High normal TSH – risk factor for subclinical hypothyroidism in GH treatment for pituitary dwarfism?

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Subclinical hypothyroidism

- Diagnosed when peripheral thyroid hormone levels are within the normal range, but thyroid stimulating hormone (TSH) is mildly elevated.
- It is common: occurring in 3-8% of the population, and carries a risk of progression to overt hypothyroidism of 2-5% per year (1).
- There is no absolute consensus on which patients to treat, although there are some clear recommendations (1).
- The therapeutic benefit of growth hormone (GH) therapy in improving height in short children is widely recognized; however, GH therapy is also associated with other metabolic actions (2).

Normal thyroid hormone secretion or appropriate L-thyroxine substitution is necessary for the optimal effect of recombinant growth hormone (rGH) on growth rate (3).

GH therapy in children with GH deficiency (GHD) has yielded conflicting results concerning its impact on thyroid function.

The decrease of free thyroxine (FT4) levels at recombinant human GH (rGH) therapy onset has been reported in several studies (3).

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 (4,5).

Methods and Results

Objective:
To evaluate the effect of rGH administration on TSH levels and FT4 serum concentrations, the frequency of SH in children with GHD during the 1st year of treatment, as well as to assess its influence on rGH therapy effectiveness.

Retrospective study:
- We reviewed the cases of 75 children with GH deficiency evaluated at the Endocrinology Department Iași during one year.
- 59 boys, 16 girls, aged between 4 and 14 years;
- 78.66 % male, 21.34. % female (Figure 1)

Methods and results:
- Clinical and hormonal data (IGF1, TSH, FT4) were collected within the first year of rhGH therapy administration.
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Results:

- All children had an improvement of growth velocity.
- Serum IGF1 levels and height SDS significantly increased after 12 months of GH therapy.
- After one year of rGH therapy, SH was the only impairment in thyroid function and it was diagnosed in 12 patients (16%).
- The risk of SH was increased among subjects with the highest tertile TSH level as compared with subjects with the lowest tertile (p<0.05).
- Despite similar IGF1 secretion increase, the improvement of height velocity was significantly lower in children with SH (0.65 cm/month) than in those who remained euthyroid (0.88 cm/month, p<0.05).
- An increase in IGF1 levels was associated with increasing levels of TSH in SH patients and led in four cases to administration of L-T4 substitution.

Discussions

- The phenomenon of FT4 concentration decrease after rGH administration in GH-deficient subjects has been reported in several studies (5,6).
- Moreover, it has been suggested that rGH therapy might disclose previously unrecognized thyroid insufficiency rather than induce hypothyroidism (7,8).
- Our observations confirm the phenomenon of „unmasking” central hypothyroidism after rGH therapy administration in some of children with previous diagnosis of isolated GHD.

Conclusions

- This study provides evidence that subclinical hypothyroidism during the first year of rGH therapy in children with GH deficiency and the influence on the growth rate should be taken into account, as it may worsen the growth response with potential indications to thyroid hormone supplementation.
- Our findings suggest that suboptimal thyroid function (highest tertile TSH level) increases vulnerability to the occurrence of SH in children treated with rGH, needing a closer monitoring.

References: