Pilot study: Targeting the inflammatory response and the induction of acute pain after breast cancer surgery with perioperative infusion of lidocaine

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We want to answer the following research questions using a peri-operative infusion of lidocaine (PIL) protocol:1. Does low dose peri-operative intravenously administered lidocaine attenuate systemic inflammatory response measured by plasma cytokine...

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

Summary

ID

NL-OMON39927

Source
ToetsingOnline

Brief title
PIL

Condition

- Other condition
- Breast therapeutic procedures

Synonym
Inflammation and pain

Health condition

Pijngeneeskunde

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Breast Cancer, Lidocaine, Pain, Surgery

Outcome measures

Primary outcome

- Cytokine and ICAM1 plasma levels pre operatively and 4 hours post operative

Secondary outcome

- NRS score pre operatively and 0 and 4 hours postoperativly

Study description

Background summary

The proposed study addresses an increasing problem in breast cancer treatment: Pain. Surgery leads to an acute phase response which is characterized by nociceptive pain and inflammation. Normally there is a recovery of pain and inflammation and healing occurs. Some patients however, develop excessive generation of inflammatory response which can lead to hyperalgesia and eventually to chronic or neuropathic pain. Surgically treated breast cancer patients have one of the highest incidences of chronic pain (20-68%). Main contributors to development of chronic pain are severity of postoperative pain and axillary lymph node dissection (ALND). Mechanisms attributable to the decline of acute and chronic pain by administering lidocaine intravenously are thought to be a reduction in discharge of A-delta and C-fibers and a reduction of misbalance in inflammatory reaction after tissue damage. Lidocaine is a widely used local anesthetic, known to block sodium channels mostly in acute pain conditions. However there are indications that intravenous lidocaine also is effective in the treatment of acute and chronic pain states in low, non toxic doses We hypothesize that intravenous lidocaine is not only a potential inhibitor of acute pain, but also acts as an anti-inflammatory agent and potentially even anti-metastasis in clinically pursuable dosages of

intravenously administered lidocaine Perioperative lidocaine infusion therefore seems to be an extremely interesting, safe and low cost therapeutic option in treatment of postoperative pain in breast cancer surgery. Furthermore we hypothesize that by attenuation of postoperative inflammation a reduction in postoperative pain and in the development of chronic pain and central hyperalgesia can be achieved.

Study objective

We want to answer the following research questions using a peri-operative infusion of lidocaine (PIL) protocol:
1. Does low dose peri-operative intravenously administered lidocaine attenuate systemic inflammatory response measured by plasma cytokine levels of interleukin (IL)-6, IL-8, IL-1beta and IL-1 receptor antagonist (IL-1RA)?
2. Does low dose peri-operative intravenously administered lidocaine attenuate levels of plasma ICAM-1 after breast surgery?
3. Does low dose peri-operative intravenously administered lidocaine reduce postoperative pain after breast cancer surgery?

Study design

The study is designed as a single centre double blind randomized controlled clinical trial.
Patients will be included at the pre operative outpatient clinical ward by anesthesiologists and physician assistants envolved with the research
Patients will supply informed consent before inclusion into the study.
Patients will allow 2 separate blood samples to be drawn.
Patients will use the NRS rating scale to quantify their acute post operative pain.

Intervention

The NRS rating scale will be used to assess severity of acute postoperative pain at 0 and 4 hours postoperatively.

Cytokine and ICAM-1 analysis
Blood will be collected from patients pre- and post-operatively (4 hours) and will be centrifugated and saved at -80 degrees celcius for cytokine determination. A Luminex® assay will be used to determine plasma cytokine levels of IL-6, IL-8, Il-1beta and IL-1RA (Milliplex, Millipore, Billerica, MA). ICAM-1 concentrations will be determined by enzyme-linked immunosorbent assay (ELISA).

Anesthesia will be standardized with propofol and sufentanil.
Additional to above regiment patients included in the treatment arm of the study will receive:

- During induction of anesthesia patients will receive 1,5mg/kg intravenous lidocaine
- After induction of anesthesia patients will receive 2mg/kg/hr intravenous lidocaine until 1 hour after the operation has ended. This will be in the recovery ward where adequate haemodynamic monitoring is available. Lidocaine concentration used in the study will be Lidocaine 1%

Patients who are not included in the treatment arm of the study will receive intravenous saline instead of lidocaine in the same timeframe and dosage (amount of ml received)

Study burden and risks

The use of lidocaine in this practical research has been proven to be associated with a low incidence of adverse events. The patients will have to
The patient will have to give a NRS score at 0 and 4 hours after surgery.
The patient will have 1 venous blood sample taken 4 hours after surgery.

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

Women undergoing primary breast cancer surgery
Women undergoing breast cancer surgery without axillary lymph node dissection
Women > 18 years old

Exclusion criteria

Allergy to amide type of local anesthetics
Recent myocardial ischemia (<6 months)
Renal or liver failure
Hypokaliemie
Chronic opioïd use
History of chronic pain
Corticosteroid use
No written informed consent by patient

Study design

Design

Study phase:	4
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):	05-11-2014
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lidocaine
Generic name:	Lidocaine
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO Date:	01-08-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	15-11-2013
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	19-05-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-07-2015
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	01-06-2016
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	16-08-2016

Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	17-04-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	EUCTR2012-002222-70-NL
CCMO	NL40729.091.13

Study results