Natural course in Dutch patients with Sanfilippo syndome (MPS III)

Published: 27-05-2008
Last updated: 07-05-2024

The first aim of this study is to extend clinical knowledge on Sanfilippo syndrome. This has several important reasons:*Clinical knowledge helps the physician to provide better care to patients diagnosed with this incurable disease and to counsel...

Ethical review	Approved WMO
Status	Pending
Health condition type	Metabolic and nutritional disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON31897

Source
ToetsingOnline

Brief title
Natural course Sanfilippo

Condition

- Metabolic and nutritional disorders congenital

Synonym
MPS III, Mucopolysaccharidosis type III

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Shire,Weeshuis der doopgezinden Haarlem

Intervention

Keyword: Lysosomal storage disorder, mucopolysaccharidoses, Natural course, Sanfilippo

Outcome measures

Primary outcome

Outcome of the study will be an increased knowledge on the natural course of

Sanfilippo syndrome. More knowledge on symptoms and life expectancy.

In addition knowledge on the pattern of GAG excretion in the urine will

increase.

Secondary outcome

Not applicable

Study description

Background summary

Mucopolysaccharidosis III (Sanfilippo syndrome) comprises 4 related inborn errors of lysosomal degradation of the glycosaminoglycan heparan sulphate. The lysosomal enzymes deficient in Sanfilippo syndrome (MPS III) are involved in the breakdown of heparan sulfate. Accumulation of heparan sulfate, an essential component of nerve cell membranes, results in progressive mental deterioration, which is the main symptom of Sanfilippo syndrome.
All types of MPS III are characterized by progressive mental deterioration and behavioral problems with only mild facial dysmorphisms and mild somatic disease.

MPS III disease is a rare debilitating and fatal disorder for which until now only symptomatic treatment is available. Therefore clinical data have only been reported on small numbers of patients and information on the natural course of the disease is limited.
This lack of knowledge on the natural history of the Sanfilippo syndrome is limiting physicians and other health professionals who wish to counsel parents of MPS III children regarding the management of this disorder.
In addition, if and when causal therapy (e.g. intracerebral enzyme replacement

therapy or gene therapy) becomes available, precise knowledge on the natural course of the disorder is essential to study efficacy.

Study objective

The first aim of this study is to extend clinical knowledge on Sanfilippo syndrome. This has several important reasons:
*Clinical knowledge helps the physician to provide better care to patients diagnosed with this incurable disease and to counsel parents and other family members.
*Because Sanfilippo is a heritable disease it is important to obtain the correct diagnosis as early as possible. This can only be achieved if physicians are familiar with the disease and/or if this knowledge is readily available.
*Presently Sanfilippo is still an incurable disease. It is however expected that therapy will be developed in the nearby future. Pre-clinical studies on enzyme replacement and gene therapy have already been initiated. To make it possible to evaluate these therapies in the future the natural course of the disease should be accurately surveyed.

The second aim of the study is expanding knowledge on the biochemical aspects, especially on excretion of GAG*s in Sanfilippo patients. This has several reasons:
*Currently the initial diagnosis of all types of MPS III is based on demonstration of increased concentrations of GAG*s in the urine. GAG excretion is known to vary with age and time. Increased knowledge on the pattern of GAG*s excretion througout the day and in different age groups can indicate the best moment to collect urine in patient with suspection of Sanfilippo syndrome and improve diagnostics.
*The most frequently used assay to demonstrate increased GAG excretion in urine is the DMB test. Urinary excretion of GAGs is only mildly elevated in some Sanfilippo patients and it is suspected that the sensitivity of the DMB test alone in detecting Sanfilippo patients may not be sufficient. We therefore intend to study the accuracy of the DMB-test and, if possible, improve this diagnostic technique.

Study design

In deceased patients:

-Study of medical records
Many of the deceased patients were previously described by Prof.J.J.P. van de Kamp in 1979 and lived in institutions. With permission of the physician of these institutions medical records will be retrieved and studied to gather follow-up data on these patients.

In living patients:

-Parents or Legal representatives will be asked to fill out 5 questionnaires. Patients are once seen in the out patients clinic and will once be visited by a psychologist at home.

Questionaires
-A questionaire on medical history
-The child behaviour checklist to evaluate behaviour
-A questionaire to assess Quality of life in patients with MPS III and parents. Age appropriate and validated Questionaires (TACQOL/TAPQOL) will be used.
-Pediatric Evaluation of Disability Inventory (PEDI): this questionnaire assesses the functional ability of children on three scales: Self Care, Mobility and Social Function.
-A questionaire to evaluate parents opinion on neonatal screening for Sanfilippo syndrome in the future

2. Physical examination

3. Developmental testing including psychological testing
Psychomotor development will be assessed using specific tests, appropriate for different age groups and severity of the mental handicap. These tests will be done in the home environment.

4. Photographs and Film
Of all patients photographs and a short film will be made. Photographs and film will be used to asses dysmorfic features in MPS III.

Biochemical/molecular analyses

5. Urinary glycosaminoglycan analysis
Several (3) urine samples will be collected by collecting bag. 100 mL of urine will be frozen and used for glycosaminoglycan analysis.

6. DNA analysis:
If possible about 2-10 ml EDTA-blood will be collected for DNA isolation. Mutational analysis will be done in the Erasmus MC, Rotterdam.
In those patients, where DNA-analyses was previously done, no blood will be drawn.
If blood is drawn for DNA-analysis, 5 ml blood is drawn in addition. This additional blood sample will be used for glycosaminoglycan analysis.

Study burden and risks

There are no risks associated with participation in the study, except for the risk of a hematoma after drawing blood.

The extend of the burden for the patients participating in the study is relatively low. Patients are once seen in the out patient clinic and a developmental test is done in the home environment.

Blood is only drawn if DNA analysis in not yet done, and urine can be collected and frozen at home.

Contacts

Public
Academisch Medisch Centrum

meibergdreef 9
1105 AZ Amsterdam
Nederland
Scientific
Academisch Medisch Centrum

meibergdreef 9
1105 AZ Amsterdam
Nederland

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-sulfatase

(MPSIIIA) or A-N-acetylglucosaminidase (MPS IIIB).

Exclusion criteria

The parent/legal representative is unwilling to participate or no clinical information is available

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-05-2008
Enrollment:	163
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	NL22296.018.08