Median Local Anaesthetic Dose (MLAD) of intrathecal Bupivacaine in primary total knee arthroplasty

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The objective of this study is to find the Median Local Anaesthetic Dose (MLAD/ED50) of Bupivacaine that allow direct postoperative mobilization and will accommodate sufficient anaesthesia during surgery.Results of this study might lead to...

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

Summary

ID

NL-OMON43405

Source
ToetsingOnline

Brief title
ED50 of intrathecal Bupivacaine in total knee arthroplasty

Condition

- Joint disorders

Synonym
Anaesthesia

Research involving
Human

Sponsors and support

Primary sponsor: Reinier de Graaf Groep
Source(s) of monetary or material Support: Vakgroep orthopedie RdGG

Intervention

Keyword: Intrathecal anaesthesia, Median effective dose, Total knee arthroplasty

Outcome measures

Primary outcome

MLAD/ED50 of Bupivacaine at t=116 minutes

Secondary outcome

Not applicable.

Study description

Background summary

Total knee arthroplasty (TKA) has become a common elective orthopaedic surgical procedure. The perioperative management has been developed in order to improve the outcomes of TKA. As a result fast-track protocols have evolved as a multimodal procedure to achieve faster rehabilitation and reduction of complications. In fast-track TKA, spinal anaesthesia with Bupivacaine is preferred over general anaesthesia due to less nausea and vomiting.
Mean surgery time for TKA at the RdGG is 71 minutes, in another study of Lozano et al. a mean surgery time of 83 minutes was found. Provided that administration of 8 mg of Bupivacaine intrathecal at level L3-L4 will lead to a motor block of 100-225 minutes according to Gautier et al. it might be possible to reduce the amount of Bupivacaine used during surgery in order to optimize rehabilitation after TKA.
Current dosage of thecal Bupivacaine are adequate for allowing surgery with total anaesthesia, however this does not provide optimization for direct postoperative mobilisation and often leave patients unable to mobilize for several hours postoperative prolonging a patients hospital stay.

Study objective

The objective of this study is to find the Median Local Anaesthetic Dose (MLAD/ED50) of Bupivacaine that allow direct postoperative mobilization and will accommodate sufficient anaesthesia during surgery.
Results of this study might lead to justification of lower doses of Bupivacaine used for anaesthesia in TKA. Henceforth, the fast-track program can be optimized and rehabilitation can start immediate postoperative.

Study design

This is an intervention study designed to find the MLAD/ED50 of Bupivacaine at a certain threshold.
In this study we used the Up-and-Down method as described by Dixon and Massey. This is a sequential allocation model where patients receive a dose of Bupivacaine according to the outcome of the preceding patient. With the Up-and-Down method we approach the MLAD/ED50 from above, leaving less patients with inadequate anaesthesia. For the cut-off point or threshold point needed in this model we use the 95th percentile of the mean surgery time for TKA, in order to expose less patients to inadequate anaesthesia during surgery.
At the cut-off point patients must be able to fully recover from sensory and motor blockage induced by Bupivacaine. Therefore, at the cut-off point (116 minutes after spinal anaesthesia is administrated) patients must reach:
- Full recovery of the motor block; measured with the modified Bromage scale (Bromage 0)
- Full recovery of sensory block; positive pinprick test at the S1 and L5 dermatome

Possible test outcome:
1. Patient reach the cut-off parameters before 116 minutes -> inadequate Bupivacaine dose
2. Patient reach the cut-off parameters after 116 minutes -> adequate Bupivacaine dose
If a patient is documented with inadequate anaesthesia (possible outcome 1) the succeeding patient receives a dose of Bupivacaine Xy+0.5 mg
If a patient is documented with adequate anaesthesia (possible outcome 2) the succeeding patient receives a dose of Bupivacaine Xy-0.5 mg

During surgery sensory block height is assessed using a pinprick test. The patient is asked to score pain on the NRS for pain. Testing will be performed in 10 minute intervals starting from the injection of Bupivacaine.
After surgery sensory block recovery is assessed using a pinprick test at dermatome L5 and S1. Supplementary, recovery from motor block is assessed by the modified Bromage scale. After surgery the testing will be performed in 10 minute intervals until the cut-off parameters are reached.

Intervention

The patients will undergo surgery according to the TKA protocol. The intervention targets the spinal anaesthesia protocol. The current protocol imposes a dose of 6 mg Bupivacaine administrated intrathecal at the L3-L4 intervertebral space. In this study we lower the dose for the succeeding patient according to the outcome of the preceding patient.
The patient will undergo testing and monitoring in 10 minute intervals starting

from the start of injection until it is recovered from the nerve blockade.

Study burden and risks

Patients will receive their scheduled TKA according to the regular planned fast track surgery programme. The Up-and-Down sequential allocation technique, rather than random allocation, is chosen due to the ease which it estimates the mean of a sample. By starting from known effective concentration and approaching the ED50 from above the number of patients subjected to potentially inadequate analgesia is minimized.

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

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
- ASA I, II or III
- 18 years or older
- Primary TKA
- Willing to participate
- Sufficient command of Dutch language

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Hypersensitivity to local anaesthetics or any of the other excipients of Bupivacaine
- Any other contraindications relate to intrathecal anaesthesia
- CNS disease, e.g. meningitis, tumor, poliomyelitis, cerebral haemorrhage
- Spinal stenosis and diseases or recent trauma to the cervical column
- Sepsis
- Pernicious anaemia with symptoms related to cervical degradation
- Pyogenic infections of the skin close to the injection site
- Cardiogenic or hypovolemic shock
- Disturbance in coagulation or treatment with anti-coagulants
- Patient is participating in a medicinal study
- Noncompliant to intrathecal anaesthesia
- No Local Infiltration Anaesthesia (LIA) possible
- Patients who are incompetent to decide

Study design

Design

Study phase:	4
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	14-04-2016
Enrollment:	25
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Marcaine 5mg/ml spinaal
Generic name:	Bupivacaïnehydrochloride
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	15-02-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
	metc-ldd@lumc.nl

Approved WMO

Date:	11-03-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden)
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Approved WMO

Date:	16-12-2016
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	EUCTR2016-000082-23-NL
CCMO	NL56547.098.16