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.

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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...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

Samenvatting

ID

NL-OMON24733

Bron
NTR

Verkorte titel
IUGR-3 STUDY

Aandoening

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

Ondersteuning

Primaire sponsor: Erasmus Medical Center/ Sophia Children's Hospital
PO Box 2060
3000 CB Rotterdam
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Tel: +31 10 463 63 63
Overige ondersteuning: Novo Nordisk Farma BV

Alphen a/d Rijn
The Netherlands

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

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.

Toelichting onderzoek

Achtergrond van het onderzoek

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.

Doel van het onderzoek

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.

Onderzoeksproduct en/of interventie

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.

Contactpersonen

Publiek

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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

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.

Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

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.

Onderzoeksopzet

Opzet

Type:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Blindering:	Enkelblind
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-03-2002
Aantal proefpersonen:	157
Type:	Verwachte startdatum

Ethische beoordeling

Positief advies

Datum:	20-02-2006
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

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

Resultaten

Samenvatting resultaten
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