

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

Submission date 09/01/2006	Recruitment status No longer recruiting	<input type="checkbox"/> Prospectively registered
Registration date 09/01/2006	Overall study status Completed	<input type="checkbox"/> Protocol
Last Edited 18/08/2009	Condition category Musculoskeletal Diseases	<input type="checkbox"/> Statistical analysis plan
		<input checked="" type="checkbox"/> Results
		<input type="checkbox"/> Individual participant data

Plain English summary of protocol
Not provided at time of registration

Contact information

Type(s)
Scientific

Contact name
Dr J.J. Hilten, van

Contact details
Leiden University Medical Center
Department of Neurology
Postzone K-05Q
P.O. Box 9600
Leiden
Netherlands
2300 RC
+31 (0)71 5262134
j.j.van_hilten.neurology@lumc.nl

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

NTR499; P05.108

Study information

Scientific Title

Acronym

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

Study objectives

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.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Received from local medical ethics committee

Study design

Randomised double blind placebo controlled crossover group trial

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Not specified

Study type(s)

Treatment

Participant information sheet

Health condition(s) or problem(s) studied

Complex regional pain syndrome type 1 (CRPS I)

Interventions

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
2. Sodium 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.

Intervention Type

Other

Phase

Not Specified

Primary outcome measure

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 measures

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:
 - 1.1. 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).
 - 1.2. Standardised measures are:
 - 1.2.1. The Fahn-Marsden dystonia rating scale
 - 1.2.2. Barry-Albright Dystonia scale
 - 1.2.3. Unified myoclonus rating scale (sections 2, 3, 4, 5, 7 and 8)
 - 1.2.4. Tremor research group rating scale
- Assessed 2 weeks before pump implantation and during both treatments at days 1, 8, 15, 22 and 29.
- 1.3. 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.
2. Sensory assessments:
 - 2.1. VAS pain scale: self-assessment (as VAS dystonia scale)
 - 2.2. McGill pain questionnaire: assessed every Monday from 2 weeks before pump-implantation to the end of the study
 - 2.3. 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).

3. Activity level:

3.1. Radboud Skills Questionnaire: in case of involvement of upper extremities

3.2. Walking Ability Questionnaire: in case of involvement of lower extremities

Overall study start date

21/11/2005

Completion date

21/11/2007

Eligibility

Key inclusion criteria

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

1.1. Continuing pain, allodynia or hyperalgesia, in which the pain is disproportionate to any inciting event

1.2. Evidence at some time of edema, changes in skin blood flow or abnormal sudomotor activity in the region of the pain

1.3. 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

Participant type(s)

Patient

Age group

Adult

Sex

Both

Target number of participants

20

Key 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)

Date of first enrolment

21/11/2005

Date of final enrolment

21/11/2007

Locations

Countries of recruitment

Netherlands

Study participating centre

Leiden University Medical Center

Leiden

Netherlands

2300 RC

Sponsor information

Organisation

Leiden University Medical Centre (Netherlands)

Sponsor details

Department of Neurology

P.O. Box 9600

Leiden

Netherlands

2300 RC

Sponsor type

Hospital/treatment centre

ROR

<https://ror.org/027bh9e22>

Funder(s)

Funder type

Government

Funder Name

Ministry of Economic Affairs (Netherlands)

Alternative Name(s)

Ministry of Economic Affairs, Netherlands Ministry of Economic Affairs, EZ

Funding Body Type

Government organisation

Funding Body Subtype

National government

Location

Netherlands

Results and Publications

Publication and dissemination plan

Not provided at time of registration

Intention to publish date**Individual participant data (IPD) sharing plan****IPD sharing plan summary**

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article	results	01/11/2009		Yes	No