Shifting pain modulation towards anti-nociceptivity: Mechanism-specific pharmacological prevention of post sternotomy pain

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Peripheral neuropathies
Study type	Interventional

Summary

ID

NL-OMON44134

Source
ToetsingOnline

Brief title
MASTER study

Condition

- Peripheral neuropathies

Synonym
chronic pain; post surgical pain

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: chronic pain, post surgical pain, sternotomy

Outcome measures

Primary outcome

Chronic pain 3 months after surgery

Secondary outcome

1. Acute postoperative pain

2. Chronic pain 1 year after surgery

Study description

Background summary

Postoperative pain and the development of chronic pain is a serious complication of surgical interventions. While the treatment of acute postoperative pain is well organized in current medical practice, the development of chronic pain still has a relatively large incidence. The latter depends on many factors including the type of surgery (a high incidence of postoperative chronic pain is observed following thoracotomies, sternotomies for coronary bypass surgery, mastectomies and inguinal hernia repairs) and specific patient-related factors. These patient-related factors include the state of the endogenous analgesia system, a modulatory and highly plastic system that is involved in modulation of afferent nociceptive input to central sites using top-down inhibitory and facilitatory pathways that inhibit or facilitate pain perception. The preoperative balance between anti- and pronociception may play a crucial role in the development of postoperative chronic pain. For example, it has been shown previously that the ability to engage endogenous inhibitory pathways (as tested by the experimental paradigm of Conditioned Pain Modulation) was associated with a lower risk of development of chronic post-thoractomy pain (odd ratio 0.52). These data suggest that improvement of preoperative nociceptive profile of the patient or pain modulatory profile (PMP), for example by pharmacological intervention to enhance endogenous inhibition or to inhibit facilitation, may reduce the risk of postoperative pain. Routinely there is no preemptive analgesic medication

for patient undergoing thoracotomies at LUMC.

Study objective

In this research project we explore anti-nociception as a state of pain modulation. Our main objectives in utilizing the plasticity of the central pain pathways are to:
(i) Shift individuals from a pro-nociceptive pain modulation profile to an anti-nociceptive profile;
(ii) Explore how this affects their chances of developing chronic pain; and
(iii) Explore whether a pharmacologically induced shift towards an anti-nociceptive state is efficient in the prevention of chronic postoperative pain.

Study design

Randomized, placebo controlled, interventional

Intervention

Maximal 3 weeks before elective surgery patients will be assessed for pain modulation using psychophysical and neurophysiological tests (as defined below; day 1). They will then be impartially randomized to one of three treatment arms: Duloxetine (DLX), Pregabalin (PGB) or placebo (PLC). A second similar assessment session will be held within 2 days before surgery (day 13/14 - 20/21). The last study intake will be on the day of surgery (day 14-21). After surgery, we will record acute pain intensity (in rest and during coughing) and analgesic consumption during the first 3-5 days hours (day 15-20). A two-weekly phone call for chronic post-operative pain and analgesic use will be pursued for 3 months (day 105). One year after surgery there will be a last assessment of pain (via telephone) and the study will end.

Study burden and risks

1. Medication: Lightheadedness/dizziness which will dissipate with a few days;
2. Pain testing: no serious burden is expected.

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

Patients of either sex with American Society of Anesthesiologists score 1, 2 or 3, aged 18 to 75 years planned to undergo elective surgery involving a sternotomy may be enrolled in the study.

Exclusion criteria

1. Pain scores > 3 (on a 11-point numerical rating scale, NRS) reported for most of the day during the past month (including angina);
2. The presence of any chronic pain disorder;
3. Regular use of analgesics for any purpose, including SNRIs, gabapentinoids, COX inhibitors or NSAIDs during the previous month;
4. Use of MAO-inhibitors within the last 14 days;
5. The presence of narrow-angle glaucoma;
6. Inability to perform psychophysical testing (eg. in case of cognitive or psychiatric disorders);
7. Patients suffering from cognitive dysfunction;
8. Patients being treated for depression, or any other mood disorder;
9. Inability to give informed consent;
10. Inability to communicate with the investigators;

11. Known allergies to the study medication:
12. Uncontrolled hypertension (diastolic blood pressure > 100 mmHg).

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	20-11-2015
Enrollment:	300
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Cymbalta
Generic name:	duloxetine
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lyrica
Generic name:	Pregabaline
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	02-02-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	20-05-2015
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	27-10-2015
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	23-03-2016
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	05-10-2016
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
EudraCT	EUCTR2014-005701-20-NL
CCMO	NL52049.058.14

Study results

Date completed: 12-09-2018

Actual enrolment: 75

Summary results
Trial ended prematurely