Leucocyte electrolytes and sodium efflux rate constants in the hypertension of pre-eclampsia

T. E. FORRESTER AND G. A. O. ALLEYNE
Department of Physiology, University of the West Indies, and Department of Medicine, University Hospital of the West Indies, Mona, Kingston, Jamaica, West Indies

Summary

1. Leucocyte electrolytes were measured in pre-eclampsia and comparison was made with leucocytes from normal primigravidae and from the original pre-eclamptic subjects 6 months after delivery when blood pressure had returned to normal.

2. In pre-eclamptic subjects, leucocyte sodium was elevated and potassium depressed, and the rate constant for sodium efflux was depressed.

3. These changes returned to normal after delivery.

4. An increase in cellular sodium as a result of altered sodium pump activity may be the cause of hypertension in pre-eclampsia.

Key words: electrolytes, hypertension, leucocyte, pre-eclampsia, sodium efflux.

Introduction

The pathogenesis of the hypertension in pre-eclampsia remains obscure. It has been related by some authors to excessive sodium retention (Mengert & Tacchi, 1961; Little, 1965; Reed, Mosel & Langford, 1968), which is not due to the renin–angiotensin–aldosterone system (Weir, Fraser, Lever, Morton, Brown, Kraszewski, McIlwaine, Robertson & Tree, 1973). The retained sodium is not intravascular as plasma volume is lower in patients with pre-eclampsia than in normotensive primigravidae (Gordon, Parsons & Symmonds, 1969). Hence this excess sodium must be distributed between the interstitial and intravascular compartments. There have been no measurements of intracellular sodium in pre-eclampsia. Thus there is no clue to the distribution between cells and interstitial fluid.

Activities of sodium + potassium-dependent ATPase and magnesium ATPase are depressed in erythrocytes from cord blood from pre-eclamptic patients, and a circulating toxin has been invoked to explain this finding (Kuhnert, Kuhnert, Murray & Sokol, 1977). If this toxic effect were widespread and affected vascular myocytes, sodium might accumulate intracellularly and cause vascular resistance to rise both from geometric changes (decreased lumen) and biochemical changes (increased smooth muscle contractility) due to increased availability of calcium (Folkow, Hallback, Lundgren, Silvertsson & Weiss, 1973; Bohr, 1974; Jones, 1974).

This study was designed to measure the intracellular sodium and potassium and the rate constant for sodium efflux in leucocytes in order to establish whether there was derangement of cellular sodium homeostasis in pre-eclampsia. The sodium content of leucocytes has been shown to be increased in essential hypertension (Edmonson, Thomas, Hilton & Patrick, 1975) but there are no such measurement in patients with transient or reversible forms of hypertension.

Methods

Fourteen primigravidae with no previous history of hypertension, who had diastolic blood pressures greater than 90 mmHg after week 24 of pregnancy, were selected from the Antenatal Clinical of the University Hospital of the West Indies, Jamaica. These patients were regarded as pre-eclamptics. Ten primigravidae with no previous history of hypertension and with normal blood pressure were chosen as controls. Eleven of
the 14 pre-eclamptic patients returned for follow-up 6 months after delivery, and measurements were repeated.

Blood was withdrawn by venepuncture, the erythrocytes were removed by dextran sedimentation and leucocytes isolated from the supernatant by centrifugation (Baron & Ahmed, 1969). The leucocytes, freed from contaminating residual erythrocytes by hypotonic lysis, were incubated in tissue culture medium (TC199) containing $^{22}$Na (0.9 $\mu$Ci/ml). After they had been loaded with $^{22}$Na, the leucocytes were washed and resuspended in two aliquots to give a final concentration of $10^{-4}$ mol/l at the start of the measurement of sodium efflux. The rate constant for total sodium efflux was determined from the residual radioactivity in three timed samples of leucocytes from the non-ouabain-treated aliquot. The rate constant for ouabain-insensitive sodium efflux was determined similarly from two timed samples from the ouabain-treated portion. $^{125}$I-labelled polyvinylpyrrolidine was added to the final wash as a marker for estimating extracellular space. The cells were dried, extracted with nitric acid (0.1 mol/l) and sodium and potassium measured by flame photometry. From these measurements the concentration (mmol/l), rate constants for total sodium efflux, the difference between total and ouabain-insensitive sodium efflux by difference. Significance of differences in data was assessed by Student's $t$-tests. Results are expressed as mean ± SEM.

Radioactive sodium and $^{125}$I-labelled polyvinylpyrrolidine were obtained from The Radiochemical Centre, Amersham, Bucks, U.K. Ouabain was from Sigma Chemical Co., St Louis, MO, U.S.A. and TC199 from Wellcome Laboratories, Beckenham, U.K. All other reagents were analytical grade.

**Results**

The blood pressure in pre-eclamptic patients was 137 ± 4.8 mmHg systolic, 95 ± 1.8 mmHg diastolic, and exceeded that in normotensive primigravidae [110 ± 2.4 mmHg systolic, 68 ± 2.5 mmHg diastolic, ($P < 0.001$)]. Pressure fell to normal levels after delivery: 124 ± 3.8 mmHg systolic, 75 ± 2.3 mmHg diastolic ($P < 0.001$).

Leucocyte sodium was elevated and potassium depressed in pre-eclamptic patients (Table 1). Both sodium content and concentration were significantly higher in leucocytes from pre-eclamptic patients when compared with normotensive primigravidae or with pre-eclamptic patients after delivery. Leucocyte potassium content was also lower in pre-eclamptic patients than in controls or in those patients 6 months after delivery. Only in controls was there a significantly greater potassium concentration.

The rate constant for total sodium efflux was significantly lower in pre-eclamptic patients before delivery, compared with the same group after delivery. A similar tendency was observed in the comparison between pre-eclamptic patients and normotensive primigravid patients.

Ouabain-insensitive sodium efflux was the same in all three groups; thus active sodium efflux, the difference between total and ouabain-insensitive efflux, followed the same pattern as total sodium efflux.

**Discussion**

These data show that leucocyte sodium is considerably elevated and potassium somewhat depressed in pre-eclampsia. The presence of raised leucocyte sodium suggests that the intracellular compartment accommodates some of the

---

**Table 1. Leucocyte sodium and potassium content and concentration and rate constants for sodium efflux in primigravidae and pre-eclamptic patients before and after delivery**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 ($n = 10$)</th>
<th>Group 2 ($n = 14$)</th>
<th>Group 3 ($n = 11$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sodium content (mmol/kg of dry solids)</td>
<td>80.5 ± 6.3 ($&lt;$0.05)</td>
<td>145.1 ± 18.3</td>
<td>70.7 ± 5.0 ($&lt;$0.005)</td>
</tr>
<tr>
<td>Sodium concn. (mmol/l)</td>
<td>30.9 ± 2.5 ($&lt;$0.01)</td>
<td>60.6 ± 7.2</td>
<td>26.8 ± 2.2 ($&lt;$0.001)</td>
</tr>
<tr>
<td>Potassium content (mmol/kg of dry solids)</td>
<td>346.9 ± 18.3 ($&lt;$0.05)</td>
<td>207.5 ± 23.6</td>
<td>357.1 ± 21.2 ($&lt;$0.05)</td>
</tr>
<tr>
<td>Potassium concn. (mmol/l)</td>
<td>150.7 ± 13.4 ($&lt;$0.01)</td>
<td>132.2 ± 9.8</td>
<td>134.9 ± 8.9 ($&lt;$0.01)</td>
</tr>
<tr>
<td>Rate constant for sodium efflux (per h)</td>
<td>3.39 ± 0.32 ($&gt;$0.10)</td>
<td>2.41 ± 0.12</td>
<td>3.49 ± 0.30 ($&lt;$0.001)</td>
</tr>
<tr>
<td>Ouabain insensitive</td>
<td>0.50 ± 0.19 ($&gt;$0.10)</td>
<td>0.63 ± 0.11</td>
<td>0.59 ± 0.05 ($&gt;$0.10)</td>
</tr>
</tbody>
</table>

Groups: 1, normotensive primigravidae; 2 and 3, pre-eclamptic patients before delivery and after delivery. Results are expressed as mean values ± SEM. Data for groups 2 and 3 were subjected to paired Student’s $t$-test and other data to unpaired $t$-test. Values for probability ($P$) are shown in parentheses.
excess sodium which is retained in pre-eclampsia. These changes in cellular electrolytes may result from a depression of activity of the sodium pump, since the rate constant for sodium efflux was depressed in the presence of a high intracellular sodium. Elevation of intracellular sodium and depression of active sodium efflux have been seen in essential hypertension (Edmonson et al., 1975), and this finding suggests that a similar derangement in cellular sodium homeostasis may exist in essential hypertension and pre-eclampsia. An elevation of cellular sodium has been demonstrated in vascular tissue in essential hypertension and renal hypertension in humans and animals (Palaty, Gustafson & Friedman, 1969), and may explain the increased vascular reactivity seen in these conditions. Although only leucocytes have been examined in pre-eclampsia, it is tempting to regard the derangement in cell sodium as affecting other tissues as in these other forms of hypertension.

Cardiac index and cardiac output are depressed in pre-eclamptic patients when compared with normal subjects or primigravid patients (Smith, Douglas & Langford, 1967): combined with a raised blood pressure this must indicate an elevation of peripheral resistance in pre-eclampsia. It is reasonable to link this increased peripheral resistance with an increase in intracellular sodium and increased vascular reactivity (Tobian, 1974; Friedman & Friedman, 1976; Blaustein, 1977).

The disappearance of the derangement of cellular electrolyte homeostasis after delivery is presumptive evidence of a cellular insult restricted to the period of pregnancy. Structural adaptation in resistance vessels to the hypertension may not be permanent since the blood pressure returns to normal. The nature of the presumed cellular insult has not been elucidated by these studies, but in this situation, where sodium retention has been clearly demonstrated and intracellular sodium now found to be markedly elevated, it is reasonable to ascribe to cellular sodium a central role in the transient hypertension of pre-eclampsia.

Acknowledgments

We are grateful to the Tropical Metabolism Research Unit, Kingston, Jamaica, for providing laboratory space and equipment.

References


