Protocolo: IBMS-SPB

Tittle: **Serratus plane block impact on pain and opioids requirements in breast surgery**

EudraCT: **2015-005773-21**

Ed. 1.1, February 19th, 2016

Official title

Serratus plane block impact on pain and opioids requirements in breast surgery.

Brief summary

The purpose of this project is to evaluate the analgesic efficacy of a regional anesthesia technique (interfascial block at the serratus muscle) performed in patient undergoing breast surgery and the effect of this technique on postoperative analgesia.

Final version of the protocol: #3 18/06/2015. Approved by Hospital la Fe review Board 30/06/2016. NCT02905149.

Detailed description

Regional analgesia techniques have shown to have benefits over conventional analgesia. The lower opioids analgesics requirements decrease side effects associated with the use of this type of medication.

It is also increasingly established scientific evidence that reducing opioids administration may play a role in prognosis of cancer patients given the immunosuppressive effect of these drugs.

In patients undergoing oncologic/reconstructive breast surgery paravertebral block has been traditionally performed, however the paravertebral space lacks a clear anatomical barrier from the spinal cord so the drugs administered can diffuse to the intervertebral foramen causing deeper levels of blocks (epidural or spinal blocks) and injections at the paravertebral level are associated with serious complications both neurological and respiratory (meningitis, spinal hematomas abscesses, pneumothorax, respiratory failure. This has led to the development of less invasive technique with an improved safety profile.

The serratus plane block falls within the framework of these newly developed techniques and the present study aims to assess its role in the management of the patient undergoing cancer / reconstructive surgery.

Methods

Inclusion criteria: (A) patients ≥18 years old; (B) American Society of Anesthesiologists (ASA) risk scale <IV; and (C) oncologic breast surgery, with or without reconstruction, with at least 24 hours' hospital stay (eg, mastectomy or partial mastectomy, also known as lumpectomy, with axillary regional or radical lymph node dissection).

Exclusion criteria: (A) patients with ASA risk scale ≥IV; (B) body mass index (BMI) >40; (C) neurologic impairment; (D) inability to give informed consent; (E) contraindications to nerve block, such as coagulopathy and local infection at the site of the block; (F) local anesthetic allergy; and (G) chronic opioid treatment. Before surgery, all participants receive education regarding the visual analog scale (VAS) pain score (0 mm=no pain and 100 mm=worst imaginable pain) and the use of electronic patient-controlled analgesia (PCA) pumps. After performing standard monitoring with pulse oximeter, ECG, non-invasive blood pressure (GE

Healthcare, Chicago, Illinois, USA), bispectral index module (BIS module, GE Healthcare, Helsinki, Finland), and TOF-Watch-S (Organon Teknika, Oss, The Netherlands), general anesthesia is induced with intravenous midazolam 0.01–0.03 mg/kg, fentanyl 1 μg/kg, and propofol 2 mg/kg. A laryngeal mask is introduced after the administration of intravenous rocuronium bromide 0.6 mg/kg for muscle relaxation. The lungs are ventilated to maintain an end-tidal carbon dioxide of 35 mm Hg. Anesthesia is maintained with an oxygen fraction (FiO2) of 0.4 and propofol continuous intravenous infusion to keep BIS index between 40 and 60. After anesthesia induction, patients are randomly allocated into two groups (1:1 allocation ratio) by a random sequence generated from a pseudorandom number seed (!RNDSEQ V.2011.09.0, JMDomenech); these sequences is kept in sealed and consecutively numbered opaque envelopes, which are opened after informed consent is obtained. Patients in the study group receive SPB with the midaxillary line approach, using levobupivacaine 0.25% 30 mL, while those in the control group do not. An anesthetist with experience in interfascial blocks perform the US-guided technique using a linear probe (8–13 MHz), a US machine (M-Turbo, SonoSite, Bothell, Washington, USA), and a 22 G, 50 mm echogenic needle (Stimuplex D; B Braun, Melsungen, Germany). With the patient lying supine and the arm abducted at 90°, the US probe is positioned in a sagittal plane at the midaxillary line. The fascial plane between the serratus anterior muscle and external intercostal muscles is identified between the fourth and fifth ribs in the midaxillary region. The gauge is advanced in-plane, and the local anesthetic is placed by hydrodissecting the interfascial space in a caudal to cranial fashion. Following the initial bolus of fentanyl during induction, perioperative analgesia is achieved by administering a bolus of 1 μg/kg fentanyl if blood pressure and/or heart rate increased ≥20% from baseline measurement (first operating room assessment). Thirty minutes before the end of surgery, intravenous paracetamol 1 g is administered in both groups. At the end of surgery, intravenous granisetron 40 μg/kg and dexamethasone 4 mg is administered; muscle relaxation is reversed if needed. During the postoperative period, all patients receive intravenous opioid medication on demand via an electronic PCA pump (CADD Solis, Smiths Medical, Minneapolis, Minnesota, USA). The pump is set to deliver a bolus dose of 1 mg, with a lockout interval of 10 min, and maximum dose of 6 mg/hour without continuous perfusion. The patient is instructed to press the PCA button whenever pain increased to VAS≥40 mm. Moreover, intravenous paracetamol 1 g/8 hours and dexketoprofen 50 mg/8 hours is administered in both groups, as part of multimodal analgesia management.

Recorded data age, BMI, type, site and duration of surgery, typeof lymphadenectomy (radical vs regional/sentinel lymph node), intraoperative fentanyl (μg), postoperative morphine (mg), and time-to-opioid first rescue dose. First 24 hours' total opioid requirements (intraoperative+postoperative, primary outcome) were calculated by converting fentanyl used intraoperatively into morphine equivalents (fentanyl conversion factor; 10 μg fentanyl=1 mg morphine). The participants are blinded to group allocation, as the blocks were performed after induction of general anesthesia. The healthcare provider (attending anesthesiologist) who administer the opioid was blinded to subject allocation as he is not present in the operating room during the standard time used by the investigator to perform the block, even for control subjects who do not receive any block. When attending anesthesiologist is called back to the operating room, the same equipment was present (US machine and disposable items needed to perform the technique, such as syringes and vials) and a white dressing that prevented injection identification is placed on all subjects. In the postoperative period, pain is

assessed by the VAS at 1, 3, 6, 12, and 24 hours after surgery. The occurrence of side effects (nausea, pruritus, apnea, urinary retention, or paralytic ileus), block-related complications, and Pain Out questionnaire answers is recorded at 24 hours after surgery. The data collector for the postoperative data is a different investigator from the one who performed the block and was blinded to the subjects' study group allocation.

The study has planned data monitoringvand auditing by the IIS la Fe according to AEMPS guidelines. Consistency will be check during analysis phase with Stata statistical software. Registries will be obtained from elecrotnic medical records available for double check procedures. All variables are obtained from the subject electronic medical record.

Sample size: Considering a decrease in postoperative morphine consumption of 40% and the average consumption of opioid after breast surgery under general anesthesia is 15 milligrams (standard deviation 8 mg) we calculated that , with an alpha error 5% power 80 % 56 patients (28 per group) were required to achieve a significant result. In anticipation of possible loss of sample , 60 patients were recruited . Analyisi will be performed by intention to treat.

Statistical Analysis Plan

Continuous variables were reported as medians with IQRs or means with SDs where applicable; categorical variables were reported as counts and percentages. We checked for the normality of continuous variables by using the Shapiro-Wilk test.

Quantitative variables (opioid consumption , pain estimated by VAS scale) will be analyzed using mixed linear model adding a randmo variable for interindividual variability for pain threshold. If the data do not meet the criteria of normality the Mann-Whitney U test will be used. If the groups differ in preoperative variables., We will make a multivariable analysis adjusting for these variables. The need for rescue analgesia over time is analyzed by Kaplan-Meier curve where the terminal state is the administration of the first dose of opioid postoperatively. The difference side effects (nausea , pruritus , apnea , urinary retention, ileus) and complications IPO questionnaire and analyzed by chi-square test and Fisher exact test. Scheffe correction will be applied for multiple comparison. Missing data are excluded from analysis.