

SUPPLEMENTAL MATERIAL

Table S1. Features of Dietary Protocols That Have Been Tested for Reproducibility in Classifying Subjects as SS or SR

| Subject class | HTN | n | Low NaCl phase Dose/d, duration, MAP(mmHg) | High NaCl phase Dose/d, duration, MAP (mmHg) | Delta MAP mmHg | Diet control | Reproducibility in repeat tests |
|-----------------|-----|-----------------|---|---|-------------------------------|-----------------------|------------------------------------|
| SS ¹ | N | 7 | 20 mmol/d, 7 days, 77.6 ± 2.8 | 220 mmol/d, 7 d, 83.2 ± 2.3 | 5.6 ^a | Y ^b | 100% |
| SR ¹ | N | 8 | 20 mmol/d, 7 days, 79.1 ± 2.6 | 220 mmol/d, 7 d, 79.0 ± 2.3 | - 0.1 | Y ^b | 87.5% |
| SS ² | N | 30 | 20 mmol/d, 7 days, 83.1 ± 1.2 | 320 mmol/d, 7 days, 91.2 ± 1.3 | 8.1 ^c | Y ^d | 100% ^e |
| SR ² | N | 108 | 20 mmol/d, 7 days, 85.1 ± 0.6 | 320 mmol/d, 7 days, 84.6 ± 0.6 | - 0.5 | Y ^d | 90% ^e |
| SS ³ | Y | 4 | 20 mmol/d, 7 days, 105 ± 3.5 | 220 mmol/d, 7 days, 116 ± 4 | 11 ^f | Y ^g | 100% |
| SR ³ | Y | 6 | 20 mmol/d, 7 days, 112 ± 5.3 | 220 mmol/d, 7 days, 108 ± 4.5 | - 4 | Y ^g | 100% |
| SS ⁴ | Y | 8 | 50 mmol/d, 6 days , 105 ± 5.0 | 250 mmol/d, 6 days , 122 ± 5.7 | 17 ^h | N ⁱ | 37.5% ^j |
| SR ⁴ | Y | 22 | 50 mmol/d, 6 days , 107 ± 2.6 | 250 mmol/d, 6 days , 108 ± 2.6 | 1 | N ⁱ | 68% ^j |
| SS ⁵ | N | 17 ^k | 56-82 mmol/d, 4 days ^l | 312-380 mmol/d, 7 days ^l | Not shown ^m | N ⁿ | 66% overall ^o |
| SR ⁵ | N | 13 ^k | 66-70 mmol/d, 4 days ^l | 488-500 mmol/d, 7 days ^l | Not shown ^m | N ⁿ | for SS + SR |
| SS ⁶ | N | 15 ^p | 62 mmol/d, 30 days ^q | 140 mmol, 30 days ^q | Not shown ^r | Y ^s | 53% overall ^t |
| SR ⁶ | N | 25 ^p | 62 mmol/d, 30 days ^q | 140 mmol, 30 days ^q | Not shown ^r | Y ^s | for SS + SR |
| SS ⁶ | Y | 22 ^u | 62 mmol/d, 30 days ^q | 140 mmol/d, 30 days ^q | Not shown ^r | Y ^s | 61% overall ^v |
| SR ⁶ | Y | 11 ^u | 62 mmol/d, 30 days ^q | 140 mmol/d, 30 days ^q | Not shown ^r | Y ^s | for SS + SR |
| SS ⁷ | Y | 4 | 40 mmol/d, 7 days | 170 mmol/d, 7 days | Not shown ^w | Y ^x | 25% ^y |
| SR ⁷ | Y | 10 | 40 mmol/d, 7 days | 170 mmol/d, 7 days | Not shown ^w | Y ^x | 90% ^y |

n indicates the sample size of subjects classified on the first test as SS or SR except in those studies^{5,6} where the sample size indicates number of subjects consistently classified as SS or SR in both rounds of testing. HTN indicates whether the subjects studied had hypertension with Y indicating yes and N indicating no. MAP values indicate the absolute MAP levels in the first round of testing in each group (mean values ± S.E.M.). Delta MAP indicates the average magnitude of the salt-induced change in MAP in each group. Diet control indicates whether a standardized diet was carefully prescribed throughout the entire study. Reproducibility indicates the percentage of subjects that were classified the same way (SS or SR) in the repeat test as in the first test. **Results in bold:** Aspects of the protocols that differ substantially from those of the proposed reference dietary protocol, and the dietary protocol recommended by the AHA. SR indicates salt resistant; SS indicates salt sensitive.

Footnotes:

- a. Blood pressure determined with an automated device from the average of 30 measurements obtained over a 1 hour period in supine subjects. Cutoff for classifying subjects as SS set as a change in MAP of ≥ 3 mmHg.
- b. Standardized diet provided 60 mmol of potassium per day. See published study for additional diet details.
- c. Blood pressure determined with an automated device from the average of 12 measurements obtained over a 1 hour period in sitting subjects. Cutoff for classifying subjects as SS set as a change in MAP of ≥ 5 mmHg.
- d. Controlled diet provided 75 mmol of potassium per day. See published study for additional diet details.
- e. Reproducibility of classifying subjects as salt sensitive or salt resistant on repeat testing was determined in a study that involved a subset of 31 subjects.
- f. Blood pressure determined from the average of 6 measurements obtained over a 30 minute period in supine subjects. Cutoff for classifying subjects as SS set as a change in MAP of ≥ 8 mmHg.
- g. Controlled diet provided 70 mmol of potassium per day. See published study for additional diet details.
- h. Blood pressure determined with a 24 hour blood pressure monitoring device from the average of readings taken every 20 minutes during the day between 6 am and 9:59 pm, and every 30 min during the night. Cutoff for classifying subjects as SS set as a change in 24 hour average MAP of ≥ 10 mmHg.
- i. Diet not controlled during the salt loading phase. Dietary instructions differed between salt restriction phase and salt loading phase. Potassium intake estimated to be approximately 90 mmol per day based on a single 24 hour urine collection study performed in each phase of the study.
- j. Reproducibility of the testing protocol for classifying subjects as salt sensitive was determined from the results of 24 hour measurements of MAP. In an additional analysis, reproducibility was determined from the results of casual measurements of blood pressure. Based on the casual BP measurements, reproducibility of classifying the same subjects as SS on both tests was 23% and reproducibility of classifying the same subjects as SR on both tests was 76%. The casual blood pressure values were determined by averaging the results of 2 measurements taken 1 minute apart in sitting subjects.
- k. In this study, the sample size represents the number of subjects consistently classified in both rounds of testing and does not represent the number of subjects that were in a particular category on initial testing. In addition to the 17 SS subjects and 13 SR subjects that were consistently classified, another 15 subjects gave inconsistent results on repeat testing. Of the subjects with inconsistent results on repeat testing, the numbers initially classified as SS versus SR were not reported.
- l. Values for salt intake represent the ranges for mean salt intake estimated from measurements of 24 hour urine sodium excretion. Absolute values for MAP in SS and SR subgroups were not reported.
- m. Blood pressure determined with a random-zero sphygmomanometer with measurements taken in sitting subjects at the end of each diet phase. Absolute values for salt-induced changes in MAP in the SS and SR subgroups were not reported. Cutoff for classifying subjects as SS set as a change in MAP of ≥ 5 mmHg.
- n. Diet not controlled throughout entire study. Diet potassium content and urinary potassium excretion not reported.
- o. Of the total number of subjects (45) entered into the study, 66% (30) were consistently classified in repeat tests. The number of subjects classified as SS on initial testing that failed to be classified as SS on repeat testing was not reported.

- p. In this study, the sample size represents the number of subjects consistently classified in both rounds of testing and does not represent the number of subjects that were in a particular category on initial testing. In addition to the 15 SS subjects and 25 SR subjects that were consistently classified, another 35 subjects gave inconsistent results on repeat testing. Of the subjects with inconsistent results on repeat testing, the numbers initially classified as SS versus SR were not reported.
- q. Values for salt intake represent the mean salt intake estimated from measurements of 24 hour urine sodium excretion. Target salt intake was approximately 50 mmol/day in the low salt phase and 150 mmol/day in the high salt phase. Absolute values for MAP in SS and SR subgroups were not reported.
- r. Blood pressure determined with a random-zero sphygmomanometer in sitting subjects. The pressure measurements were not made on the last day of each diet phase as recommended in the preferred dietary protocol. Rather, blood pressure was determined from the mean of 5 pairs of measurements taken over the period between day 21 and day 30 of each dietary intervention period. Cutoff for classifying subjects as SS was set as a change in SBP greater than the median change in SBP of all subjects tested which was 6.4 mmHg. Absolute values for salt-induced changes in MAP in the SS and SR subgroups were not reported.
- s. Controlled diet provided ~ 45 mmol potassium per day. See published study for additional diet details.
- t. Of the total number of normotensive subjects (75) studied, 53% (40) were consistently classified in repeat tests. The number of subjects classified as SS on initial testing that failed to be classified as SS on repeat testing was not reported.
- u. In this study, the sample size represents the number of subjects consistently classified in both rounds of testing and does not represent the number of subjects that were in a particular category on initial testing. In addition to the 22 SS subjects and 11 SR subjects that were consistently classified, another 21 subjects gave inconsistent results on repeat testing. Of the subjects with inconsistent results on repeat testing, the numbers initially classified as SS versus SR were not reported.
- v. Of the total number of hypertensive subjects (54) studied, 61% (33) were consistently classified in repeat tests. The number of subjects classified as SS on initial testing that failed to be classified as SS on repeat testing was not reported.
- w. Blood pressure determined with a 24 hour blood pressure monitoring device from the average of readings taken at 15 minute intervals during the day between 7 am and 10:00 pm, and every 30 min during the night. Absolute values for salt-induced changes in MAP in the SS and SR subgroups were not reported. Cutoff for classifying subjects as SS set as a change in 24 hour average MAP of ≥ 10 mmHg.
- x. Controlled diet provided 65 mmol of potassium per day. See published study for additional diet details.
- y. Results reflect the analysis performed on 24 hour blood pressure recordings. When the analysis was performed on clinic blood pressure values determined from the average of 3 measurements obtained over 15 minutes in sitting subjects, the reproducibility of classifying subjects as SS in repeat testing was 50% and of classifying subjects as SR on repeat testing was 70%.

References:

1. Sharma AM, Schattenfroh S, Kribben A, Distler A. Reliability of salt-sensitivity testing in normotensive subjects. *Klin.Wochenschr.* 1989;67:632-634.
2. Overlack A, Ruppert M, Kolloch R, Gobel B, Kraft K, Diehl J, Schmitt W, Stumpe KO. Divergent hemodynamic and hormonal responses to varying salt intake in normotensive subjects. *Hypertension.* 1993;22:331-338.
3. Draaijer P, de Leeuw P, Maessen J, van Hooff J, Leunissen K. Salt-sensitivity testing in patients with borderline hypertension: reproducibility and potential mechanisms. *J Hum Hypertens.* 1995;9:263-269.
4. Gerdts E, Lund-Johansen P, Omvik P. Reproducibility of salt sensitivity testing using a dietary approach in essential hypertension. *J Hum Hypertens.* 1999;13:375-384.
5. Mattes RD, Falkner B. Salt-sensitivity classification in normotensive adults. *Clin Sci (Lond).* 1999;96:449-459.
6. Obarzanek E, Proschan MA, Vollmer WM, Moore TJ, Sacks FM, Appel LJ, Svetkey LP, Most-Windhauser MM, Cutler JA. Individual blood pressure responses to changes in salt intake: results from the DASH-Sodium trial. *Hypertension.* 2003;42:459-467.
7. Zoccali C, Mallamaci F, Cuzzola F, Leonardis D. Reproducibility of the response to short-term low salt intake in essential hypertension. *Journal of Hypertension.* 1996;14:1455-1459.