Influence of exogenous growth hormone administration on circulating levels of Klotho in healthy and chronic kidney disease subjects

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To assess the impact of 7 daily subcutaneous gifts of GH on circulating Klotho levels in human sugjects with CKD stage III and healthy age-matched controls.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Nephropathies
Study type	Interventional

Summary

ID

NL-OMON40366

Source
ToetsingOnline

Brief title
Klotho & Growth hormone

Condition

- Nephropathies

Synonym
Chronic kidney disease, renal insufficiency

Research involving
Human

Sponsors and support

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

Intervention

Keyword: Chronic Kidney Disease, Growth Hormone, Klotho

Outcome measures

Primary outcome

1. To demonstrate the absolute change from baseline to day 7 in sKlotho levels

in serum and urine before and after seven daily subcutaneous gifts of rhGH in

patients with CKD stadium III and age-matched healthy controls.

2. To compare the difference in response between subjects with CKD stage III

and age-matched healthy controls after 7 days of subcutaneous injection of rhGH

on sKlotho levels in serum and urine.

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.

Several data suggest that IGF-1 has an important interaction with Klotho expression and circulating Klotho levels. We hypothesize that exogenously delivered GH may induce higher levels of Klotho.

In this study, we want to determine the effect of administration of rhGH on serum levels of Klotho in patients with CKD stage III and compare them with age-matched controls.

Study objective

To assess the impact of 7 daily subcutaneous gifts of GH on circulating Klotho levels in human sugjects with CKD stage III and healthy age-matched controls.

Study design

Open, prospective, single-center, nonrandomized, single-arm, explorative trial.

Intervention

All subjects will be administered subcutaneous injections of Somatropin (= rhGH) of 20 µg/kg/day for 7 subsequent days.

Study burden and risks

The burden and risks associated with participation in this study are:
* 3 extra visits to the VU Medical Center in order to take blood samples and bring first morning spot urine.
* The subject must receive seven times a subcutaneous dose of Somatropin which can give local problems at the injection spot like itching and pain.
* The subject can experience side effects of Somatropin, for example peripheral oedema, headache, joint and muscle complaints.

There are no benefits in participating in this study.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Patients with CKD stage III, control group: patients without CKD.
- Patients * 18 years and < 65 years old.
- Providing informed consent.

Exclusion criteria

- Patients who, in the opinion of the study investigator may present a safety risk.
- Patients who are unlikely to adequately comply with the trial*s procedures (due for instance to medical conditions likely to require an extended interruption or discontinuation, history of substance abuse or non-compliance).
- Patients taking medications or having concomitant illnesses likely to confound endpoint assessments (e.g. growth hormone suppletion, thyroid hormone suppletion, use of estrogens, corticosteroids, androgens or anabole steroids, insulin).
- Patients taking other experimental (i.e., non marketed) therapies within a month before preceding screening.

- Patients with any pituitary disease.
- Women who are pregnant, breastfeeding, intend to become pregnant, or not using or willing to use adequate contraception.
- Unwillingness to comply with reproductive precautions. Women who are capable of becoming pregnant must be willing to comply with approved birth control from two-weeks prior to, and for 60 days after taking the investigational product.
- Known growth hormone deficiency.
- History of any malignancy, or active current malignancy.
- Active intracranial tumours.
- BMI > 30.
- History of respiratory disorders or obstructive sleep apnea syndrome (OSAS).
- Critical illness as defined by the need for respiratory or circulatory support (e.g., in an intensive care unit).
- Patients with thyroidal disease.
- Treatment with immunosuppressive agents.
- Patients with active vasculitis.
- Patients with heart failure or a history of heart failure.
- Severe hepatic disease (defined as serum alanine aminotransferase or aspartate aminotransferase levels greater than three times the upper limit of normal).
- Severe chronic systemic infections or inflammatory disease.
- Uncontrolled hypertension (systolic blood pressure > 180 mmHg and/or diastolic blood pressure > 110 mmHg two times measured).
- Active respiratory infection.
- Patients with diabetes.
- Patients with signs of malnutrition.
- Patients with autosomal dominant polycystic kidney disease (ADPKD).
- Patients with a single kidney.
- Known or suspected allergy to trial product(s) or related products

Study design

Design

Study phase:	2
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:	Recruitment stopped
Start date (anticipated):	28-01-2015
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:	23-09-2014
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	08-01-2015
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	26-06-2015
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
EudraCT	EUCTR2013-003354-24-NL
CCMO	NL45916.029.14