ISRCTN14865526 https://doi.org/10.1186/ISRCTN14865526

Epidural blockade affects the pharmacokinetics of propofol in surgical patients

Submission date
16/01/2014

Recruitment status
No longer recruiting

Registration date
30/01/2014

Overall study status
Completed

Last Edited
30/01/2014

Condition category
Surgery

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
It still remains unclear why an epidural or spinal analgesia (an injection given into the back that numbs the lower half of the body and stops any pain being felt) reduces the need for sedatives. The study aims to find the relationship between epidural analgesia and reduction in the need for sedatives.

Who can participate?
You can participate in the study if you are between 18 and 65 years old, are relatively healthy and are scheduled for surgery under epidural analgesia and sedation or anaesthesia.

What does the study involve?
Participants were randomly allocated to one of four groups. One group received dummy medication, and the other three groups received three different doses of ropivacaine in the epidural space (an area of the spinal column). Everybody received the same dosage of propofol sedation to induce a certain level of sleep.

What are the possible benefits and risks of participating?
There are no benefits in participating. The study requires an extra line in the arm and could result in bruises. The study would take up 150 minutes of the participants time before the scheduled operation.

Where is the study run from?
Leiden University Medical Center, Netherlands.

When is the study starting and how long is it expected to run for?
The study started in December 2010 and completed in February 2012.

Who is funding the study?
Leiden University Medical Center, Department of Anesthesiology, Netherlands.

Who is the main contact?
M.E. Sitsen, MD, mesitsen@lumc.nl

J Vuyk, MD, PhD, J.Vuyk@lumc.nl
A.Dahan, MD, PhD, a.dahan@lumc.nl

Contact information

Type(s)
Scientific

Contact name
Mrs Elske Sitsen

Contact details
Albinusdreef 2
Leiden
Netherlands
2333 ZA
+31 715 262301
mesitsen@lumc.nl

Additional identifiers

Clinical Trials Information System (CTIS)
2010-020050-34

Study information

Scientific Title
The influence of epidural blockade with ropivacaine on the pharmacokinetics and pharmacodynamics of propofol sedation in patients

Study objectives
We hypothesized that epidural blockade would affect the pharmacokinetics of propofol and that altered hemodynamics may be involved. We therefore studied the influence of epidural blockade on the pharmacokinetics of propofol in a double-blind randomized manner.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Medical Ethics Committee, Leiden University Medical Center, 28/07/2010, ref.: T10.087.NL32295.058.10

Study design
Randomized double-blind placebo-controlled study design, single centre

Primary study design
Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied
The effect of epidural analgesia with ropivacaine on the pharmacokinetics and pharmacodynamics of propofol in patients

Interventions
28 patients were randomly assigned to one of four study groups.

After written informed consent the patients received an intravenous cannula, a lumbar epidural catheter at L2-L3, placed 5 cm in the epidural space after skin infiltration with lidocaine, and an intra-arterial canulla in the radial artery for hemodynamic monitoring and blood sampling. The patient is then attached to the standard peri-operative anaesthetic monitoring. This includes a 3-lead ECG, blood pressure monitoring, pulse oximetry (SaO2), and cerebral activity registration through BIS monitoring. The cardiac output was monitored noninvasively.

The patients in group 1 received no ropivacaine (10 ml of epidural NaCl 0.9%), the patients in group 2 received 50 mg of epidural ropivacaine 7.5 mg/ml, the patients in group 3 received 100 mg of epidural ropivacaine 7.5 mg/ml and the patients in group 4 received 150 mg of ropivacaine 7.5 mg/ml. During the 30 minutes after the medication was given data were gathered; it took 30-40 minutes to achieve a steady block level. Thereafter patients received a target controlled infusion with propofol with an initial target concentration of 1 µg/ml. After 6, 12 and 18 min this target propofol concentration was increased to 2.5 µg/ml, 4 µg/ml and 6 µg/ml. Twenty-four min after the start of the propofol administration the administration was terminated. After waking up, depending on the time available before scheduled surgery, the patient was monitored and samples were taken until 90-120 min after termination of the propofol sedation.

The study was ended and the epidural catheter was used to administer ropivacaine at a dose sufficient for surgery. Patients were then continued for the scheduled surgical procedure.

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
Ropivacaine, propofol

Primary outcome(s)
To evaluate the influence of epidural blockade with ropivacaine on the pharmacokinetics of propofol.

Assessments of the epidural blockade level will be performed every 5 min during the first 30 min until a stable level of analgesia is established. A stable level is defined as an unchanged upper blockade level during two consecutive assessments. The level of sensory loss is determined by loss of cold sensation bilateral in the anterior axillary line and by the pin prick test. Motor function loss is tested using the Bromage scale.

Every 3rd min, the Ramsay sedation score, the eyelash reflex, the BIS score and state of consciousness will be tested and an arterial blood sample will be taken for blood propofol

concentration determination. The state of consciousness is tested by asking the patient to perform a simple task after gently tapping at the shoulder ('open your eyes please'). Unconsciousness will be defined as no response to this command.

Samples (5 ml) for the determination of the plasma propofol concentrations will be taken 3, 6, 9, 12, 15 and 18 min after the start of the target controlled propofol infusion and 2, 5, 10, 20, 30, 60, 90 and 120 min after termination of the propofol infusion. Samples for the ropivacaine concentration will be taken 5, 10, 15, 30, 60, 90 and 120 minutes after the epidural loading dose.

Key secondary outcome(s))
To evaluate the influence of epidural blockade with ropivacaine on the pharmacodynamics of propofol. This includes both the sedative and the hemodynamic effects.

Completion date
03/02/2012

Eligibility

Key inclusion criteria
1. American Society of Anesthesiologists (ASA) class I-II
2. Age 18-65 years
3. Patients scheduled for surgery requiring epidural anaesthesia and sedation

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Upper age limit
65 years

Sex
All

Key exclusion criteria
1. Patients with a body mass index (BMI) >30
2. Participation in a trial on investigational drugs within 3 months prior to the study
3. Known history of hepatic, renal disease or other disease as judged by the investigators
4. Bleeding or coagulation disorders
5. Patients receiving chronic analgesic therapy
6. Patients using alpha-blockers
7. Pregnancy or lactation
8. Alcohol or drug abuse or history of alcohol/drug abuse

9. Documented or suspected soybean protein and/or drug allergy
10. Allergy for amide-type local anesthetics

Date of first enrolment
13/12/2010

Date of final enrolment
03/02/2012

Locations

Countries of recruitment
Netherlands

Study participating centre
Albinusdreef 2
Leiden
Netherlands
2333 ZA

Sponsor information

Organisation
Leiden University Medical Center (Netherlands)

ROR
https://ror.org/05xvt9f17

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Leiden University Medical Center, Department of Anesthesiology (Netherlands)

Results and Publications

Individual participant data (IPD) sharing plan

IPD sharing plan summary

Not provided at time of registration