Growth Hormone Treatment for Children born Small for Gestational Age

Mohammad Hassan Moaddab, MD
Pediatric Endocrinologist
SGA: Definition

- It requires the following:
  - accurate knowledge of gestational age (ideally based on first trimester ultrasound exam),
  - accurate measurements at birth of weight, length, and head circumference.
SGA: Definition

• Small for gestational age (SGA) describes a baby with a birth weight and/or length below -2SD

• Approximately 5% of children are born SGA

• Additionally, those SGA babies who have small head circumference should be recognized.
What are the causes of SGA?

**Maternal**
- Infections
- Nutrition
- Medical conditions
- Substance abuse
- Pregnancy pathology
- Age, height, birth weight
- Ethnic background

**Placental**
- Insufficiency
- Abruption
- Infarction
- Structural abnormalities

**Fetal**
- Genetic abnormalities
- Down, Bloom, Fanconi syndrome
- Congenital malformations
- Metabolic problems
- Multiple gestations
SGA: Other characteristics

- In addition to having short stature, children born SGA:
  - have less body fat than children born AGA\(^1\)
  - may be psychosocially disadvantaged\(^2\)
  - may be at increased risk of developing metabolic syndrome if there is a rapid weight gain in childhood\(^3\)
  - have low bone mineral density\(^4\)

1Sas et al 2000, 2 Strauss 2000, 3 Jaquet et al. 2005, 4 Arends et al 2003
SGA: Early Growth & Catch-up Growth

- Children born SGA are shorter during childhood and as adults (app. 1SD lower than the mean)

- Typical infant born SGA;
  - experiences a period of accelerated linear growth during the first 12 months of life,
  - this results in a stature above -2 SD in up to 90%,
  - most of the catch-up growth occurs during the first year and is near completion by 2 yr of age.
  - those born very prematurely are less likely to reach a normal range.
%8-10 of SGA babies are with short stature in adulthood

SGA: Early Growth & Catch-up Growth

- Catch-up growth may be incomplete in recognized syndromes, such as **Silver Russell or Turner syndromes**.

- Circulating concentrations of GH, IGF-I, IGF-binding protein-3 are not predictive of subsequent growth.
Etiology of poor growth in SGA:

- An irreversible deficit in cell number,
- inadequate calorie intake during the first years of life,
- and abnormalities in GH secretion have been hypothesized.
Hormonal status in SGA children

Very small proportion of children with SGA has classical GH or IGF deficiency; but many of them has:

• mild GHD and partial endogeneous GH or IGF-1 irresponsiveness.

SGA: Treatment with GH

- **The aim of GH therapy** in short SGA children is to:
  - **normalize height** in early childhood
  - maintain normal height gain during childhood
  - achieve adult height within normal target range

- **Other benefits**
  - GH has normalizing effects on:
    - **body mass index**\(^1\)
    - **lipid profile**\(^2\)
    - **blood pressure**\(^3\)
    - **psychosocial profile**\(^3\)
    - **bone mineral density**\(^4\)

---

1 Sas et al. 2000, 2 Van Pereren et al 2003, 3 Van Pereren et al. 2004, 4 Arends et al. 2003
Neurological and intellectual consequences

- In large observational studies, cognitive impairment is independently associated with:
  - low birth weight,
  - short birth length,
  - small head circumference for gestational age.

- Those without catch-up in height and/or head circumference have the worst outcome.

- **GH treatment**;
  - induces catch-up growth in head circumference particularly in those with small head circumference at birth.
  - there is some evidence that GH also improves IQ in short SGA children.
Indication of GH

- In the United States, growth hormone is approved for use in short SGA children whose height remains less than 2 SDS below the mean for age and sex at 2 - 4 years of age.
Indication of GH

• In **Europe**, the approved indication is for short SGA children whose height is less than **2.5 SDS** below the mean for age and sex **at 4 years of age**.

• In addition, the European indications include **low growth velocity** (ie, height velocity less than average for age) and **predicted height (>1 SD below midparental height)**.
SGA: Treatment with GH

• The optimal dose and duration of GH therapy have not been established.

• Usually GH begins with doses similar to those used for treatment of GH deficiency in children. (33 – 67 micgr/kg)

• During GH therapy, dose of GH readjusted to maintain IGF-1 levels at approximately 1 SD above the mean for age and/or Tanner stage of development.

• At present, there is no convincing evidence that the addition of GnRH analog treatment to inhibit pubertal progression is associated with additional height gain.
SGA: Treatment with GH

- If there is an inadequate response, re-evaluation is indicated,
  - including consideration of compliance,
  - GH dose,
  - diagnosis,
  - the decision to discontinue treatment.

- In those with a positive response to GH, withdrawal of GH therapy after 2–3 yr leads to catch-down growth and is not recommended.

- In children receiving GH, IGF-I monitoring as a tool for dose optimization may be useful.
SGA: Treatment with GH

- Treatment-emergent adverse events are not more common in this population than in other conditions treated with GH, nor have additional safety concerns arisen.
SGA long-term GH treatment: Safety follow-up

- GH is insulin antagonist.

- Short SGA children may have reduced insulin sensitivity and metabolic changes.

- Long-term GH treatment does not increase the risk of DM type 2 and MS in young adults.

- Novo Nordisk continues long-term safety follow-up in SGA young adults.

van Dijk et al., J Clin Endocrinol Metab 92: 160-165, 2007
Norditropin label: Contraindications

- Active malignant tumours
- Acute critical illness (complications following open heart surgery, abdominal surgery, multiple accidental trauma, acute respiratory failure or similar conditions)
- Hypersensitivity to somatropin or excipients
- **In CRI, treatment with Norditropin should be discontinued at renal transplantation**
SGA, is more than a stature issue.

Thank you for your attention