A prospective study of children 0-8 years with congenital adrenal hyperplasia and adrenal insufficiency on treatment with hydrocortisone granules monitored by 17-OHP saliva sampling

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INTRODUCTION

Children with congenital adrenal hyperplasia (CAH) and adrenal insufficiency (AI) require hydrocortisone replacement from birth, and continuous monitoring of therapy during growth is necessary. A licensed paediatric formulation that allows accurate dosing down to 0.5mg is now available.

AIM

To investigate safety and efficacy of hydrocortisone (HC) granules in capsules for opening in 0-8 year old children with CAH and AI monitored through 17-OHP saliva profiles.

METHOD

- 17 children with classic CAH (9 male)
- 1 child with hypopituitarism (male)

Age at study entry:
- cohort 1 (2-6 years): n=9
- cohort 2 (1 month-2 years): n=6
- cohort 3 (<28 days): n=3

Study visits included:
- physical examination, measurement of weight, length, blood pressure.
- Monitoring of HC-therapy
- daily 17-OHP-saliva profile every three months.
- HC doses were adapted according to the predose 17-OHP salivary profiles. If the value for 17-OHP was out of range, the dose 8 hours before that sample time point was adjusted.

RESULTS

Children were treated with HC granules three times daily every eight hours. Median duration of treatment (range) was 795 (1-872) days with 150 follow-up visits. Six children withdrew early. Hydrocortisone dose was adjusted at 40/150 visits (in 32 based on 17-OHP saliva profiles and 8 based on blood sampling).

Hydrocortisone doses used at different time points varied from 0.5mg to 10mg. Height and weight showed no trends for accelerated or reduced growth. No adrenal crisis was observed despite 193 treatment-emergent adverse events, which were mainly common childhood illnesses.

Average dose and dose distribution of hydrocortisone (morning – afternoon – nighttime dose) across visits according to the age of the children:

<table>
<thead>
<tr>
<th>Average dose distribution</th>
<th>Mean HC-dose</th>
<th>Proportion of administrations containing 0.5 mg granule dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Children aged 0-3 months</td>
<td>33.3 ± 33.3</td>
<td>1.5 – 1.5 – 1.5 mg</td>
</tr>
<tr>
<td>Children aged 4 months – 2 years</td>
<td>46 – 22 – 32</td>
<td>2.3 – 1.1 – 1.6 mg</td>
</tr>
<tr>
<td>Children aged 2-4 years</td>
<td>40.6 – 18.3 – 40.6</td>
<td>2.8 – 1.2 – 2.6 mg</td>
</tr>
<tr>
<td>Children aged 4-8 years</td>
<td>36 – 14 – 50%</td>
<td>3.2 – 1.3 – 4.6 mg</td>
</tr>
</tbody>
</table>

* half of the patients were treated with a hydrocortisone dose of 2-2 mg and half of the patients with 1-1 mg resulting in a mean dose of 1.5-1.5 mg dose.

CONCLUSIONS

This first prospective study of glucocorticoid treatment in children with AI demonstrates that an individualised therapy consisting of a 3-monthly 17-OHP saliva profile and an accurate dosing from birth with hydrocortisone granules in capsules for opening results in hydrocortisone doses at the lower end of the recommended dose range and normal growth without occurrence of an adrenal crisis.

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REFERENCES


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