Treatment trial with Losartan of a patient with stiff skin syndrome.

Published: 25-07-2011
Last updated: 27-04-2024

1. The effect of Losartan on the joint excursions and the Hardening of the skin in a patient with SSS.2. Gain insight in the pathogenesis of SSS3. Gain insight in the functional effect of Losartan in SSS.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Musculoskeletal and connective tissue disorders congenital
Study type	Interventional

Summary

ID

NL-OMON36060

Source
ToetsingOnline

Brief title
Treatment trial of stiff skin syndrome with Losartan

Condition

- Musculoskeletal and connective tissue disorders congenital

Synonym
congenital scleroderma, stiff skin syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Angiotensin II blockade, Congenital scleroderma, Fibrosis, Losartan, signaling, Stiff skin syndrome, TGF&beta, Treatment

Outcome measures

Primary outcome

1. Improvement of joint excursions.

2. Improvement of the hardening of the skin.

3. Change of fibrosis in the skin.

4. Change of the TGFβ signaling

Secondary outcome

Side effects of Losartan

Study description

Background summary

Stiff skin syndrome (SSS)is a rare disorder. Losartan (Cozaar) is a registered drug with blood pressure lowering properties which is expected to have a therapeutic effect in SSS. In our center only one patient is known with this disorder. She is severely affected. Physiotherapy and ultraviolet radiation therapy did not reduce the joint limitations or skin hardening. Losartan is a widespread used medicine devoid of significant adverse effects. To relieve the complaints of the patient use of Losartan could be tried without severe objections. Recently specific mutations in the fibrillin-1 gene were found in some families with SSS. Fibrillin can interact with TGFβ signaling. It is hypothesized that in SSS TGFβ signaling is increased. Losartan is a TGFβ anatagonist and is believed to suppress the TGFβ activation in SSS. To gain insight in the pathogenesis of SSS and the effect of Losartan, histopathologic and functional investigations of the TGFβ pathway will be performed. Before and after 3 months of treatment the joint excursions and the hardening of the skin will be measured.

Study objective

1. The effect of Losartan on the joint excursions and the Hardening of the skin

in a patient with SSS.
2. Gain insight in the pathogenesis of SSS
3. Gain insight in the functional effect of Losartan in SSS.

Study design

Observational study in which the therapeutical effect of a registered drug (Losartan) will be tested in a patient with SSS. The effect will be measured by goniometric measurement of joint excursions, ultrasound of the skin, histopathologic and functional analysis of the TGFβ-signaling in fibroblasts.

Intervention

Treatment with the maximal tolerated dose till a maximum of 100 mg Losartan during 3 months.

Study burden and risks

The patient will be asked to undergo physical examination, blood pressure, 2 skin biopsies, goniometric measurement of joint excursions and ultrasound of the skin at different sites of the body. The initial dose of 50 mg Losartan per day will be prescribed with a check of bloodpressure and electrolytes, renal and liver function after 2 weeks. if Losartan is well tolerated the maximum dose of 100 mg per day will be prescribed with a check-up after 2 weeks (blood pressure and blood parameters). After 3 months of treatment the above described examinations will be repeated. The risk (adverse side effects) of the treatment is very low. The dose will be modified if side effects occur.

Contacts

Public
Leids Universitair Medisch Centrum

Postbus 9600
2300 RC Leiden
NL
Scientific
Leids Universitair Medisch Centrum

Postbus 9600
2300 RC Leiden
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Clinical diagnosis of stiff skin syndrome.

Exclusion criteria

Pregnancy.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	16-09-2011
Enrollment:	1
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cozaar
Generic name:	Losartan
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	25-07-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	15-08-2011
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2011-002995-17-NL
CCMO	NL35820.058.11