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Examination of 'Salt Memory' in the Development of Hypertension and Its Molecular Mechanisms

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Summary

Objectives: We and others have shown that treatment of spontaneously hypertensive rats (SHR) or Dahl salt-sensitive rats with an renin-angiotensin-aldosterone (RAA) system inhibitor at the time of hypertension development causes a sustained reduction of blood pressure. The aim of this study was to examine the effects of temporary exposure to a high-salt diet on blood pressure and markers of end-organ damage in hypertensive rat models.

Methods: (Experiment 1) Dahl salt-sensitive rats were divided into 4 groups, and fed from age 6 to 14 weeks with low-salt (0.12% NaCl), normal-salt (0.8% NaCl) high-salt (7% NaCl) or high-NaAA (12.7% NaAA) diet. After these treatments, all group were returned to a normal-salt diet. (Experiment 2) Male SHRs were divided into five groups, and fed from age 6 to 14 weeks with a low-salt (0.12% NaCl), normal-salt (0.8% NaCl) or high-salt (7% NaCl) diet. Other rats were given a high-sodium/normal-chloride (12.7% NaAA) or normal -sodium/high-chloride diet (11.6% AACl). After these treatments, all groups were returned to a normal-salt diet. The effects on systolic blood pressure and urine protein excretion were examined regularly until age 24-28 weeks.

Results: (Experiment 1) Transient treatment with a high-salt diet caused an elevation in blood pressure not only during the treatment period, but also after returning to the normal-salt diet. 3 months after treatment cessation, blood pressures were still elevated in the rats transiently exposed to a high-salt diet. Similarly, urine albumin excretion was elevated in the high-salt rats at the end of the study. No such effect was seen in the NaAA group. At age 28 weeks, the high-salt group rats demonstrated increases in plasma renin activity, aldosterone, with a similar trend for renal renin mRNA. (Experiment 2) Transient treatment with a high-salt diet caused an elevation in blood pressure not only during the treatment period, but also after returning to the normal-salt diet. An increase in proteinuria and renal arteriolar hypertrophy was recognized in the high salt group, together with a marginal elevation in renin-angiotensin-aldosterone (RAA) system activity.

Conclusion: These results suggest that transient high-salt diet treatment results in a sustained elevation of blood pressure and activation of RAA system in Dahl salt-sensitive rats and SHR.