Influence of exogenous growth hormone administration on circulating levels of Klotho in paediatric patients with isolated growth hormone deficiency.

Published: 12-09-2014
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To assess the impact of treatment with rhGH on circulating Klotho levels in paediatric patients with IGHD.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hypothalamus and pituitary gland disorders
Study type	Observational non invasive

Summary

ID

NL-OMON44245

Source
ToetsingOnline

Brief title
KLOGIC

Condition

- Hypothalamus and pituitary gland disorders

Synonym
Klotho levels in isolated growth hormone deficiency

Research involving
Human

Sponsors and support

Primary sponsor: Vrije Universiteit Medisch Centrum
Source(s) of monetary or material Support: Nederlandse Nierstichting

Intervention

Keyword: Children, Growth hormone, Isolated growth hormone deficiency, Klotho

Outcome measures

Primary outcome

The absolute change in sKlotho levels in serum and urine before and after

treatment with rhGH in paediatric patients with IGHD.

Secondary outcome

not applicable.

Study description

Background summary

The GH - IGF-1 axis is a major controller of cell and tissue growth and development in human. Stimulation of the pituitary gland under the influence of hypothalamic hormones leads to pulsatile output of GH from the pituitary, leading to increased activation of hepatic GH receptors and IGF-1 production. IGF-1 is a key peptide involved in growth and cellular proliferation. GH and IGF-1 also have major effects on kidney growth, structure and function and their overall activities are reduced in patients with CKD.

Klotho is an anti-aging gene and overexpression leads to an extended life span. Klotho deficiency however, as is the case with patients with CKD, is associated with premature aging, progression of renal function loss, development of arterial stiffness, vascular calcification, cardiac hypertrophy, and secondary hyperparathyroidism. Restoring Klotho levels in different CKD mouse-models resulted in an impressive amelioration of the kidney injury. Therefore, upregulation of endogenous Klotho might provide novel treatment strategies not only to preserve remnant kidney function but also to minimize complications of CKD. Recent data show that patients with acromegaly, in which the production of GH and IGF-1 by the anterior pituitary gland is excessive, also have dramatically elevated levels of sKlotho. After transsphenoidal resection of the GH-producing adenoma, these elevated sKlotho levels returned rapidly towards normal. This strongly suggests that GH or IGF-1 are physiological inducers of Klotho. We hypothesize that exogenously delivered GH may induce higher levels of Klotho.

As far as we know, no research is ever done to assess sKlotho levels in paediatric patients with IGHD. In this observational study we will determine the levels of sKlotho and IGF-1 in serum samples from paediatric patients with IGHD before and after treatment with GH.

Study objective

To assess the impact of treatment with rhGH on circulating Klotho levels in paediatric patients with IGHD.

Study design

Open, prospective, multi-center, explorative study.

Study burden and risks

Not applicable.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Children (2-11 years)

Inclusion criteria

- Subjects with newly diagnosed GHD according to the guideline *Guideline for GH treatment in children* with an indication for treatment with rhGH .
- Boys < 9 years old and girls < 8 years old (pre-pubertal).
- No history of rhGH treatment in the last 6 months.
- Providing informed consent by the parents.

Exclusion criteria

- Subjects with a combined pituitary hormone deficiency.
- Patients taking medications or having concomitant illnesses likely to confound endpoint assessments (e.g.use of corticosteroids, androgens or anabole steroids, insulin).
- Patients with hypothyroidism not adequately supplied with thyroid hormone.
- Patients taking other experimental (i.e., non marketed) therapies.
- Patients with any kind of kidney disease.
- Patients with a single kidney.

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-05-2015

Enrollment:	20
Type:	Actual

Ethics review

Approved WMO Date:	12-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	23-09-2015
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	09-11-2016
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	NL48068.029.14