Studies of red cell cation transport in white and black essential hypertensives

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Summary

It has been reported previously in white patients with essential hypertension that red cell sodium pump activity as measured by ouabain-sensitive uptake of the potassium analogue ^{86}Rb from a potassium-free medium, is very significantly greater than in white controls. In a further study of black (West Indian) subjects reported here no similar abnormality was present in black hypertensives when compared with black normotensive individuals. Red cell rubidium uptake was significantly lower in normotensive blacks than in normotensive whites although sodium pump activity was the same. These results may be relevant to observed racial differences in sodium handling and in the pathophysiology of essential hypertension.

Introduction

There is now a large body of evidence to indicate that in whites with essential hypertension the distribution of sodium between intra-cellular and extra-cellular compartments is abnormal and a number of cation transport abnormalities have been described in both erythrocytes and leucocytes (Garay *et al.*, 1980; Poston *et al.*, 1981). The mechanism underlying these abnormalities is disputed. It has recently been reported from this laboratory that there is an apparent increase in the activity of the erythrocyte sodium-potassium ATPase ('sodium pump') in essential hypertensive whites although this is probably secondary to raised intracellular sodium (Woods, Beevers and West, 1981). Preliminary work suggested racial differences in normal red cell electrolyte transport which has now been examined in more detail.

When normotensive black and white individuals are given an i.v. saline load the former group excrete sodium more slowly and have a greater and more sustained rise in blood pressure while doing so (Luft *et al.*, 1979). This difference in natriuretic

response might account for the greater prevalence of essential hypertension among blacks than among whites living in similar urban environments with a high dietary sodium intake (Stamler *et al.*, 1974; Sever *et al.*, 1979). Essential hypertension in blacks is more commonly associated with low plasma renin than in whites (Dunn and Tannen, 1974; Brunner *et al.*, 1972) and has been reported to be less responsive to β -blockade (Seedat, 1980). These indications of pathogenetic and pathophysiological differences in essential hypertension among blacks and whites prompted the present study in which red cell cation transport was compared in matched groups of normotensives and hypertensives from both races resident in the catchment area of a single hospital.

Methods

The ^{86}Rb procedure has been described previously (Woods *et al.*, 1981) and was based on the method of Aronson *et al.* (1977). Washed red cells were suspended in potassium-free Ringer's solution containing $3\text{ }\mu\text{mol/l}$ ^{86}Rb chloride and uptake of the isotope was measured over one hr at 37°C in the presence and absence of ouabain 1 mg/ml . The inter- and intra-assay coefficients of variation were $<5\%$. The non-parametric Mann-Whitney test was used to compare all uptake data.

None of the subjects included in the study was taking any prescribed or proprietary drug treatment. The hypertensive individuals were newly referred cases who had received no anti-hypertensive treatment for at least 6 weeks and the great majority had never been treated for hypertension. Their blood pressures were in excess of $140/90\text{ mmHg}$ (diastolic V). Whites and blacks were well matched for blood pressure ($177/106$ and $178/104\text{ mmHg}$ respectively) and were also of similar age (mean 47 and 50 years respectively). The normotensive controls

included patients awaiting minor surgical procedures, factory workers taking part in blood pressure screening, and medical and laboratory staff. None of the controls had any known or suspected family history of hypertension. Black and white controls were also well matched for blood pressure (124/76 and 119/74 mmHg respectively) and mean age (35 years for both groups). Each group contained approximately equal numbers of males and females. Earlier studies had failed to show any influence of either age or sex on ^{86}Rb uptake.

Results

The pooled results are shown in Fig. 1. Total ^{86}Rb uptake was significantly greater in normotensive whites than in normotensive blacks owing to a very significantly greater ouabain-resistant ^{86}Rb uptake in the whites. Ouabain-sensitive transport of ^{86}Rb was identical in the 2 groups. Ouabain-resistant influx includes passive movement of ^{86}Rb into the cells and also several saturatable pathways. It is not yet clear which of these is responsible for the racial difference in normotensives.

When white hypertensives were compared with white normotensive controls a very significant increase in sodium pump activity was found in the former as has been reported previously. Ouabain-resistant ^{86}Rb transport was identical in white hypertensives and white normotensives.

When black hypertensives were compared with black normotensive controls there was no abnormality in either component of ^{86}Rb influx under the

conditions of the experiment. This is in clear contrast to the results found in white essential hypertensives. Sodium pump transport of ^{86}Rb was in fact lower in black hypertensives than in black controls although this difference did not reach significance.

Discussion

The increased red cell sodium pump activity observed among white essential hypertensives may well be a secondary phenomenon in response to another abnormality in transmembrane sodium movement such as a defect in the sodium-potassium co-transport mechanism described by Garay *et al.* (1980) or even an increase in membrane sodium permeability as suggested by Postnov *et al.* (1977). Whatever the explanation, it is of great interest that no similar change was seen in black hypertensives in comparison with normotensive black controls. These contrasting results suggest either that there is no abnormality in cation movement across the red cell membrane in black hypertensives or, alternatively, that there is a defect but one which is different from that occurring in white hypertensives and not detected by the technique used here. The latter possibility is supported by the observation of Adenomonu and Salako (1979) that red cell sodium concentration is indeed significantly higher in hypertensive than in normotensive Nigerians. A fuller understanding of the physiological basis for the differences in electrolyte transport between normotensive blacks and whites and between normotensive and hypertensive whites may clarify the interaction

FIG. 1. Pooled uptake data for white hypertensives (WH) ($n=16$), white normotensives (WN) ($n=22$), black normotensives (BN) ($n=23$) and black hypertensives (BH) ($n=10$). Statistics by Mann-Whitney test.

between genetic and environmental factors in the development of essential hypertension.

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