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Three year follow-up of children with abnormal newborn screening results for congenital hypothyroidism: Who needs treatment and who needs permanent treatment?

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INTRODUCTION

Incidence of congenital hypothyroidism (CH)

- 1/3,000–4,000 live births according to the literature
- 1/2,000–3,000 live births in countries with newbone screening test (NST)
- 1/6,700 live births before the screening era

The aim of this study

- To analyze predictive factors suggesting transient congenital hypothyroidism (TCH) compared to permanent congenital hypothyroidism (PCH) or transient thyroid function test (TFT) abnormalities among those who had positive screening results in our centers over the past decade.

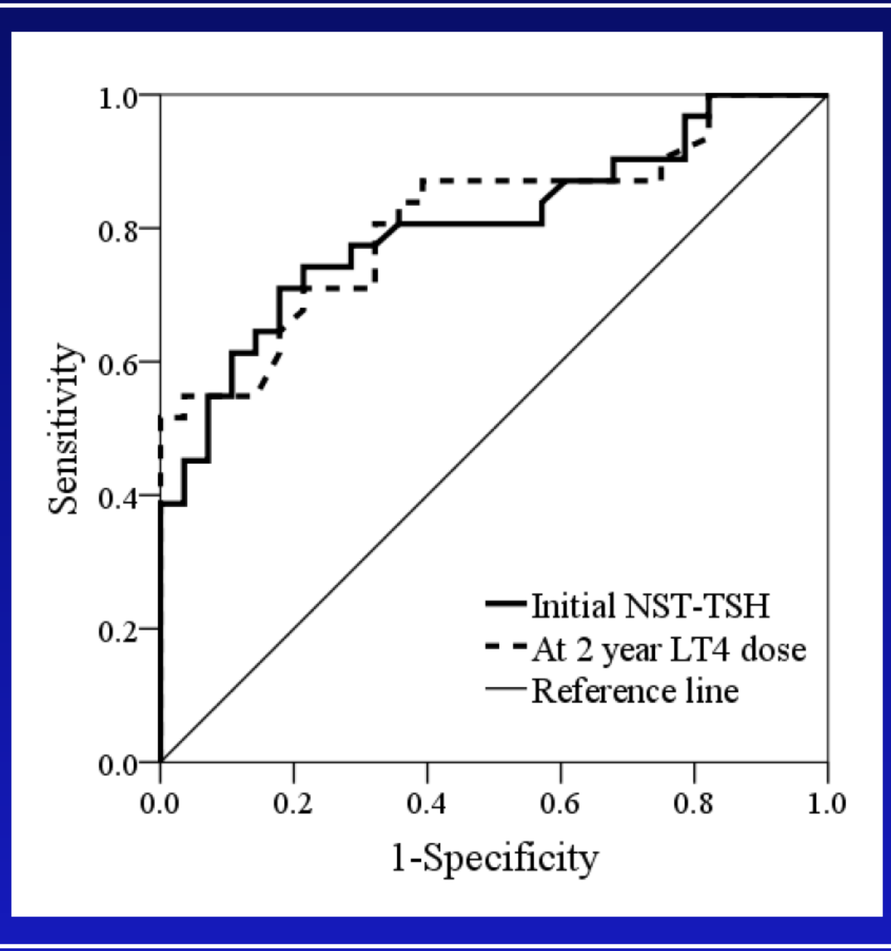
SUBJECTS & METHODS

- A chart review of 105 subjects (50 boys and 55 girls)
- Who had an elevated TSH levels detected by a NST
- Definition
  - TCH: when trial-off therapy was successful and kept their TFT within a tolerable range (TSH<10 μIU/mL and normal free T4 levels) for at least 6 months of follow-up after the cessation of levothyroxine (LT4) medication.
  - PCH: when trial-off therapy failed or subjects were kept on medication over 3 years of age due to thyroid dysgenesis or dyshormonogenesis
  - Transient TFT abnormality: when subjects did not require LT4 replacement therapy and their follow-up serum TFTs were normalized (TSH<6 μIU/mL and free T4≥0.9 ng/dL after 2 weeks of age)

RESULTS

- Prevalence
  - CH: 75.2% (TCH 35.2% and PCH 40.0%)
  - Transient TFT abnormalities: 24.8%
- Abnormal thyroid imaging in CH subjects: 56.4% (n=44/78)
- Serum levels of free T4 and TSH of TCH subjects (median and interquartile ranges)
  - At 6 month: 1.35 (1.20–1.49) ng/dL, 5.2 (4.2–7.1) μIU/mL
  - At 12 month: 1.39 (1.14–1.62) ng/dL, 6.3 (4.2-7.9) μIU/mL
- The nadir free T4 and peak TSH in transient TFT abnormality subjects: 1.21 (1.09–1.40) ng/dL, 9.8 (5.4–20.8) μIU/mL

- Predictive factors suggesting TCH compared to PCH
  - Initial NST-TSH levels (optimal cutoff point, 31.0 μIU/mL)
  - LT4 dose at 2 years of age (4.1 μg/kg/day)
  - Maximal LT4 dose (50 μg/day)



- Predictive factors suggesting TCH compared to transient TFT abnormalities
  - Initial serum level of free T4 (1.06 ng/dL),
  - Not TSH (27.2 μIU/mL)

Risk factor	Odds ratio	95% C.I	*P*-value
Initial Free T4 (ng/dL)	0.008	0.000-0.297	0.009
Initial TSH (μIU/mL)	1.052	0.996-1.111	0.067

CONCLUSIONS

1. As both NST-TSH levels and treatment histories are important to predict a successful trial-off-therapy, the earlier re-evaluation of children younger than 3 years of age might be possible when their initial NST-TSH levels and maximal or 2-year LT4 doses are low.
2. When the initial serum level of free T4 is above the average values in neonates with mild TSH level elevation, the normalization of TFTs could be waited without LT4 medication.
3. On the basis of optimal cutoff point analysis, NST-TSH levels might be readjusted to prevent unnecessary or over-treatment of TCH.

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