Neonatal screening program for Central Congenital Hypothyroidism


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Background

Congenital hypothyroidism (CH) is a heterogeneous entity that includes hypothyalamo-hypophyseal system disorders: Combined pituitary hormone deficiency (CPHD), TRH-R defects, β-TSH deficiency and IGF1 mutations. Newborns with CH of central origin (CH-C) are missed on TSH based screening programs. Additional T4 determination might help to early detect CH-C leading to reduce morbidity and mortality from CPHD which represents ~ 75% of all CH-C.

Aim

To conduct a neonatal screening based on TSH and T4 determinations for early detection of CH-C.

Population & Methods

37045 term newborns aged 2-7 days were screened. From June 2014 to June 2015 TSH (IFMA Delfia); cutoff 10 mU/L & T4 (FIA Delfia); cutoff 4.5 ug/dl (-2.3 SDS) measured in filter paper blood samples positive for CH-C

Clinical Assessment

Biochemical Assessment

Brain & Thyroid US

- Serum TSH, T4, FT4, T3, Thyroglobulin, Antithyroid-ab
- TSH (in patients likely to have hypoTBGemia)
- Cortisol, GH, prolactin, LH/FSH, Testosterone (boys)
- Glycemia, electrolytes

Results

<table>
<thead>
<tr>
<th>TSH &gt;10 mU/L</th>
<th>Low-normal T4</th>
<th>Primary hypothyroidism (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TSH ≤10 mU/L</td>
<td>Normal T4</td>
<td>Central hypothyroidism (n=24)</td>
</tr>
</tbody>
</table>

**Permanent CH-C (n=3)**

**Prevalence 1:12348**

**HypoTBGemia (n=5)**

**Transient hypothyroidism (n=16)**

**Non thyroidal illness (15)**

**In patients (13):**

- Respiratory distress, sepsis

**Urinary tract infection (1)**

**Healthy (1)**

**Isolated ACTH deficiency (1)**

**Combined Pituitary Hormone Deficiency**

<table>
<thead>
<tr>
<th>Gender</th>
<th>Case I</th>
<th>Case II</th>
<th>Case III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Boy</td>
<td>ACTH, TSH, ADH</td>
<td>ACTH, TSH</td>
<td>GH, TSH, PRL</td>
</tr>
<tr>
<td>Girl</td>
<td></td>
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</tbody>
</table>

**Hormone replacement**

- LHX4 +/+ HESX1 +/+
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- POU1F1 +/– R271W, de novo

**Conclusions**

T4 determination allows the identification of CH-C as a prevalent condition. Diagnosis of CH-C helps to early identify CPHD preventing major morbidity and mortality. This screening strategy requires experienced specialists to **confirm the diagnosis of CH-C** as well as to rule out transient low T4 disorders.

The elevated prevalence of CH-C highlights the importance of evaluating its cost-effectiveness in current neonatal screening programs.

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