The goal of congenital hypothyroidism (CH) treatment is rapid normalization and maintenance of TSH and FT4 in the reference range. Recommended starting dose of levothyroxine (LT4) ranges from 10-15 mcg/kg/d. Hyperthyroxinemia can be accepted in the context of normal TSH and LT4 should only be reduced in case of symptoms or repeatedly increased FT4.

OBJECTIVES

• Perform retrospective data analysis on FT4 kinetics during the first six months of treatment for each CH severity group

• Quantify duration, maximum peak fold above upper FT4 reference limit and daily maximum peak fold of hyperthyroxinemic periods based on pharmacokinetics model

METHODS

• Simulation of FT4 kinetics for individual patients based on our recently developed mathematical pharmacokinetics model [2]

• Retrospective longitudinal multi-center study during follow-up (first 180 days) with data from n ~ 56 infants (female 71%, GA 40.9 [36.8, 41.4] weeks)

• A total of 236 FT4 and 232 TSH measurements

• CH severity groups are defined based on FT4 level at diagnosis [1]:

<table>
<thead>
<tr>
<th>Severity Group</th>
<th>FT4 at diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severe CH</td>
<td>FT4 &lt; 5 pmol/l</td>
</tr>
<tr>
<td>Moderate CH</td>
<td>FT4 5-10 pmol/l</td>
</tr>
<tr>
<td>Mild CH</td>
<td>FT4 &gt; 10 pmol/l</td>
</tr>
</tbody>
</table>

THE RESULTS

• TSH levels at diagnosis were not significantly differing between moderate and severe CH.

• Severity groups had comparable numbers of consultations during follow-up.

COMPARISON OF LT4 STARTING AND MAINTENANCE DOSE

Figures 4 and 5 illustrate the starting and maintenance dose of LT4 for each severity group. The dose is displayed as a percentage of the initial dose, with LT4 starting dose normalized to the reference range. The results indicate that the LT4 starting dose is lower for severe CH, moderate CH, and mild CH patients.

REFERENCES


ACKNOWLEDGMENTS

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CONCLUSIONS

• Given available data, no significant difference in TSH at start of treatment and initial LT4 dosing for severe and moderate CH patients was found.

• Simulations revealed longer hyperthyroxinemic periods for moderate and mild CH patients compared to severe CH patients.

• From a pharmaceutical point of view, severity-based dosing during follow-up might help reducing duration and extent of hyperthyroxinemia.

• Prospective data are necessary to confirm these preliminary findings.