136. Effects of etomidate on adrenocortical function


Sedation with etomidate in intensive-care patients has been associated with increased mortality [1]. Moreover, the British Committee on Safety of Medicines has issued a warning that etomidate may impair adrenal function [2]. We observed severe adrenal insufficiency in a patient with tetanus receiving long-term etomidate therapy for sedation [3]. This study was designed to assess the effect of a routinely employed induction dose of etomidate on cortisol secretion.

16 patients (14 males, 2 females) scheduled for minor surgery and without evidence of adrenal disease were randomly allocated to either etomidate (0.3 mg/kg) or thiopentone (5 mg/kg). Anaesthesia was induced with intravenous fentanyl (0.1 mg) and the assigned drug. In all patients surgery was completed within two hours. Blood samples for cortisol, testosterone and ACTH were taken at zero time and in frequent intervals for 5 hrs after induction. Steroid hormones were measured by RIA using commercially available reagents. Plasma ACTH was determined by RIA after extraction with QUSO G 32.

In both groups a striking fall of serum cortisol was observed within 30 min after induction (see table). However, depression of serum cortisol was more pronounced and lasted longer in the etomidate group compared to controls (p < 0.02). Recovery from adrenal suppression after etomidate became evident after 4 hours. Plasma ACTH tended to be higher in the etomidate group (130±49 vs. 45 ± 33 pg/ml at 240 min) indicating a direct action of etomidate at the adrenal cortex. Serum testosterone showed no significant change after etomidate.

Conclusions: A single bolus of etomidate leads to a significant reversible suppression of serum cortisol by acting directly at the adrenal cortex. As serum testosterone is not influenced, the effect of etomidate is probably limited to adrenocortical steroid synthesis.

Table: Serum cortisol after induction of anaesthesia with thiopentone (TH) or etomidate (ET)

<table>
<thead>
<tr>
<th></th>
<th>0'</th>
<th>30'</th>
<th>60'</th>
<th>90'</th>
<th>120'</th>
<th>150'</th>
<th>180'</th>
<th>210'</th>
<th>240'</th>
<th>300'</th>
</tr>
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<td>10.8</td>
<td>12.7</td>
<td>13.9</td>
<td>12.9</td>
<td>13.1</td>
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<td>18.0</td>
</tr>
<tr>
<td></td>
<td>±SEM</td>
<td>2.4</td>
<td>1.2</td>
<td>4.8</td>
<td>3.6</td>
<td>4.4</td>
<td>5.0</td>
<td>5.3</td>
<td>5.3</td>
<td>5.2</td>
</tr>
<tr>
<td>ET</td>
<td>15.2</td>
<td>9.2</td>
<td>6.4</td>
<td>6.4</td>
<td>6.4</td>
<td>5.9</td>
<td>7.9</td>
<td>8.1</td>
<td>9.8</td>
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</tr>
<tr>
<td></td>
<td>±SEM</td>
<td>3.8</td>
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<td>1.2</td>
<td>1.2</td>
<td>1.5</td>
<td>1.6</td>
</tr>
</tbody>
</table>

References

2. Editorial: Lancet II (1983), 24

Supported by Landesamt für Forschung, Nordrhein-Westfalen.

137. The influence of ketoconazole on serum levels of cortisol, 11-deoxycortisol, corticosterone and 11-deoxycorticosterone in normals and in patients with Cushing's syndrome

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Ketoconazole (K), an antifungal agent, has a blunting effect on the serum cortisol (F) response to adrenocorticotropic hormone (ACTH) in healthy men after a single oral dose [1]. Furthermore it could be shown that repeated oral doses of K induced a reproducible clear-cut fall of serum cortisol levels below 2.5 µg/dl in a patient with Cushing's syndrome due to adrenal adenoma. The inhibitory