Intra-subject variability in pain scoring and the consequences for analgesia treatment

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Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON44114

Source
ToetsingOnline

Brief title
The VAPAANA Study

Condition

- Other condition
- Muscle disorders
- Peripheral neuropathies

Synonym
Chronic and acute pain, fibromyalgia, obesity, polyneuropathy

Health condition

obesitas

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: alfentanyl, analgesia, fibromyalgia, obesity, pain scores, variability

Outcome measures

Primary outcome

Heat and electrical pain VAS scores

Secondary outcome

Questionnaires for obese patients

QST values

corneal confocal microscopy results

conditioned pain modulation

offset analgesia

temporal summation

Study description

Background summary

Predicting the analgesic effect of pain medication is an important topic in chronic pain research, especially in the field of neuropathic pain. Treating neuropathic pain is based on a trial-and-error principle where the probability of effective treatment is low (about 30% per treatment per patient).1 Both pain responses and efficacy of treatment display a large between-subject but also within-subject variability. This large variability is difficult to explain. In recent years research behavioral tools have been developed that allow (some) prediction of analgesic effect in chronic pain patients. One such tool is quantitative sensory testing.2 With this method sensory profiles are produced

of patients with a certain chronic pain syndrome. Profile characteristics may be used to predict analgesic properties.

In acute pain relief large variability exists in the analgesic properties of pain medication. For example, in post-operative patients variability is present in the amount of opioid dose necessary (up to factor 10 difference) to induce adequate pain relief after surgery in patients with equivalent weights. In experimental studies on acute pain similar effects are observed, where some subject experience profound analgesia after the administration of an analgesic where others experience no to little effect (dosage administered is adjusted to weight).

In a recent study on capsaicine patches (Dahan, data on file) for the treatment of painful diabetic neuropathy many predicting markers were obtained prior to treatment. A finding of major interest in that study was that the amount of pain relief produced by the capsaicine patch could be predicted by the amount of variability of the pre-treatment spontaneous pain scores of the patients. Patients with a high variability in pre-treatment spontaneous pain scores had a high probability to experience pain relief opposed to patients with a low variability in spontaneous pain scores who had a low chance to experience any pain relief.

Furthermore, postoperative analgesia is difficult to establish stably in obesitas patients and it is indicated that these patients are unable to score pain consistantly.
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Study objective

In the current study we want to further explore the predictability of pre-treatment pain variability on the probability to experience pain relief. Knowledge on the understanding of individual differences in analgesic properties of a drug is of importance to individualize pain treatment. Specified individual treatment regimens will eventually lead to more adequate pain relief in patients and an improvement of effect-side effect ratios. We hypothesize that a high variability in pre-treatment experimental pain scores is a predictive marker of pain relief. To this end we will determine variability on experimentally induced heat and electrical pain stimuli to determine its predictive potential for opioid-induced analgesia (i.e. alfentanil). Furthermore, variability tests will be repeated after opioid administration to evaluate the effect of opioids on pain variability.
For obese patients, variability in pain scoring will be established, and furthermore a questionnaire will be filled out to assess variables that might influence the patients' ability to score pain.
Furthermore we will evaluate endogenous pain mechanisms in the obese subjects.

Study design

Protocol outline
The study will be performed using a double-blind, randomized, placebo controlled design. Subjects will be tested on 2 separate occasions with a wash-out period of at least one week. Upon arrival subjects will be familiarized with the heat and electrical pain tests and baseline pain test will be performed to determine the lower and upper boundaries (pain stimulus inducing a score of 0 out of 10 and 10 out of 10 respectively on a visual analogue scale) of the heat and electrical stimuli. These boundaries will be used for the remainder of the study. Next, baseline pain variability will be determined by applying 10 random temperatures and 10 electrical potentials between the pre-defined boundaries as described below.

After baseline pain variability is determined, an intravenous canule will be placed in one of the arms for drug administration. Alfentanil will be administered using target controlled infusion at analgesic plasma concentrations for 120 minutes. The first 30 minutes will be used to induce a stable alfentanil plasma concentration. In the remaining 90 minutes heat and electrical pain variability tests will be re-assessed to determine the effect of alfentanil on pain variability and the analgesic effect of the drug. Using the TCI system alfentanil concentrations will be set at 100 ng/ml, 200 ng/ml in 2 groups of 10 subjects.

For the post-operative patient group subjects will be tested prior to the surgery where only the pain variability tests will be performed (no alfentanil will be administered). 1-2 hours after surgery the pain variability tests will be repeated and the amount of opioid necessary to induce adequate pain relief will be registered for 24 hours post-operative.

Conditioned pain modulation, offset analgesia and temporal summation will be measured in the obese subject group by means of heat pain stimuli and electrical pain stimuli. Endogenous pain modulation will be evaluated this way.

Intervention

Alfentanil. Alfentanil is a μ-opioid receptor agonist used for the treatment of acute pain. Using the TCI system alfentanil concentrations will be set at 100 ng/ml, 200 ng/ml in 2 groups of 10 subjects. Blood samples will be obtained at 20 min intervals to assess the stability of the alfentanil concentration over time.

Study burden and risks

Zie boven

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Healthy subjects of either sex between the age of 18 and 75; ;Patient inclusion criteria: (i) Patients diagnosed with fibromyalgia or peripheral polyneuropathy according to the guidelines of the IASP or other professional pain societies (eg., Netherlands Society of Anesthesiologists); or patients scheduled for elective surgery with post-operative opiate treatment; (ii) a pain score of 5 or higher for chronic pain patients; (iii) age between 18 and 75 years;
Obesity patients: BMI > 35

Exclusion criteria

Medical disease such as pulmonary, renal, liver, cardiac, gastro-intestinal, vascular

disease; allergy to study medication; use of strong opioids; use of benzodiazepines; raised intracranial pressure;(x) pregnancy and/or lactation

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	18-01-2013
Enrollment:	180
Type:	Actual

Ethics review

Approved WMO Date:	15-01-2013
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO Date:	13-03-2013
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO
Date: 17-06-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 21-08-2013

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 17-03-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 28-04-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 06-06-2014

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO
Date: 06-02-2015

Application type: Amendment

Review commission: METC Leiden-Den Haag-Delft (Leiden)

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Approved WMO Date:	24-11-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	23-02-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
CCMO	NL42388.058.12