The interconnectivity between growth hormone replacement therapy and subclinical hypothyroidism on growth response in children with pituitary dwarfism

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Introduction

- Administration of recombinant growth hormone rhGH to GH-deficient children has yielded conflicting results concerning its impact on thyroid function.
- Data about patients developing subclinical hypothyroidism (SH) are scanty, but it is thought to be associated with impairment of metabolic profile and lower growth response.

Method

- We reviewed the cases of 42 children:
  - 29 boys, 13 girls (chart 1),
  - aged between 4 and 14,

Chart 1: Distribution of patients by sex:

- There were 31% boys and 69% girls.

Criteria for inclusion in the study:

- Growth hormone deficiency confirmed;
- Constant periodic revaluations (6 months to one year);
- Duration of treatment with rhGH for at least one year without interruption;
- Normal thyroid function at diagnosis and onset of therapy.
- Clinical and hormonal data (IGF-1, TSH, fT4), as well as radiographic bone assessments were documented at the beginning and after 1-st year of rhGH treatment.

Chart 2: IGF-1 values

- Euthyroid patients
- Subclinical hypothyroidism
- 87.44±63.52
- 244.42±217.31
- 216.4±137.9
- 81.4±±37.53

At the beginning of treatment
After 1 year

Chart 3: Dose modification for rhGH

- Euthyroid patients
- Subclinical hypothyroidism
- 0.03
- 0.04
- 0.02
- 0.037

At the beginning of treatment
After 1 year

Objective

- To investigate:
  - The frequency of SH in children with pituitary dwarfism treated with rhGH;
  - The influence of SH on rhGH therapy effectiveness.

Results

- At therapy onset:
  - all patients had the height below the -2.5 SD (mean SD of -3.2),
  - bone age was delayed (with mean of 2,32 years compared to chronological age),
  - IGF-I concentration was either decreased or close to lower limit of normal range,
  - there was no impairment in thyroid function.

- After one year of rhGH therapy:
  - SH was the only impairment in thyroid function and it was diagnosed in 6 patients (16.6% of cases).
  - Despite similar IGF-I secretion increase, the improvement of height velocity was significantly lower in children with SH (0.7± 0.16 cm/month) than in those who remained euthyroid (0.57± 0.1 cm/month, p<0.05) and also for the bone age (Chart 2-5).
  - Furthermore, an increase in IGF-I levels was associated with increasing levels of TSH in SH patients and led to 2 cases to administration of L-T4 substitution.

Chart 4: Growth rate and height gain: children with subclinical hypothyroidism vs. children with normal thyroid function:

- Normal thyroid function
- Subclinical hypothyroidism
- Growth rate (cm/month)
  - 0.7±0.16
  - 0.57±0.1
- Height gain (cm)
  - 8.0±1.94
  - 6.95±1.25

Chart 5: Evolution of bone age for patients with subclinical hypothyroidism compared with euthyroid patients:

- Subclinical hypothyroidism
  - 9 months
- Normal thyroid function
  - 36 m

Conclusions

- After one year of rhGH therapy, SH was the only impairment in thyroid function and it was diagnosed in 16.6% of cases. Despite similar IGF-I secretion increase, the improvement of height velocity was significantly lower in children with SH than in those who remained euthyroid.
- Also, an increase in IGF-I levels was associated with increasing levels of TSH in SH patients.
- The incidence of subclinical hypothyroidism during the first year of rhGH treatment in children with pituitary dwarfism should be taken into account, as it may worsen the growth response and may be worsened by the rhGH therapy.

References: