High dietary salt intake increases carotid blood pressure and wave reflection in normotensive healthy young men

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TYPICAL DIETARY SALT INTAKES in many countries range between 9 and 12 g (7), and there is considerable evidence that these levels of intake are associated with increased cardiovascular morbidity and mortality (10, 22). Studies have shown a strong and consistent relationship between dietary salt intake and brachial blood pressure (BP) (1); however, some of the excess cardiovascular risk due to high salt intake appears to be independent of the effect on brachial BP (10, 16). In addition, relationships between salt intake and left ventricular hypertrophy have been reported to be independent of brachial BP (5).

It is increasingly recognized that BP measured in the brachial artery may not be representative of aortic BP and wave reflection in the common carotid artery of healthy volunteers.

MATERIALS AND METHODS

Recruitment and study design. Ten men [median age 32 (22–40) yr] were recruited from the staff of Imperial College London and Imperial College Healthcare National Health Service Trust to participate in the study. All volunteers were healthy, normotensive non-smokers without diabetes and had no evidence of cardiovascular or other diseases. Written informed consent was obtained, and the study was approved by the local Research Ethics Committee.

Prior to participation, all subjects were consuming a typical UK diet, which for this age group is estimated to supply a median salt intake of 9.14 g/day (equivalent to 160 mmol sodium/day) (17). Diet diaries or urinary sodium were not collected prior to the study. After a 1-wk run-in period, subjects were randomized to receive either sodium chloride (128 mmol sodium/day) or matched placebo capsules for 2 wk in a double-blind crossover design. All volunteers ingested a low-salt diet (60–80 mmol sodium/day) throughout the 6-wk duration of the study so that their total sodium intake during the high-salt period was ~188–208 mmol sodium/day. Each 2-wk treatment period was followed by a 1-wk washout period on low sodium intake, and subsequently the subjects crossed over to the alternative medication for an additional 2 wk. Measurements were made at the end of each treatment period.

Measurements. All measurements were performed by a single observer after ≥15 min of rest. The subjects abstained from caffeine, smoking, alcohol, and vigorous exercise for ≥12 h prior to assessments. Sitting clinic BP and heart rate were measured in the left arm with a validated automated device (Omron HEM-705CP, Omron, Tokyo, Japan) (19). The mean of the last two of three recordings, measured at 2-min intervals, was calculated. Arterial pressure in the common carotid artery was measured by applanation tonometry with a high-fidelity strain, gauge-tipped pencil probe (SPT 301; Millar Instruments, Houston, TX) and calibrated to diastolic and mean pressure, as described previously (12).

Blood flow velocity in the common carotid artery was measured using an HDI 5000 ultrasound system with a 7.5-MHz linear array scan head (Phillips Healthcare, Guildford, UK). Examinations were performed in the supine position, with the neck extended and rotated slightly to the contralateral side. All measurements were made ~1 cm proximal to the carotid bulb. B-mode ultrasound was used to ensure correct positioning of the transducer, and flow velocity was measured by pulsed-wave ultrasound using a Doppler angle of 60°. Data were as a result of wave reflections occurring in the circulation (18). Increased wave reflection has also recently been shown to be an independent risk factor for cardiovascular events (14), but the effect of changes in salt intake on central BP and wave reflection is unknown. The aim of the present study was to compare the effects of high and low salt intake on central BP and wave reflection in the common carotid artery of healthy volunteers.
analysed offline using custom written software in Matlab (Matlab R2009b; MathWorks, Natick, MA), as described previously (25). To obtain representative pressure and flow velocity waveforms for analysis, at least five pressure and flow velocity waveforms were ensemble averaged, using the ECG R-wave as a fiducial marker.

Data analysis. Figure 1 shows an illustrative trace of a pressure and wave intensity waveform.

Carotid augmentation index (cAIx) was calculated as pressure augmentation measured from the shoulder of the pressure wave to the late systolic peak as a ratio of the pulse pressure (20). \( P_h/P_f \) was calculated as the ratio of the peak backward \( (P_b) \) and forward \( (P_f) \) separated pressure. The timing and peak intensity of three major waves was measured: a forward-traveling compression wave \( \left( c_1 \right) \), a backward-traveling compression wave \( \left( c_1^{-1} \right) \), and a forward-traveling decompression wave \( \left( D \right) \). Carotid wave velocity, a measurement of carotid arterial stiffness, was calculated using a pressure-flow velocity loop, as described previously (25). Resistive index (RI) was calculated as required to detect a difference of 3 mmHg in carotid systolic BP at a 5% significance level with 90% power. Data are presented as means (SD), and high and low salt treatments were compared using linear mixed model analysis. \( P < 0.05 \) was considered significant.

RESULTS

The effects of high and low salt intake are compared in Table 1. Urinary 24-h sodium excretion was increased more than twofold at the end of the high salt period, and mean 24-h urinary sodium excretion during the high- and low-sodium periods was in keeping with expected dietary sodium intakes, suggesting that participants complied with dietary instructions. Urinary potassium excretion was reduced, and body weight also increased during the high-salt period, suggesting some degree of volume expansion. Brachial systolic BP tended to be increased during the high-salt intake periods, but this difference was not statistically significant. Diastolic BP and heart rate did not differ between high- and low-salt periods. In contrast, carotid systolic BP was significantly higher after the period of high salt intake, and \( P_b/P_f, \) cAIx, and \( c_1^{-1} \) were increased. The intensity of the S- and D-waves did not differ significantly between high and low salt treatment, and carotid wave speed was unchanged, but there was an increase in RI. Timings of waves did not differ between high- and low-salt treatments.

DISCUSSION

High dietary salt intake increases carotid systolic BP in young healthy men despite minimal changes in brachial BP. The accompanying increases in \( P_h/P_f, \) \( c_1^{-1} \), and cAIx indicate that this rise in carotid systolic pressure is attributable to increased wave reflection. The observation that high vs. low salt intake is associated with increased carotid BP due to enhanced wave reflection provides additional insight into the relationship between di-

| Table 1. Comparison of the effect of high and low salt intakes |
|-----------------------------|-----------------------------|-----------------------------|
| Variable                      | Low Salt | High Salt | \( P \) |
| Brachial SBP, mmHg            | 112 (6)   | 114 (9)   | 0.1    |
| DBP, mmHg                     | 65 (7)    | 65 (8)    | 0.9    |
| HR, min \(^{-1}\)             | 56 (5)    | 56 (4)    | 0.9    |
| Carotid SBP, mmHg             | 91 (13)   | 98 (11)   | <0.01  |
| cAIx, %                       | 7.5 (14.0) | 17.3 (13.4) | <0.01 |
| \( P_h \), mmHg               | 10.5 (2.6) | 12.7 (2.2) | 0.02   |
| \( P_h/P_f \)                 | 0.11 (0.03) | 0.13 (0.02) | 0.04   |
| S-wave intensity, Wm\(^{-2}\) | 18.5 (11.2) | 20.1 (10.2) | 0.2    |
| Time of peak S-wave, s        | 0.16 (0.02) | 0.16 (0.02) | 0.2    |
| \( c_1^{-1} \) intensity, Wm\(^{-2}\) | 1.5 (0.7) | 2.1 (1.0) | 0.06   |
| Time of \( c_1^{-1} \), s     | 0.25 (0.05) | 0.26 (0.03) | 0.02   |
| D-wave intensity, Wm\(^{-2}\) | 4.3 (2.7)    | 4.5 (3.3)   | 0.8    |
| Time of D-wave, s             | 0.52 (0.04) | 0.53 (0.06) | 0.5    |
| Resistive index               | 0.7 (0.1)    | 0.8 (0.1)   | 0.04   |
| Carotid wave velocity, ms\(^{-1}\) | 5.3 (1.6) | 5.8 (2.1) | 0.5    |
| Sodium excretion, mmol/24 h   | 94 (35)    | 191 (51)   | <0.01  |
| Potassium excretion, mmol/24 h| 86 (41)    | 94 (35)    | <0.01  |
| Urine volume, ml/24 h         | 1,439 (512) | 1,551 (629) | 0.5    |
| Weight, kg                    | 74.3 (15.2) | 75.1 (15.5) | <0.01  |

Data are means (SD). SBP, systolic blood pressure; DBP, diastolic blood pressure; HR, heart rate; cAIx, carotid augmentation index; \( P_h \), backward pressure; \( P_f \), forward pressure; \( P_h/P_f \), ratio of backward to forward pressure; \( c_1^{-1} \), backward (reflected) compression wave. \( P \) values were derived from linear mixed model analysis.
eterary salt intake and increased cardiovascular risk (10, 22). Our data suggest that measurements of brachial BP may substantially underestimate the adverse effects of salt intake on central BP. A meta-analysis of previous studies of the effect of changes in salt intake on brachial BP in young normotensive subjects indicated that an average reduction of 74 mmol of sodium was associated with a 2- and 1-mmHg fall in systolic and diastolic BP, respectively (7). These estimates are very similar to our current findings and much smaller than the ~7-mmHg difference in central systolic BP we observed. Central BP may be more relevant to risk of stroke, myocardial infarction, and left ventricular hypertrophy. Furthermore, increased wave reflection predicts cardiovascular events and left ventricular mass independently of central BP, possibly because of adverse effects on left ventricular performance (13, 24). This may also explain why the relationship between increased salt intake and left ventricular hypertrophy has been reported to be independent of brachial BP (5).

The mechanisms linking increased dietary salt intake to increased central systolic BP and enhanced wave reflection remain to be defined, but previous reports (2, 6) show that increased salt intake impairs release of nitric oxide (NO) in vivo. NO is an important regulator of arterial diameter, and impairment of NO release will result in impedance mismatching and increased wave reflection (4). Alternatively, increased arterial stiffness due to increased salt intake as observed in previous studies (1a, 8) could also contribute to impaired downstream impedance matching and increased wave reflection (4). Whether these effects are related to sodium-induced volume expansion and changes in shear stress (21) or changes in plasma sodium (9) remains speculative at present.

Our study has a number of limitations. All participants were healthy normotensive young men of European origin, and findings cannot necessarily be extrapolated to women, other ethnic groups, older subjects, or subjects with elevated blood pressure, all of whom may show different responses to changes in salt intake (15). The study is of relatively small size and short duration, and the effect of salt intake on BP is likely to act over decades (15); whether changes in central BP are maintained during longer periods of high salt intake requires further study, and it should be noted that participants were consuming a typical high-salt diet prior to the study. All measurements were made in the carotid artery rather than the aorta since it was not feasible to perform invasive measurements on healthy subjects; however, carotid and aortic BP are very similar (3).

CONCLUSIONS

Increased salt intake in young normotensive men elevates carotid systolic BP and increases wave reflection. These effects may account for the adverse effects of high dietary salt intake on the risk of cardiovascular disease.

GRANTS

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the authors.

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