NCT02848599

ID: 25-1:6563-3/2014

The Influence of Postoperative Analgesia on Systemic Inflammatory Response and POCD After Femoral Fractures Surgery

Document Date: May 26, 2017

The study was approved by the University Hospital Osijek Ethics Committee (Approval number 25-1:6563-3/2014, 19.5.2014.) and written informed consent was obtained from all subjects. The study design was a prospective, randomized, controlled trial. All patients received spinal anesthesia and one of two techniques of postoperative analgesia: intravenous patient-controlled analgesia (PCA) with morphine or patient-controlled epidural analgesia (PCEA) with 0.125% levobupivacaine. According to technique of postoperative analgesia which was applied, patients were allocated into two groups, the morphine group and the levobupivacaine group. Randomization was done before surgery by pulling out the envelope in which it was written the group division. Inclusion criteria were age ≥ 65, American Society of Anesthesiologists (ASA) physical status I-III, Mini-Mental State Examination (MMSE) score ≥ 17.Exclusion criteria were age < 65, ASA physical status > III, MMSE score < 17, history of dementia, schizophrenia, Parkinson's disease and cerebrovascular disease, use of opioids and benzodiazepines longer than one month before surgery, alcoholism, severe liver disease (class C according to Child-Pugh classification), severe kidney disease requiring hemodialysis, multiple trauma and the presence of head injury, communication issues such as serious hearing or visual impairment, any contraindication for regional anesthesia and for the both techniques of postoperative analgesia. Cefazolin 1g was given to all patients 30 minutes before incision and two other doses were given postoperatively. All patients were sedated with midazolam, 2 to 3 mg intravenously, before induction of anesthesia. In the morphine group spinal anesthesia was induced with subarachnoidally injection of 12.5-15 mg 0,5% levobupivacaine. In the levobupivacaine group combined spinal-epidural anesthesia was performed. First, the epidural space was entered with Tuohy epidural needle and the spinal needle was introduced via the lumen of the epidural needle into the subarachnoid space through which 12.5-15 mg of 0.5% levobupivacaine was injected. After that epidural catheter was inserted in the epidural space and its position was checked radiologically and confirmed with the test dose of 0.5% levobupivacaine after the spinal anesthesia was released. During the operation blood pressure was measured non-invasively every 5 minutes and its decrease greater than 20% from preoperative values was corrected by fluid administration and incremental IV injections of vasoconstrictors. The ECG and peripheral oxygen saturation by pulse oximeter were continuously monitored. Postoperative analgesia was obtained using patient-controlled analgesia (PCA) for the first 72 h. In the morphine group intravenous PCA was provided with the following settings: 0.5-2 mg/h basal flow, 0.5 mg bolus dose, and a 20-min lockout. Postoperative epidural PCA analgesia was obtained with 0.125% levobupivacaine with 6-12 ml/h basal flow, 2 ml bolus dose, and a 20-min lockout. Analgesia was assessed by Numerical Rating Scale (NRS), from 0 (no pain) to 10 (maximum pain) every three hours 72h postoperatively and then 3 times a day until discharge. In all patients complete blood count, differential blood count, CRP and fibrinogen were calculated 30 min before induction of anesthesia, 24h, 72h and 120h postoperatively. Blood glucose level was measured every 4 hours for 72h after

surgery and further depending on the values. The plasma concentrations of IL-6 was measured 30 min before induction of anesthesia, 24h and 72h postoperatively. Duration of surgery, blood loss, erythrocyte transfusion, body temperature and postoperative hospital stay were recorded. Cognitive functions were assessed using Mini-Mental State Examination (MMSE) preoperatively (baseline) and from the 1st to the 5th postoperative day and on the day of discharge(the day of surgery was marked as 0 day), once a day between 6 and 8 am. Anxiety and depression were assessed using Hospital Anxiety and Depression Scale (HADS) preoperatively (baseline) and on the 1st and 5th postoperative day and on the day of discharge once a day, at the same time when cognitive functions were evaluated.