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Effect of moderate salt restriction and high potassium intake on pressor hormones, response to noradrenaline and baroreceptor function in man

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Summary

1. Twenty-one normotensive subjects were studied to assess any possible benefits of moderate salt restriction and of high potassium intake in the prevention of hypertension in man.

2. The effects of salt reduction from 200 to 50 mmol/day and/or of an increase of potassium intake from 80 to 200 mmol/day over a 2 week period, on blood pressure, plasma noradrenaline, adrenaline, vasopressin, renin and aldosterone, were measured both at rest and after mental stress. The effects of graded infusion of noradrenaline on blood pressure and heart rate were also studied.

3. Salt restriction lessened the increase of blood pressure during noradrenaline infusion; the combination with high potassium intake also reduced the pressure rise after mental stress. There were no major changes in plasma levels of vasopressin and adrenaline. Plasma noradrenaline increased during the low sodium diet.

4. High potassium intake improved baroreceptor function as revealed by the greater decrease in heart rate for a given rise in pressure after noradrenaline infusion.

5. The results of this study are compatible with a protective effect of a practicable low sodium/high potassium diet on the development of human hypertension.

Key words: baroreceptors, noradrenaline, potassium intake, sodium intake, stress.

Introduction

The aim of the present study was to demonstrate whether the usual high sodium/low potassium diet of civilized people is detrimental to normal blood pressure regulation and a cause of essential hypertension in man. This hypothesis was developed by Meneely & Battarbee (1976) on the basis of the work of Addison (1928), Priddle (1931) and Meneely, Ball & Youmans (1957), among others. Therefore we investigated blood pressure regulation and blood pressure-regulating hormones in normotensive subjects on their usual 'high sodium/low potassium' diet and after independently decreasing their sodium intake or increasing potassium intake. The effects of reduction of sodium intake in human subjects have been better documented (for reviews see Dahl, 1972; Freis, 1976) than the effects of a high potassium intake though most studies on variations of sodium intake were performed at extremes of 400 mmol of sodium/day and 10 mmol/day, the former being consumed hardly anywhere in the world and the latter not being practicable.

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Material and methods

Twenty-one normotensive medical students, all male (aged 21–25 years) were studied. Half of the subjects had a family history of hypertension.

The subjects were studied in a randomized fashion, either on their usual diet or after being on (a) a low sodium diet, (b) a high potassium diet or (c) a combined low sodium/high potassium diet for 2 weeks. The diets were provided by the dietary department of the University Hospital: The usual diet ('high sodium/low potassium' diet) contained 12 g of salt and 3 g of potassium/day, the 'low sodium' diet 3 g of salt and 3 g of potassium, the 'high potassium' diet contained 12 g salt and 8 g potassium and the 'low sodium/high potassium' diet contained 3 g of salt and 8 g of potassium.The high potassium intake was

achieved by giving large amounts of vegetables and fruit, by using a commercial salt substitute containing potassium chloride (Sina-Salz, Nordmark-Werke, Hamburg, F.R.G.) and by additionally giving 1 tablet of Kalinor (Nordmark-Werke) per day, containing 40 mmol of potassium.

After a 24 h urine collection, a needle was placed in a forearm vein of the fasting subject at 08·00 hours. After 90 min of supine bed rest heparinized blood was taken for determination of plasma renin, aldosterone, vasopressin, noradrenaline and adrenaline. In addition, systolic, diastolic and mean blood pressure as well as pulse rate were recored every minute with the Dinamap model 849 with recorder 950. (Applied Medical Research Corp., Tampa, Florida, U.S.A.)

The subjects then had to perform a standardized calculation stress for 3 min with further continuous blood pressure and pulse monitoring and blood was taken after 3 min for plasma catecholamines and vasopressin determination.

In the afternoon of the same day, after 30 min supine bed rest, a graded infusion of noradrenaline in a dose of 0·1 $\mu g/min^{-1}/kg^{-1}$, 0·2 $\mu g/min^{-1}/kg^{-1}$, 0·4 $\mu g/min^{-1}/kg^{-1}$, each over a 5 min period, was performed with automatic continuous blood pressure and pulse rate measurement every minute.

Methods of hormone determinations were: plasma renin by the method of Boyd, Adamson, Fitz & Peart (1966), plasma aldosterone by the method of Ito, Woo, Haning & Horton (1972), vasopressin by the method of Robertson, Mahr, Athar & Sinha (1973) and plasma catecholamines by the method of Hörtnagl, Benedict & Grahame Smith (1977). For comparison of blood pressure and pulse rates on the different diets, the mean of recorded values during the resting period was taken: after mental stress the highest pulse rates recorded and the mean of the two highest blood pressure values were compared.

For the evaluation of pressor response to noradrenaline, mean values of blood pressure and pulse rates of the resting period and of each 5 min

TABLE 1. *Effects of sodium restriction and high potassium intake on blood pressure, pressor hormones and responses to noradrenaline and mental stress in normal man*

Mean values ± SEM.

	Usual diet	Low sodium diet	High potassium diet	Low sodium/high potassium diet
Body weight (kg)	75·8 ± 2·66	−1·02 ± 0·07	−0·89 ± 0·13	−1·20 ± 0·10
Systolic blood pressure (mmHg)	125·0 ± 2·99	122·3 ± 2·35	122·0 ± 3·21	116·8 ± 3·38
Diastolic blood pressure (mmHg)	69·5 ± 2·62	65·6 ± 2·66	66·0 ± 2·50	61·2 ± 2·82
Heart rate (beats/min)	62·2 ± 2·44	67·4 ± 3·29	62·4 ± 2·06	71·0 ± 6·88
Serum sodium (mmol/l)	141·2 ± 1·25	144·3 ± 1·29	142·6 ± 0·90	149·1 ± 0·49
Serum potassium (mmol/l)	4·69 ± 0·13	4·64 ± 0·09	4·51 ± 0·10	4·75 ± 0·20
Plasma renin ($pg/h^{-1}/ml^{-1}$)	328·3 ± 32·02	602·8 ± 72·20	274·8 ± 46·10	1439·4 ± 413·67
Plasma aldosterone (ng/100 ml)	5·3 ± 1·34	15·9 ± 1·79	11·1 ± 1·58	43·1 ± 9·75
Plasma noradrenaline (basal) (ng/ml)	0·353 ± 0·075	0·605 ± 0·177	0·440 ± 0·101	—
(mental stress) (ng/ml)	0·413 ± 0·108	0·590 ± 0·169	0·401 ± 0·078	—
Plasma adrenaline (basal) (ng/ml)	0·053 ± 0·009	0·062 ± 0·017	0·062 ± 0·011	—
(mental stress) (ng/ml)	0·087 ± 0·009	0·071 ± 0·019	0·066 ± 0·015	—
Plasma vasopressin (basal) (pg/ml)	10·1 ± 0·76	11·9 ± 1·49	10·5 ± 0·88	—
(mental stress) (pg/ml)	11·8 ± 0·90	13·4 ± 1·41	11·9 ± 1·00	—
24-h urinary sodium (mmol//day)	210·5 ± 23·60	40·3 ± 7·50	155·1 ± 20·90	28·4 ± 5·30
24-h urinary potassium (mmol/day)	71·4 ± 5·80	65·4 ± 5·6	115·5 ± 11·50	172·4 ± 4·30
Response to noradrenaline:				
Increase to mean arterial pressure (mmHg)				
at 0·1 $\mu g\ min^{-1}\ kg^{-1}$	2·02 ± 2·410	2·65 ± 0·979	3·75 ± 1·079	−1·25 ± 0·966
at 0·2 $\mu g\ min^{-1}\ kg^{-1}$	9·90 ± 1·328	6·70 ± 1·750	9·34 ± 1·424	3·68 ± 1·242
at 0·4 $\mu g\ min^{-1}\ kg^{-1}$	20·80 ± 2·155	15·50 ± 1·4466	20·50 ± 1·146	10·30 ± 1·499
at 0·8 $\mu g\ min^{-1}\ kg^{-1}$	—	—	—	19·60 ± 1·790
Change of heart rate (beats/min)				
at 0·1 $\mu g\ min^{-1}\ kg^{-1}$	−6·38 ± 0·958	−5·07 ± 0·557	−8·90 ± 0·975	−8·68 ± 0·893
at 0·2 $\mu g\ min^{-1}\ kg^{-1}$	−12·20 ± 1·237	−12·20 ± 0·973	−15·00 ± 1·110	−11·36 ± 1·626
at 0·4 $\mu g\ min^{-1}\ kg^{-1}$	−16·80 ± 1·302	−18·20 ± 1·188	−21·10 ± 0·914	−17·60 ± 1·962
at 0·8 $\mu g\ min^{-1}\ kg^{6-1}$	—	—	—	−21·60 ± 1·982
Response to mental stress:				
Heart rate at 1 min (beats/min)	83·50 ± 5·23	93·60 ± 5·98	88·30 ± 5·25	100·00 ± 9·81
Systolic blood pressure at 2 min (mmHg)	134·50 ± 4·92	134·50 ± 4·27	134·30 ± 3·70	124·40 ± 4·25

period of noradrenaline infusion were compared and 'steady-state' baroreceptor reflex properties were assessed by the procedure of Korner, West, Shaw & Others (1974).

Since each subject was his own control, paired *t*-tests were used for statistical comparison of all results, except where not normally distributed values were observed; these were evaluated by the Wilcoxon test.

Results

As can be seen from Table 1, resting blood pressure fell only after the combined low sodium/high potassium diet. During a high potassium intake, noradrenaline produced significantly greater reductions in pulse rate at comparable blood pressure increases. A low sodium diet caused significantly smaller rises of blood pressure at 0·2 and 0·4 μg of noradrenaline min^{-1}/kg^{-1} as compared with the usual high sodium/low potassium diet. The combined low sodium/high potassium diet was associated with the least increase of blood pressure and with the highest pulse rate reductions, so that the dose of noradrenaline had finally to be raised to 0·8 μg of noradrenaline min^{-1}/kg^{-1} to achieve increases of blood pressure comparable with that achieved with 0·4 $\mu g\ min^{-1}\ kg^{-1}$ on the usual high sodium/low potassium diet.

The sensitivity of the baroreceptors, calculated from the ratio decrease pulse rate/increase mean arterial pressure at 0·2 μg of noradrenaline $min^{-1}\ kg^{-1}$ was calculated to be 1·43 $\pm$ 0·262 (mean $\pm$ SEM) in subjects on a potassium intake of 3 g/day and 4·17 $\pm$ 1·223 in subjects on a potassium intake of 8 g/day. With the Wilcoxon matched pairs signed rank test the difference was found to be significant ($P < 0·01$).

The low sodium/high potassium diets resulted in the expected changes in renin and aldosterone: vasopressin and plasma adrenaline remained unchanged. Plasma noradrenaline increased during the low sodium diet, but not during high potassium intake. The response of plasma catecholamines to calculation stress was similar with all diets.

Mental stress led to comparable increases of blood pressure during the usual diet and the low sodium or high potassium diet, but pulse rates 1 min after initiation of mental stress were significantly higher during the low sodium or high potassium diet. During the combined low sodium/high potassium diet, however, systolic blood pressure rose significantly less than during the diet and increases in pulse rates were greatest.

Discussion

The present study shows (a) a decrease in body weight during moderate salt restriction and during high potassium intake, (b) an increase of basal plasma noradrenaline during sodium restriction, which has been demonstrated previously (Luft, Rankin, Henry, Bloch, Grim, Weyman, Murray & Weinberger, 1979), (c) a reduced pressor response to exogenous noradrenaline during moderate salt restriction and during low sodium/high potassium intake and an increased 'steady-state' baroreceptor sensitivity during a high potassium intake.

Previous studies, most of them performed at impracticable levels of sodium intake or after pharmocological intervention with sodium balance (Raab, Humphreys & Lepeschkin, 1950; Wanko & Freis, 1958), have given inconclusive results as to whether sodium depletion decreases vascular sensitivity to catecholamines in normal subjects (Raab *et al.*, 1950; Tank & Herrin, 1953; Wanko & Freis, 1958; Ames Borkowski, Sicinski & Laragh, 1965) or not (Bohr, Brosie & Cheu, 1958; Friedman, Jamieson & Friedman, 1959; Kirkendall, Connor, Abboud, Rastogi, Anderson & Fry, 1972). Our results suggest that apparently a low salt diet may decrease vascular sensitivity to noradrenaline, whereas an increase of potassium intake might improve baroreceptor function as revealed by the greater fall in heart rate in response to noradrenaline. Therefore, a combined low sodium/high potassium intake may have a cumulative suppressive effect on noradrenaline-induced blood pressure increments. This effect is also seen during mental stress, where higher rises in heart rates (and presumably also greater increases of cardiac output) are needed to achieve equal blood pressure increments during low sodium and/or high potassium diets as compared with the usual diet.

It is still not clear whether a high potassium intake has a beneficial effect on blood pressure (Addison, 1928; Priddle, 1931; Meneely & Battarbee, 1976) or not (Freed & Friedman, 1951; Ruskin, 1954; Bohr *et al.*, 1958) and how any beneficial effect could be exerted.

In animal experiments baroreceptors have been shown to be sensitive to changes of extracellular potassium concentration (Saum, Ayachi & Brown, 1977) as well as to changes of sodium balance or extracellular sodium concentration (Kunze, Saum & Brown, 1977; Rocchini, Cant & Barger, 1977). Our evidence for improvement of baroreceptor function with high potassium intake (which was observed without any concomitant change in serum sodium and potassium con-

centration) could explain, at least partly, any beneficial effect of high potassium intake on blood pressure.

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