**INTRODUCTION**

Short Synacthen tests (SST) are used widely for the diagnosis of adrenal insufficiency (AI) in children. LDSST are more sensitive but less specific than the SDSST. Concerns regarding accuracy of dosing and reproducibility of the LDSST have been raised, leading to concerns of over diagnosis and treatment.

**AIM**

To report:
1. Prevalence of AI, defined as suboptimal or abnormal responses to the LDSST, according to indication for testing
2. Effect of age and gender on baseline and peak cortisol measurement

**METHOD**

Retrospective study of children tested between 2008-2020

Test protocol:
500ng/1.73m² Synacthen as IV bolus. Sampling at 0, 15, 25 and 35 minutes

Only the first LDSST were analysed if child tested more than once

Serum cortisol measured using Siemens Immulite 2000XPi immunoassay system.

Classification of test results:
- Peak cortisol ≥ 450nmol/L
- Suboptimal: Peak cortisol 350-449 nmol/L
- Hydrocortisone during stress periods only (IH)
- Baseline cortisol <100nmol/L
- Prescribed daily hydrocortisone

**RESULTS**

**Table 1:** Age and sex of children undergoing the LDSST by diagnostic category.

<table>
<thead>
<tr>
<th>Indication for test (N)</th>
<th>Percentage of all tests</th>
<th>Age (years)</th>
<th>Male, N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients (481)</td>
<td>-</td>
<td>9.5 ± 5.2</td>
<td>295 (61)</td>
</tr>
<tr>
<td>Inhaled steroids (ICS) (106)</td>
<td>22</td>
<td>10.5 ± 3.6</td>
<td>66 (62)</td>
</tr>
<tr>
<td>Iatrogenic not ICS (40)</td>
<td>8</td>
<td>9.7 ± 5.8</td>
<td>20 (50)</td>
</tr>
<tr>
<td>Structural brain abnormality (136)</td>
<td>28</td>
<td>9.4 ± 1.0</td>
<td>77 (57)</td>
</tr>
<tr>
<td>Poor cortisol response to GH stimulation test (29)</td>
<td>6</td>
<td>8.2 ± 4.5</td>
<td>19 (66)</td>
</tr>
<tr>
<td>GHD* (27)</td>
<td>6</td>
<td>10.6 ± 3.5</td>
<td>21 (78)</td>
</tr>
<tr>
<td>Infants (35)</td>
<td>7</td>
<td>0.3 ± 0.3</td>
<td>24 (69)</td>
</tr>
<tr>
<td>Fatigue (37)</td>
<td>8</td>
<td>11.7 ± 4.5</td>
<td>19 (51)</td>
</tr>
<tr>
<td>Autoimmune (13)</td>
<td>3</td>
<td>15.1 ± 1.9</td>
<td>6 (46)</td>
</tr>
<tr>
<td>Miscellaneous (58)</td>
<td>12</td>
<td>9.5 ± 5.4</td>
<td>43 (74)</td>
</tr>
</tbody>
</table>

*GHD: Growth hormone deficiency confirmed on stimulation testing

**Baseline cortisol**
- **Age:** Cortisol increased by 2.7% (95% CI: 1.8%, 3.7%) / 1 year increase in age
- **Sex:** Cortisol measurements 11.5% higher in girls than boys (p = 0.030, 95% CI: 1.1%, 23.1%) after adjusting for diagnostic group and age
- Cortisol concentrations were highest in patients with isolated GHD and autoimmune disease and lowest in those with structural brain abnormalities (F-test p = 0.006)

Differences between diagnostic groups persisted after adjusting for age and gender

**Peak cortisol**
- **Age:** No relationship between age and peak cortisol
- **Sex:** Cortisol 60nmol/L (95% CI: 31.4, 88.6, p<0.001) higher in girls than in boys after adjusting for diagnostic group and age

Cortisol concentrations were lowest in children treated with pharmacological doses of steroids, structural brain abnormalities and infants (F-test p<0.0001), who were most likely to be prescribed hydrocortisone

Differences between diagnostic groups persisted after adjusting for age, gender and using baseline cortisol as a predictor

**CONCLUSIONS**

The relatively small number of children treated with daily hydrocortisone and the clustering of children with an abnormal result in diagnostic groups we consider to be at greatest risk of AI, suggest that overdiagnosis and treatment of AI is unlikely to be very common.

While a statistically significant effect of age and sex was seen on baseline cortisol, and an effect of sex on peak cortisol, these differences are modest and we suggest do not justify the complexity of introducing age and sex related reference ranges.

**REFERENCES**

1. Courtney, M, Allister et al. 2004
2. Nye, Grice et al. 2001
3. Kazlauskaite, Evans et al. 2020
5. Tan, Manfredonia et al. 2018

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