nin activity before and after preclinical resuscitation performed on-site and on admission to the intensive care unit. As serum, and not plasma, was used, the correlation between renin activity in serum and plasma had to be assessed beforehand.

20 ml blood were collected from 50 non-selected patients in a general medical ward. 10 ml were used for EDTA plasma and 10 ml for serum. Both were stored at -20 °C within 1 h after sampling. 1 ml portions of serum and plasma were taken for lyophilization before freezing. In 37 patients with out-of-hospital cardiac arrest blood was taken from a central venous catheter before resuscitation was started on-site. A second blood sample was taken on admission to the intensive care unit (end of the preclinical phase) or at cessation of unsuccessful resuscitation attempts. Plasma and serum renin activity were determined with a commercial kit (Renin-RIA bead, Abbott Diagnostics).

In the control group (n = 50) a positive correlation between plasma (x) and serum (y) values was found, the data for the regression line y = a + bx being: r = 0.99, aₓ = -0.19, bₓ = 0.85, aᵧ = 0.39, bᵧ = 1.14.

During lyophilization of plasma and serum samples, an identical loss by 10.9% on average was seen. The median serum renin activity in these patients was 4.75 µg/l/h.

In successfully resuscitated patients (n = 15) there was a significant rise in the median serum renin activity from 8.9 µg/l/h on-site to 15.0 µg/l/h on delivery (p < 0.001).

In contrast, the median serum renin activity in patients with fatal outcome (n = 22) failed to increase during resuscitation attempts (4.2 vs. 3.6 µg/l/h; n.s.).

Conclusions: 1. Serum plasma and serum renin activity correlate closely, determination in serum being of greater practicability in emergency or restricted situations. Lyophilized samples are suitable for external quality control assessment schemes. 2. The rise in serum renin activity after successful resuscitation is part of the early endocrine response to injury and may serve as a prognostic parameter.

211. Potassium-canrenoate possesses less antiandrogenic effects than spironolactone.

Demonstration in patients treated for essential hypertension


Potassium canrenoate (KC) is a water-soluble derivative of spironolactone (SP). Long-term treatment with KC seems to cause less antiandrogenic effects than SP. We have recently established a sensitive method for measuring substances in plasma which act on kidney androgen receptors (AR). By this method we have demonstrated that the androgen receptor active materials (ARM) in the plasma of castrated mice treated with SP are 10-fold higher than in mice treated with KC. In a parallel in vivo bioassay we have found that the antiandrogenic activity of SP is 5-fold higher than KC [1]. The aim of the present study was to evaluate ARM in the plasma of patients with essential hypertension.

Patients and methods: 15 adult male patients (age 50 ± 8 years, mean ± SD) were the object of the study. The diagnosis of essential hypertension was made by conventional biochemical, hormonal, radiological and isotopical examinations. The patients were treated for 3 months with KC (98 ± 12 mg/day) and blood for the assay of ARM and plasma testosterone was taken 12 hours after the last administration of the drug. The method for measuring ARM has been previously described [1]. Briefly, kidney cytosol from castrated mice was incubated with a tracer amount of 3H-RU1881, a synthetic androgen having no affinity for plasma proteins. Incubations were performed for 2 hours at 4 °C with stripped plasma, with increasing concentrations of cold RU1881 in stripped human plasma and with the plasma of each patient. Separation of receptor-bound tracer was effected by the charcoal dextran method. The results are expressed as nM Eq of RU-1881 on the standard curve. No triamcinolone was added for preventing binding of the tracer to progesterone receptors because the affinity and the capacity of AR did not change with or without the addition of this steroid.

The results are shown in Table 1 as mean ± SD of the single values.
Table 1

<table>
<thead>
<tr>
<th></th>
<th>Blood pressure mm Hg</th>
<th>s. K⁺ mEq/l</th>
<th>ARM nM Eq</th>
<th>Pl. testos. nM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before KC</td>
<td>165 ± 21/105 ± 4</td>
<td>4.0 ± 0.5</td>
<td>2.4 ± 0.6</td>
<td>20.6 ± 5.8</td>
</tr>
<tr>
<td>After KC</td>
<td>124 ± 4/ 93 ± 5</td>
<td>4.5 ± 0.3</td>
<td>2.1 ± 0.6</td>
<td>19.8 ± 6.8</td>
</tr>
<tr>
<td>Normal range</td>
<td>4–5</td>
<td>1.6–3.4</td>
<td>10–20</td>
<td></td>
</tr>
</tbody>
</table>

Antiandrogenic side-effects did not occur in any case.

Conclusions: The results demonstrate that KC is a drug capable of regulating blood pressure in essential hypertension without causing the antiandrogenic effects frequently seen under SP treatment. Side-effects may appear in patients with compromised liver function but to a lower extent than after SP, as demonstrated in liver cirrhosis [2]. The different amount of ARM after KC and SP is probably due to a minor metabolite of SP which possesses a high affinity for androgen receptors and/or has a long half-life in vivo. Since the values of ARM and testosterone did not change before and after therapy we conclude that all KC metabolites are eliminated 12 hours after administration.

References

212. Parathyroid hormone secretory function and serum levels of carboxyl-terminal flanking peptide (PDN-21) of the human calcitonin gene in normal subjects and osteoporotic patients

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Parathyroid hormone secretory responses were investigated in osteoporotic patients (56 ± 5 yr; mean ± SEM; 2 men and 6 women, aged 37–74 yr) and compared to 7 age-matched normal subjects (56 ± 5 yr; 2 men and 5 women, aged 38–73 yr) at 15, 45, 120, 180 and 480 min after peroral phosphate (48 mmol) administration. Serum phosphate was increased in osteoporotic and normal subjects (ΔPO₄ at 120 min 0.46 ± 0.07 mM, p < 0.001, and 0.54 ± 0.05 mM, p < 0.001, respectively).

As a consequence serum ionized calcium was similarly decreased (ΔCa⁺⁺ at 15 min 0.06 ± 0.02 mM, p < 0.02, and 0.05 ± 0.01 mM, p < 0.05, respectively; and at 120 min 0.05 ± 0.02 mM, p < 0.02, and 0.06 ± 0.01 mM, p < 0.001, respectively). Serum total calcium did not change consistently in normal subjects or osteoporotic patients (basal: 2.23 ± 0.03 mM, at 15 min 2.21 ± 0.03 mM, p > 0.1; at 120 min 2.18 ± 0.03 mM, p < 0.05; at 15 min 2.25 ± 0.03 mM, p > 0.1, at 120 min 2.20 ± 0.05 mM, p < 0.05, respectively).

Serum levels of immunoreactive PTH (N-RIA recognizing predominantly intact PTH on gel permeation chromatography) were increased in normal subjects within 15 min from 156 ± 25 pg/ml to 260 ± 37 pg/ml (p < 0.05) and remained elevated after 120 min (215 ± 42 pg/ml) (p < 0.05). In osteoporotic patients PTH remained largely unaltered (basal: 104 ± 26 pg/ml, at 15 min 127 ± 33 pg/ml, at 120 min 146 ± 31 pg/ml (p > 0.1). Moreover, a statistically significant rise of urinary cyclic AMP occurred in normal subjects after 4 h from 2.9 ± 0.8 to 8.1 ± 0.7 nmol/100 GF (p < 0.05), but not in osteoporotic patients (basal: 2.4 ± 0.3, after 4 h 2.8 ± 0.6 nmol/100 GF (p > 0.1).

Analysis of variance revealed a significant difference of PTH response at 15 to 480 min after phosphate loading (p < 0.01) and urinary cAMP excretion from time "0" to 4 hours (p < 0.01) between normal and osteoporotic subjects.