Efficacy and safety of growth hormone treatment in short children born small for gestational age (IUGR-3 STUDY); Effects of GH-levels on growth, insulin sensitivity and body composition.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON24733

Source
Nationaal Trial Register

Brief title
IUGR-3 STUDY

Health condition

Small for Gestational Age (SGA), Kinderen met persisterend korte gestalte

Sponsors and support

Primary sponsor: Erasmus Medical Center/ Sophia Children's Hospital
PO Box 2060
3000 CB Rotterdam
The Netherlands
Tel: +31 10 463 63 63
Source(s) of monetary or material Support: Novo Nordisk Farma BV
Alphen a/d Rijn
The Netherlands

Intervention

Outcome measures

Primary outcome

1. To determine before, during and after stop of long-term growth hormone treatment:
a. Insulin sensitivity (via frequent sampling intravenous glucose tolerance test);
b. Body composition.
In relation with each other and with baseline serum GH levels during an overnight GH profile and in relation with 6 months of treatment with 2 different GH doses.
2. To assess the long-term efficacy of biosynthetic GH treatment in a dose of 3 IU\m2\day on final height and other various auxological parameters.

Secondary outcome

To assess the safety of GH treatment by studying the short- and long-term effects on:
a. Blood pressure;
b. Thyroid function;
c. Fasting glucose and insulin andHbA1c levels.

Study description

Background summary

BACKGROUND
Most children born small for gestational age (SGA) show catch-up growth to a normal height during the first two years of life, but approximately 10-15 % of them remain short with a height below –2 SD scores. It has been demonstrated that growth hormone (GH) treatment results in a normalization of height during childhood as well as adulthood. Several epidemiological studies have shown an association between low birth size and diabetes mellitus type 2, hypertension and cardiovascular disease. Short SGA children with relatively higher GH levels in serum also had more signs of insulin insensitivity, both before and during GH treatment. Further research is needed to evaluate this.
The present study aims to evaluate the effect of growth hormone therapy in prepubertal short children born SGA on growth parameters, GH levels, insulin sensitivity and body composition and their relationship, before and during GH therapy.

STUDY DESIGN
Open-labelled, randomised multicenter GH trial involving 120 children with short stature born SGA aged 3 to 8 years of age. The children will be treated with biosynthetic GH until attainment of final height. Every three months there will be a physical examination and anthropometry. Yearly laboratory evaluation (routine chemistry and haematology) (the first

year twice) and a bone age determination (X-ray of the left hand). Every 2 year (the first year twice) dual energy X-ray absorptiometry (DEXA) to evaluate the body composition and in children aged 5 years or more a frequent sampling intravenous glucose tolerance test (FSIGT) to evaluate the insuline sensitivity. In 60 children aged 5 years or more overnight GH profile test during 12 hours will be performed at the start of the study and after 6 months.

OBJECTIVES
PRIMARY
1. To determine before, during and after stop of long-term growth hormone treatment: Insulin sensitivity (via frequent sampling intravenous glucose tolerance test) and body composition. In relation with each other and with baseline serum GH levels during an overnight GH profile and in relation with 6 months of treatment with 2 different GH doses
2. To assess the long-term efficacy of biosynthetic GH treatment in a dose of 3 IU/m2/day on final height and other various auxological parameters.

SECONDARY
To assess the safety of GH treatment by studying the short- and long-term effects on: blood pressure, thyroid function and fasting glucose and insulin and HbA1c levels.

Study objective

Children born small for gestational age (SGA) might be at increased risk for developing hypertension, cardiovascular disease and diabetes mellitus type 2. It has been shown that those SGA children with relatively higher GH levels during an overnight GH-profile had more signs of insulin resistance. GH treatment does not seem to increase the risk on these diseases, but insulin sensitivity has not yet been evaluated in detail and has not yet been studied in relation to age, body composition, and baseline serum levels of GH, insulin-like growth factor (IGF)-I and IGF-binding proteins. This type of research is very important since it might give clues which children are more prone to develop the metabolic syndrome in later life an whether GH treatment during childhood and puberty has any effect on the development of this metabolic syndrome.

Intervention

Growth hormone treatment; Norditropin SimpleXx 15 mg/1.5 ml

The first 60 patients of five years and older who are included in the study, will undergo an overnight GH-profile, FSIGT and Dual Energy X-ray absorptiometry (DXA). After stratification for gender, age, GH status, these patients will be randomised into two different groups: During the first 6 months, groups A and B will receive GH therapy in a dose of 1 and 2 mg/m2/day, respectively. Subsequently, all patients will continue GH treatment with a dose of 1 mg/m2/day.

Those patients of five years and older who will not undergo an overnight GH profile, FSIGT and DXA and all patients younger than 5 years will receive 1 mg GH/m2/day.

Contacts

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Eligibility criteria

Inclusion criteria

1. Children born with a birth length and/or weight < - 2 SD for gestational age (Usher McLean (22));
2. Neonatal period without signs of severe asphyxia (defined as Apgar score < 3 after 5 minutes), and no serious diseases such as long-term artificial ventilation and oxygen supply, broncho pulmonary dysplasia or other chronic lung disease;
3. Short stature defined as a height SD score below –2.5 according to the Dutch National Growth References of 1997;
4. Height velocity (cm/year) for chronological age £ P50 (25);
5. Chronological age at start of treatment: 3.00 - 7.99 years (boys and girls);
6. Prepubertal signs defined as Tanner stage 1 or testicular volume < 4 ml (26);
7. Well documented growth data from birth up to 2 years and at least 1 year before the start of the study;
8. Both growth hormone deficient and growth hormone insufficient patients;
9. Informed consent.

Exclusion criteria

1. Chromosomal disorders, known syndromes and serious dysmorphic symptoms suggestive for a syndrome that has not yet been described, except for Silver Russell Syndrome;
2. Coeliac disease and other chronic or serious diseases of the gastrointestinal tract, heart,

genito-urinary tract, liver, lungs, skeleton or central nervous system, metabolic disease or chronic or recurrent major infectious diseases, nutritional and/or vitamin deficiencies;
3. Any endocrine or metabolic disorder such as diabetes mellitus, diabetes insipidus, hypothyroidism, or inborn errors of metabolism, except of GHD;
4. Use of medications or interventions at this moment or during the previous 6 months that might have interfered with growth, such as corticosteroids (including high dose of corticosteroid inhalation), sex steroids, growth hormone, or major surgery (particularly of the spine or extremities);
5. Active malignancy or increased risk of leukaemia;
6. Serious suspicion of psychosocial dwarfism (emotional deprivation);
7. Expected non-compliance.

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Masking:	Single blinded (masking used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-03-2002
Enrollment:	157
Type:	Anticipated

Ethics review

Positive opinion

Date:	20-02-2006
Application type:	First submission

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
NTR-new	NL550
NTR-old	NTR606
Other	: N/A
ISRCTN	ISRCTN65230311

Study results

Summary results
van Dijk M, Mulder P, Houdijk M, et al. High Serum Levels of Growth Hormone (GH) and IGF-I during High Dose Growth Hormone Treatment in Short Children Born Small for Gestational Age. J Clin Endocrinol Metab 2006