Double-blind randomised placebo-controlled cross-over study to investigate the safety and effectiveness of intrathecal glycine on pain and dystonia in Complex Regional Pain Syndrome type 1.

No registrations found.

Ethical review	Positive opinion
Status	Recruitment stopped
Health condition type	-
Study type	Interventional

Summary

ID

NL-OMON27048

Source
NTR

Brief title
The ITG study (ITG is an abbreviation for intrathecal glycine)

Health condition

Complex Regional Pain Syndrome type 1 (CRPS I)

Sponsors and support

Primary sponsor: Dept. of Neurology, Leiden University Medical Centre
Source(s) of monetary or material Support: Ministry of Economic Affairs

Intervention

Outcome measures

Primary outcome

Primary outcome is the safety of ITG.

Safety evaluations include history taking, physical examination and neurological examination, blood and cerebrospinal fluid assessments and 12-lead electrocardiography (ECG).

Secondary outcome

Secondary outcome is the efficacy of ITG compared to placebo.
- Patients are assessed: 2 weeks before pump implantation, during both treatments at days 1, 8, 15, 22 and 29;
- at days of dose adjustment, assessments are performed first.

These assessments include:
1. Movement disorders assessments:
A. Visual analogue (VAS) dystonia scale:
self-assessed every monday at 9:00, 14:00 and 20:00 from 2 weeks before pump-implantation to the end of the study.
Symptom severity is rated from 0 (absent) to 10 (most severe).
B. Standardised measures are:
- the Fahn-Marsden dystonia rating scale,
- Barry-Albright Dystonia scale,
- unified myoclonus rating scale (sections 2, 3, 4, 5, 7 and 8) and
- tremor research group rating scale are assessed 2 weeks before pump implantation and during both treatments at days 1, 8, 15, 22 and 29.
C. Change of dystonia is rated on a global impression scale. The blinded investigator assesses the change from baseline on a global impression scale at the end of both treatments.
Sensory assessments:
A. VAS pain scale: self-assessment (as VAS dystonia scale).
B. McGill pain questionnaire: assessed every monday from 2 weeks before pump-implantation to the end of the study.
C. Thermal sensory analyzer:
to assess pain and temperature perception thresholds (Medoc Ltd, Israel, model TSA-II, using the method of limits) and is done during both treatments at days 1 and 29.
A thermode is placed on the volar side of the wrists (if involved) and the dorsal side of the feet (if involved).
Activity level:
A. Radboud Skills Questionnaire: in case of involvement of upper extremities.
B. Walking Ability Questionnaire: in case of involvement of lower extremities.

Study description

Background summary

Introduction:

A large proportion of chronic patients with complex regional pain syndrome type 1 (CRPS I) suffer from both neuropathic pain and dystonia.
Findings from neurophysiological and intrathecal baclofen studies highlight an impaired inhibitory neurotransmission.
Since glycinergic neurotransmission plays an important inhibitory role in afferent and motor processing, glycine administration may offer new options for the treatment of both pain and movement disorders in patients with CRPS I.

Aim of the study:

- Primary aim of the study is to evaluate the safety of intrathecal glycine (ITG) in CRPS I patients.

- Secondary aim is to study the effectiveness of ITG treatment during 4 weeks (in an increasing dose schedule).

SUBJECTS:

Subjects will be male or female out-patients, at least 18 years of age, with a clinical diagnosis of CRPS I related dystonia who are referred to the movement disorders out-patients' clinic of the department of Neurology at the Leiden University Medical Centre (LUMC) for intrathecal baclofen treatment.

Methods:

The ITG study is a double-blind randomised placebo-controlled cross-over study.
For future intrathecal baclofen treatment, in all patients a programmable pump for continuous intrathecal administration is implanted.
Study treatment is started at a dosage of 8/21 mL/24 hours and will be weekly increased with 8/21 mL/24 hours.
In case of adverse events, dose will be halved (and if needed repeated) or stopped, depending on the opinion of the investigators.
Safety and efficacy are assessed by means of standardized evaluation.
Patients are assessed 2 weeks before pump implantation and during both treatments at day 1, day 2, day 4, day 8, day 15, day 22 and day 29.

Study objective

A large proportion of chronic patients with complex regional pain syndrome type 1 suffer from both neuropathic pain and dystonia. Findings from neurophysiological and intrathecal baclofen studies highlight an impaired inhibitory neurotransmission. Since glycinergic neurotransmission plays an important inhibitory role in afferent and motor processing, glycine administration may offer new options for the treatment of both pain and movement disorders in patients with CRPS I.

Study design

N/A

Intervention

For future intrathecal baclofen treatment, in all patients a programmable pump for continuous intrathecal administration (SynchroMed® pump, Medtronic, Minneapolis MN, USA, 40 mL reservoir) and a lumbar reservoir for cerebrospinal fluid sampling will be implanted.
Each subject receives two treatments:
1. 2.1% glycine solution during 4 weeks and
2. natrium chloride 0.9% during 4 weeks (placebo).
Study treatment is started at a dosage of 8/21 mL/24 hours (during treatment with glycine 2.1% this corresponds to 8 mg/24 hours) and will be weekly increased with 8/21 mL/24 hours.
There is a tapering and wash-out period after each treatment: tapering in 1 week (3 equal dose decreases with an interval of 48 hours, e.g. monday 22, wednesday 12 and friday 0 mg/24 hours) and wash-out in 1 week.
Treatment is started on mondays.

Contacts

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Eligibility criteria

Inclusion criteria

1. Patients must fulfil the diagnostic criteria of the consensus report of CRPS I:

a. continuing pain, allodynia or hyperalgesia, in which the pain is disproportionate to any inciting event;

b. evidence at some time of edema, changes in skin blood flow or abnormal sudomotor activity in the region of the pain;

c. no condition that would otherwise account for the degree of pain and dysfunction;

2. Patients must suffer from clinically significant tonic or intermittent dystonia in one or more extremities;

3. Patients must have symptoms for at least 1 year.

Exclusion criteria

1. Patients are excluded if they can obtain satisfactory relief of symptoms with conventional treatments;

2. Patients with a history of alcohol or drugs abuse within the past year;

3. Patients with clinically significant psychiatric illness;

4. Pregnant, nursing women and females of childbearing potential not using effective contraception;

5. Patients who are unlikely to comply with study requirements or have a history of poor compliance to medical regimens or study requirements;

6. Patients with an insufficient command and understanding of the Dutch language;

7. Patients involved in legal proceedings (claiming compensation for their CRPS I).

Study design

Design

Study type:	Interventional
Intervention model:	Crossover
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2005
Enrollment:	20
Type:	Actual

Ethics review

Positive opinion

Date:	07-11-2005
Application type:	First submission

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
NTR-new	NL458
NTR-old	NTR499
Other	: P05.108
ISRCTN	ISRCTN75413193

Study results

Summary results
N/A