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Title page

The efficacy of combined intrathecal morphine and Pericapsular Nerve Group (PENG) block on postoperative pain and recovery quality in anterior hip arthroplasty: A prospective, double-blind, randomized clinical trial

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Study Protocol

In this study, the combination of Pericapsular Nerve Group (PENG) block and low-dose intrathecal morphine with spinal anesthesia in hip arthroplasty is aimed to be compared with PENG alone and intrathecal morphine alone in terms of morphine consumption, postoperative pain, and recovery quality scores during the postoperative 48-hour period.

After approval from the Ethics Committee of Bezmialem Vakif University Medical Faculty, the study will be conducted on 90 adult patients aged 18-90 years, classified as ASA I-IV, who will undergo hip surgery. This prospective, randomized, and double-blind clinical trial has been planned. Randomization will be achieved by assigning patients to study groups entirely by chance, and selection bias will be prevented. For this purpose, MedCalc version 16 statistical software for Windows (medcalc.com.tr) will be used. Patients will be divided into three groups: Pericapsular nerve group block plus spinal anesthesia with bupivacaine (Group P: n=30), Spinal anesthesia with bupivacaine and morphine (Group M: n=30), and pericapsular nerve group block plus spinal anesthesia with bupivacaine and morphine (Group P+M: n=30). After the patients are taken to the operating room, standard monitoring with non-invasive blood pressure (NIBP), heart rate (HR), peripheral oxygen saturation (SpO2), and electrocardiography (EKG) will be conducted. All patients will receive 2-6 L/min of oxygen through a nasal cannula. Preoperative visual analog scale (VAS) for pain and Quality of Recovery (QoR-15) values will be recorded for all patients. As premedication, all patients will receive 0.03 mg/kg midazolam.

In this prospective, double-blind, randomized clinical trial, researchers will be unaware of which treatment will be applied to patients in the study groups and which of these treatments is beneficial or not. Patients will also be unaware of which treatment is administered to them.

Groups:

Group P: Patients in this group will undergo ultrasound-guided block using a linear or convex ultrasound probe in the supine position before spinal anesthesia. The block procedure will involve the use of a local anesthetic solution (10-20 ml of 0.25% bupivacaine, 2 mg dexamethasone, and 5 mcg.ml-1 epinephrine) and a Stimuplex Ultra 360 22G 80 mm block needle (B. Braun Medical AG, Melsungen, Germany). Subsequently, spinal anesthesia will be administered at the L3-L4 intervertebral level with 10-15 mg of heavy bupivacaine while the patient is in a sitting position.

Group M: Patients will receive subarachnoid block without Pericapsular Nerve Group block. Subarachnoid block will be administered at the L3-L4 intervertebral level by adding 10-15 mg bupivacaine with 100 μg of morphine.

Group P+M: Patients will undergo ultrasound-guided block using a linear or convex ultrasound probe in the supine position before spinal anesthesia. The block procedure will involve the use of a local anesthetic solution (10-20 ml of 0.25% bupivacaine, 2 mg dexamethasone, and 5 mcg.ml-1 epinephrine)

and a Stimuplex Ultra 360 22G 80 mm block needle (B. Braun Medical AG, Melsungen, Germany). Subarachnoid block will be administered at the L3-L4 intervertebral level by adding 10-15 mg bupivacaine with 100 μg of morphine.

Sensory block control at T8-T10 level will be assessed in all three groups. Visual analog scale (VAS) for pain and 15-degree leg elevation will be measured in all groups 10 minutes after the completion of the block. Postoperative nausea and vomiting will be monitored and recorded. The same anesthesiologist will administer both the block and spinal anesthesia to all patients.

After the block, all patients will be continuously monitored for signs of local anesthetic toxicity every 5 minutes with non-invasive blood pressure, continuous EKG, and pulse oximetry, for 30 minutes. During the perioperative period, VAS (at 1st, 6th, 12th, 24th, and 48th hours), QoR-15 score values, and rescue analgesic requirements of patients will be recorded.

Intravenous Patient-Controlled Analgesia (IV PCA) device will be installed, and patients who are hemodynamically and respiratory stable in the recovery unit will be transferred to the ward.

During the postoperative period, all patients will receive 1 g of intravenous paracetamol every 8 hours. Morphine PCA (concentration: 0.1mg/ml, bolus dose: 1 mg, lockout time: 10 minutes, basal infusion rate: 0 mg) will be adjusted, and intravenous Patient-Controlled Analgesia (PCA) will be applied.

Rescue analgesia will be provided with 50 mg tramadol upon request or when VAS≥4 and will be recorded.

Patients experiencing nausea or vomiting at any time will receive ondansetron intravenously at a dose of 0.15 mg/kg, and this dose will be repeated if necessary.

Statistical Analysis

Descriptive statistics for qualitative variables in the study are presented as counts and percentages, while descriptive statistics for quantitative variables include mean, standard deviation, median, minimum, and maximum values. For comparisons based on the occurrence rates of relevant variables among groups, Pearson chi-square or Fisher Freeman Halton tests will be employed. In the detailed comparison of groups with observed differences, the Bonferroni correction will be applied. The normal distribution conformity of quantitative variables will be assessed using the Kolmogorov-Smirnov test. One-way analysis of variance (ANOVA) will be utilized for the comparison of means among more than two groups, with the Tukey test employed as a post hoc test for multiple comparisons. Kruskall-Wallis test will be applied for the median comparison of more than two independent groups, and Dunn test will be used for pairwise comparisons. For repeated measurements of variables showing normal distribution changes between periods, analysis of variance will be applied, while the Friedman test will be used for variables not showing normal distribution. Additionally, two-way analysis of variance will be used to

examine changes between groups and periods. The statistical significance level will be set at 0.05, and the SPSS (version 26) package program will be used for calculations. Consent to conduct the study was obtained from Local Ethic Committee of Bezmialem Vakif University.