SPECIAL ISSUES IN BREAST CANCER

REGIONAL ANALGESIA AND BREAST CANCER SURGERY

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ABSTRACT • Breast cancer surgery is frequently associated with postoperative nausea, vomiting, pain and painful restricted movement. It is well established that thoracic paravertebral block with or without general anesthesia provides better postoperative analgesia and reduces the risk of nausea and vomiting after breast surgery as well as the incidence of chronic pain.

Paravertebral block improves the quality of recovery after breast cancer surgery and provides the patient with the option of ambulatory discharge.

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RESUME • La chirurgie du sein est fréquemment associée à un risque important de nausées et de vomissements ainsi que d'une douleur postopératoire avec limitation des mouvements. Le bloc paravertébral thoracique, avec ou sans une anesthésie générale, assure une analgésie postopératoire efficace et réduit l'incidence des nausées et vomissements postopératoires ainsi que l'incidence des douleurs chroniques.

Le bloc paravertébral améliore la qualité de réveil après chirurgie carcinologique et facilite la réalisation de la chirurgie en ambulatoire.

INTRODUCTION

Breast cancer is the most common major malignancy in women worldwide and the second leading cause of cancer death [1]. Patients undergoing breast surgery are normally associated with a high incidence of postoperative nausea and vomiting (PONV), pain and painful restricted movement. The incidence of PONV during the 24-hour interval after breast cancer surgery has been reported around 59% [2]. PONV is greater in patients undergoing general anesthesia, in female patients, in patients experiencing postoperative pain, and in women undergoing breast surgery. Troublesome pain and PONV can prolong recovery and hospitalization, and are some of the most common causes of hospital admission following ambulatory surgery [3].

Postoperative pain continues to be under-treated and it is known that bad pain relief may contribute to a high risque of developing a chronic pain in the operative site [4]. Patient-controlled intravenous analgesia with opioids remains a common strategy for management of postoperative pain; however, this method is far from ideal because efficacy is suboptimal and side effects frequent [5]. Opioids produce adverse effects such as nausea, vomiting and sedation so alternative analgesic regimes in the perioperative period may reduce unwanted side effects. Regional anesthetic techniques, such as thoracic epidural analgesia, offer better quality analgesia than systemic opioids in major abdominal and thoracic surgery [6]. Local and regional techniques, including local anesthetic infiltration has indisputable benefits in postoperative pain relief in many clinical settings, however, its efficacy in patients undergoing breast surgery remains controversial [7-9]. Regional anesthesia using paravertebral block (PVB) is a good alternative to general anesthesia for breast cancer surgery. PVB provides superior analgesia and fewer side effects related to a standard opiate-based postoperative analgesia [10-16]. It has been used as the sole anesthetic [10, 14, 16] and for ambulatory breast surgery [12].

In the course of the development of systemic analgesics and epidural anesthesia, PVB has fallen into disfavor. Numerous reports attest the safety and efficacy of PVB to provide better postoperative analgesia and its ability to shorten hospitalization after breast surgery compared to general anesthesia [10-14]. Here, we briefly review some of the background to this technique and some interesting new developments that provide additional reasons why this block should be considered as part of the anesthetic for breast surgery [15-16].

PARAVERTEBRAL BLOCK

Thoracic PVB, first reported by Leipzig in 1905 and revisited by Easton and Wyatt in 1979, involves injection of local anesthetic, just lateral to the vertebral spinal process, at the site where the spinal nerve emerges from

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the intervertebral foramina [17-18]. The paravertebral space contains dorsal and ventral rami and the sympathetic chain. Hence, infiltration of this space results in a unilateral sensory, motor, and sympathetic blockade. Nerve blockade is achieved in dermatomes above and below the injection site [19]. There are two common variations in the technique for breast surgery. The first is a single-site injection that involves a large volume, usually 15-20 ml or 0.3 ml/kg of 0.375-0.5% bupivacaine at one paravertebral space, usually at T4 level. This technique provides unilateral anesthesia from four to five dermatomes [17]. The other variation is the multiple-site technique in which 3-4 ml of local anesthetic are injected into multiple levels, usually as many as six different levels [8, 10-11]. There are numerous indications for PVB, such as thoracic, renal and intra-abdominal surgery, however, the most common appears to be breast surgery. PVB has been used to relieve acute chest wall pain from rib fractures, herpes zoster, and pleurisy, to manage acute and chronic post-thoracotomy pain and chest and shoulder surgery. There are a few contraindications to PVB which include infection at the site, coagulopathy, or allergy to local anesthetic drugs [15].

Both single and multilevel paravertebral injections have been reported to provide good analgesia. The single puncture technique gives the opportunity to place a paravertebral catheter that allows giving supplemental dosing and providing prolonged unilateral perioperative analgesia. Cheema et al. [20] investigated in a thermographic study the spread after a single thoracic percutaneous paravertebral injection of 15 ml of bupivacaine 0.5%. They found a large unilateral somatic and sympathetic block extended over 5 (range: 1-9) and over 8 (range: 6-10) dermatomes respectively. However, one single-injection PVB may not be sufficient to cover all relevant dermatomes. In fact, Naja et al. showed in a recent study that 97% of patients had adequate loss of sensation with four injections compared with only 11% for single injections. So a multilevel injection PVB produces a more reliable sensory block than a single injection technique and assessment of longitudinal anesthetic spread in the paravertebral space revealed a more caudal spread of local anesthetic compared with a cephalic distribution [21].

PVB for breast surgery is an efficient technique. In a prospective study, Cooter et al. showed that 87% of PVB were successful for surgical anesthesia and 94% of the blocks were successful for postoperative analgesia [13]. It reduces postoperative pain and opioids consumption, thus decreasing postoperative nausea and vomiting. As compared with patients managed using general anesthesia, PVB markedly improves the quality of recovery after breast cancer surgery and provides the patient with the option of ambulatory discharge [11-12]. This regional technique has resulted in a very high patient satisfaction [10-12].

Multiple studies find out that single injection PVB, at the level of T4, is advantageous compared to general anesthesia in breast surgery with respect to postoperative analgesia, painful restricted movement and postoperative vomiting [9, 12-13]. In an observer-blinded study, Pusch et al. [11] randomized 86 patients to receive either a single injection of 0.3 ml/kg of bupivacaine 0.5% or general anesthesia. Single-injection PVB provided adequate intraoperative analgesia in 93% of women scheduled for unilateral breast surgery going from lumpectomy to a radical mastectomy with axillary dissection. The recovery time from anesthesia and frequency of vomiting was significantly reduced in the PVB group. Postoperative pain scores and pain medication were significantly lower in women with PVB at 1, 6, and 12 h after surgery, while a better comfort in relation to painful restricted movement and earlier mobilization was achieved [9]. Similar results were obtained in a randomized study by Klein et al. [10] using a multilevel injection PVB at T1-7. Naja et al. [14] randomized 60 patients to receive either a PVB at T1-5 using a nerve-stimulator guided technique compared to general anesthesia. Pain scores both at rest and during movement and consumption of analgesics were significantly lower in the PVB group during the first three postoperative days.

Studies have shown that PVB has the potential to reduce pain and side effects after breast surgery when used in addition to general anesthesia or sedation. However, none of the studies cited above were placebo-controlled, which may have caused an over estimation of the positive effects. Kairaluoma et al. [15] randomized 60 patients, undergoing a breast tumor resection or mastectomy with lymph node biopsy (sentinel), to receive a single-level injection at T3 using bupivacaine 5 mg/ml (0.3 ml/kg) or saline (2 ml). Patients who received bupivacaine reduced the consumption of IV opioids by 40% in the postanesthesia care unit, and had less pain at rest after 24 h. Moller et al. [22], in a randomized double-blind placebo-controlled study examined the effect of a multilevel injection PVB from level C7 through T5 (30 ml of ropivacaine 0.5%) before general anesthesia compared to placebo (30 ml of saline) on postoperative analgesia. They found in the PVB group a significant decrease in intraoperative use of fentanyl and propofol, less consumption of PCA fentanyl IV in the PACU as well as a significant decrease in the number of patients with pain scores ≥ 3 in the PACU. This multilevel PVB provided good analgesia for breast surgery, but the duration of analgesia was briefer than described in previous studies.

McElwain et al. [23] applied in a prospective, double-blind, randomized trial, a patient-controlled analgesia to paravertebral catheter (level T2 or T3) and evaluated the efficacy and tolerability of two distinct dosing regimens, levobupivacaine 0.2% at 8 ml/h with 3-ml bolus and 15-min lockout group v/s levobupivacaine 0.2% at 4 ml/h with 8-ml bolus and 30-min lockout. Patient-controlled analgesia to paravertebral catheter offered an excellent postoperative analgesia with few side effects and high patient satisfaction for the two groups. Only total volume of levobupivacaine received and boluses administered

were significantly greater in 15-min than 30-min lockout groups. Drugs used for PVB include bupivacaine, ropivacaine, and levobupivacaine with or without epinephrine. Hura et al. [24] recently randomized 70 patients scheduled for mastectomy to receive a single injection of 0.4 ml/kg of ropivacaine 0.5% or bupivacaine 0.5% at the T4 level. Repeated assessments of the sensory blockade were performed at frequent intervals. Both drugs provided good analgesia, but ropivacaine was characterized by a more rapid onset, a larger initial spread, and a longer duration of the blockade.

Although complications associated with PVB can be serious, their incidences from published data actually are quite low, varying from 2.6% to 5% [12, 25]. A prospective multicentre study of Lonnqvist et al. [26] assessed the safety of the single-injection PVB for different surgical procedures. The block proved to have a safety profile similar to those observed in comparable regional anaesthesia techniques and a frequency of complications equal to, or even lower than those seen in epidural, intrapleural or intercostal block studies. Bupivacaine deposited paravertebrally produced greater preservation of lung function and fewer side effects due to bupivacaine toxicity than interpleural application [25]. Complications include local anesthetic toxicity, pneumothorax (0.5%), pleural puncture (0.2-2%), vascular puncture (3.8%), hypotension (4.6%), epidural spread (1%), intrathecal spread (rare), and failed block (6-18.6%) [26-27]. Although the incidence of pneumothorax resulting from PVBs is quite small, it is logical that the risk of complications per patient increases when multiple injections are performed [27].

Karmakar et al. [28] showed that the addition of epinephrine reduces and delays the rapid phase of systemic absorption of ropivacaine from the paravertebral space and can be useful to reduce systemic ropivacaine toxicity. Slow injection of local anesthetic, reduction in the dose for the elderly or frail patients, and the addition of adrenaline to local anesthetic are useful strategies for minimizing systemic local anesthetic toxicity. Placing a paravertebral catheter makes possible to fractionate the amount of injected local anesthetic solution, which might increase the safety of PVB. Considering that the PVB has a certain complication rate, the risk/benefit ratio does not favor the routine use of PVB for minor breast surgery such as lumpectomies or quadrantectomies without axillary lymph node dissection and radiograph wire-localized breast biopsies [29]. The PVB, which provides profound inhibition to painful stimuli and reduces general anesthesia-related complications, would be recommended for major breast surgery such as lumpectomies or quadrantectomies with axillary lymph node dissection and radical mastectomies.

In some patients, postsurgical pain persists long after natural healing processes have been completed. The incidence of chronic postsurgical pain (CPSP), defined as pain developed of at least two months duration, is variable after breast surgery. CPSP is common but often underrecognized, neglected, or misdiagnosed. Forty-nine percent of patients who undergo mastectomy with reconstruction have pain one year later, compared with 31% of those undergoing mastectomy alone and 22% of those undergoing breast reduction [30]. Women who undergo breast surgery experience chest wall, breast, or scar pain (range, 11%-57%), phantom breast pain (13%-24%), and arm and shoulder pain (12%-51%) [4]. The intensity of acute postoperative pain, the type of operation, involvement of regional lymph nodes and radiotherapy have been considered the most important factors predisposing to chronic pain in patients with breast cancer [31].

The intensity of postoperative pain and the increased requirement of analgesics during the first days after surgery may play an important role in the development of CPSP [4]. Iohom et al. [32] evaluated the association between continuous paravertebral block for 48 h, concentration of nitric oxide products and development of chronic postsurgical pain after breast surgery. No patient in the continuous PVB developed chronic postsurgical pain, evaluated 10 weeks postoperatively, compared with 80% in the standard management group. There is no association between perioperative nitric oxide concentration and the development of CPSP. Patients in the PVB group reported significantly lower visual analog scale pain scores with movement until 96 hours postoperatively.

In addition to providing acute postoperative pain relief, preoperative PVB seems to reduce the prevalence of chronic pain up to one year after breast cancer surgery. Kairaluoma et al. [33] performed a one-year follow-up of 60 patients, half of whom had received PVB, scheduled for conservative breast cancer surgery with lymph node biopsy (sentinel) or axillary dissection. At one month after surgery, the intensity of motion-related pain was significantly lower in the paravertebral group. At one-year follow-up, the prevalence of pain symptoms, the intensity of motion related pain, and the intensity of pain at rest were also significantly lower in the PVB compared to general anesthesia (GA) group. Considering radiotherapy was performed six months after surgery, patients who received a PVB still seemed to report less pain than patients without block, and regardless of whether an axillary dissection was performed, patients in the PVB group had less motion-related and chronic pain 12 months after surgery than patients in the GA group [33].

A recent study yielded another potential benefit to PVB. Exadaktylos et al. [34] performed a retrospective study of the medical records of 129 consecutive patients who underwent mastectomy and axillary node dissection for breast cancer. Seventy-nine of these patients had GA while 50 patients had surgery with paravertebral anesthesia combined with GA. Metastasis and recurrence-free survival rate was 94% in the paravertebral group compared with 82% at 24 months and 77% at 36 months in the GA group. Authors suggested that the paravertebral anesthesia rather than morphine for postoperative analgesia reduced the risk of cancer recurrence rate during the initial years of follow-up. In fact, PVB decreased the stress response of surgery and opioid consumption that both would impair cellular and humoral immune func-

tions [34-36]. Decreased morphine use would presumably allow improved immune function. Compared with postoperative opiates, continuous PVB infusion of local anesthetic improves subcutaneous tissue oxygenation, thus possibly reducing infection risk and improving wound healing [37]. These studies have relatively small numbers of patients and confirmatory studies are needed for the additional benefits of this procedure.

LOCAL ANESTHETIC INFILTRATION

Administration of local anesthetics in the surgical wound is a simple and attractive technique to improve postoperative pain relief. Local infiltration may avoid some of the difficulties associated with thoracic PVB or thoracic epidural analgesia, and still provide superior analgesia and fewer side effects to a standard opiate-based postoperative analgesia in some clinical settings, but its efficacy in patients undergoing breast surgery remains controversial.

Several authors report a reduction in IV analgesic requirement and postoperative pain relief after local anesthetic infiltration pre- and postoperatively [9, 38], while other trials failed to show any benefit from pre- and postoperative wound infiltration of local anesthetic [7-9]. A prospective, randomized, double-blind study, including 60 patients, found no differences in postoperative pain management between 3.75 mg/ml ropivacaine and saline wound infiltration before breast surgery. Data shows similar postoperative needs of analgesics and antiemetics with a similar frequency of PONV [8].

Sidiropoulou et al. [39] examined the efficacy of continuous wound infiltration compared with a preoperative thoracic PVB regarding the analgesic efficacy of the two techniques after mastectomy with axillary dissection. Absolute pain scores were low in both groups. Four hours after surgery, the PVB showed a significant reduction in postoperative pain and reduced painful restricted movement, whereas the infiltration group had lower pain scores and painful restricted movement 16 and 24 h after surgery. PONV was significantly less frequent in patients who received a PVB. There is no clear benefit of one technique over the other regarding postoperative analgesia, although it should be noted that the continuous wound infiltration requires no skill and therefore might constitute a superior technique.

CONCLUSION

Thoracic paravertebral analgesia is a useful technique in patients requiring breast cancer surgery and has seen increasing popularity over the last 10 years. PVB has been shown to provide a better acute postoperative pain management following breast surgery. Benefits include a reduction in postoperative nausea and vomiting, prolonged postoperative pain relief, and potential for ambulatory discharge. It has significantly improved the quality of recovery after major breast surgery. Thoracic PVB as part of a balanced analgesic regimen provides effective pain relief with few side effects.

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