Potassium citrate feeding protects against nephron loss in severe sodium chloride hypertension in rats

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Summary

1. Potassium citrate did not significantly increase plasma flow to the renal papilla in normotensive Dahl R rats on either low or high NaCl diets. Similarly, potassium citrate did not significantly increase papillary plasma flow in mildly hypertensive Dahl S rats on low NaCl diets. Thus potassium citrate feeding did not ordinarily alter papillary plasma flow.

2. When S rats were fed on a high (4%) NaCl diet for 24 weeks, they became severely hypertensive and developed nephrosclerosis with nephron loss. This accounted for the significant reduction in papillary plasma flow in S rats on 4% high NaCl diet with no potassium supplementation.

3. When S rats on high NaCl diet were given a supplement of KCl, they still developed severe hypertension and almost the same fall in papillary plasma flow, suggesting a similar degree of nephron loss from nephrosclerosis.

4. However, when S rats on high NaCl diet were given a supplement of potassium citrate, they still developed the same severe hypertension but, in contrast, they did not have a decrease in papillary plasma flow. This actually increased to 7% higher than in comparable S rats eating the low NaCl diet. Moreover, S rats receiving potassium citrate supplements in their high NaCl diet had a papillary plasma flow which was 34% higher than that of S rats receiving no potassium supplement in the high NaCl diet (P < 0.005) and was 19% higher than that of S rats receiving KCl supplements in the high NaCl diet (P < 0.04). This occurred even though the rats receiving potassium citrate were severely hypertensive.

5. Thus potassium citrate feeding protected against nephron loss from nephrosclerosis during severe NaCl-induced hypertension, whereas KCl feeding did not provide such protection.

Key words: nephron, papillary plasma flow, potassium citrate, sodium.

Introduction and methods

This report explores the protective effect of potassium salts in NaCl-induced hypertension. In this study we used males from the two strains of Dahl rats [1]. On a 24 week low salt diet, with 0.3% NaCl, the Dahl R strain remained normotensive with a mean blood pressure of 131 mmHg and the Dahl S rats became mildly hypertensive with an average blood pressure of 169 mmHg. However, when the two strains of rats were on a moderately high NaCl diet, with 4% NaCl, for 24 weeks, the R rats continued to be normotensive with a mean blood pressure of 132 mmHg, whereas the S rats became severely hypertensive with a mean blood pressure of 208 mmHg. This 4% salt diet would be roughly equivalent to 20 g of salt/day for an adult man eating 500 g of dry food per day. Both the low and the high NaCl diets were tested in three variations: (1) without any potassium supplement; (2) with a 2.6% KCl supplement; (3) with a 3.8% potassium citrate supplement. The two potassium salts were added in equimolar amounts. After 24 weeks of feeding with these six different diets, the plasma flow to the renal papilla was measured with our version of the Lilienfield 131I-labelled albumin method [2, 3, 4].

Results

Fig. 1 shows the results. The 14 Dahl R rats on a low (0.3%) NaCl diet had a mean plasma flow to the renal papilla of 25.7 ml min⁻¹ 100 g⁻¹. When
13 similar R rats ate the 4% high NaCl diet, the papillary plasma flow averaged 26.1 ml min⁻¹ 100 g⁻¹, which is slightly higher, but this difference was not significant. In 11 Dahl S rats eating the low NaCl diet, the average papillary flow was 16.4 ml min⁻¹ 100 g⁻¹ (Fig. 1). This is 36% lower than the papillary flow in R rats. Our previous work has shown that S rats, even on a low salt diet, have significantly lower papillary flows than R rats and we suggested that this attribute could contribute to the greater susceptibility of the S rats to NaCl-induced hypertension [4]. Ten other S rats were fed on the 4% high NaCl diet and developed a mean papillary flow of 13.5 ml min⁻¹ 100 g⁻¹. Thus, although the high NaCl diet slightly increased the papillary flow of the R rats, it definitely decreased the papillary flow of the S rats by 18%, a significant reduction (P < 0.05). These S rats on the high NaCl diet had a severely elevated blood pressure of 204 mmHg, and the nephrosclerosis resulting from this probably accounts for the 12% fall in papillary flow on the high NaCl diet. Apparently KCl did not significantly prevent the hypertension and the nephrosclerosis. Again the ratio of papillary flow in S rats to that in R rats was 68% on a low NaCl diet and only 55% on the high NaCl diet.

When both of the diets were supplemented with 3-8% potassium citrate, again the R rats showed an 8.9% increase in papillary flow on the high NaCl diet, just about the same increase as occurred on the diets with KCl. However, in the S rats, the high NaCl diet containing potassium citrate actually increased papillary flow by 6-5%, instead of the decrease that was seen when the high NaCl diet contained either KCl or no added potassium. These S rats on the high NaCl diet with potassium citrate became severely hypertensive with a blood pressure of 206 mmHg, which is similar to the levels in S rats on KCl or no added potassium. Nevertheless, the papillary flow actually increased, indicating a protection against nephron loss.

Fig. 1 shows the papillary flows for the R and S rats on all six diets. The flows were in general very slightly higher on high NaCl diets [7% higher including all rats (P < 0.05)] but potassium citrate added to either low or high NaCl diets did not cause any significant increase in papillary flow.

The potassium citrate diet did not produce a rise in papillary flow in S rats on a low (0-3%) NaCl diet. The results indicate that potassium citrate does not ordinarily bring about a rise in papillary flow. The S rats developed a similarly severe hypertension on all three high NaCl diets. Nevertheless, papillary flows decreased when the high NaCl diet contained either KCl or no added
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Potassium, whereas the flow increased when potassium citrate was added to the high NaCl diet. Thus the papillary flow in the high (4%) NaCl--potassium citrate group was 34% higher than that of the S rats on the high (4%) NaCl diet without any added potassium. This difference was significant \( P < 0.005 \). The papillary flow of the high (4%) NaCl--potassium citrate group was 19% higher than that of the high (4%) NaCl--KCl group \( P < 0.04 \). These differences occurred even though the blood pressure of the rats receiving potassium citrate was at a similar severely hypertensive level.

Discussion

The most likely reason for the higher papillary flows in high salt S rats fed with potassium citrate is that the potassium citrate somehow protects against nephron loss from nephrosclerosis during severe NaCl-induced hypertension. Moreover, feeding with KCl at an equimolar level does not provide this same measure of protection. The reasons for this difference in protection are obscure. However, ancient man for 3 million years consumed a diet very high in potassium content. Moreover this high potassium content was combined with organic anions or phosphate anions whereas the chloride anion was present to a negligible extent. Substances like potassium citrate were consumed in large quantities in this prehistoric human cuisine. It is conceivable that nephrosclerosis is somehow retarded by this ancient ancestral diet.

Acknowledgments

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References