

Effective analgesia in patients after knee surgery

Submission date	Recruitment status	<input type="checkbox"/> Prospectively registered
20/11/2017	No longer recruiting	<input type="checkbox"/> Protocol
Registration date	Overall study status	<input type="checkbox"/> Statistical analysis plan
22/11/2017	Completed	<input type="checkbox"/> Results
Last Edited	Condition category	<input type="checkbox"/> Individual participant data
21/11/2017	Surgery	<input type="checkbox"/> 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 stress response in patients after total knee replacement (TKR).

Who can participate?

Adults over the age of 50 who will undergo 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 researchers at Clinic of Orthopedics and Traumatology Lovran (Croatia) and University of Rijeka, Faculty 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

Contact name

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Additional identifiers

Protocol serial number

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)

Study design

Prospective randomised observational single centre

Primary study design

Observational

Study type(s)

Treatment

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 diazepam (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 mononuclear cells and plasma. Isolated mononuclear cells were 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(s)

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

Key secondary outcome(s)

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

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

Healthy volunteers allowed

No

Age group

Adult

Sex

All

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

Clinic for Orthopedics and Traumatology Lovran

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51415

Sponsor information

Organisation

Clinic for Orthopaedics and Traumatology Lovran

Funder(s)

Funder type

Hospital/treatment centre

Funder Name

Results and Publications

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

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
<u>Participant information sheet</u>	Participant information sheet	11/11/2025	11/11/2025	No	Yes