PAPERS AND SHORT REPORTS

Leucocyte cation transport in essential hypertension: its relation to the renin-angiotensin system

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Abstract

Leucocyte cation transport measured when patients received a normal sodium intake and the response of the renin-angiotensin system to changes in sodium intake were studied in 22 patients with essential hypertension. The rate constant for total leucocyte sodium efflux measured during a normal diet was significantly correlated with the plasma renin activity measured during a low sodium diet. Impairment of leucocyte sodium transport was significantly greater in eight patients whose plasma renin activity failed to rise into the normal range during the low sodium diet as compared with the 14 other patients, whose renin system responded normally to sodium restriction.

These results provide further suggestive evidence for the hypothesis that there is a circulating sodium transport inhibitor that may be important in the pathogenesis of essential hypertension.

Introduction

There is increasing evidence of a disturbance of intracellular electrolyte composition and sodium transport in essential hypertension. This was first described by Tobian and Binion in 1955,[1] who found an increase in the sodium content of renal arteries. Abnormalities in red cells were first reported in 1960 by Losse *et al*[2] and subsequently confirmed by others.[3-7] A mean increase in intracellular sodium content and a reduction in the rate constant for active sodium efflux were first reported in leucocytes by Edmondson *et al*[8] in 1975. Recently Poston *et al* showed that the plasma of hypertensive patients contains a sodium transport inhibitor that may be the cause of the impairment of sodium efflux in the white cells.[9] This finding supports the hypothesis that the development of essential hypertension is due to a sodium transport inhibitor with natriuretic properties that is continuously correcting an underlying tendency of the kidney to retain sodium.[10]

Many reports have shown that about 30-50% of patients with essential hypertension have a suppressed renin-angiotensin system that does not repond normally to sodium restriction.[11] Laragh *et al* suggested that in these patients with low renin activity the blood volume was effectively expanded owing to a greater tendency of the kidneys to retain sodium and water compared with patients with normal renin activity,[12] though measurements of blood volume and extracellular water are within normal limits.[13] If this suggestion is correct then, according to the hypothesis mentioned above, the abnormality in sodium transport should be greatest in those patients who have low-renin hypertension. We, therefore, studied the relation between leucocyte cation transport and the activity of the renin-angiotensin system in patients with essential hypertension.

Patients and methods

We investigated 22 unselected patients with essential hypertension who had had no previous treatment. Patients whose diastolic pressure when sitting was greater than 95 mm Hg over two months were included. Patients who had an underlying cause for their high blood pressure were excluded as well as those with accelerated hypertension. renal failure, or previous cerebrovascular or cardiovascular disease or who were taking oral contraceptives or any other drugs. The diastolic pressure ranged from 95 to 135 mm Hg with a mean of 108 mm Hg. The patients, all caucasian, comprised 11 men and 11 women, whose mean age was 46 years. Leucocytes were obtained from whole blood and the rate constant for sodium efflux measurement by methods previously described.[14] Plasma renin activity[15] and plasma angiotensin II[16] and aldosterone[17] were measured by radioimmunoassay. The correlation coefficients were estimated by the method of least squares. All mean values are given ±SEM.

Measurements were made of 24-hour urinary sodium excretion, blood pressure, plasma renin activity, and plasma angiotensin II and aldosterone when the patients were taking a normal diet, on the fifth day of a high sodium diet (normal diet plus 200 mmol (mEq) sodium (Slow Sodium, CIBA)), and on the fifth day of a low sodium diet (10 mmol/day). Similar measurements were made in 40 normotensive control subjects with similar age and sex distributions. The leucocyte

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studies in the hypertensive patients were performed only when they were taking their normal diet; these studies were not done in the normotensive controls.

Results

Plasma renin activity after sodium restriction in eight of the hypertensive patients failed to rise into the normal range, which had been established in the 40 normotensive controls. These eight patients were designated as the low-renin group. Plasma renin activity in the remaining 14 patients rose normally after sodium restriction. These were designated as the normal-renin group. Mean urinary sodium excretion on the fifth day of the low sodium diet in the eight low-renin patients was $19{\cdot}6 \pm 3{\cdot}0$ mmol/day, which was not significantly different from that in the 14 normal-renin patients with ($13{\cdot}1 \pm 2{\cdot}6$ mmol/day; $p > 0{\cdot}2$). Weight loss by the fifth day of the low sodium diet was $1{\cdot}3 \pm 0{\cdot}3$ kg in the low-renin patients and $1{\cdot}4 \pm 0{\cdot}2$ kg in the normal-renin patients ($p < 0{\cdot}6$, not significant).

In all 22 hypertensive patients the mean rate constant for total leucocyte sodium efflux was $3{\cdot}13 \pm 0{\cdot}2$ h and the mean rate constant for glycoside-sensitive (active) sodium efflux $2{\cdot}38 \pm 0{\cdot}13$/h. The mean rate constant for total leucocyte sodium efflux in the eight low-renin patients was $2{\cdot}74 \pm 0{\cdot}12$/h, which was significantly lower than that in the 14 normal-renin patients ($3{\cdot}35 \pm 0{\cdot}15$/h; $p < 0{\cdot}02$) (fig 1). The rate constant for total leucocyte sodium efflux (measured while the patients were receiving a normal sodium diet) was compared with the plasma renin activity and angiotensin II and aldosterone concentrations measured during the normal, high, and low sodium diets. During the low sodium diet plasma renin activity and concentrations of angiotensin II and aldosterone correlated significantly with the rate constant for total leucocyte sodium efflux ($r = 0{\cdot}60$, $p < 0{\cdot}01$, $n = 22$ (fig 2); $r = 0{\cdot}66$, $p < 0{\cdot}05$, $n = 11$; and $r = 0{\cdot}66$, $p < 0{\cdot}01$, $n = 15$ respectively). These plasma concentrations of angiotensin II and aldosterone during the low sodium diet also correlated significantly with the rate constant for active glycoside-sensitive leucocyte sodium efflux; the correlation with plasma renin activity just failed to reach conventional levels of significance. There was no significant correlation between the rate constant for total leucocyte sodium efflux or glycoside-sensitive sodium efflux and plasma renin activity or concentrations of angiotensin II and aldosterone when measured during the normal and high sodium diets. The greatest impairment of leucocyte sodium efflux was therefore in those patients who had the lowest plasma renin activity during sodium restriction.

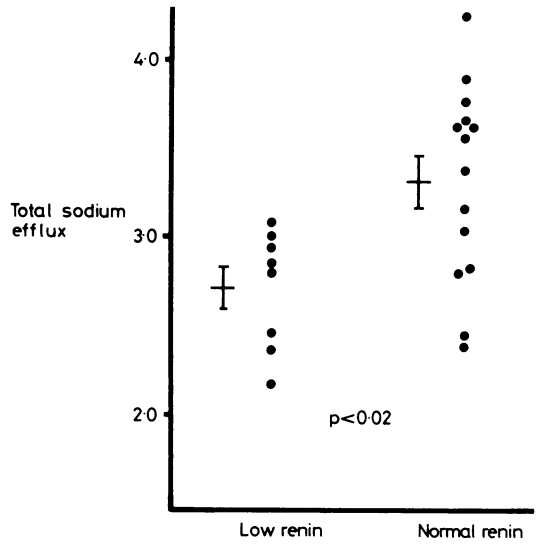

FIG 1—Rate constants per hour for total leucocyte sodium efflux measured during normal sodium diet in eight low-renin and 14 normal-renin patients. Bars indicate means ± SEM.

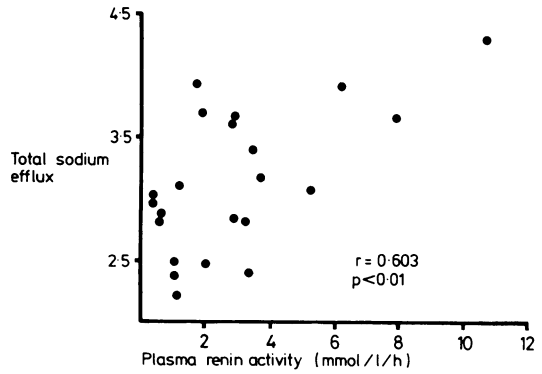

FIG 2—Relation between plasma renin activity measured on fifth day of 10 mmol sodium diet and rate constant for total leucocyte sodium efflux per hour measured during normal diet in 22 hypertensive patients.

Conversion: SI to traditional units—Plasma renin activity: 1 mmol/l/h ≈ 1·3 ng/ml/h.

Discussion

These patients showed a similar impairment of leucocyte cation transport to that described previously.[8 9] The severity of this defect while the patients were receiving a normal sodium diet was significantly related to the plasma renin activity and concentrations of angiotensin II and aldosterone when they were receiving a low sodium diet. The results show that the defect in leucocyte transport in essential hypertension is greatest in those patients with a renin-angiotensin system that does not respond normally to sodium restriction.

The hypothesis that there may be a circulating sodium transport inhibitor in essential hypertension is based on a suggestion by Dahl[18] to account for the results of experiments on parabiotic rats. This was subsequently modified by Haddy and Overbeck[19] to explain the rise in blood pressure that occurs with demonstrable volume expansion. De Wardener and MacGregor[10] recently extended the hypothesis to essential hypertension. They suggested that in patients with established essential hypertension or who are going to develop essential hypertension the blood contains a sodium transport inhibitor with natriuretic properties secreted in response to a tendency of the kidneys of such patients to retain sodium and water. This rise in the plasma concentration of the sodium transport inhibitor is the reason that extracellular fluid volume measurements in essential hypertension are within normal limits. The sodium transport inhibitor also inhibits sodium transport in other cells. In the arteriole this leads to an increase in tone and the subsequent development of hypertension by the mechanism outlined by Blaustein.[20]

The hypothesis, therefore, proposes that patients with essential hypertension are in a state of continuously correcting a tendency for extracellular volume expansion. Those patients whose kidneys have the greatest tendency for sodium retention and for extracellular fluid volume expansion and, therefore, a less pronounced rise in renin activity with sodium restriction should have the highest level of the circulating sodium transport inhibitor and thus the greatest impairment in leucocyte sodium transport. Our results, showing that the impairment of leucocyte sodium transport is greatest in hypertensive patients with a subnormal response of the renin-angiotensin system to sodium restriction, support the hypothesis.

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Is your enema really necessary?

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Abstract

Two hundred and seventy-four women admitted for delivery of singleton infants were studied for the effects of a preparatory enema on faecal contamination, duration of labour, and the incidence of infection in the newborn. Altogether 149 of the women were given an enema (controls) and 125 were not.

The two groups showed no significant difference in the degree of faecal contamination during the first and second stages of labour, and the incidences of gross contamination were similar. Contamination after an enema was especially difficult to control, since it was more likely to be fluid. Seven neonates in each group showed evidence of infection, bowel organisms being isolated from four in the no-enema group and two in the control group. Durations of labour, though not strictly comparable, were similar in the two groups.

The findings suggest that when preparing for normal labour the enema should be reserved for women who have not had their bowels open in the past 24 hours and have an obviously loaded rectum on initial pelvic examination.

Introduction

In a recent study[1] we looked at the value of shaving the pubic area of women admitted to the delivery suite in labour. Having established that shaving was not beneficial to the patient, we decided to examine other midwifery procedures.

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It has long been established practice in many midwifery units to administer an enema to all patients in labour. This is claimed to have three major benefits. An empty bowel facilitates the descent of the presenting part, reduces faecal contamination, and reflexly stimulates uterine activity. We have tried to establish the truth of these claims.

Pre-existing attitudes

MEDICAL STAFF

With only two exceptions, the medical staff of the unit of all grades (senior house officer to consultant) thought that the lack of an enema could delay the descent of the presenting part, complicate labour, and lead to unacceptable faecal contamination, especially in the second stage.

MIDWIVES

The midwives were also united in their attitude. Most objected strongly to managing patients in labour unless an enema had been given and the bowel emptied. They thought that without an emena labour would be prolonged and the incidence of instrumental delivery increased. They foresaw faecal contamination of the baby and thought that offensive odour would embarrass both staff and patients.

PATIENTS

One hundred and twenty antenatal patients were interviewed. Thirty-six were primigravid, had never had an enema, and were unable to comment. They were, however, willing to accept whatever professional advice they were given. The remaining 84 parous patients were divided in their opinions. Forty-two considered the procedure degrading and uncomfortable but accepted it as the price of a "clean delivery." The others thought that they should be offered some choice, and several mentioned suppositories as an acceptable alternative.