Efficacy of dietary suppletion genestein in patients with the MPS III (A follow-up study)

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The objective of the study is to establish the effect of genestein in patients with MPS III on urinary and serum GAGs levels, hair morphology, GAG accumulation in skinbiopsy, cognitive functions and behavior (Piotrowska et al, 2008). MPS III is a...

Ethical review	Approved WMO
Status	Pending
Health condition type	Inborn errors of metabolism
Study type	Interventional

Summary

ID

NL-OMON35077

Source
ToetsingOnline

Brief title
Follow-up study genestein in MPS III

Condition

- Inborn errors of metabolism

Synonym
MPS III, Sanfilippo

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Stichting Kinderen en Kansen (www.kinderenenkansen.nl)

Intervention

Keyword: Genestein, Lysosomal storage disorder, Nutriceutical, Sanfilippo disease

Outcome measures

Primary outcome

- urinary GAG excretion

Secondary outcome

- serum heparan sulphate levels

- GAG-accumulation in skin biopsies.

- hair morphology

- behaviour

- neurocognitive function

Study description

Background summary

Sanfilippo syndrome (MPS III) is a rare lysosomal storage disorder, characterized by progressive mental and motor deterioration and premature death. MPS III is caused by a deciency in the degradation of heparansulphate (one of the glucosaminoglycans) with subsequent accumulation of heparansulphate. Until now no causal therapy is available.

Genestein is a isoflavone from soy occuring in the natural diet. Genestein is widely used as a food additive (*nutriceutical*). Several potentially beneficial health effects have been attributed to genestein.

In vitro research demonstrated genestein inhibits the synthesis of GAG's, probably through inhibition of an epidermal growth factor. Since accumulation of GAG's (heparansulphate) is a key symptome in Sanfilippo syndrome, dietary supplementation of genestein could potentially have clinically relevant beneficial effects in children with MPS III. In a recent small open-label pilot study in children with MPS III positive results on GAG excretion in the urine, cognitive function measured by questionairs and hairmorphology were demonstrated after oral treatment with genestein.

The positive results of the Polish study gave hope to many parents and in several countries parents already started to give their children genestein, which is available as a dietary supplement, despite of proven efficiency.

In June 2009 a double blind placebo controlled study on the effect of genestein was initiated in the Netherlands. Thirty patients with MPS III type A, B or C are included in this study and receiving either placebo or genestein (10 mg/kg) during two 6 month periods in a cross-over design
results will be expected at the end of this year. Our study will be a follow-up study of previous mentioned study en will examine the efficacy of genestein as nutriceutical in patients with MPS III.

Study objective

The objective of the study is to establish the effect of genestein in patients with MPS III on urinary and serum GAGs levels, hair morphology, GAG accumulation in skinbiopsy, cognitive functions and behavior (Piotrowska et al, 2008). MPS III is a devastating disorder for which until now no treatment is available. Results will be used in the management of patients with MPS III. When genestein proves to be effective it can be used as dietary supplementation in the treatment of MPS III. When genestein has no effect, the use of genestein can be discouraged.

Given that this study is a follow-up study, the effect of genestein, mainly on neurocognitive functioning could be examined over a longer time period.

Study design

Study design is a follow up study of the double-blind randomised controlled trial with cross-over design. This follow-up study is an open-label study. Patients will receive Genestein 10 mg/kg for a period of 12 months.

Intervention

All participating patients will receive genestein capsules (10mg/kg) for a period of 12 months.

Study burden and risks

The effects of genestein on development of breast cancer, prostate cancer, plasma lipid levels ed have been extensively studied. Until now, no short time negative effects have been reported. In the Polish pilot study no adverse events occured. Use of genestein appears to be save. Besides genestein occurs in the natural diet, and infants fed soy-based formulas even ingest 5-9 mg/kg isoflavines a day (Setchell et al 1997). A possible negative effect of genestein is a decreased fertility and this is compared to the symptoms of MPS

III a neglegible risc. The riscs and burden of the study for the patients are relatively small: 2x venapuncture, 1x skinbiopsy, 2x collection urine, 1x assessing hairmorpholgy, 1 x questionairs for patients, and 2x assessment of cognitive function (In subset of patients with developmental age > 1 years). Invasive procedures, including venapuncture, skinbiopsy and hairmorphology at 6 and/or 12 months will only be done when results of placebo controlled trial demonstrate a postive effect of genestein in these patients.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

The patient should have a biochemically confirmed deficiency of heparan-N-Sulphatase (MPS IIIA) or A-N-acetylglucosaminidase (MPS IIIB) or Acetyl CoA: alpha-glucosaminide N-acetyltransefrase (MPS IIIC). All patients who participated in the placebo controlled cross-over trial with genestein are allowed to participate in this study.

Exclusion criteria

The parent/legal reprensentative is unwilling to participate
Patient underwent umbilical cord blood cell transplantation

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-07-2010
Enrollment:	30
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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	NL31974.018.10