Inheritance of Abnormal Erythrocyte Sodium Counter Transport in Children of Parents with Essential Hypertension

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ABSTRACT

Aims: To assess the rate of sodium-counter transport in healthy offsprings of parents suffering from essential hypertension comparing to those with normotensive parents. And see if this marker could be used as a diagnostic marker in essential hypertension.

Subjects and Methods: The study was conducted on 15 offspring of normotensive parents (G1), 15 offspring with one hypertensive parent (G2) and 15 offspring of both essential hypertensive parents (G3). All groups were between 10-20 years of age and with equal gender distribution. All cases were labeled normotensive after taking detailed history, complete physical examination and laboratory investigations. Lithium efflux and maximum rate (Vmax) of lithium-sodium counter transport (a mode of Na-Na counter transport) was measured in red blood cells.

Results: There was a highly significant (p<0.001) increase in lithium efflux at two and four hours and non-significant increase at zero hours, in subjects with family history of essential hypertension as compared to that in normotensive offsprings born of normotensive parents. Increase in Vmax of lithium-sodium counter transport of normotensive offsprings with both essential hypertensive parents was highly significant (P<0.001) than that of normotensive offspring with one hypertensive parent and with both normotensive parents.

Conclusions: Lithium efflux and Vmax of sodium counter transport is raised in subjects with family history of essential hypertension as compared to those without family history of hypertension And therefore it can be used as a marker for the diagnosis of hypertension.

Key words: Sodium-counter transport, Healthy offsprings, Parents Essential hypertension, Parents normotensive.

INTRODUCTION

Observations in cat ion movements into red blood cells suggested different membrane pathways. Up till now kinetic studies have clearly shown that no specific red blood cell transport defect characterizes the whole population of essential hypertensive patients. Conversely several complex patterns including some inherited abnormality in membrane sodium transport are involved in the pathogenesis of essential hypertension.

Evidence is now available that elevated Vmax of lithium-sodium counter transport is not only one of the characteristic features of essential hypertensives but it is also found in normotensive offspring of hypertensive patients. Moreover this abnormality of ion transport is not reported in secondary hypertension.

Lithium-sodium counter transport is a membrane system, which exchanges intracellular lithium for extra cellular sodium in vitro. High counter transport reflects abnormal kinetic properties of red blood cell membrane sodium exchange. It is under genetic control and is raised in patients with essential hypertension and their first degree relatives.

This study was carried out to assess the rate of sodium-counter transport in healthy offspring of parents with essential hypertension as compared to those with normotensive parents. It was also aimed to examine the role of sodium-counter transport mechanism as a diagnostic marker in essential hypertension.

SUBJECTS AND METHODS

The study was conducted on 15 offsprings with normotensive parents (G1), 15 offspring with one hypertensive parent (G2) and 15 offspring with both essential hypertensive parents (G3). All groups were
between 10-20 years of age and with equal gender distribution. All cases were labeled normotensive after taking detailed history, complete physical examination and laboratory investigations.

Lithium-sodium counter transport in subject’s red blood cells was measured according to method described by Woods et al. Blood was drawn in tubes containing ethylenediaminetetra-acetic acid (EDTA). The red blood cells were separated, washed and loaded with lithium by suspending in a medium containing lithium chloride. The lithium-loaded cells were incubated in sodium free and sodium enriched media for measurement of lithium efflux.

Fractions of cell suspension were diluted with distilled water and lithium counter transport was measured by flame photometer. Vmax of counter transport (millimoles of lithium efflux per liter of red blood cells per hour) was computed from the linear regression of lithium loss as a function of time. Results were expressed as mean significance of difference between groups by applying student ‘t’ test.

**RESULTS**

There was no significant difference in lithium efflux values at zero hour between subjects with and without family history of essential hypertension. Increase in lithium efflux at two and four hours in subjects with family history of essential hypertension was very highly significant (P<0.001) as compared to that in normotensive offspring born of normotensive parents (Table-1).

Table-1: Comparison of Vmax of lithium efflux between subjects (G1) without family history of Essential Hypertension with subjects (G2, G3) having family history of Essential Hypertension.

<table>
<thead>
<tr>
<th>Time (Hour)</th>
<th>Lithium efflux in mM/L RBCs (mean ±SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1</td>
<td>0.006 ± 0.010</td>
<td>G2</td>
</tr>
<tr>
<td>G2</td>
<td>0.033 ± 0.04</td>
<td>G3</td>
</tr>
<tr>
<td>G3</td>
<td>0.67 ± 0.06</td>
<td></td>
</tr>
</tbody>
</table>

G1: Normotensive offspring with normotensive parents (controls)
G2: Normotensive offspring with one essential hypertensive parent.
G3: Normotensive offspring with both essential hypertensive parents.
NS: Non-significant (G2 vs G1; G3 vs G2).
VHS: Very highly significant (G2 vs G1: G3 vs G1)

An increase in Vmax of lithium-sodium counter transport of normotensive offspring with one hypertensive parent was highly significant (P<0.001) as compared to that of offspring with normotensive parents. There was also a highly significant (P<0.001) increase in Vmax of lithium-sodium counter transport of normotensive offspring with both hypertensive parents than that of normotensive of offspring with normotensive parents and with one hypertensive parent (Table 2).

Table-2: Comparison of Vmax of lithium-sodium counter transport between subjects (G1) without family history of Essential Hypertension with subjects (G2, G3) having family history of Essential Hypertension.

<table>
<thead>
<tr>
<th>Vmax lithium-sodium (millimoles / liter of RBCs per hr) Means ±SD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>G1 0.17 ± 0.01</td>
<td>G2 0.29 ± 0.04</td>
</tr>
</tbody>
</table>

**DISCUSSION**

Abnormalities in erythrocyte membrane sodium transport in patients of essential hypertension have been recognized for many years. The present interest in the field was sparked by a number of the studies. An increased lithium-sodium countertransport was reported in some of the normotensive offspring of essential hypertensive patients. It was suggested that such studies could be used to differentiate between essential and secondary hypertension and could also help to detect normotensive offspring of hypertensive parents who would also have a potential risk of developing essential hypertension.

An increased lithium-sodium counter transport reflects abnormal kinetic properties of sodium-sodium counter transport either functional or structural. This induces sodium and water retention and smooth muscle contraction thus causing hypertension. We observed that elevation in Vmax of lithium-sodium counter transport was very highly significant (P< 0.001) in normotensive offspring with family history of essential hypertension as compared to that in normotensive offspring without family history of essential hypertension. Moreover, it was seen that increase in Vmax of lithium-sodium counter transport was significant (P< 0.001) in normotensive offspring with both hypertensive parents. Our study shows that the genetic role in the pathogenesis of essential hypertension cannot be ruled out. The genetic transfer of abnormally raised sodium countertransport actively predisposes the normotensive offspring with positive family history of essential hypertension to the potential risk of hypertension in future. Several other workers reached the same conclusion.
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REFERENCES