Postoperative Analgesia in Breast Cancer Surgery: Efficiency and Safety of Ultrasound Guided Erector Spinae Plane Block, a randomized controlled double blinded trial

Analgésie post-opératoire dans le cancer du sein: Sécurité et efficacité du bloc Erecteur Spinal échoguidé, étude randomisée contrôlée en double aveugle

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Abstract

Introduction: Breast cancer surgeries are the mainstay and usually the first step of treatment.

Aim : To assess the efficiency and safety of ultrasound guided Erector Spinae Plane Block (ESPB) for the management of postoperative pain in patients undergoing elective breast cancer surgery.

Methods: Between December 2018 and June 2019, a prospective, controlled, randomized, double-blinded study was conducted at the maternity and neonatology center of Tunis. We included fifty ASA I-II female patients who were scheduled for elective breast cancer surgery. They were randomly divided into two groups : Group R (n=25) with Ropivacaine, while Group P (n=25) received a placebo. The study recorded PCA morphine consumption and patient demand for PCA. The primary outcome was to compare the visual analogue scale (VAS) pain scores at various points throughout the 24 hours postoperatively (1st, 2nd, 4th, 8th, 12th, 16th, 20th, 24th) between the two groups.

Results : Except for the first hour and 16th hour post-surgery, the mean VAS pain scores were significantly lower in Group R compared to Group P. The 24-hour morphine consumption was significantly lower in Group R (5.5±0.9 mg) compared to Group P (16.6±2.8 mg); p<0.001. Per-operative fentanyl consumption was also significantly lower in Group R (9.1±4.2 mcg; Group P: 50±9.1 mcg; p< 0.001). Moreover, the mean total morphine demand was significantly lower in Group R.

Conclusion : ESPB with Ropivacaine is effective and safe for pain management after breast cancer surgery with a consequent morphine sparing and less use of systemic analgesia.

Key-words : Breast cancer, analgesia, ropivacaine, erector spinae

Résumé

Introduction: Les chirurgies du cancer du sein sont la première étape du traitement.

Objectif : Nous avons étudié l'efficacité et la sécurité du Bloc Erecteur Spinal (BES) echo-guidé pour soulager la douleur postopératoire chez les patientes subissant une chirurgie élective du cancer du sein.

Méthodes : Entre décembre 2018 et juin 2019, une étude prospective, contrôlée, randomisée en double aveugle a été menée au centre de Matérnité de Tunis. Cinquante patientes ont été réparties aléatoirement en deux groupes : le groupe R (n=25) a reçu de la ropivacaïne, tandis que le groupe P (n=25) a reçu un placebo. Le critère principal était de comparer les scores de douleur sur l'échelle visuelle analogique (EVA) à différents moments postopératoires (heures : 1re, 2e, 4e, 8e, 12e, 16e, 20e, 24e).

Résultats : À l'exception de la première et de la seizième heure postopératoire, les scores moyens de douleur sur l'EVA étaient significativement plus bas dans le groupe R. La consommation de morphine sur 24 heures était significativement plus faible dans le groupe R (R: 5,5 ± 0,9 mg ; P: 16,6 ± 2,8 mg ; p<0,001). La consommation de fentanyl sur 24 heures était également plus faible dans le groupe R (R : 9,1 ± 4,2 µg; P:50 ± 9,1 µg ; p<0,001).

Conclusion : L'ESPB avec de la ropivacaïne est efficace et sûr pour soulager la douleur après une chirurgie du cancer du sein, réduisant ainsi la consommation de morphine et l'utilisation d'analgésie systémique.

Mots clés: cancer du sein, analgésie, ropivacaine, érecteur spinal

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INTRODUCTION

Breast cancer is the leading type of cancer among women, with over two million women being diagnosed with this disease worldwide each year. Surgery is the primary and typically initial approach for treatment [1]. Breast conserving treatment (BCT) has become the standard surgical procedure for primary breast cancer, offering both oncological safety and satisfactory aesthetic results [2].
Patients who undergo breast cancer surgery (BCS) often experience moderate to severe acute pain after the operation, and up to 50% of them may experience chronic pain that interferes with their daily activities [3]. Despite the availability of various treatment options to alleviate postoperative BCS pain, it continues to be a significant problem. New regional anesthesia techniques have been introduced to manage postoperative pain effectively, but the complex innervation of the breast makes it challenging. Consequently, different regional anesthesia techniques may target different areas of the surgical site [4].
Of all the available options, the paravertebral block has been extensively studied and found to be the most effective analgesic technique. Recently, a new interfacial plane block called the Erector Spinae Plane Block (ESPB) has been introduced. This technique involves injecting a local anesthetic (LA) under the erector spinae muscle, with the expectation of achieving paravertebral spread three vertebral levels cranially and four levels caudally. This, in turn, blocks the dorsal and ventral rami of the spinal nerves, making it a promising technique for managing postoperative pain. Our aim was to evaluate the safety and efficacy of Ultrasound-guided ESPB in managing postoperative pain in patients undergoing elective BCS.

METHODS

From December 2018 to June 2019, a single center prospective, controlled, randomized, double-blinded and interventional study was conducted in Maternity and Neonatology Center of Tunis, Tunisia. After approval of the study protocol by the local ethics committee and written informed consent, fifty ASA I-II female patients scheduled for BCS were enrolled. Patients with any of the following criteria were not included: patient refusal, body mass index>40 kg/m2, ASA >II, history of psychiatric or neurological disease, chronic pain syndromes, recent use of opioid drug, long-term use of antiarrhythmic drug, contraindications to peripheral nerve block: coagulation disorders or treatment with anticoagulants, allergy to LAs and infection at the thoracic injection site. Patients were excluded in case of failure to perform ESPB or inappropriate use of the patient-controlled analgesia (PCA) device. Patients were randomized in two Groups to receive either ESPB with 40 ml of 0.375%ropivcaine (Group R) or ESPB with 40ml of normal saline solution (Group P). They were briefed on PCA pumps and visual analogue scale (VAS) pain scores for assessing the level of their pain during the preanesthetic visit. Participants were not informed to which group they will be assigned. In order to respect blinding, a first investigator performed randomization and prepared labeled solutions, a second investigator performed ESPB and managed intraoperative period. After standard monitoring (Electrocardiography, noninvasive arterial blood pressure, and pulse oximetry), venous access was established with 18 gauge intravenous cannula in the contralateral upper limb of the surgical site before the procedure. All blocks were performed by the same investigator approximately 20 minutes before induction of general anesthesia.

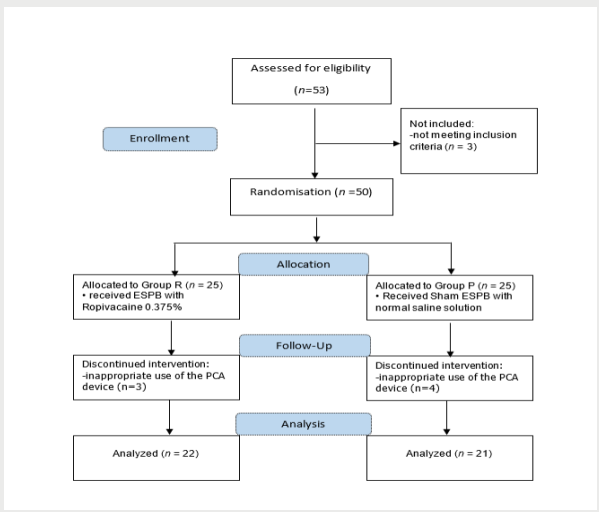

Figure 1. Flowchart

ESPB was performed in the sitting position and on the same side of the surgery. The fifth thoracic (T5) spinous process was identified using the vertebra prominens (C7) as a surface landmark. Skin preparation was performed using 10% povidone iodine. A high-frequency linear array ultrasound probe (L10) of MySonoU6® fully covered by a sterile probe cover was placed in a transverse orientation over the midline of the back to identify the spinous process. The probe was then rotated to a longitudinal orientation to produce a parasagittal view and was slidden approximately 3cm laterally towards the targeted side. Once the probe is placed in the appropriate position, the following layers are identified from the superficial to the deep plane: skin and subcutaneous tissue; trapezius muscle, rhomboid major and erector spinae muscle, TP shadow, intertransverse ligament, costotransverse ligament, finally pleura and lung. LA infiltration over the superficial tissues is performed using Lidocaine to prevent pain. The block needle is then inserted. An echogenic 22 G, 85 mm needle was used to perform the block. During the ESPB procedure, the needle was inserted in plane of the ultrasound, approximately 1–2 cm away from the probe, in a 30–45-degree direction. It usually crosses the trapezius fascia, the rhomboid and the erector spinae fascia to reach the intertransverse ligament plane. The correct location of the needle tip between the erector spinae muscle plane and the TP, intertransverse ligament is checked by injecting 1ml of normal saline solution. Once the position of the needle is checked, the solution is injected according to randomization. All patients received standard general anesthesia protocol. Anesthesia was induced with 2–3 mg/kg IV Propofol, 2 mcg/kg Fentanyl and 0.5 mg/kg IV Atrcurium. Endotracheal intubations were performed using a 7.0 or 7.5 tube Patients were ventilated by a 50%O2 in air and 2% Sevoflurane. Analgesia was provided using intermittent injection of fentanyl 0.5mcg/kg administered only when heart rate or mean blood pressure increased more than 20% of baseline values. Paracetamol 1g and Ketoprofen 100mg were given to all patients 30 minutes before the end of the surgery. The postoperative pain management schedule was identical in both groups. After awakening, all patients were transferred to the recovery room where morphine PCA pump was connected to all study participants. PCA device was set for a 1mg bolus

dose with 5min lockout interval and a 4-hour limit of 24 mg without continuous delivery. Postoperative pain was assessed using VAS pain scores at 1st, 2nd, 4th, 8th, 12th, 16th, 20th, and 24th postoperatively Rescue analgesia was given when VAS pain scores were over than 6cm. In these cases, patients received Paracetamol 1g i.v. and Ketoprofen 100mg was given intramuscularly only if VAS pain scores were over than 8cm. Ondansetron 4mg was given intravenously in case of nausea or vomiting. Patient satisfaction regarding postoperative analgesia was assessed using a 3-point scale (3: Very satisfied, 2: neutral, 1: dissatisfied) for 24 h postoperatively. For the post-operative follow up the physician was blinded to the study groups. The main outcome was to compare visual analogue scale (VAS) pain scores at various points throughout the 24 hours postoperatively (1st, 2nd, 4th, 8th, 12th, 16th, 20th, 24th).

The sample size calculation was based on a pilot study of 5 patients indicated that 18 patients per group would give a power of 90% at a level of 0.05 to detect a difference of 0.5 mg of morphine. Secondary outcomes were total fentanyl consumption, time to first PCA morphine request, PCA morphine demands during the 24 hours, rescue analgesia (percentage of patients requiring rescue analgesia was recorded), incidence of postoperative nausea and vomiting, incidence of morphine related side effects (pruritus, urinary retention, hypotension, respiratory distress and sedation), patient satisfaction regarding post-operative analgesia, incidence of adverse events related to ESPB (LA systemic toxicity, pneumothorax, major hematoma or intravascular injection). Data entry and processing were performed using SPSS® software 23 and Microsoft Office Excel® 2013. Quantitative variables were expressed as means ± standard error or medians and were compared using the Student's t test or ANOVA test when appropriate. Qualitative variables were expressed as frequencies (%) and were compared using Pearson's χ2 test or Fisher's test when appropriate. P values less than 0.05 were considered as statistically significant.

RESULTS

The mean postoperative VAS pain scores were significantly lower in the Group R than in Group P at all points of assessment except at H1 and H16. Regarding secondary outcomes, the 24 h patient PCA consumption, was significantly lower in Group R than in Group P (5.5±0.9 mg vs 16.6±2.8 mg respectively; p<10-3). The need for postoperative PCA morphine was significantly lower in Group R at all points of assessment. A subgroup analysis based on the type of surgery found a significantly lower PCA morphine consumption in Group R than in Group P regardless the type of surgery: PCA morphine consumption in Lumpectomy with axillary dissection subgroup was 5.4 ±1.2mg in Group R vs 17 ±3.9mg in Group P; p=0.013. In Mastectomy with axillary dissection subgroup, PCA morphine consumption was 5.6 ±1.2mg in Group R vs 12.8 ±3.6mg in Group P; p=0.036. We found that total fentanyl consumption was significantly lower in Group R than in Group P. In fact, only 18% (4) patients from the Group R required fentanyl reinjection versus 67% (14) patients from Group P (p<10-3). The mean given dose of fentanyl was significantly lower in Group R than in Group P: (9.1±4.2mcg vs 50±9.1 mcg respectively; p<10-3). Mean time to first request for morphine was similar in both Groups: 1.8± 0.4 H in Group R versus 1.1± 0.1H in Group P (p=0.081). The Mean total morphine demand during the first postoperative 24h was significantly lower in Group R than in Group P: 6.5±1.3 versus 21±4.5 respectively (p=0.003). The mean morphine demand values were significantly lower in Group R than in Group P at all points of assessment. Only one patient in Group R required Paracetamol 1g at H16 postoperatively. In Group P, one patient needed only Paracetamol at H4. One other patient needed both paracetamol and ketoprofen at H16 postoperative. Globally, no significant differences between the groups were recorded (p=0.607). No differences were observed between groups regarding the incidence of nausea and vomiting. In Group P, two patients developed nausea and vomiting and required parenteral ondansetron. None of the patient in Group R developed nausea or vomiting. None of the patients had any other complications related to morphine in the first postoperative 24 h. A higher level of satisfaction was reported in Group R than in Group P: 91% versus 47.6% respectively; p=0,003. No adverse events related to ESPB were recorded during the first 24h postoperative.

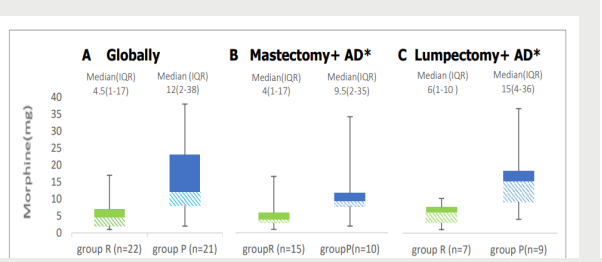

Figure 2. 24 Hours PCA morphine consumption

A, Globally. **B**, active versus placebo block in the mastectomy with axillary dissection subgroup. **C**, Active versus placebo block in the lumpectomy with axillary dissection subgroup.*AD : axillary dissection.

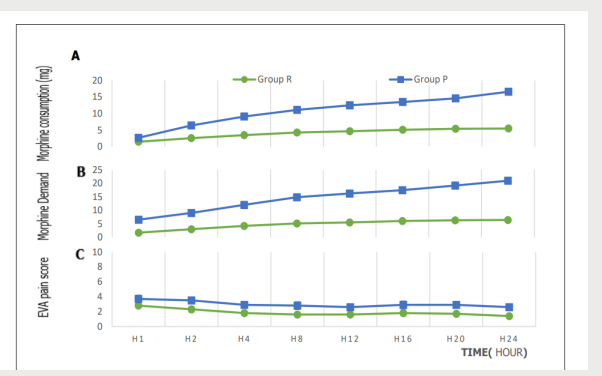

Figure 3. Cumulative PCA morphine consumption and demands and EVA pain scores at different time intervals.

A, Cumulative PCA morphine consumption **B**, Cumulative PCA morphine demands **C**, EVA pain scores.

DISCUSSION

In this prospective controlled randomized double blinded trial, PCA morphine consumption over the 24h postoperative, has shown a significant decrease in the active group which makes a significant morphine sparing. In fact, PCA morphine consumption decreased of 2/3 with Ropivacaine ESPB. As previously shown, fifty percent of the active group requested less than 4.5mg of morphine which represent a significant benefit. Regarding intraoperative fentanyl consumption, we noted a dramatic decrease of fentanyl needs. In fact, more than 19% of patients in the active group did not require analgesia maintenance which suppose that regional analgesia was established in less than 45 min in the. It means that ESPB is effective regardless the type of surgery in the active group. These results were similar in subgroups.

Moreover, lower PCA morphine demands in the active group R but a similar need of rescue analgesia. Similar incidences of morphine related side effects were noted. In our study, we found a higher level of satisfaction with the quality of analgesia in the active group. No adverse events related to ESBP was noted in our study. So, ESPB seems to be a safe procedure.

Paravertebral block has been commonly accepted as the most effective regional technique for pain relief. Nevertheless, it is considered as an invasive block requiring advanced skills. Clinicians have been seeking for safer and easier alternatives |5]. The ESPB has recently emerged as a novel technique with several advantages. It is an interfacial plane block first described in a case report by Forero et al for thoracic neuropathic pain [6]. It has later been used as post-operative regional analgesia technique in 34 different surgical procedures and performed to treat chronic pain. LA is usually injected between the erector spinae muscle plane and transverse process, intertransverse ligament plane with ultrasound guidance. Although the mechanism of the ESPB remains unclear, cadaveric studies suggest that ESPB acts on the ventral rami of spinal nerves in the paravertebral space via the penetration of the intertransverse connection tissues [7-8-9]. Magnetic resonance imaging studies showed that the injectate spreads not only to paravertebral and epidural spaces but also to lateral cutaneous branches of the intercostal nerves [10-11]. ESPB provides extensive cranio-caudal spread which could be affected by various concentrations and volumes of LA [12-13]. The optimal doses and volumes are still not known. However, Luftig et al proposed a weight-based LA dose and volume guide for ESPB which recommends the dose of 2 mg/kg of bupivacaine with the maximum of 175 mg or 3mg/kg of ropivacaine with the maximum of 300mg. Altiparmak et al performed ESPB using two different concentrations of bupivacaine. Ultrasound-guided ESPB performed with 20 ml of 0.375% bupivacaine reduced postoperative tramadol consumption more significantly than ESPB performed with 20 ml of 0.25% bupivacaine [14]. ESPB was compared to PECS [15], to multimodal analgesia [16], to morphine analgesia [17-19] or tramadol PCA [20] (table 2). ESPB seemed to be more effective in these studies. For example, the ESPB provided effective analgesia with minimal morphine consumption in patients who underwent total mastectomy and axillary dissection with or without a tissue expander [17,18,21]. It was also effective in patients who underwent various types of mastectomy [20,22].

This is a prospective double blinded placebo versus active group, which make our results more reliable. Reducing opioid consumption during the perioperative period remains one of the purposes of enhanced recovery programs. Further, conducting opioid-free anesthesia is now a goal of anesthesiologists all over the world as it contributes to enhance recovery programs. Regional anesthesia is one of the biggest tools to reach this purpose. ESPB seems to be a promising technique in this context. Although morphine and fentanyl consumption were dramatically decreased, there still is a little need for them. In this study, safety is established. In fact, complications are currently reported with paravertebral block such as pneumothorax. A single study has reported the occurrence of iatrogenic pneumothorax with ESPB [23]. Pneumothorax is not expected when ESPB is performed under US guidance. It may be the result of hand-eye coordination loss or depth miscalculation. We think that this kind of complication would disappear with practice. The ESPB is easy to learn and to perform thanks to its simple sonoanatomy. The injection site is far from major vascular structures and pleura. The motor block occurred when ESPB was performed at lower thoracic or lumbar level [24]. The authors hypothesize that it is due a lumbar plexus spread of LA. Systemic toxicity remains a real danger in ESPB [25], it included mild neurological signs but not cardiovascular signs.

Our findings showed that ESPB a simple, safe and effective method for the management of postoperative pain after BCS. But there are some limitations: First, the blinded conditions did not allow us to perform a clinical assessment of the sensory blockade. Sensory level may determine the exact limits of the analgesic effect of the block. Second, it would also be advisable to record dynamic VAS scores, still we noted that our patients did not specially complain when moving their arms.

CONCLUSION

ESPB with 40ml of 0.375% ropivacaine seems to be effective and safe for pain management after breast cancer surgery with a consequent morphine sparing, less systemic analgesia, better patient satisfaction and minor complications.

ESPB is a promising technique for pain management. Further studies are necessary to enhance the efficiency of the block while studying volumes, concentrations, LAs and adjuncts. It should be commonly used and more studied as a part enhanced recovery programs and opioid-free anesthesia protocols.

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