Salivary Cortisone is Reduced in Addison’s disease Receiving Hydrocortisone Replacement, but Salivary Cortisol Day Curves do Not Differ from Controls

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Introduction

Immediate release conventional hydrocortisone and cortisone acetate are the most commonly used replacement therapies in Addison’s disease.

The cortisol concentration profile and overall quality of conventional hydrocortisone replacement has been examined using urine and serum cortisol, plasma ACTH and salivary cortisol, but all measurements have limitations.

Salivary cortisol measured in spot samples taken at various times after the administration of hydrocortisone has been shown to correlate with simultaneously measured serum cortisol in patients with Addison’s disease.

We previously reported that salivary cortisol concentrations measured by electric chemiluminescence immunoassay in Addison’s patients on hydrocortisone replacement were greater than endogenous cortisol concentrations in healthy subjects.

Salivary cortisol may be a more accurate measure of serum free cortisol than salivary cortisol, since it is less affected by cortisol binding globulin.

Liquid chromatography tandem mass spectrometry makes it possible to accurately identify and quantify cortisol and other steroids.

Methods

To explore the utility of LC-MS/MS in measuring salivary cortisol and cortisone and determining the pharmacokinetic parameters for hydrocortisone and endogenous cortisol production in Addison’s disease and controls.

To explore the correlation of salivary cortisol and cortisone dose in Addison’s patients, hypothesising that salivary cortisol may reflect post dose exposure more accurately than salivary cortisol.

Discussion

Salivary cortisol was approximately 10-fold higher in controls than in patients

Salivary cortisol AUC in patients did not differ from controls

Salivary cortisol and cortisone concentrations in patients were highly variable

Total daily hydrocortisone dose adjusted for body weight or body surface area were highly correlated with the peak cortisol concentration, our data cannot be utilised to identify or quantify cortisol.

We propose that there is higher activity of salivary 11BHSD2 in healthy controls than in patients

Alternatively, the bidirectional pathway of 11BHSD2 may be down-regulated, whereas 11-beta-hydroxysteroid dehydrogenase type 1 (11BHSD1) may be up-regulated in patients

References


<table>
<thead>
<tr>
<th>Ethnicity</th>
<th>Gender</th>
<th>N (%)</th>
<th>Age (IQR) years</th>
<th>Total daily dose of hydrocortisone adjusted for body weight (IQR) mg</th>
<th>Total daily dose of fludrocorRsone (IQR) mg/kg</th>
<th>Total fludrocorRsone dose adjusted for body weight (IQR) µg/kg</th>
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<tbody>
<tr>
<td>White</td>
<td>Female</td>
<td>10 (38)</td>
<td>21 (20-22)</td>
<td>8.96 (6.96-12.23)</td>
<td>23.65 (6.10-54.76)</td>
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<td>5 (20)</td>
<td>48 (38-63)</td>
<td>32.61 (6.75-146.19)</td>
<td>11.11 (2.91-35.85)</td>
<td>55.63 (15.75-35.85)</td>
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<tr>
<td>Black</td>
<td>Female</td>
<td>5 (19)</td>
<td>21 (20-22)</td>
<td>33.12 (25.97-39.95)</td>
<td>3.00 (1.88-5.60)</td>
<td>213.33 (127.51-314.13)</td>
</tr>
</tbody>
</table>

Note: Data presented as median (IQR).