

# Effective analgesia in patients after knee surgery

<b>Submission date</b> 20/11/2017	<b>Recruitment status</b> No longer recruiting	<input type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
<b>Registration date</b> 22/11/2017	<b>Overall study status</b> Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
<b>Last Edited</b> 21/11/2017	<b>Condition category</b> Surgery	<input type="checkbox"/> Individual participant data <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 stops 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?

1. Sandra velcic Brumnjak, MD  
elvel1@yahoo.com
2. Vlatka Sotosek Tokmadzic  
vlatkast@medri.uniri.hr

## Contact information

### Type(s)

Scientific

### Contact name

Dr Sandra Velcic Brumnjak

### Contact details

Clinic for Orthopaedics and Traumatology Lovran  
Šetalište maršala Tita 1  
Lovran  
Croatia  
51415  
+385 915 023 262  
elvel1@yahoo.com

## 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)

Clinic for Orthopedics and Traumatology Lovran, Lovran, Croatia and Faculty of Medicine, University of Rijeka, ref: 317/2015

## **Primary study design**

Observational

## **Study design**

Prospective randomised observational single centre

## **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 DatInf Ranolist computer program (DatInf GmbH, Tübingen, 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 Trading 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 is managed 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

Šetalište maršala Tita 1

Lovran

Croatia

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