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Effective analgesia in patients after knee surgery

Submission date
20/11/2017

Recruitment status
No longer recruiting

Registration date
22/11/2017

Overall study status
Completed

Last Edited
21/11/2017

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
In the majority of invasive surgical procedures, such as total knee replacement, pain and surgical stress cause profound pro-inflammatory response often followed by down-regulation of immune response. Therefore, it is mandatory to perform the most effective analgesia in order to maintain effective analgesia and immune balance. The aim of this study is to analyze the impact of epidural analgesia, peripheral nerve blockade and multimodal systemic analgesia on acute stess response in patients after total knee replacement (TKR).

Who can participate?
Adults over the age of 50 who will underwent elective surgery for primary degenerative osteoarthritis scheduled at Clinic of Orthopedics and Traumatology Lovran, Lovran, Croatia for total knee replacement.

What does the study involve?
Participants undergo their surgical procedure for their total knee replacement. Participants are randomly allocated to one of three groups which dictates the type of postoperative analgesia (pain relief). Those in the first group receive an epidural analgesia (an injection that stops pain in a certain part). Those in the second group receive a peripheral nerve blockade of sciatic and femoral nerve (an injection that stop signals along a nerve to stop pain) and those in the third group receive the multimodal systemic analgesia (two or more analgesic agents). Participants are followed up for their pain levels.

What are the possible benefits and risks of participating?
There is a benefit for the present and future patients because the results of the study will provide the answers which type of analgesia is more effective for those patients. There are no direct risks with participating.

Where is the study run from?
The study is being run by researches at Clinic of Orthopedics and Traumatology Lovran (Croatia) and Univeristy of Rijeka, Facutly of Medicine (Croatia)

When is the study starting and how long is it expected to run for?
June 2015 to December 2017

Who is funding the study?
1. Clinic of Orthopedics and Traumatology Lovran (Croatia)
2. University of Rijeka (Croatia)

Who is the main contact?
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Contact information

Type(s)
Scientific

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
13.06.1.1.12

Study information

Scientific Title
The impact of different techniques of analgesia on stress response in patients after total knee replacement

Study objectives
Regional analgesia could better reduce the levels of stress mediator than multimodal systemic analgesia, thus improving patients recovery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Clinic for Orthopedics and Traumatology Lovran, Lovran, Croatia and Faculty of Medicine, University of Rijeka, ref: 317/2015

Study design
Prospective randomised observational single centre

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Health condition(s) or problem(s) studied
Total knee replacement and pain

Interventions
Application of different type of postoperative analgesia (lubar epidraul analgesia, peripheral nerve blocks, and systemic multimodal analgesia) in patients after total knee replacement

Participants who are admitted to the Clinic of Orthopaedics and Traumatology Lovran are included in this prospective, randomised study. Participants are randomly allocated using by Datlnf Ranolist computer program (Datlnf GmbH, Tubingen, Germany) to one of three groups according to the type of postoperative analgesia received.

For all patients included in the study the same anesthesia procedure will be applied. Twelve hours before surgery 3800 IU of dalteparin (Fraxiparine, Aspen Pharma Tradding Limited, France) is given subcutaneously and 10 mg diazapam (Roche, Basel, Switzerland) orally. The same surgeon performs all operations and the same anesthesiologist perform all anesthesia. All participants undergo regional lumbar spinal anesthesia.

Postoperative pain ismanaged applying epidural analgesia (Group 1), peripheral nerve blockade of sciatic and femoral nerve (Group 2) or multimodal systemic analgesia (Group 3). In patients of Group 1 the epidural catheter are applied immediately after surgery with 18 gauge Tuohy epidural needle (Espocan ®, B.Braun, Melsungen AG, Germany) through loss-of resistance technique with air between L3-L4 lumbar vertebra. The mixture of 0.25% levobupivacaine (Chirocaine 0.5%, Abb Vie S.r.l. Campoverde Di Aprilia, Italy) and 0.5 mcg/mL sufentanyl

(Sufentanil Renaudin, France) (2-15 mL/hour depending on patients VAS score) is applied. After 24 hours intermittent epidural boluses of 10 mL of 0.25% levobupivacaine every 4 to 6 hours depending of patients VAS scores are applied.
The catheter is removed on the third postoperative day. In Group 2 peripheral nerve blockade of sciatic and femoral nerve on the operated leg are used to manage the pain in these patients. The blocks are performed using ultrasound guided technique “in plane” technique for displaying the needle on ultrasound machine (Sonosite EDGE Ultrasound system, SonoSite, Inc., SAD). The 0.25% levobupivacaine are applied near the nerves. In Group 3 multimodal systemic analgesia are used to manage the postoperative pain. On the beginning of surgery wound closure, intravenous application of paracetamol (Paracetamol Kabi, Fresenius Kabi, Friedberg, Germany) starts, and continue by intravenous application of 1 g paracetamol every 6 hours, 200 mg tramadol every 10 to 12 hours (Tramal, Grunenthal Gmbh, Aachen, Germany) and 2.5 g metamizolsodium (Alkagin, Alkaloid-Int d.o.o., Ljubljana, Slovenia).

Twenty milliliters of blood is sampled from each patient included in the study are obtained to isolate peripheral blood monoculear cells and plasma. Isolated mononulear cells ware labeled with the combination of different antibodies (mouse anti human CD3, CD4, CD8, CD56). Labeled samples are analysed by flow cytometer (FACS Calibur, Becton Dickinson & Co, USA). In plasma concentration of catecholamines, cortisol and cytokines (interleukin-1 beta, interleukin-6 and tumor necrosis factor alpha) are detected by ELISA (enzyme-linked immunosorbent assay).

The following data are recorded: gender, age, duration of the operation, duration of anesthesia, duration of hospitalisation. The subjective perception of intensity of pain for each patient is recorded using a 10 cm Visual Analogue Scale (VAS) with end points labeled "no-pain“ and "the worst possible pain“ before surgery (T1), after surgery (T2), 24 hours (T3) and 72 hours (T4) after surgery at rest and on movement.

Intervention Type
Other

Primary outcome measure
1. Pain intensity is measured using the VAS at rest and on movement before surgery,after surgery, 24 hours and 72 hours after surgery
2. Absolute number of leukocytes is measured using electronic counter Technicom H-1 system, USA, using laser's optical principle of dark colors
3. Frequency of different types of lymphocytes is measured using the flow cytometry before surgery,after surgery, 24 hours and 72 hours after surgery
4. Concentration of cytokines and hormones are measured using ELISA before surgery, after surgery, 24 hours and 72 hours after surgery

Secondary outcome measures
1. Patient outcome is measured using hospital electronic documentation system at before surgery, after surgery, 24 hours and 72 hours after surgery
2. Complications is measured using hospital electronic documentation system at before surgery, after surgery, 24 hours and 72 hours after surgery

Overall study start date
15/06/2015

Completion date
01/12/2017

Eligibility

Key inclusion criteria
1. Patients who underwent elective surgery for primary degenerative osteoarthritis scheduled at Clinic of Orthopedics and Traumatology Lovran, Lovran, Croatia for total knee replacement (TKR), American Society of Anesthesiologists (ASA) physical status I to III
2. Fully able to understand the study contents were included in the study
3. Adults over 50

Participant type(s)
Patient

Age group
Adult

Sex
Both

Target number of participants
Forty patients in each group (3 groups)

Key exclusion criteria
1. Patients with allergies to anesthetics and analgesics
2. Received blood transfusion
3. Those with neurologic conditions of the lower limbs
4. Immune disorders
5. Malignant disease
6. Secondary form of knee osteoarthritis or rheumatoid arthritis

Date of first enrolment
15/10/2015

Date of final enrolment
01/06/2017

Locations

Countries of recruitment
Croatia

Study participating centre
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Sponsor information

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Sponsor type
Hospital/treatment centre

Funder(s)

Funder type
Hospital/treatment centre

Funder Name
Clinic for Orthopaedics and Traumatology Lovran

Results and Publications

Publication and dissemination plan
The results of the study are going to be submitted for publication in 01/12/2017.

Intention to publish date
01/12/2017

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are/will be available upon request from Sandra Velcic Brumnjak (elvel1@yahoo.com).

IPD sharing plan summary
Available on request