POST-OPERATIVE SERUM CORTISOL LEVELS AS PREDICTORS OF RECURRENTENCE IN CUSHING’S DISEASE

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Introduction
Cushing’s disease (CD) is characterized by increased secretion of ACTH generally as a result of a pituitary adenoma. The surgical success rates after transsphenoidal pituitary surgery (TSS) range from 53-96% in different centres. Postoperative cortisol levels have been proposed as the standard criteria for prediction of surgical remission.

Objectives
Evaluate the potential of post-transsphenoidal pituitary surgery cortisol levels to predict surgical remission or recurrence of CD.

Material and methods
Retrospective cohort study of patients with clinical and biochemical diagnosis of CD, submitted to TSS and followed in our centre, from 1977 to 2013 (n=84). Patients who lost follow-up or with insufficient data (n=52), were excluded.

Remission criteria:
- absence of clinical and laboratory signs of hypercortisolism;
- normal urinary free cortisol (UFC);
- cortisol levels < 1.8 µg/dL at 8.00 am after 1mg overnight dexamethasone suppression test.

Recurrence criteria:
- absence of clinical and/or analytical signs of hypercortisolism at least 1 year after TSS
- Statistical analysis: IBM SPSS 21.0 software.
- Statistical significance: *p < 0.05

Results (I)

Baseline data

| Patients included: 33 | Median age: 33 years (range 14-70) |

87.9% Women
12.1% Men

Types of lesion (Imagiology):
- 18 patients (54.6%) - Microadenoma
- 6 patients (18.2%) - Macroadenoma
- 3 patients (9.0%) - Invasive macroadenoma
- 6 patient (18.2%) - No adenoma visible on MRI/CT-SCAN

Surgical approach
- 31 patients (93.9%) – Transsphenoidal approach
- 2 patients (6.1%) – Transfrontal approach

Outcome after surgery
- 19 patients (57.6%) – Remission
- 11 patients (33.3%) – Recurrence
- 3 patients (9.1%) – Persistence

Results (II)

Serum cortisol and UFC – Pre-operative and post-operative assessment

<table>
<thead>
<tr>
<th>Analyte</th>
<th>Pre-operative assessment</th>
<th>Post-operative assessment</th>
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<tbody>
<tr>
<td>UFC (µg/dL)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>186.50</td>
<td>0.955</td>
<td>240.00</td>
</tr>
<tr>
<td>Cortisol 0 am (µg/dL)</td>
<td>14.00</td>
<td>0.478</td>
</tr>
</tbody>
</table>

Table 1. UFC and midnight cortisol before and after TSS

Serum cortisol evolution

<table>
<thead>
<tr>
<th>Cortisol measurement (µg/dL)</th>
<th>Remission</th>
<th>P Remission/Recurrence</th>
<th>Recurrence</th>
<th>Persistence</th>
<th>P Remission/Recurrence and Persistence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol 9 am (µg/dL)</td>
<td>9.47</td>
<td>0.047</td>
<td>10.92</td>
<td>16.05</td>
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</tr>
<tr>
<td>Cortisol 0 am (µg/dL)</td>
<td>4.66</td>
<td>0.008</td>
<td>9.24</td>
<td>14.50</td>
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<tr>
<td>Cortisol 9 am (µg/dL)</td>
<td>2.58</td>
<td>0.011</td>
<td>7.76</td>
<td>8.57</td>
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Table 2. Cortisol levels: one week (A) and 2 months after TSS (B).

Conclusions

1) This study states that treatment of Cushing’s disease is difficult.

2) 57.6% of the patients of this cohort achieved remission after TSS.

3) Serum cortisol levels at 0:00am in the post-operative period were significantly different in patients with remission compared with the other groups.

4) The usefulness of midnight cortisol levels after TSS was demonstrated.

5) Lower accuracy in predicting remission with morning serum cortisol values at one week evaluation after TSS.

6) The disease free period had a strong inverse correlation with morning cortisol levels.

Bibliography