IGF-1 serum concentrations and growth in children with Congenital Leptin Deficiency (CLD) before and after replacement therapy with Metreleptin

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Summary

Most studies show that obese children have normal or increased IGF-1 levels, and it is known that IGF-1 levels decrease under caloric restriction (1). Interestingly, in 8 children with congenital leptin deficiency we found that:

- IGF-1 serum levels were low at baseline and increased during 12 months Metreleptin substitution despite reduced caloric intake and significant weight loss. IGFBP3 SDS and IGF-1/IGFBP3 ratio SDS also showed an increase under Metreleptin substitution.
- Height SDS after 12 months of Metreleptin substitution was increased in 4/5 children (2-12 yrs). This age range is the period in which IGF-1 plays a major role in growth.

Our findings support the hypothesis that leptin, as a signal of the energy status, promotes IGF-1 production and growth in children.

Background and Objective

Leptin is a key signal of the body’s energy status and exhibits pleiotropic effects:

- Congenital Leptin Deficiency (CLD) in humans results in intense hyperphagia and early-onset severe obesity, along with multiple metabolic, hormonal and immunological abnormalities (2).
- In vitro and animal model studies suggest that leptin promotes linear growth (3).

With the aim to investigate the possible effect of leptin on growth in humans, we evaluated IGF-1 serum levels and growth before and after 12 months of leptin replacement therapy in children with CLD.

Patients and Methods

Our case-series contains n=8 patients (6 males) with CLD due to defective leptin production (n=5) or bioinactive leptin (n=3). We retrospectively analyzed data regarding:

- BMI SDS (4)
- Height SDS (5)
- IGF-1 SDS (6)
- IGFBP3 SDS, IGF-1/IGFBP3 molar ratio SDS (7)

before and after 12 months of leptin replacement therapy (0.024mg/kg Metreleptin LBW/day; Aegerion Pharmaceuticals GmbH).

Results

Patients characteristics:
- N= 8 (6 males)
- Range of age at T0= 0.9-14.8 yrs

Fig. 1: Mean BMI SDS before (T0) and after 12 months (T12) of leptin replacement therapy.

Fig. 2: IGF-1 SDS before (T0) and after 12 months (T12) of leptin replacement therapy.

Fig. 3: Height SDS before (T0) and after 12 months (T12) of leptin replacement therapy in children of age 2-12 years.

Fig. 4: Mean IGFBP3 SDS (A) and mean IGF-1/IGFBP3 molar ratio SDS (B) before (T0) and after 12 months (T12) of leptin replacement therapy.

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References