that was replicated in this study (Figure 2). These findings were also consistent with the deleterious effect of sodium on fasting FMD in the short term (8, 9, 28). We showed that impairment in FMD was correlated with increases in SBP and DBP after the high-sodium meal without potassium. This effect was not seen in the postprandial study by Dickinson et al. (7). Furthermore, we previously showed that a high-potassium meal (without sodium) can attenuate postmeal responses in FMD to a low-potassium meal (13). Previous studies that investigated the effect of increasing potassium on fasting FMD have reported mixed results (12, 15, 29); however, dose appears to play an important role with increasing potassium on fasting FMD have reported mixed results (13).

One salt-substitution study (simultaneously reducing sodium and increasing potassium) showed significant improvements in central AIx in response to a high-fat meal over time. Previous studies showed a small postmeal decrease in BP at 30 min (13). However, postmeal increases in BP that provoked increases in PWVc-f in hypertensive (10, 33, 34) but not normotensive (35) populations showed a small postmeal decrease in BP at 30 min. Previous studies showed mixed results in populations that showed an increase in AIx (36) and other studies that showed a decrease (37). Furthermore, Dickinson et al. (38) reported a further increase in AIx after a high-sodium meal. Our study showed no meal × time interaction for AIx. Previous studies showed no change in PWVc-f between meals; however, we saw a small but significant trend for increased PWVc-f over time. Previous studies showed an improvement in fasting PWVc-f in hypertensive (10, 33, 34) but not normotensive (35) populations with reduced sodium intake. The influence of potassium on vascular function measures is unclear, with BP likely to influence any observed effect (14).

Our study showed a significant reduction in central AIx in response to each of the test meals. This result remained after correction for heart rate (augmentation index corrected to heart rate at 75 beats/min). Previous studies showed mixed results in AIx in response to a mixed meal with some studies that showed an increase in AIx (36) and other studies that showed a decrease (37). Furthermore, Dickinson et al. (38) reported a further increase in AIx after a high-sodium meal. Our study showed no meal × time interaction for AIx. Previous studies showed no effect of potassium interventions on fasting AIx (15, 39, 40). One salt-substitution study (simultaneously reducing sodium and increasing potassium) showed significant improvements in measures of arterial stiffness (central pulse pressure and pulse wave reflection time) after 12 mo of intervention but did not see an effect on AIx (41).

This study showed that a meal that contained 38 mmol K raised serum potassium by 0.6 mmol/L in healthy individuals. We hypothesized that this increase in serum potassium affects the FMD response by one of 2 mechanisms. First, we speculate that
the rise in serum potassium may directly affect the small and intermediate calcium-activated potassium channels of endothelial cells, which are then electrically coupled to the smooth cells (i.e., an endothelium-derived hyperpolarizing factor effect) (42). Second, increased serum potassium may increase nitric oxide release because cellular studies showed an increase in release of nitrates (an index of nitric oxide release) in response to increased extracellular potassium (43). Serum sodium was raised by a maximum of 1.2 mmol/L after the 65-mmol sodium meals. This change in serum sodium was expected because previous studies showed an increase in serum sodium in response to a 65-mmol sodium meal (38). Dickinson et al. (7) hypothesized that the mechanism for the observed decrease in FMD after a high-sodium meal is increased serum sodium resulting in a reduction in nitric oxide bioavailability. Evidence from in vitro studies suggested increases of 5–10 mmol in serum sodium reduce nitric oxide bioavailability and nitric oxide synthase activity (44, 45). We did not measure serum concentrations of nitrate and nitrite in this study because previous studies did not detect changes in nitrate and nitrite concentrations after a 65-mmol Na meal (38). In our study, we observed a relation between BP and FMD after the high-sodium meal that was not seen in the study by Dickinson et al. (7); therefore, the rise in BP could be the mechanism for the reduction in FMD.

We observed small but significant differences in serum endothelin-1 and ICAM-1 with diminished postmeal falls with the addition of potassium to the meal, but baseline values were higher with the high-sodium meal, and this finding alone may account for the difference. Endothelin-1 was previously shown to decrease after a reduced sodium diet (9). Furthermore, Liu et al. (46) showed that endothelin-1 decreased after a 7-d low-sodium diet (51.3 mmol/d) and increased after a 7-d high sodium diet (307.7 mmol/d), and the addition of potassium (60 mmol/d for 7 d) attenuated the response to the high-sodium diet. Conversely, Dickinson et al. (38) failed to detect a difference in postprandial endothelin-1 concentrations between a low-sodium meal and a high-sodium meal alone (5 compared with 65 mmol). Previously, reductions in fasting ICAM-1 were reported after a 6-wk high-potassium diet in woman only (15), but we did not see a sex-related treatment effect in our study. The role of variations in endothelin-1 and ICAM-1 in alterations in endothelial function in the postprandial state are unknown, but they are unrelated to changes in FMD.

Limitations of this study included the use of a relatively healthy population sample, which might have limited the potential to see improvements in BP and vascular variables. However, we saw significant improvements in measures of endothelial function after the addition of potassium to the high-sodium meal. Furthermore, it is unclear whether these results persist in the longer term, and the effect of high potassium in the presence of high sodium on fasting FMD warrants additional investigation. We acknowledge that, in populations with renal impairment, there may be risk of hyperkalemia by increasing dietary potassium, and in our study, serum potassium remained elevated at 120 min. Another limitation was that we did not adjust for any effect of menstrual cycles of premenopausal women. However, we did not see an effect of sex and did not observe any differences in baseline FMD measurements between treatments; therefore, the menstrual cycle does not appear to have affected our data. It was a limitation that we are unable to provide a mechanistic explanation for the effect of potassium and sodium on endothelial function; however, this study provides some insight into the changes in endothelial mediators that occur in response to high-potassium and -sodium loads.

In conclusion, this study showed that the amount of potassium present in 3 servings of fruit can significantly attenuate reductions in endothelial function induced by a high-sodium (65-mmol) meal. A transient increase in serum potassium is a plausible mechanism for this response; however, increased potassium does not appear to affect other measures of vascular function. This finding suggests that, in populations in whom reducing sodium intake may be problematic (e.g., primarily of processed foods), increasing potassium intake may reduce CVD risk. Although the long-term implications of this result in the pathogenesis of atherosclerosis and CVD is unknown, this study provides additional evidence that increases in dietary potassium should be encouraged, particularly in the presence of a high-sodium westernized diet.

The authors’ responsibilities were as follows—JBK and PMC: developed the hypotheses tested in the study, designed the research (project conception, development of overall research plan, and study oversight), and contributed to statistical analyses and interpretation of data; NB: contributed to the study design, planned and conducted the study, performed vascular measurements (hands-on conduct of experiments and data collection), performed initial statistical analyses, and drafted the manuscript; KSP: assisted in conducting the study and performed some vascular measurements (hands-on conduct of experiments and data collection); and all authors: critically reviewed the manuscript. None of the authors reported a conflict of interest related to the study.

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