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Anesthesia and analgesia in breast surgery: the benefits of peripheral nerve block

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Abstract. – Breast surgery is frequently associated with postoperative pain, nausea and vomiting, that result in increased patient's suffering, prolongation of hospital stays and related costs. Thoracic paravertebral nerve block (TPVB) is a viable option to the classic multimodal analgesia in breast surgery as it enhances surgical anesthesia and postoperative analgesia.

In this review, we report the results of a number of studies on the role of TPVB in breast surgery. This technique is associated with a superior control of the pain, a reduction in opioids consumption after surgery, a decrease in postoperative nausea and vomiting, and an overall decrease in length of hospital stay. In particular, TPVB seems to provide the most benefits in patients undergoing an unilateral or bilateral mastectomy followed by immediate reconstruction. Some studies also suggest that the use of regional anesthesia-analgesia could attenuate perioperative immunosuppression and minimize metastases in breast cancer patients.

TPVB can be also coupled with other regional anesthetic techniques such as pectoral nerve block (PNB), thus increasing the reduction in postsurgical pain, opioids consumption and length of hospital stays.

Key Words
Thoracic paravertebral block, Pectoral nerve block, Anesthesia, Breast cancer, Pain.

Introduction

Breast cancer is the most common malignancy in women and its incidence has steadily increased over the last decade[1]. Despite the latest advances in breast cancer surgery, this procedure is frequently associated with postoperative pain, nausea and vomiting, which lead not only to increased patient's suffering, but also to a prolongation of hospital stays and related costs[2-4]. This issue is particularly relevant for patients undergoing mastectomy combined with prosthetic reconstruction, as they usually experience a higher peak pain intensity than women undergoing breast-conserving therapy[5]. One of the main causes of postoperative complications is general anesthesia (GA), which is frequently used for sedation and is associated with nausea and vomiting in 50% of the cases[6]. Alternatives to GA such as preoperative medications, neuropathic analgesia and local or regional anesthesia have been explored to reduce postoperative complications and increase perioperative pain control[7-10]. Among these, regional infiltration of anesthetic agents or botulinum toxin resulted in improved analgesia, decreased perioperative morbidity and shorter hospital stays[11-14]. In particular, thoracic paravertebral nerve block (TPVB) is considered a viable option to the classic multimodal analgesia as it offers benefits enhancing surgical anesthesia and postoperative analgesia. This technique has been associated with faster recovery rates after surgery[15], less postoperative pain[15,16] and reduced postoperative analgesic requirements compared to GA[15]. In this review we will discuss the advantages of TPVB in breast cancer surgery, also underlining the superior outcomes of the combination of TPVB with other anesthetic techniques such as pectoral nerve block.

Thoracic Paravertebral Block

Thoracic Paravertebral block (TPVB) is a regional anesthetic technique that consists in the injection of a local anesthetic in the paravertebral space, nearby the point where the thoracic spinal nerves emerge from the intervertebral foramina.

From the anatomical point of view the thoracic paravertebral space is defined in anterolateral position by the parietal pleura, posteriorly by the superior costotransverse ligament, medially by the vertebrae and intervertebral foramina, superiorly and inferiorly by the heads of the ribs. The

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endothoracic fascia, behind which are located the thoracic spinal nerves, is interposed between the parietal pleura and the superior costotransverse ligament[17].

The TPVB consists in the injection of local anesthetic posterior to the parietal pleura, in the same tissue plane as the neurological structures and results in ipsilateral somatic and sympathetic nerve block. The resulting block involves the thoracic dermatomes above and below the injection site, thanks to the cranio-caudal anatomical continuity of the paravertebral space at the thoracic level.

The TPVB procedure is performed with the patient in the sitting or lying down. The needle, positioned 2.5 to 3 cm lateral to the T4 spine, is advanced directly posteroanterior, perpendicular to the skin, until contact with the pars intervertebralis, articular column, or transverse process of the particular vertebra is established. The needle is then "walked off" the structure in an inferolateral (lateral and caudal) direction and advanced approximately 1 cm (maximum 1.5 cm), pointing laterally, away from the medial structures. The paravertebral space is reached once the needle penetrates the costotransverse ligament, feeling a "pop" and loosing resistance to air[17].

Some studies have shown that TPVB is effective in reducing postoperative complications and hospital stays compared to general anesthesia alone[18].

Klein et al[16] conducted a randomized prospective study to compare the effects of TPVB with GA in postoperative complications in women undergoing unilateral or bilateral breast augmentation or reconstruction. The study showed that TPVB provided improved analgesia, measured with the visual analog score (VAS), when compared to GA alone; this superior pain control was especially evident during the first 24h but it could last up to 72h after the initial block. Moreover, a trend of decreased vomiting and nausea scores was detected in the TPVB group compared to the GA group, but the difference between treatments was statistically significant only at 24 h. This result was probably correlated with a decreased opioid consumption registered in the TPVB group. Indeed after the surgery, patients treated with TPVB required 3 times fewer analgesics than patients receiving GA alone[17].

One important advantage of TPVB is that it seems to provide the most benefits in patients undergoing an unilateral or bilateral mastectomy followed by immediate reconstruction. These patients usually suffer from higher pain levels and require longer hospital stays because of the length and the complications of the surgical procedure and the longer time under general anesthesia.

The results of a retrospective study conducted by Fayh et al[19] reported that among patients undergoing mastectomy, those who received TPVB had reduced need for postoperative antiemetic (39% *vs*. 57%) and opioid equivalent use (mean ± SD 40.1 ± 15.2 *vs*. 47.6 ± 17.7 morphine equivalents) compared to those who received another anesthetic treatment. In particular, they observed that patients who underwent bilateral mastectomy with immediate reconstruction, and therefore experienced the highest levels of postoperative pain, were those with the most significant quantitative difference in opioid use. Nevertheless, even those treated with unilateral mastectomy without reconstruction had a small but still significant decrease in opioid consumption. In addition, the proportion of patients discharged within 36 h of surgery was significantly higher in the TPVB group compared to the non TPVB group[19].

Similar results were reported by Coopey et al[20] who showed that in patients undergoing breast surgery TPVB significantly decreased the length of hospital stay. The decrease in length of hospital stay was associated with an improved pain control, a shorter time to conversion to oral narcotics after surgery and a reduction in intraoperative and postoperative narcotics use, with a consequential decrease in postoperative nausea and vomiting[20]. The authors underline the importance of the routine use of TPVB in this kind of patients, especially considering the increasing proportion of women opting for this type of surgery[21].

TPVB in chronic pain

Acute postoperative pain due to insufficient or ineffective pain control is a major risk factor for the development of chronic pain after breast surgery. This condition includes paresthesia, intercostobrachial neuralgia and phantom breast pain and it overall affects 20-50% of the women who undergo breast surgery[22]. Some studies investigated the efficacy of TPVB in reducing persistent postoperative pain, reporting positive results for patients at 6 and 12 months follow-up. However this result must be considered with caution given the overall limited incidence of chronic pain in the population analyzed[22].

The results of a randomized study on 180 women undergoing modified radical mastectomy revealed that although TPVB cannot reduce the occurrence of relative risk of chronic pain, it can

reduce the intensity of chronic pain compared to GA. Indeed, patients who received a TPVB reported less severe chronic pain and exhibited fewer symptoms and signs of chronic pain compared to those who received GA. In addition, patients treated with TPVB experienced better physical and mental health-related quality of life[23].

One possible explanation for these results is that the effective analgesia provided by TPVB could avoid the spinal hypersensitization and the alteration in the normal stimulation of nociceptive neurons induced by the damages to tissues during surgery. This hypothesis should, however, be better investigated in future studies to assess the role of TPVB in reducing chronic pain after breast surgery.

TPVB and immune function in breast cancer

Some studies have recently investigated how several perioperative factors, including the use of anesthetics and opioids, can influence the anti-tumor immune response after cancer surgery. In particular, the use of regional anesthesia-analgesia seems to attenuate perioperative immunosuppression and minimize metastases.

One study focused on the effect of different treatments (propofol/paravertebral anesthesia-analgesia *vs.* sevoflurane/opioid analgesia) on the levels of protumorigenic factors – such as cytokines and matrix metalloproteinases (MMP) – and antitumorigenic cytokines. The results of the study showed that TPVB with propofol altered the levels of some cytokines that regulate perioperative cancer immunity. In particular, the analysis reported a decrease in postoperative IL-1b – a cytokine that promotes tumor invasiveness and tumor-mediated immune suppression – and MMP-3 – a key enzyme that favors tumor invasion and metastasization by promoting the proteolytic degradation of the extracellular matrix. In addition TPVB with propofol was associated with a significant increase in IL-10 levels. Although the role of this cytokine in breast cancer has not been clarified yet, it is known that IL-10 inhibits the production of pro-inflammatory cytokines and exerts an antitumor and antimetastatic activity. Overall these results suggest that regional anesthesia combined with propofol may help preserve the immune defenses against tumor progression[24].

The influence of anesthesia on the immune regulation has been reported also in another study that focused on Natural Killer (NK) cells, which are considered a critical element in the anti-tumor immune response. Buckley et al[25] showed that serum from women receiving different anesthetic treatments for breast surgery had different effects on the cytotoxic activity of healthy human NK cells against hormone-responsive breast cancer cells. Indeed NK cells cytotoxicity *in vitro* was greater in women treated with propofol TPVB compared to those who received sevoflurane-opioid GA[25].

Despite the advantages observed in these studies for TPVB technique, these results are only preliminary and need further confirmation to verify their reliability.

TPVB and Pectoral nerve block

Pectoral nerve block (PNB) is a relatively simple and effective presurgical procedure that targets the two medial and lateral pectoralis nerves, branches of the brachial plexus and responsible motor innervation of pectoralis major and minor muscles (Pecs I). Of note different versions of this method have been described, such as Pecs II (modified Pecs I) that targets the axilla that is vital for axillary clearances and the intercostal nerves[26] and the serratus plain block that primarily targets the thoracic intercostal nerves and is designed to provide complete analgesia of the lateral part of the thorax[27].

The PNS is mainly used in breast surgical procedures that require breast expanders or subpectoral prosthesis, which are usually associated with marked postsurgical pain due to the stretching of the pectoralis major. The employment of this technique together with other pain control measures helps reduce postsurgical muscle spasm and associated pain thanks to the nerve block of pectoralis major. In fact, the sole TPVB hardly reaches the roots of the brachial plexus and then leaves unprotected these muscles that are frequently manipulated during the reconstructive surgeries.

Wahba et al[28] compared the analgesic effect and morphine consumption of Pecs (Pecs I) and TPVB in women undergoing modified radical mastectomy. Overall they observed that within 24 h after surgery patients treated with Pecs block consumed a significantly smaller amount of morphine compared to those in the TPVB group; moreover the time for first request of morphine was longer in the Pecs group. In addition, Pecs was associated with a decreased intensity of postsurgical pain, measured with numerical rating score, within 12h. Noteworthy, at 18h and 24h after surgery pain intensity was lower in the TPVB group. Based on the results of the study the authors suggest that Pecs is a potential analgesic technique alternative to TPVB after breast surgery[28].

Although no data are available on the use of Pecs block as sole anesthetic technique, a recent study evaluated the combination of Pecs I and TPVB, comparing it with TPVB associated with standard sedation in 60 patients undergoing breast surgery with subpectoral implants[29]. The block of pectoral nerve was introduced in combination with TPVB as a way to obtain a more comfortable perioperative period. The results of the study showed that the combination of the two techniques was associated with a better post-operative analgesic control immediately after surgery: pain level assessed with VAS was significantly lower in the group treated with the combination of pectoral and thoracic paravertebral block 8 hours but not 24 hours after surgery. In addition, the combination of the two techniques reported a reduced need for intra-operative sedation. Last of all, no statistically significant differences were observed between the two groups in terms of postoperative nausea and vomiting[29].

Conclusions

The use of TPVB during breast surgery presents a number of advantages for women as it is associated with a reduction in post-surgical complications. Several studies showed that patients who receive TPVB experience reduced levels of postoperative pain, have a decreased need for opioids after surgery and therefore suffer less nausea and vomiting, and eventually shorten their hospital stay, compared to patients who receive general anesthesia. Of note, TPVB is particularly important for patients undergoing complicated procedures, such as unilateral or bilateral mastectomy followed by immediate reconstruction, as they usually experience more complications after surgery.

In addition, TPVB seems to be associated with benefits regarding avoidance of immunosuppression and inflammation. We suggest that this aspect is particularly important and further studies should be performed to assess the impact of TPBV on the anti-tumor immune response and on the number of relapses after breast surgery.

Other techniques are under investigation as alternatives to or in combination with TPVB. We believe that the combination of TPVB and PNB may result in additional benefits for the patients, especially in terms of reduction of postoperative pain. Despite the positive results obtained so far, the number of studies on this combination are still limited and we, therefore, suggest that future clinical trials, performed on a larger number of patients, should be performed to assess the benefits of the combination of TPVB and PNB.

Conflicts of interest

The authors declare that no conflicts of interest relevant to this study.

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