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

Ioana Bodescu[1], Jeanina Idriceanu[1], Ioana Vasiliu[1], Adina Manolachie[1], Irina Oana Chifu[1], Iulia Crumpei[1], Cristina Cristea[1], Cristina Preda[1], Voichița Mogoș[1], Carmen Vulpoi[1]

1 – Department of Endocrinology, University of Medicine and Pharmacy "Gr.T. Popa" Iasi, Romania

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.

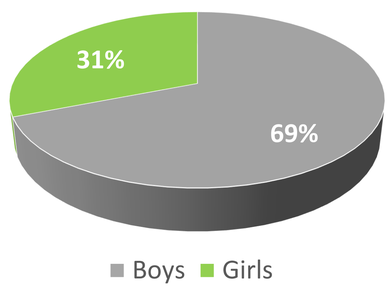
Objective

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

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:



- *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

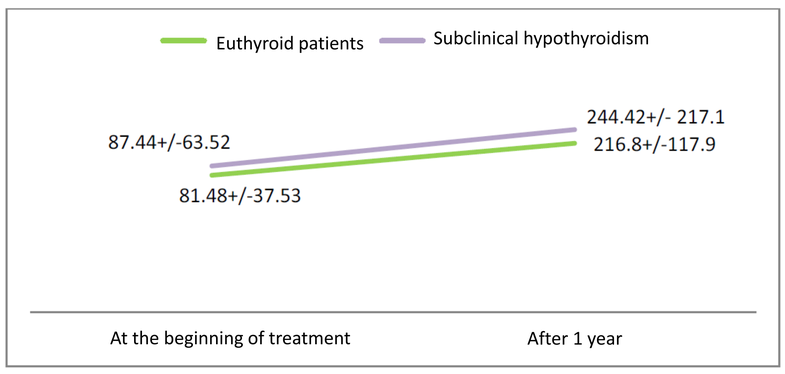
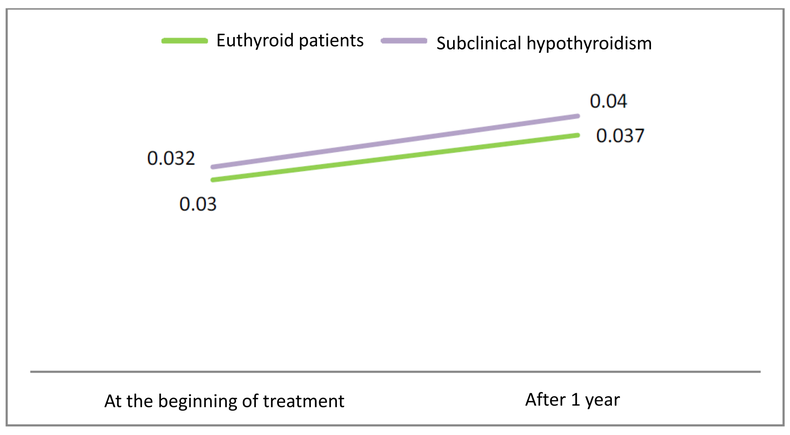


Chart 3: Dose modification for rhGH



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 in 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:

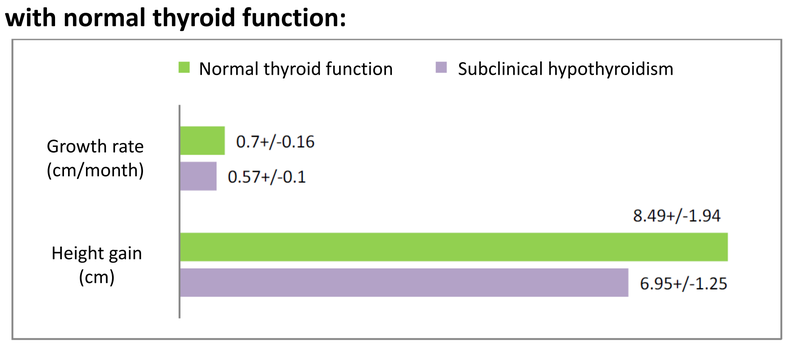
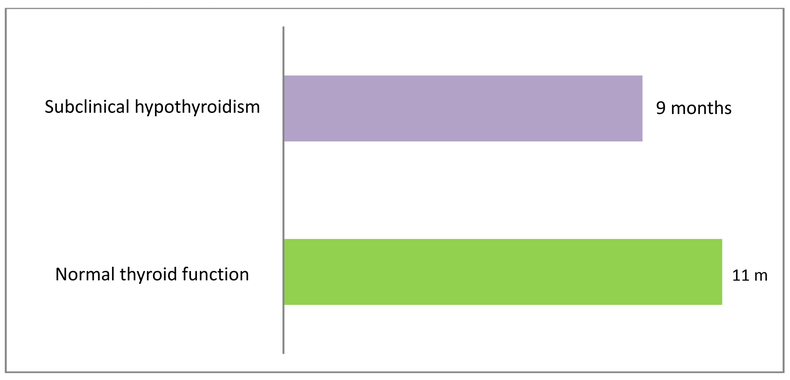


Chart 5: Evolution of bone age for patients with subclinical hypothyroidism compared with euthyroid patients:



Conclusions

❖After one year of rhGH therapy, SH was the only impairment in thyroid function and it was diagnosed in16.6% 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:

Smyczynska J et al, Thyroid function in children with growth hormone (GH) deficiency during the initial phase of GH replacement therapy – clinical implications, *Thyroid Research* 2010, 3(1):2-11.
Kalina-Faska B, Kalina M, Koeler B, Effects of recombinant growth hormone therapy on thyroid hormone concentrations. *Int J Clin Pharmacol Ther* 2004, 42(1):30-34.