Prospective study on the metabolic and linear growth effects of growh hormone treatment in children with Kabuki Syndrome

Published: 27-03-2012
Last updated: 26-04-2024

The primary objective of this study is to assess the relation between the short term metabolic changes after start of rhGH therapy and the long term change in height SDS after one and two years of treatment. Secondly, we want to assess the effects...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Interventional

Summary

ID

NL-OMON39985

Source
ToetsingOnline

Brief title
Metabolic effects of Growth Hormone

Condition

- Hypothalamus and pituitary gland disorders
- Inborn errors of metabolism

Synonym
Kabuki syndrome (KS)

Research involving
Human

Sponsors and support

Primary sponsor: Medisch Universitair Ziekenhuis Maastricht
Source(s) of monetary or material Support: Ministerie van OC&W,Pfizer

Intervention

Keyword: Growth, Growth hormone, Kabuki syndrome, Metabolic effects

Outcome measures

Primary outcome

Is there an increase in TEE during 6 weeks treatment with rhGH in children with Kabuki Syndrome?

What is the relation between the short-term (6 weeks) change in TEE as measured with the DLW technique and the long term change in height SDS during treatment with rhGH?

What is the effect of rhGH treatment on metabolic risk parameters typical for the metabolic syndrome in adults?

Secondary outcome

To assess the long (2 years) term safety of growth hormone therapy on metabolic risk parameters and body composition.

What are the characteristics of hyermobility in the Dutch children with Kabuki Syndrome and does rhGH treatment lead to a diminished degree of hypermobility?

What are the characteristics of body proportions in children with Kabuki Syndrome and does the body composition changes during rhGH treatment?

Study description

Background summary

Kabuki Syndrome (KS, OMIM 147920) is a multiple anomaly syndrome. The spectrum of medical problems seen in Kabuki syndrome is diverse but all patients have similar facial features. Recently, an available genetic test strongly confirm the diagnosis KS with mutations in KDM6A or KMT2D (MLL2) gene. One of the features in KS children is postnatal growth retardation, final stature is short in KS children, mostly below -2 SDS. The cause of the growth retardation is unknown, but growth hormone deficiency has been reported several times in literature. Further clinical signs and symptoms in KS children are obesity, hypertension, hypotonia and short stature. Features resembling the metabolic syndrome (MS) and hypothalamic disturbance. Some of these features are also seen in syndromes like Turner (TS) and Prader-Willi (PWS) patients. They do not have a real growth hormone deficiency, but have proven benefit from growth hormone therapy at supra-physiological doses obtaining a higher final height than the expected one according to the natural history. Moreover, there is a paucity of data regarding the cardiovascular and metabolic risk factors in children with TS and PWS and the positive effect of GH treatment on these risk factors. These children have an abnormal body composition, presence of hypertension, dyslipidemia and hyperinsulemia and therefore fulfilment of the criteria of the metabolic syndrome.

Study objective

The primary objective of this study is to assess the relation between the short term metabolic changes after start of rhGH therapy and the long term change in height SDS after one and two years of treatment. Secondly, we want to assess the effects of GH on metabolic risk parameters which are typical parameters for the metabolic syndrome in adults. Furthermore, want to map the severity of hypermobility and whether growth hormone therapy affects the degree of hypermobility. We also want to look at the body proportions in children with Kabuki syndrome and / or growth hormone treatment will affect this.

Study design

The study design is a prospective study monitoring the metabolic effects and efficacy of rhGH in Kabuki syndrome subjects. Total body water (TBW), total energy expenditure (TEE), basal metabolic rate (BMR) and physical activity level (PAL) measurements are performed over a 2-wk period using the doubly labeled water (DLW) method before and during GH treatment. Markers of metabolic risk factors will be determined during routine blood controls. Baseline characteristics of growth patterns, body proportions, laxity, blood pressure, BMI and waist circumference are collected every three months during routine controls. Furthermore, the measurements will be linked with the anthropometric parameters of each individual assembling a prognostic growth profile, therefore the children will be followed during one year of treatment to evaluate the change in height standard deviation score (SDS).

Intervention

Growth hormone treatment 1-1.4 mg/m2/day in 1 dd subcutaneous (Genotropin).

Study burden and risks

Growth hormone treatment is licensed for short stature in Turner syndrome (TS) and Prader-Willi Syndrome (PWS) (EMEA), syndromes with the same characteristics as KS. Studies on growth hormone treatment did not reveal any detrimental effects of this therapy so far. Before the start of the study, subjects will be screened for underlying growth pathology according to the Dutch Growth Research Foundation guidelines , including growth hormone test. When enrolled in the study, rhGH treatment will be started. All visits are linked with the routine visit controls accordingly to the guidelines, except the visit before start of GH treatment and the six week visit. Throughout these visits, routine blood controls are used for determining metabolic risk markers, no extra blood controls are used. The total amount of additional blood drawn would be maximum 20 ml. Risks of the doubly labeled water (DLW), Ventilated Hood (VH) method, hyperlaxity evaluation and photometry are negligible. Making a X-rayed left hand for bone age provides a minimal radiation.

Contacts

Public
Medisch Universitair Ziekenhuis Maastricht

P.Debyelaan 25
Maastricht 6229 HX
NL
Scientific
Medisch Universitair Ziekenhuis Maastricht

P.Debyelaan 25
Maastricht 6229 HX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

-Children with the KDM6A orKMT2D (MLL2) mutation.;-Children who meet at least four out of five KS characteristics:;#Facial features: long palpebral fissures with eversion of outer third, arched eyebrows with sparse outer half, prominent and/or misshapen ears, and depressed nasal tip.;#Skeletal abnormalities.;#Intellectual disability (mild to moderate).;#Postnatal short stature.;#Abnormalities of dermal ridges.;-Informed consent.;-Age >= four years.

Exclusion criteria

-Children with a chronological or bone age greater than 8 years for girls and 10 years for boys, because of the influence of puberty.;-Extremely low dietary intake (less than minimal required intake for age according to WHO criteria). ;-Use of medication that might interfere with growth during GH therapy, such as corticosteroids and sex steroids.

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	07-04-2013
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Genotropin
Generic name:	somatropin
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	27-03-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-09-2012
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	24-06-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	19-09-2013
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	26-05-2014
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	28-05-2014
Application type:	Amendment

Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
EudraCT	EUCTR2012-000432-26-NL
ClinicalTrials.gov	NCT3342
CCMO	NL39636.068.12