Early discrimination between transient and permanent congenital hypothyroidism in children with eutopic gland

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INTRODUCTION

Congenital hypothyroidism (CH) is a common condition that occurs in approximately 1: 3000- 4000 live births and is one of the most common preventable cause of mental retardation. Owing to the CH screening programs this condition is now diagnosed and treated at an early age and is no longer a social problem but the increased thyrotropin (TSH) assay sensitivity has led to adopt lower TSH cut-offs that caused a progressive increase in detecting mild forms of CH. As consequence of these changes, significant increase in CH frequency has been reported in the last years and an elevated percentage of screened children treated for CH ultimately prove to not require L-thyroxine (L-T4) treatment after the first 3 years of age and are classified as having a transient (T) CH. In the present study we have retrospectively investigated a series of CH children with eutopic gland, in order to identify the factors that could allow an early discrimination between the cases with either P or T CH.

PATIENTS AND METHODS

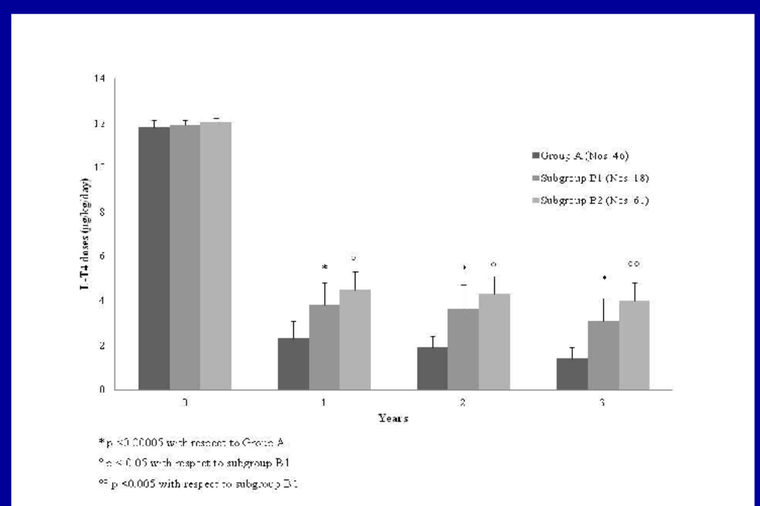
Clinical, biochemical and imaging data of 125 children with CH, who were positively screened and treated during the period 1998-2011, were retrospective analyzed

RESULTS

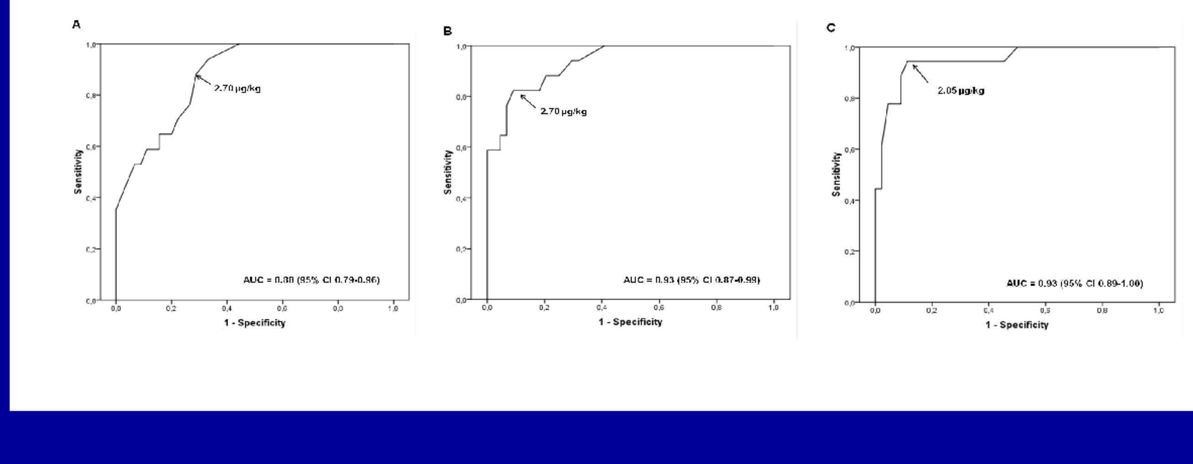
46/125 patients (36.8%) were included in the group with T CH (Group A) and 63.2% were judged to be affected by P CH and were included in Group B. 79 patients of Group B (77.2%) exhibited, at thyroid scan, a gland dysgenesis (athyreosis in 33 cases, thyroid ectopia in 28 cases) and were classified as subgroup B_2; 18 patients (22.8%) were diagnosed to be affected by a P CH form with gland in situ (subgroup B_1).

None of Group A children required any increment of L-T4 per kg dose from therapy start onwards to maintain over time normal TSH values, whereas some increase of doses was occasionally needed in 16/18 children of subgroup B_1 ($p<0.0001$).

Whereas L-T4 per kg doses at therapy start were very similar in Group A patients (11.8 ± 0.3 µg/kg body weight) and in those from subgroups B_1 (11.9 ± 0.2) and B_2 (12.0 ± 0.2), L-T4 per kg doses at subsequent times were significantly lower in Group A than in subgroup B_1. Significant differences in terms of L-T4 per kg doses at subsequent times were also found between subgroups B_1 and B_2.



The ROC curves predicting T CH diagnosis using the L-T4 dose requirements at 1, 2 and 3 years in the children with eutopic gland are shown in panels A, B and C. The optimal cut-off value of L-T4 per kg doses that was predictive of T CH for each year is listed below (Table). The L-T4 doses with the highest sensitivity (100%) were 1.70, 1.45 and 0.98 µg/kg/day, respectively, at 1, 2 and 3 years, whereas the L-T4 doses with the highest specificity (100%) were, respectively, 4.90, 4.27 and 4.70 µg/kg/day.



Age (years)	L-T4 dose (µg/kg/day)	Sensitivity (%)	Specificity (%)	Youden Index
1	≤2.70	88.2	73.3	0.61
2	≤2.70	82.4	90.9	0.73
3	≤2.05	94.4	88.6	0.83

CONCLUSIONS

a) L-T4 requirements >4.9 µg/kg/day at 12 months or >4.27 µg/kg/day at 24 months are highly suggestive of P CH, irrespective of gland ultrasonography;

b) b) L-T4 requirements <1.7 µg/kg/day at 12 months or <1.45 µg/kg/day at 24 months are highly suggestive of T CH, at least in the cases with eutopic gland;

c) the analysis of L-T4 requirements during the first years of treatment might allow an early discrimination between T and P CH in the cases with eutopic gland

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Thyroid

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