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Neurodevelopmental and body composition outcomes in children with congenital hypothyroidism treated with high-dose initial replacement and close monitoring

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Background: Despite newborn screening and early levothyroxine replacement, there are continued reports of mild neurocognitive impairment in children with congenital hypothyroidism (CHT). In Auckland, New Zealand, cases are identified by a neonatal screening program with rapid institution of high-dose levothyroxine replacement (10–15 mcg/kg/day), producing prompt normalisation of thyroid function. Subsequently, frequent monitoring and dose alterations are performed for 2 years. We aimed to assess whether the Auckland treatment strategy prevents impairment of intellectual and motor development.

Methods: This study encompassed all children with CHT born in 1993–2006 in Auckland, and their siblings. Neurocognitive assessments included: i) IQ via Weschler Preschool and Primary Scale of Intelligence III or Weschler Intelligence Scale for Children IV; ii) Movement Assessment Battery for Children; and iii) Beery Visuomotor Index. Body composition was assessed by dual-energy x-ray absorptiometry.

Results: 44 CHT cases and 53 sibling controls aged 9.6±3.9 years were studied. Overall IQ was similar among CHT cases and controls (95.2 vs 98.6; p=0.20) and there were also no differences in motor function. Severity of CHT did not influence outcome, but greater time to normalise free thyroxine was associated with worse motor balance. There were no differences in anthropometry or body composition between groups.

Conclusions: These findings suggest that a strategy of rapidly identifying and treating infants with CHT using high-dose levothyroxine replacement is associated with normal intellectual and motor development. The subtle negative impact on motor function associated with time to normalize free thyroxine levels is consistent with benefit from rapid initial correction.

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Screening for Congenital Hypothyroidism: Comparison of Borderline Screening Cut-Off Points and the Effect on the Number of Children Treated with Levothyroxine

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Abstract

Background: The newborn screening programme for congenital hypothyroidism (CH) has led to the prevention of severe developmental delay associated with this condition. In the UK, thyroid-stimulating hormone (TSH) screening cut-off points have changed over time, in some instances prompted by changing methodological platforms. The use of borderline cut-off points varies throughout the country. ***Objective:*** To use discordance in cut-off points to assess the performance of the UK Newborn Screening Programme Centre (UKNSPC) definitions. ***Methods:*** Between January 2006 and December 2007, 223,658 newborn infants were screened by the Great Ormond Street Hospital (GOSH) for CH. All children with positive results and those with blood-spot TSH concentrations >6 mU/l on repeat screening were referred to GOSH. We compared the numbers of children detected and treated for CH using the GOSH cut-off points (>6 mU/l) and those of the national screening programme (>10 mU/l). Children were defined as transient CH if levothyroxine treatment had been discontinued by 3 years. ***Results:*** Of the children screened between January 2006 and December 2007, 167 out of 223,658 fulfilled the GOSH screening criteria; 136 of these required levothyroxine treatment, but 29 (21%) of the children treated would not have been detected by the current UKNSPC guidelines. Transient CH was found in 17/47 (36%) of the treated children detected with a cut-off point >6 mU/l. Raising the cut-off point to >10 mU/l reduced the number of children treated for transient CH to 4/18 (22%). ***Conclusion:*** A significant number of children with true and transient CH are missed with a screening cut-off point of >10 mU/l. Our data suggests that a cut-off point of 6 mU/l is appropriate.

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REVIEW
ENDOCRINE DISORDERS IN CHILDHOOD AND ADOLESCENCE

Natural history of subclinical hypothyroidism in children and adolescents and potential effects of replacement therapy: a review

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Abstract

Objective: Subclinical hypothyroidism (SH) is quite common in children and adolescents. The natural history of this condition and the potential effects of replacement therapy need to be known to properly manage SH. The aim of this review is to analyze: i) the spontaneous evolution of SH, in terms of the rate of reversion to euthyroidism, the persistence of SH, or the progression to over hypothyroidism; and ii) the effects of replacement therapy, with respect to auxological data, thyroid volume, and neuropsychological functions.
Methods: We systematically searched PubMed, Cochrane, and EMBASE (1990–2012) and identified 39 potentially relevant articles of which only 15 articles were suitable to be included.
Results and conclusions: SH in children is a remitting process with a low risk of evolution toward overt hypothyroidism. Most of the subjects reverted to euthyroidism or remained SH, with a rate of evolution toward overt hypothyroidism ranging between 0 and 28.8%, being 50% in only one study (nine articles). The initial presence of goiter and elevated thyroglobulin antibodies, the presence of celiac disease, and a progressive increase in thyroperoxidase antibodies and TSH value predict a progression toward overt hypothyroidism. Replacement therapy is not justified in children with SH but with TSH 5–10 mIU/l, no goiter, and negative antithyroid antibodies. An increased growth velocity was observed in children treated with levothyroxine (L-T_4; two articles). L-T_4 reduced thyroid volume in 25–100% of children with SH and autoimmune thyroiditis (two studies). No effects on neuropsychological functions (one study) and posttreatment evolution of SH (one study) were reported.

European Journal of Endocrinology **168** R1–R11

Concluding remarks

i) SH in children seems to be a remitting process with a low risk of evolution toward overt hypothyroidism.
ii) The initial presence of goiter and elevated TG-Abs and a progressive increase in TPO-Abs and TSH values predict a progression toward overt hypothyroidism.
iii) There is no clear evidence on the beneficial effects of L-T_4 on growth and thyroid volume in SH due to insufficient data.
iv) No effects on neuropsychological functions were reported.

v) Replacement therapy is not justified in children with SH but with TSH 5–10 mIU/l, no goiter, and negative antithyroid antibodies.
vi) Further randomized double-blind studies are needed to clearly evaluate the effects of replacement therapy on growth, goiter, neuropsychological, and cardiovascular outcomes.