Mutation of the TSH receptor gene: a longitudinal study in children with non-autoimmune subclinical hypothyroidism


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BACKGROUND
Neonatal screening strategies revealed an increase in hypothyroidism associated with an in-situ thyroid gland due to TSH receptor (TSHR) mutations.

OBJECTIVE AND HYPOTHESIS
Determine the impact of TSHR mutations on clinical course, biochemical parameters and therapeutic approach in children carrying this mutation.

Hypothesis: therapy may be unnecessary in partial TSH resistance due to a TSHR mutation.

METHODS
• We retrospectively evaluated diagnosis and re-evaluation parameters in 34 patients (pts) with non-autoimmune subclinical hypothyroidism and a diagnosed TSHR mutation.
• Ultrasound exam (US), Auxological parameters, DEXA, Bone age, Biochemical parameters (total cholesterol, HDL, triglycerides, AST, ALT, ALP, CPK) and Developmental Quotient (DQ) were compared between pts

RESULTS
Diagnosis of all TSHR mutation pts:
• 53% at screening, 23% for familial thyroid disease,
• 15% for signs/symptoms, 9% casually.
• Age range: 0 - 11 years
• Mean I spot: 8.4 ± 4 mU/L
• Mean TSH: 14.2 ± 13 mcU/ml (range 5.3 – 74.9)
• Mean FT4: 1.27 ± 0.2 ng/dl (range 0.27- 2.09)

Ultrasound:

<table>
<thead>
<tr>
<th>In treatment</th>
<th>Hypoplastic</th>
<th>Normal</th>
<th>Hyperplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>First US</td>
<td>27%</td>
<td>72%</td>
<td>0%</td>
</tr>
<tr>
<td>Last US</td>
<td>55%</td>
<td>44%</td>
<td>0%</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>NO treatment</th>
<th>Hypoplastic</th>
<th>Normal</th>
<th>Hyperplastic</th>
</tr>
</thead>
<tbody>
<tr>
<td>First US</td>
<td>15%</td>
<td>84%</td>
<td>0%</td>
</tr>
<tr>
<td>Last US</td>
<td>12%</td>
<td>75%</td>
<td>12%</td>
</tr>
</tbody>
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Therapy vs No Therapy:

| height sds, weight sds, BMI sds, target height sds, bone mineral density z-score, chronological age-bone age and biochemical parameters. | n.s. |
| height sds-target height sds | p < 0.05 |
| Mean DQ scores were within the average range in all pts | n.s. |

Re-evaluation: 15 pts underwent etiological re-evaluation
• 60% discontinued treatment (mean TSH 7.6 ±3.2 mcU/ml, mean FT4 1.16 ± 0.2 ng/dl)
• 40% resumed treatment (mean TSH 22.2 ±10.2 mcU/ml, mean FT4 1.0 ± 0.23 ng/dl)
• 4 pts: Compound heterozygote for a TSHR mutation
• 1 pt: SGA

CONCLUSIONS
In conclusion, our data indicates that children diagnosed with non-autoimmune subclinical hypothyroidism due to a TSHR mutation might not be in need of treatment unless they are compound heterozygous for the mutation or in case of selected cases of single heterozygous children born SGA

Disclosure Statement: Authors declare no conflict of interest related to this work.