SHORT COMMUNICATION

FAECAL SODIUM/POTASSIUM RATIO AND ALDOSTERONISM IN EXPERIMENTAL HYPERTENSION IN THE RAT

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SUMMARY

1. Renal artery constriction and sham operation produced a temporary fall in the faecal sodium/potassium (Na/K) ratio of rats. When contralateral nephrectomy had been performed, the ratio rose to normal with the development of hypertension. With an intact opposite kidney the ratio remained low, but was elevated by spironolactone. With or without contralateral nephrectomy, the ratio was normal in chronically hypertensive animals (>28 days).

2. Balance studies showed sodium depletion in hypertensive rats with a normal kidney in situ. It is suggested that this stimulates aldosterone secretion and the faecal electrolyte changes.

Key words: faecal sodium/potassium ratio, sodium balance, aldosterone, renal hypertension.

The development of secondary aldosteronism in experimental hypertension appears to be critically dependent upon the procedure used. In the sheep and rat there is evidence that hypertension produced by unilateral renal ischaemia is associated with an increased aldosterone secretion rate: when the contralateral kidney is removed, no such change occurs (Blair-West, Coghan, Denton, Orchard, Scoggins & Wright, 1968; Singer, Losito & Salmon, 1963; Schwartz, Bloch & Velly, 1964). However, anaesthesia may cause artifacts in such studies (Pettinger, Marchelle & Augusto, 1971).

The human faecal Na/K ratio provides a good index of aldosterone activity (Charron, Leme, Wilson, Ing & Wrong, 1969). Such measurements can be made frequently without anaesthesia. Accordingly we have studied changes in this ratio in the rat during the development of hypertension produced by unilateral renal ischaemia with and without contralateral nephrectomy, and we have correlated these changes with sodium balance.

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METHODS

Female Wistar rats (150–200 g) ate a pellet diet containing 0·17–0·215 mmol sodium/g and 0·155–0·176 mmol of potassium/g. Metabolic cages (Cope & Cope Ltd) were used for 24 h faecal collections and balance studies.

Group 1 (Sham operation). In six animals the left kidney was exposed and mobilized and the renal artery dissected free. The kidney was returned to its bed and the wound closed.

Group 2 (Clip only). Nine animals were made hypertensive by constriction of the left renal artery (Wilson & Byrom, 1941). Faeces were collected for 3 weeks from six animals. The other three animals were given food containing spironolactone (9 mg daily) for 5 days during the third post-operative week with faecal collections before, on days 2–5 of spironolactone and days 2–5 following it.

Group 3 (Clip-nephrectomy). Six animals were made hypertensive by constriction of the left renal artery 2 weeks after contralateral nephrectomy. Faeces were again collected for 3 weeks.

Group 4 (Chronic hypertension). In fifteen animals hypertension was produced by constriction of the left renal artery. In another six animals hypertension was produced by this procedure 2 weeks after contralateral nephrectomy. Single collections of faeces were made 4 weeks to 3 months after the development of hypertension (mean blood pressure 130 mmHg or more).

Mean blood pressure was measured indirectly once or twice weekly by a photoelectric method (Swales & Tange, 1970).

Food intake, urinary and faecal sodium and urinary volume were estimated on seven animals treated as in group 2 and twelve animals treated as in group 3, and daily sodium balance was calculated (Swales, Thurston, Queiroz & Medina, 1972). Cumulative sodium balance was estimated from the time of operation until the end of 10 days of sustained hypertension, and the faecal Na/K ratio calculated over the final 24 h.

Sodium and potassium content of food and faeces was estimated by flame photometry after incineration and dissolving the residues in 0·1 m-HCl.

RESULTS

All mean values are logarithmic means (i.e. antilog mean loge Na/K). The mean faecal Na/K ratio of thirty-two normal rats was 1·25.

Group 1 (Sham clipping). Sham renal artery clipping produced a significant decrease in faecal Na/K ratio to 0·76 at 24 h and 0·97 at 3 days (P<0·001). At 6 days the value was 1·48; this is just significantly higher than normal (P<0·02).

Group 2 (Clip only). The faecal Na/K ratio decreased after renal artery clipping and remained significantly low (P<0·01) throughout the 3 post-operative weeks (Fig. 1). The mean pre-spironolactone Na/K ratio of 0·63 rose significantly during spironolactone to 1·20 (P<0·05) and then fell to 0·73 (n = 12 for each group).

Group 3 (Clip-nephrectomy). The faecal Na/K ratio fell as in group 2, but then rose again to values above 1·0 which were almost identical with the pre-operative mean (Fig. 1).

The faecal Na/K ratio showed no difference upon the days that blood pressure was measured compared with other days.
Mean daily food intake in group 2 was 12.55 (±SEM 0.41) g/day and in group 3, 12.50 (±0.26) g/day. These differences are not statistically significant (P>0.05). Mean weights of each group changed by <4% during the period of study. Mean cumulative sodium balance of the seven additional clip-only rats after 10 days hypertension was −2.25 (±0.68) mmol; for twelve additional clip-nephrectomy animals the value was +1.90 (±0.53) mmol. The correlation between log$_e$ (Na/K ratio) and sodium balance at this stage was statistically significant ($r = +0.60; P<0.01$).

Group 4 (Chronic hypertension). Average blood pressure of clip-only rats was 161 mmHg and blood pressure of clip-nephrectomy rats was 167 mmHg. The mean faecal Na/K ratio of the former had risen from the subnormal values found in the acute phase (Fig. 1) to 1.19. Neither of these values is significantly different from normal.

**Fig. 1.** Changes in mean faecal Na/K ratio (±1 SD) in rats after left renal artery constriction. (a) Intact contralateral kidney; (b) previous right nephrectomy. Mean blood pressure rose to 153 and 151 mmHg respectively.
DISCUSSION

In man the faecal Na/K ratio correlates well with aldosterone activity, as judged by its response to aldosterone and spironolactone: it has the advantage that no escape from the sodium-retaining effect of steroids occurs in chronic aldosteronism (Charron et al., 1969), whereas urinary sodium excretion 'escapes' after a few days of deoxycorticosterone acetate administration (August, Nelson & Thorn, 1958).

Our results show a similar logarithmic distribution and range to that found in the human, although the mean value is approximately five times higher in the rat. The ratio was readily lowered by aldosterone and shows no 'escape' after prolonged salt depletion (J. D. Swales, H. Thurston, F. P. Queiroz & J. D. Tange, unpublished observations).

The faecal Na/K ratio decreased transiently in both groups 2 and 3 after renal artery constriction. The similar response to sham renal artery constriction (group 1) shows that this was a non-specific effect resembling that described in sheep after renal artery clipping (Blair-West et al., 1968).

Later changes in the Na/K ratio after renal artery constriction are determined by the presence of an intact contralateral kidney. When this was present (group 2) the ratio remained well below the pre-operative figure for at least 3 weeks although it rose between 4 weeks and 3 months (group 4). The response to spironolactone suggests that this was due to an increased secretion of aldosterone. Although another mineralocorticoid, 18-hydroxy-deoxycorticosterone, has been implicated in hypertension (Rapp & Dahl, 1971) it is unlikely that this contributes to faecal electrolyte changes in view of its weak mineralocorticoid action (Melby, Dale & Wilson, 1971). By contrast, when contralateral nephrectomy was performed (group 3) the Na/K ratio soon returned to pre-operative values. Sodium retention has been demonstrated in this form of hypertension (Tobian, Coffee & McCrea, 1969) and there is evidence that it plays a pathogenetic role (Swales & Tange, 1971). The positive correlation between the final cumulative sodium balance and Na/K ratio suggests that sodium balance is at least a contributory factor to the amount of aldosterone secretion and that the 'secondary aldosteronism' in group 2 is at least partly due to sodium depletion produced by the natriuretic effect of hypertension upon an intact kidney (Koch, Aynejdian & Bank, 1968).

It may be of relevance that the results of Schwartz et al. (1964) suggest that the elevation of aldosterone secretion rate does not continue beyond 3 weeks. There are parallel physiological and pharmacological differences between acute and chronic hypertension (Page, Kaneko & McCubbin, 1966).

Our results provide support for the view that there are important differences in sodium metabolism in these two models of experimental hypertension (Swales, Thurston, Queiroz, Medina & Holland, 1971).

REFERENCES


Faecal sodium–potassium


