Pregabalin in Patients with Central neuropathic pain: A randomized, double-blind, placebo-controlled trial of a flexible-dose regimen.

No registrations found.

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

Summary

ID

NL-OMON26939

Source
NTR

Brief title
N/A

Health condition

central neuropathic pain

Sponsors and support

Primary sponsor: Academic Medical Center, Amsterdam
Department of anesthesiology
Pain Relief Unit
Source(s) of monetary or material Support: None

Intervention

Outcome measures

Primary outcome

The primary efficacy parameter is a pain intensity score recorded by patients (at baseline, and 4 weeks following treatment), using a visual analog scale (VAS).

Secondary outcome

Health status and quality of life (QOL) questionnaires (secondary outcomes) were completed before start of treatment and 4 weeks following start of treatment. Health status and QOL measurements included the Pain Disability Index (PDI), the EQ-5D, and the Medical Outcomes Short-form Health Survey questionnaire 36 (SF36).

Study description

Background summary

Central neuropathic pain (pain associated with lesions of the central nervous system) has been estimated to occur in up to 8% of patients after a stroke, and about 10% to 30% of patients with spinal cord injury are affected during the course of their illness.
(1)The mechanisms underlying central neuropathic pain are not completely understood. A dominating feature of central pain, however, is an abnormal spinothalamic function with altered sensitivity to temperature and pinprick.
(2) Disruption of the spinothalamic pathways may contribute to neuronal hyperexcitability, loss of descending inhibitory control mechanisms in the spinal cord, and alterations in the processing of incoming noxious and non-noxious stimuli resulting in an abnormal pain perception (1, 3). In addition, loss of balance between noxious and non-noxious sensory inputs gives rise to neuronal reorganization in the thalamus contributing to the onward flow of nociceptive information to the postcentral gyrus of the cortex (4). Despite recent advances in identification of peripheral and central sensitization mechanisms related to central nervous system injury, the effective treatment of patients suffering from central pain remains a clinical challenge. Nevertheless the numerous treatment options available (including opioids, anticonvulsants, antidepressant, baclofen, á-adrenergic agonists, and ketamine), some of these patients still experience severe neuropathic pain. In addition, the use of these agents is often limited by significant side effects.

Recently, pregabalin was reported to possess antihyperalgesic and antiallodynic properties in a wide range of animal models, and to be effective in randomized clinical trials of nonmalignant chronic neuropathic pain (including postherpetic neuralgia and diabetic peripheral neuropathy). (5, 6, 7) Additionally, this anticonvulsant has excellent bioavailability and a favorable safety profile with minimal concern for drug interactions and no interference with hepatic enzymes. The exact mechanism of action of pregabalin is unclear. Although structurally related to gamma-aminobutyric acid (GABA), pregabalin is inactive at GABAA and GABAB receptors and it does not alter GABA uptake or degradation. Pregabalin (like gabapentin), however, binds with high affinity to the á2-ä protein (subtype 1 and 2) (situated in various regions of the brain and in the superficial dorsal horn), an auxiliary protein of (presynaptic) voltage-gated N-type calcium channels in stimulated neurons. (7-9) Voltage-

gated calcium channels in the central nervous system provide rapid and fine-tuned modulation of neurotransmitter release by controlling fusion of synaptic vesicles to presynaptic membranes. (10) Their blockade by pregabalin reduces the calcium influx at nerve terminals (preventing synaptic vesicles from fusing) and hence reduces the release of several neurotransmittors including glutamate, norepinephrine, gene-related peptide, and substance P that are particularly relevant for potential neuronal hyperexcitability. (11, 12).

Although recent trials confirm the effectiveness of pregabalin in peripheral neuropathic pain, the role of pregabalin in the treatment of central neuropathic pain remains unknown. Given the absence of other effective pharmacological treatments for central pain, any medication providing some benefits in terms of symptom amelioration and quality of life improvement in patients with neuropathic pain have to be evaluated.

Study objective

We tested, in a randomized, double-blind, placebo-controlled trial, the effects of pregabalin on pain relief, tolerability, health status, and quality of life in patients with central neuropathic pain.

Study design

N/A

Intervention

Pregabalin versus placebo.

Contacts

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Eligibility criteria

Inclusion criteria

1. Age 18 years or older;

2. Written informed consent;

3. Patients suffering from severe neuropathic pain caused by lesion or dysfunction in the central nervous system. Neuropathic pain was described by at least one of the following: burning pain, paroxysmal episodes of shooting pain, or pain on light touch. Additionally, patients had to score above 12 on the Leeds Assessment of Neuropathic Symptoms and Signs questionnaire (LANSS) (13).

Exclusion criteria

1. Pregnant;

2. Had a history of intolerance, hypersensitivity, or known allergy to pregabalin;

3. Had a known history of significant hepatic, renal, or psychiatric disorder;

4. Had a history of galactose-intolerance, lactase deficiency, or glucose-galactose malabsorption syndrome;

5. Subjects with a calculated creatinine clearance rate below 60 mL/m (estimated from serum creatinine using Cockroft-Gault equation) were specifically excluded.

6. No new analgesic therapies were to be initiated at any time during the trial.

7. Patients who had been exposed previously to gabapentin, regardless of dose and treatment duration, were permitted to enter the study. However, treatment with gabapentin was to be discontinued at least 3 days before receiving study medication.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-01-2006
Enrollment:	40
Type:	Actual

Ethics review

Positive opinion

Date:	27-12-2006
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	NL838

Register	ID
NTR-old	NTR852
Other	: N/A
ISRCTN	ISRCTN67414160

Study results

Summary results
N/A