Assessing the cost-effectiveness of withdrawing growth hormone treatment after mid-puberty in adolescents with idiopathic isolated growth hormone deficiency

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The aim of this study is to assess whether withdrawing GH treatment after mid-puberty in adolescents with idiopathic isolated GH deficiency, who showed a normal result in a GH stimulation test at retesting, is as effective as continuing GH until...

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

Summary

ID

NL-OMON55366

Source
ToetsingOnline

Brief title
Withdrawing growth hormone treatment after mid-puberty

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Growth hormone deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC
Source(s) of monetary or material Support: ZonMw

Intervention

Keyword: Cost-effectiveness, Growth hormone, Puberty, Withdrawal

Outcome measures

Primary outcome

Primary: adult height (AH) minus target height (TH) SDS. Secondary: adult height SDS, total pubertal growth (cm), and satisfaction with attained adult height.

Secondary outcome

Secondary: adult height SDS, total pubertal growth (cm), and satisfaction with attained adult height.

Study description

Background summary

If children who are diagnosed as idiopathic isolated growth hormone deficiency are retested for growth secretion after adult height has been reached, a normal test result is often observed. It appears plausible that if a normal GH secretion is observed in mid-puberty, GH treatment may only have a minor effect on adult height. We hypothesize that withdrawing GH treatment in mid-puberty has no negative effect on attained adult height and on patients' satisfaction with adult height.

Study objective

The aim of this study is to assess whether withdrawing GH treatment after mid-puberty in adolescents with idiopathic isolated GH deficiency, who showed a normal result in a GH stimulation test at retesting, is as effective as continuing GH until adult height.

Study design

Prospective patient preference design with additional historic control group, studied up to adult height. All children with IIGHD will be retested in mid-puberty, according to the current treatment protocol. If GH secretion is normal, patients will be asked if they prefer to continue GH treatment until near-adult height is reached (traditional approach) or discontinue GH treatment. We expect that the preference of each choice will be approximately 50%. It is expected that groups will differ in baseline characteristics (e.g. those who choose discontinuing GH may be older and taller). Because the number of included patients will be too low (and the between-group differences too large) to show statistically significant *non-inferiority* of discontinuing GH at mid-puberty, a retrospective analysis will be performed of growth, pubertal stages and bone age of a historic control group (anonimized) with IIGHD, in whom a normal GH provocation test was found after stopping GH treatment at final height. Based on these data, a model will be constructed of expected height gain on GH treatment as a function of sex, age, bone age, Tanner stage, GH peak in childhood, GH peak at retesting, and GH dosage. For both prospectively followed groups the expected height gain at inclusion will be calculated based on the model. At the end of the observation period, the effectively attained height gain in both groups will be compared with the predicted one. We hypothesize that the difference in attained minus predicted height gain in both groups will not be significantly different from zero, and that the 95% CI will exclude a difference >0.5 SD to the detriment of the group who discontinued GH in mid-puberty.

Intervention

The intervention is withdrawing growth hormone treatment in mid-pubertal adolescents with adequate growth hormone secretion at retesting. At the start of growth hormone treatment growth hormone secretion was insufficient. Patients were retested in mid-puberty and growth hormone secretion appeared normal.

Study burden and risks

The burden is minimal, and approximately 50% of the participants will benefit by stopping daily injections for 2-3 years, less venepunctures and visits to the clinic. A theoretical, but very low risk is that the group who stops GH at mid-puberty may achieve a slightly shorter adult height. Besides a benefit for 50% of participants, there is a substantial benefit for health budget. The average GH dose for a GH deficient adolescent is 1.6 mg/day. The cost of 1 mg GH is ¤ 25. GH treatment costs ¤ 14.600 per year per adolescent. Resource utilization is estimated as ¤ 365 per year per adolescent. If our study shows that GH treatment can be withdrawn 2 years earlier with a similar and equally satisfying adult height, the reduction in costs are substantial (¤ 2.394.400). This study can only be done in this patient group.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)

Inclusion criteria

GH treated adolescents with partial idiopathic isolated GH deficiency (IIGHD)
GH peak at diagnosis >5 mU/L and <30 mU/L
mid-puberty (boys: Tanner stage G3 or G4, testicular volume > 12 ml and bone age 13-16 years; girls: Tanner stage B3 or B4 and bone age 11-14 years)
GH peak of > 20 mU/L at retesting in mid-puberty
GH treatment for at least 3 years
Informed consent

Exclusion criteria

Medical or psychologic disorder, or medication other than GH, that could

potentially influence growth

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	19-04-2017
Enrollment:	128
Type:	Actual

Ethics review

Approved WMO Date:	26-10-2016
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	04-07-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-09-2017
Application type:	Amendment
Review commission:	METC Amsterdam UMC

Approved WMO Date:	08-02-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	07-01-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	12-04-2021
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	13-01-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	27-02-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
CCMO	NL57916.029.16