Does Initial Dosing of Levothyroxine in Infants with Congenital Hypothyroidism Lead to Frequent Dose Adjustments Secondary to Iatrogenic Hypothyroidism on Follow-up Laboratory Evaluation?

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Abstract

Background: Congenital hypothyroidism is the most common preventable cause of intellectual disability. The current guidelines recommend starting levothyroxine at or initial dose between 10 to 15 µg/kg on an empty stomach.

The dosage is influenced by the available thyroid extract (25 µg, 37.5 µg, 50 µg, 75 µg, 100 µg/mL), an empty stomach is administered twice daily for 5 days and then the patient is followed up.

HYPOTHESIS: We hypothesized that a sizable proportion of the newborns treated for congenital hypothyroidism at the higher end of the dosage range become biochemically hypothyroid at follow up visit, requiring a reduction of the dose.

Method

• Single-center retrospective chart review from January 1st, 2002 through December 31st, 2012
• Inclusion Criteria: Newly diagnosed CT identified by New York State screening program diagnosed in first month of life
• Exclusion Criteria: Down Syndrome
  Transient hypothyroidism (off levothyroxine by 3 years) Patients lost to follow up due to switching practices.bb
Primary outcome: % of patients requiring dose reduction

Results

• n = 104
• Male: female 60:44
• Mean age at diagnosis: 11 ± 6 days
• Mean TSH at diagnosis: 286 mIU/L
• Mean starting dose of levothyroxine: 12 ± 2.5 µg/kg
• Mean age at initial dose adjustment 49 ± 23 days
• Mean dose at TSH normalization: 11.3 ± 2.4 µg/kg

Comparison of Dosing Between Groups

<table>
<thead>
<tr>
<th>Category</th>
<th>No Dose Change</th>
<th>Dose Decrease</th>
<th>Dose Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td>CT</td>
<td>11.5</td>
<td>13.2</td>
<td>10.3</td>
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<tr>
<td>TSH</td>
<td>15.5</td>
<td>12.0</td>
<td>13.5</td>
</tr>
</tbody>
</table>

Clinical Practice Versus Laboratory Testing

• Among infants treated for CT, 36.5% required a dose reduction for iatrogenic hyperthyroxinemia.
• These infants received a higher dose of levothyroxine than the infants who either required no adjustment or required an increase in the dose.
• A narrower range for initial dosing in congenital hypothyroidism may be appropriate.
• Further prospective studies will be needed to determine this range.

Conclusion

• 38/104 of the patients were assessed to be hyperthyroid requiring a dose reduction. Of these, 29 were for a low/suppressed TSH and 9 for an elevated T4.
• 13/104 of the patients were assessed to be hypothyroid requiring a dose increase. Of these, 12 were for an elevated TSH (ranging from 8.59-82.65 uIU/mL) and 1 was for a low T4.
• Of these 12, 5 had a TSH of > 15 µuIU/mL; four of which were started on a low dose of ≤ 11.5 mcg/kg.
• 57.1% of patients treated with ≥12.5 µg/kg of L-thyroxine became hyperthyroid versus 26.1% of patients treated with ≤ 12.5 µg/kg (p = 0.007).
• Routine monitoring of T4s every two weeks was not performed due to both compliance and large variability of practice strategies among providers.
• Variability included: dosage adjustments based on T4 levels, measurement of free T4 versus total T4 for monitoring with TSH, and the strategy of using a higher dose for the first two weeks and then lowering the dose once the TSH becomes suppressed.

Hypothesis

A sizable proportion of the newborns treated for congenital hypothyroidism at the higher end of the dosage range become biochemically hypothyroid at follow-up visit, requiring a reduction of the dose.