ALDOSTERONE RESPONSE TO MODULATION
OF POTASSIUM IN PATIENTS ON DIALYSIS
OR WITH ESSENTIAL HYPERTENSION

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Summary

This investigation demonstrates in patients with essential hypertension an
abnormal response of the adrenal glands to modulation of potassium metabolism
by infusion of insulin-glucose. Similar results have been reported in anephric
patients, while the inverse response of non-nephrectomised patients on dialysis
corresponded to that of normal subjects. It is suggested that the abnormal
response of patients with essential hypertension may be of importance to the
understanding of the pathogenesis of this important disease.

Introduction

The pathogenesis of essential hypertension (EH) remains unknown, although an
altered adrenal responsiveness to angiotensin II has been suggested [1]. Previ-
ously we have found that the aldosterone response to modulation of potassium
metabolism is significantly different in anephric and non-nephrectomised patients
on haemodialysis [2] as shown in Figure 1.

The present investigation, therefore, examines the adrenal response to potas-
sium modulation in a group of patients with essential hypertension, all with
low plasma renin activity as found in anephric patients. For comparison a group
of control subjects has been studied.

Methods

All investigations were carried out with the patient in the supine position. After
one hour of resting, basal renin activity, aldosterone, cortisol, potassium, sodium,
glucose, and blood pressure were measured three times at five minute intervals.
Then 100ml of 50 per cent glucose, with 16IU of crystalline insulin added, was
given intravenously within five minutes. Blood samples were then drawn every
30 minutes for the next three hours. The patients were allowed to drink moder-
ately during the tests and extra IV glucose was given at the slightest symptom of
insulin hypoglycaemia.
Figure 1. Mean ± SE values of plasma aldosterone and plasma potassium in six non-nephrectomised and seven anephric chronic dialysis patients after infusion of insulin-glucose. In all patients a transient decline of the plasma potassium concentration was found. However, the plasma aldosterone concentration declined transiently in the non-nephrectomised patients, while a temporary rise was seen in the anephric patients.

The investigations were repeated after 14 days of treatment with bendroflumethiazide 5mg twice daily.

Plasma renin activity was measured by RIA [3]. Control values in normal subjects were 0.4 to 0.9ng/ml/hr. Plasma aldosterone was measured by a modification of a specific RIA method [4], control values 22–223pg/ml. Potassium and sodium were determined by flame photometry. Cortisol was measured by a competitive protein binding method [5].
Data of patients with essential hypertension and of control subjects are presented in Table 1. None received any medication before the investigation. Secondary hypertension was excluded.

**TABLE 1. Basal data before insulin-glucose**

<table>
<thead>
<tr>
<th>Subjects</th>
<th>No.</th>
<th>Age (yrs)</th>
<th>Thiazides</th>
<th>BP</th>
<th>Cr (mmol/L)</th>
<th>K (mmol/L)</th>
<th>Plasma Renin (ng/ml/hr)</th>
<th>Aldosterone (pg/ml)</th>
<th>Cortisol (µg/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>7</td>
<td>24</td>
<td>-</td>
<td>116/77</td>
<td>3.6</td>
<td>0.4</td>
<td>39</td>
<td>15.0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td></td>
<td>+</td>
<td>120/75</td>
<td>3.3</td>
<td>2.5</td>
<td>114</td>
<td>16.5</td>
<td></td>
</tr>
<tr>
<td>Essential hypertension</td>
<td>8</td>
<td>36.5</td>
<td>-</td>
<td>175/121</td>
<td>3.7</td>
<td>0.3</td>
<td>90</td>
<td>14.7</td>
<td></td>
</tr>
<tr>
<td></td>
<td>7</td>
<td></td>
<td>+</td>
<td>147/111</td>
<td>3.3</td>
<td>1.7</td>
<td>125</td>
<td>16.6</td>
<td></td>
</tr>
</tbody>
</table>

Mean values

**Results**

The plasma potassium concentration in patients with EH showed a transient decline during insulin-glucose infusion of the same magnitude as that of patients on dialysis. No difference was demonstrated between the response of EH-patients and control subjects.

The plasma aldosterone concentrations of the control subjects declined transiently as seen in non-nephrectomised patients on dialysis, while a temporary increase was found in the EH-patients, as previously seen in anephric dialysis patients. Figure 2 demonstrates the mean percentage changes (±SE) of the plasma aldosterone concentration in the control and EH-groups. The different responses were further magnified after treatment by thiazide.

The plasma cortisol concentrations in response to insulin-glucose followed the same pattern as that of aldosterone, although the response was not influenced by treatment by thiazide. Figure 3 demonstrates the mean percentage changes (±SE) of the plasma cortisol concentration in the control and EH-groups.

No significant changes were found in the plasma renin activity or in the plasma sodium concentrations.

**Conclusions**

1. A transitory decrease of the plasma potassium concentration without a change of the total body potassium content was induced by an intravenous
infusion of insulin-glucose. The decrease of plasma potassium was of the same magnitude in patients with essential hypertension and subjects with normal blood pressure. It seems most likely that the decrease of plasma potassium was secondary to a displacement of potassium from the extra- to the intracellular space.

Figure 2. Percentage changes (mean ±SE) of plasma aldosterone after insulin-glucose in the control group and in the group with essential hypertension, before and after treatment with thiazide for two weeks. A significant increase of plasma aldosterone (p<0.001) was found in the group with essential hypertension compared to the control group. This difference was further magnified by treatment with thiazide.

Figure 3. Percentage changes (mean ±SE) of plasma cortisol after insulin-glucose in the control group and in the group with essential hypertension before and after treatment with thiazide for two weeks. A significant increase of plasma cortisol (p<0.01) was found in the group with essential hypertension compared to the control group. No influence was found of treatment with thiazide on the cortisol response.
2. In untreated patients with essential hypertension a significant increase of the plasma aldosterone concentration was found in response to insulin-glucose. In contrast, a significant decrease of plasma aldosterone was found in a corresponding group of control subjects with normal blood pressure. The different response between the two groups was even greater after sodium depletion.

3. Similarly, the response of the plasma cortisol concentration was significantly increased after insulin-glucose in patients with essential hypertension, but not in control subjects with normal blood pressure. No effect of sodium depletion was found on the plasma cortisol response.

4. The effect of insulin-glucose on aldosterone and cortisol was probably not mediated via changes in plasma renin activity.

5. Thus, the present investigation has demonstrated an abnormal response of the adrenal gland to modulation of potassium by insulin-glucose in patients with essential hypertension. It is suggested that this may be a factor of pathogenetic importance.

Acknowledgement

This work was supported by the Danish Medical Research Council.

References

1 Williams GH, Hollenberg NK, Moore TS et al. J Clin Invest 1979; 63: 419
3 Olggaard K, Ladedoged J. Ugeskr Laeg 1977; 139: 1590
5 Olggaard K, Madsen S. Clin Biochem 1976; 9: 265

Open Discussion

TOURKANTONIS (Thessaloniki) I would like to ask you what was the plasma renin activity in patients with essential hypertension? May be that in such a group of patients with various values of plasma renin activity (low, normal or high) the response of aldosterone and cortisol to insulin infusion is different.

OLGAARD These are all low in essential hypertension patients and the renin value in the resting stage, not sodium depleted, was a mean value of 0.3ng/ml/hr.

COLUMSIGHT (Milan) Did you check the blood glucose in your patients? Can you exclude that hypoglycaemia could have induced an increase in ACTH function?

OLGAARD Yes, I don’t know the mechanism of this. I don’t know if this is going to take place via modulation of potassium or changes in the phosphate concentration. The blood glucose was the same in the two groups at 4.8mmol/L and this increased to a maximum value of 6.5mmol/L, while the lowest value was about 3.3mmol/L. I don’t think there has been any stimulation by hypoglycaemia.