The Blood Pressure Response to Antihypertensive Treatment With Lisinopril or Bendrofluazide Is Related to the Calcium and Magnesium Contents in Skeletal Muscle

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To evaluate the association between skeletal muscle mineral balance and effect of antihypertensive treatment, 37 patients with essential hypertension, randomly treated with either lisinopril or bendrofluazide, were investigated with skeletal muscle biopsies before and after 6 months of treatment. The ratio between calcium and magnesium concentrations in skeletal muscle prior to treatment predicted the blood pressure response during active treatment (r = -0.38, P < .02). During treatment the change in blood pressure was related to the change in muscle Ca/Mg ratio (r = 0.35, P < .05), especially in the patients treated with lisinopril. Thus, an association between the calcium and magnesium balance in skeletal muscle and the blood pressure response to antihypertensive treatment was found in the present study. Am J Hypertens 1996;9:273-276

KEY WORDS: Bendrofluazide, lisinopril, hypertension, muscle minerals, calcium, magnesium.

A deficient intracellular magnesium content, together with an increased intracellular calcium concentration, has been observed in erythrocytes and platelets from hypertensive subjects. The conditions in erythrocytes and platelets may not, however, reflect the conditions in other tissues.

We have recently reported on the effects of lisinopril and bendrofluazide on glucose and lipid metabolism during antihypertensive treatment with these drugs in a randomized double-blind, parallel-group study. A secondary aim was to investigate the effects on ion concentrations in skeletal muscle in relation to the blood pressure response.

SUBJECTS AND METHODS

A random sample of 37 of the 50 patients with essential hypertension entered a trial that has previously been described in detail. Sixteen patients, mean age 57, of whom four were female, were treated with lisinopril; and 21 patients, mean age 59, of whom six were female, received bendrofluazide medication. After a period of placebo treatment of 4 to 6 weeks, in which the supine diastolic blood pressure (DBP) was 95 to 115 mm Hg at least twice, the patients were randomly assigned to treatment with lisinopril 10 or 20 mg once daily or bendrofluazide 2.5 or 5 mg once daily for 24 weeks, the dose depending on the blood pressure control. Blood pressure was measured in duplicate with a sphygmomanometer after 5 min in the supine position and after 2 min in the standing position.

Skeletal muscle biopsies were performed in the right femoral vastus lateralis muscle. The muscle biopsy specimen was dissected free from visible fat and con-
TABLE 1. MINERAL CHARACTERISTICS OF THE HYPTERTENSIVE PATIENTS (N = 37) DURING THE INITIAL PLACEBO RUN-IN (0). ADJUSTED MEANS (± SD) FOR SODIUM, POTASSIUM, CALCIUM, AND MAGNESIUM CONCENTRATIONS (mmol/kg DRY MATTER), AND Ca/Mg AND Na/K RATIOS IN SKELETAL MUSCLE TISSUE, AND THE CHANGES DURING 6 MONTHS OF TREATMENT WITH LISINOPRIL (L) (N = 16) OR BENDROFLUAZIDE (B) (N = 21)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Treatment</th>
<th>Placebo (O)</th>
<th>Effect of Treatment %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>L</td>
<td>148 (55)</td>
<td>+8% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>147 (100)</td>
<td>+16% NS</td>
</tr>
<tr>
<td>K</td>
<td>L</td>
<td>382 (155)</td>
<td>-2% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>400 (110)</td>
<td>-7% NS</td>
</tr>
<tr>
<td>Ca</td>
<td>L</td>
<td>4.5 (2.3)</td>
<td>-1% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>4.6 (2.2)</td>
<td>+16% NS</td>
</tr>
<tr>
<td>Mg</td>
<td>L</td>
<td>34 (14)</td>
<td>-4% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>40 (8)</td>
<td>-13% NS</td>
</tr>
<tr>
<td>Ca/Mg ratio</td>
<td>L</td>
<td>0.14 (0.06)</td>
<td>0% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.16 (0.04)</td>
<td>+13% NS</td>
</tr>
<tr>
<td>Na/K ratio</td>
<td>L</td>
<td>0.43 (0.19)</td>
<td>-2% NS</td>
</tr>
<tr>
<td></td>
<td>B</td>
<td>0.42 (0.18)</td>
<td>+17% NS</td>
</tr>
</tbody>
</table>

DISCUSSION

The present study showed that the Ca/Mg ratio in skeletal muscle is associated with blood pressure regulation, as a relative increase in the magnesium content in skeletal muscle, compared with the calcium content, was associated with a fairly pronounced decrease in blood pressure during treatment. Furthermore, the Ca/Mg ratio in skeletal muscle was found to be a predictor for the blood pressure response to antihypertensive treatment.

In previous studies, Lindner et al noted a correlation between the calcium concentration in erythrocytes and blood pressure, and observed a reduced calcium concentration in erythrocytes from patients in whom the blood pressure was reduced during treatment with antihypertensive drugs such as lisinopril.
blocking of calcium entry into cells. Thus, assum-
ing that parallel mineral changes occur in skeletal and
vascular smooth muscle, a reduced Ca/Mg ratio
exerted by both in skeletal and in vascular smooth muscle.
Calcium is a primary regulator of contrac-
tion that is emphasized by the work of Dyckner and Wester,
and magnesium balance in skeletal muscle and the
association between the changes in calcium and mag-
nesium concentrations in skeletal muscle and the anti-
hypertensive response to lisinopril was more pro-
nounced than that for the thiazide is not known, but
the ability of diuretic therapy to concommitantly
help to explain the poor correlation between changes
in blood pressure with changes in Ca/Mg ratios. This
speculates that parallel mineral changes occur in skeletal and
and further lowered blood pressure. It has previously been found that an adequate intra-
cellular magnesium concentration is necessary for the
intracellular potassium balance, as the Na⁺-K⁺-
pump transporting potassium into the intracellular
space is conducted by magnesium-dependent phos-
phorylation, and as magnesium inhibits the K⁺ ef-
flux via potassium channels. The close relation-
ship observed in the present study confirms these
observations.

In summary, an association between the calcium and
magnesium balance in skeletal muscle and the
blood pressure response to antihypertensive treatment
was found in the present study, suggesting that ion balance is involved in blood pressure regulation.

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