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# 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

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| **Submission date**<br>09/01/2006 | **Recruitment status**<br>No longer recruiting | [_] Prospectively registered<br>[_] Protocol<br>[_] Statistical analysis plan<br>[X] Results<br>[_] Individual participant data |
| **Registration date**<br>09/01/2006 | **Overall study status**<br>Completed | |
| **Last Edited**<br>18/08/2009 | **Condition category**<br>Musculoskeletal Diseases | |

**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. 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.

## 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 |