Preincisional Paravertebral Block Reduces the Prevalence of Chronic Pain After Breast Surgery

Pekka M. Kairaluoma, MD
Martina S. Bachmann, MD, PhD
Per H. Rosenberg, MD, PhD
Pertti J. Pere, MD, PhD

We reported earlier that preincisional paravertebral block (PVB) provides significant immediate postoperative analgesia after breast cancer surgery. In the same patients (n = 60), a 1-yr follow-up was performed to find out whether PVB could also reduce the prevalence of postoperative chronic pain. The follow-up consisted of a 14-day symptom diary and telephone interviews 1, 6, and 12 mo after surgery. The 14-day consumption of analgesics was similar in the 30 PVB and the 30 control patients. However, 1 mo after surgery, the intensity of motion-related pain was lower (P = 0.005) in the PVB group. Six months after surgery, the prevalence of any pain symptoms (P = 0.029) was lower in the PVB group. Finally, at 12 mo after surgery, in addition to the prevalence of pain symptoms (P = 0.003) and the intensity of motion-related pain (P = 0.003), the intensity of pain at rest (P = 0.011) was lower in the PVB group. These findings were independent of whether or not axillary dissection had been performed. The incidence of neuropathic pain was low (two and three patients in the PVB and control groups, respectively). In addition to providing acute postoperative pain relief, preoperative PVB seems to reduce the prevalence of chronic pain 1 yr after breast cancer surgery.

Chronic pain symptoms in the operated area and the ipsilateral arm are prevalent 1 yr after breast surgery (1,2). Unexpectedly, chronic pain has been found to be more common after breast-conserving surgery than radical surgery (3). The intensity of acute postoperative pain, the type of operation, involvement of regional lymph nodes, and radiotherapy have been considered the most important treatment-related factors predisposing to chronic pain in patients with breast cancer (2,4). Paravertebral block (PVB) can be used as the sole anesthetic technique for breast surgery (5,6); but, perhaps more frequently today, PVB is used before or after the induction of general anesthesia to provide postoperative analgesia after breast surgery (7–10). We have reported earlier good immediate postoperative analgesia after preincisional PVB in patients undergoing breast surgery for cancer (8). Good acute pain relief is associated with a lower risk of development of chronic pain in the operative area (4,11,12). Therefore, we performed a 1-yr follow-up in 60 breast cancer patients who participated in our PVB study (8) to determine whether the preincisional PVB would be associated with less long-term pain after breast surgery.

METHODS

We obtained Institutional Ethics Committee approval and written informed patient consent for a prospective, randomized, placebo-controlled, and single-blind outcome study in 60 patients who underwent breast surgery for cancer (8). Before general anesthesia, 30 patients were given a PVB (PVB group) with 0.5% bupivacaine 1.5 mg/kg at T3, and 30 patients received a sham block (sham group) with saline subcutaneously at the corresponding puncture site (8). Regarding the safety of the patients, we did not find it necessary to identify the paravertebral space in the sham patients after contacting the transverse process with the epidural needle, but otherwise, the block was performed similarly in both groups. A staff anesthesiologist, not participating in the follow-up assessment, performed the procedure behind a drape curtain so that the patient, her attending anesthesiologist, and the nursing staff were blinded to the block and study drugs. The patients were scheduled for conservative breast cancer surgery with associated radioisotope guided (SENTINEL) lymph node biopsy. Axillary dissection was performed if lymph node metastases were detected. Patients with a large primary tumor, hormone receptor negative, stage II–III cancer, or axillary metastases received postoperative chemotherapy (13,14). Patients with a large primary tumor, axillary metastases, infiltration into skin or muscle, and all with breast-conserving surgery received postoperative radiotherapy.

From the Department of Anesthesia and Intensive Care Medicine, Helsinki University Hospital, Finland.

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Address correspondence and reprint requests to Pekka Kairaluoma, MD, Department of Anesthesia and Intensive Care Medicine, Helsinki University Hospital, PO Box 580, Helsinki, FIN-00029 HUS, Finland. Address e-mail to pekka.kairaluoma@hus.fi.

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The follow-up consisted of a postoperative 14-day symptom diary and telephone interviews by a blinded interviewer 1, 6, and 12 mo after the operation. All patients were encouraged to take ibuprofen 10 mg/kg and acetaminophen 1 g 3 times daily at home for analgesia as required, with an option of taking acetaminophen 500 mg + codeine 30-mg tablets (instead of mere acetaminophen) or tramadol 50–100 mg for rescue analgesia. The patients were instructed to contact the study doctor by telephone if they experienced inadequate pain relief. The patients and the study anesthesiologists who performed the analysis remained blinded to the use of PVB with bupivacaine or a sham block throughout the entire study period.

At the preanesthesia visit, the patients were instructed to use a symptom diary (8). In their diaries at predetermined times during hospital stay and twice daily at home until the 14th postoperative evening, the patients recorded their daily medication, location of pain, and visual analog scale (VAS) scores (0–10) for pain, nausea and vomiting, sedation, and ipsilateral shoulder movement restriction.

To evaluate the association of mood with recovery, the patients were requested to fill out the Finnish version of the Profile of Mood Scales (POMS) questionnaire (15). The Finnish version of POMS has been validated in a standard female population and used in the evaluation of premedication (15). The questionnaire consists of 7–8 adjectives related to each of 6 aspects of mood: depression, fatigue, anxiety, hostility, vigor, and confusion. The questionnaire was first filled out at the preanesthesia visit and then repeatedly on the first postoperative day and 1, 6, and 12 mo later during the telephone interviews.

A group-blinded study assistant conducted all telephone interviews. Patients were asked to use the Numeric Rating Scale (0–10) to evaluate their current condition regarding motion-related pain and pain at rest. The patients were asked if they could localize any pain specifically to the breast, axilla, arm, or some other site. If the patient still had pain at the time of the interview, she was also asked about the occurrence of various types of pain or sensibility disturbances. An overall incidence of pain symptoms was determined as the number (0–5) of reported different pain symptoms (pain at rest, movement-related pain, sharp pain, continuous pain, and pain from light tactile stimulus) at each interview. The patients were asked whether they were still taking analgesics and whether they had received chemotherapy or radiation therapy (when and how many times).

Patients who reported pain symptoms during the interviews were contacted, and those who had pain symptoms related to the breast operation were seen at the pain clinic of the hospital. Qualitative skin sensibility testing was performed to find possible deterioration of nerve ending function, which is typical in neuropathic pain. The tests included manual palpation and exposure to hot and cold objects, a brush, and the tip of a pinprick needle.

The data were analyzed on an “intention-to-treat” basis using Mann-Whitney, χ², or Kruskal-Wallis tests and presented as the number of patients, mean ± sd, or median (range) as appropriate. P < 0.05 was considered statistically significant. The logistic regression module of the statistical program NCSS 2000 (NCSS, Kaysville, UT) was used. The multiple stepwise logistic regression was performed by the backward elimination method with cutoff 0.20, elimination midpoint 0.50, and maximum iterations 50. The effect of a second operation was analyzed by recalculating all data after exclusion of all patients who had more than one operation.

RESULTS

Fifty-eight patients (96.7%) returned the 14-day symptom diary. We were able to interview all 60 patients at 1 and 6 mo and 59 patients at 12 mo after surgery because one patient had died before the 12-mo interview. The death was not related to breast cancer or cancer therapy.

Patients in the sham group experienced more VAS >3 intense pain during the first 14 postoperative days (Fig. 1). There was no difference in analgesic consumption, number of patients taking pain medication regularly (Fig. 2), or localization of pain between the groups.

The Numeric Rating Scale (0–10) scores for motion-related pain and pain at rest were lower in the PVB group 12 mo after surgery (Table 1). There was no difference between the groups in the incidences of rigidity in the scar area, sensitivity disturbances, musculoskeletal symptoms, and restriction of movement, edema, radiotherapy, or chemotherapy. None of the patients reported phantom pain. The patients in the PVB group had fewer pain symptoms 6 and 12 mo after surgery (Table 2). The localization of pain was similar in both groups 1 and 12 mo after surgery, but the patients in the sham group experienced significantly more breast pain 6 mo after surgery regardless of whether or not the axilla had been dissected.

Breast resection with associated lymph node biopsy was performed in 21 (70%) patients in the PVB group and 22 (73%) patients in the sham group, and thus, mastectomy was performed at the primary operation in 9 (30%) patients in the PVB group and 8 (27%) patients in the sham group (P = 0.774). Lymph node involvement requiring axillary dissection was diagnosed in 12 patients in the PVB group and 11 patients in the sham group (P = 0.79). Five patients in the PVB and 3 in the sham group (P = 0.45) had axillary dissection in a second operation 2–4 wk later. Mastectomy was performed in 3 patients in the PVB group and in 2 in the sham group (P = 0.64) 2–4 wk after the primary operation, which had included axillary dissection in all but 1 patient. One patient in the PVB
group had both axillary dissection and mastectomy performed in the second operation. The patients did not receive any regional anesthetic block for the second operation. Patients who had axillary dissection at the primary operation consumed more pain medication during the first 14 postoperative days (Table 3). The study results did not change markedly when all data were recalculated without the patients who had more than one operation.

Chemotherapy was given to 15 (50%) patients in the PVB group and 13 (43%) patients in the sham group ($P = 0.49$), whereas radiotherapy was given to 24 (80%) patients in the PVB group and 22 (73%) in the sham group ($P = 0.41$). Chemotherapy was given to the 22 (71%) patients who required axillary dissection and to 6 (21%) who did not ($P < 0.01$), whereas radiotherapy was given to 28 (90%) patients who required axillary dissection and to 18 (62%) who did not ($P < 0.05$). Chemotherapy started 1–4 mo (median, 2 mo) after surgery and continued until 4–7 mo (median, 6 mo) after surgery. Most of the patients who did not require axillary dissection or chemotherapy had completed their radiotherapy before the 6-mo interview, whereas 21 of 22 patients who required axillary dissection, chemotherapy, and radiotherapy received their radiotherapy after the 6-mo interview.

Logistic regression was used to analyze the relationship between known and suspected risk factors (2,4) and the pain symptoms 12 mo after surgery (Table 4). The independent variables used in the logistic regression analysis were PVB, axillary dissection, pain (VAS) in the postanesthesia care unit, pain (VAS) on hospital ward, pain (VAS) at home (14-day), motion restriction (VAS) (14-day), occurrence of breast...
had tumor resection without axillary dissection, and one patient in the sham group had radical mastectomy with axillary dissection. Neuropathic pain was diagnosed in the other five patients seen at the pain clinic. Neuropathic pain was characterized by continuous burning or sharp pain with dynamic and static allodynia, hypersensitivity, or dysesthesia to light tactile and thermal stimuli. The five patients who suffered from neuropathic pain had higher depression scores 1 mo after surgery (12 [9–21] versus 6 [0–25]; scale, 0–32) than the other 55 patients (P = 0.040) and had consumed more rescue analgesics during the first 14 postoperative days than the other 55 patients (Table 3). All five patients with neuropathic pain had received postoperative radiotherapy.

Both groups scored similarly with regard to five aspects (depression, anxiety, hostility, fatigue, and confusion) in the POMS questionnaire during the entire 12-mo follow-up period. However, the PVB group had significantly higher scores for vigor at all measurement points, including the preanesthesia visit, except at 6 mo after the operation, when the scores were similar. The depression score 1 mo after surgery was higher (10 [0–23] versus 5 [0–25]; P = 0.016) in the patients who required axillary dissection during or after the primary operation.

**DISCUSSION**

Our follow-up showed that preoperative PVB reduced the prevalence and severity of pain up to one year after breast cancer surgery. The prospective fashion of the study and the excellent patient compliance strengthen the validity of our results. There have been no reports on the long-term effects of PVB on chronic pain after breast surgery for cancer (16,17). Interestingly, the application of EMLA® (lidocaine and prilocaine) cream on the breast and the axilla, started before surgery and continued for four days, has been reported to reduce the incidence of chronic pain in the area of surgery three months after surgery (18).

The intensity of postoperative pain and the increased requirement of analgesics during the first days after surgery may play a role in the development of chronic postoperative pain (3,4,11,12,18). We found that a preincisional PVB with bupivacaine provided significant immediate postoperative analgesia, reducing the consumption of IV opioid by 40% in the postanesthesia care unit (8). The correlation between the consumption of the rescue analgesics during the first 14 postoperative days and pain at rest, and any pain in the axilla 12 months after surgery is in accordance with the concept that significant early postoperative pain predisposes to chronic pain symptoms (4).

The benefits of PVB were evident at every interview, with increasing benefits culminating at the 12-month interview when the PVB group had less motion-related pain and less pain at rest. Radiotherapy about 6 months after surgery may have aggravated the pain symptoms recorded at 12 months.
Dissection (AX) and in Those Who Had None (NO-AX)

**Table 3. The Consumption of Analgesics (mean ± sd) During the First Postoperative 14 days in Patients Who Had Axillary Dissection (AX) and in Those Who Had None (NO-AX)**

<table>
<thead>
<tr>
<th></th>
<th>AX (n = 23)</th>
<th>NO-AX (n = 37)</th>
<th>NP (n = 5)</th>
<th>NO-NP (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acetaminophen (g)</td>
<td>15.0 ± 7.7*</td>
<td>7.6 ± 6.7</td>
<td>14.3 ± 8.1</td>
<td>10.2 ± 7.9</td>
</tr>
<tr>
<td>Ibuprofen (g)</td>
<td>11.5 ± 7.7*</td>
<td>7.9 ± 7.3</td>
<td>11.3 ± 5.0</td>
<td>9.0 ± 7.3</td>
</tr>
<tr>
<td>Acetaminophen 500 mg + codeine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30 mg (tablets)</td>
<td>4.0 ± 11.6</td>
<td>0.7 ± 2.5</td>
<td>15.5 ± 22.5</td>
<td>0.7 ± 2.3</td>
</tr>
<tr>
<td>Tramadol (mg)</td>
<td>59 ± 174</td>
<td>69 ± 249</td>
<td>240 ± 331*</td>
<td>48 ± 204</td>
</tr>
</tbody>
</table>

In the third and fourth columns, a similar comparison between the patients who were diagnosed to have neuropathic pain (NP) later on with the ones that were not (NO-NP) is shown. * P < 0.05.

**Table 4. Statistically Significant Relationships Between Perioperative Factors and Chronic Pain Symptoms 12 mo After Surgery**

<table>
<thead>
<tr>
<th>Response variable</th>
<th>Related variable</th>
<th>Regression coefficient</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Motion-related pain</td>
<td>Paravertebral block</td>
<td>−1.664</td>
<td>0.031*</td>
</tr>
<tr>
<td>Motion-related pain</td>
<td>Pain (VAS) at home (14-day)</td>
<td>1.688</td>
<td>0.012*</td>
</tr>
<tr>
<td>Pain at rest</td>
<td>Use of rescue analgesic (14-day)</td>
<td>0.286</td>
<td>0.049*</td>
</tr>
<tr>
<td>Pain at rest</td>
<td>Radiotherapy</td>
<td>5.937</td>
<td>0.036*</td>
</tr>
<tr>
<td>Pain at rest</td>
<td>Occurrence of breast pain (14-day)</td>
<td>0.413</td>
<td>0.035*</td>
</tr>
<tr>
<td>Chronic pain symptoms</td>
<td>Paravertebral block</td>
<td>−1.295</td>
<td>0.039*</td>
</tr>
<tr>
<td>Chronic pain symptoms</td>
<td>Pain (VAS) at home (14-day)</td>
<td>0.953</td>
<td>0.039*</td>
</tr>
<tr>
<td>Neuropathic pain</td>
<td>Use of rescue analgesic (14-day)</td>
<td>0.156</td>
<td>0.046*</td>
</tr>
<tr>
<td>Pain in the axilla</td>
<td>Pain symptoms (1 mo)</td>
<td>0.551</td>
<td>0.045*</td>
</tr>
<tr>
<td>Pain in the axilla</td>
<td>Axillary dissection</td>
<td>2.069</td>
<td>0.008*</td>
</tr>
<tr>
<td>Pain in the axilla</td>
<td>Use of rescue analgesic (14-day)</td>
<td>0.378</td>
<td>0.037*</td>
</tr>
<tr>
<td>Pain in the breast</td>
<td>Axillary dissection</td>
<td>−2.151</td>
<td>0.009*</td>
</tr>
<tr>
<td>Pain in the arm</td>
<td>None</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

VAS = Visual Analog Scale.

* P < 0.05.

after surgery, but even in such cases, PVB seems to have had a positive effect.

The patients in the PVB group had fewer pain symptoms 6 and 12 months after surgery. One month after surgery, the many pain symptoms seen in both groups were probably the result of new acute postoperative pain after the secondary axillary dissection/mastectomy that had to be performed in 12 patients (20% of patients) 2–4 weeks after surgery.

Chronic pain is reportedly more common after breast-conserving surgery than after radical surgery (3). The patients in the PVB group had less pain 12 months after the operation regardless of whether the axilla had been dissected (52% of patients). In our hospital, after the studies by Tasmuth et al. (4,19) on chronic pain in breast cancer patients, the surgeons have paid special attention to sparing the intercostobrachial and other nerves during axillary clearance, at least when there is no metastatic involvement of the axillary lymph nodes. After 12 months, the incidence of pain in the arm was very low, i.e., 3% in both study groups. Sparing of the intercostobrachial and other nerves together with breast-conserving surgery (70% breast resections) are probably the reasons for the absence of phantom pain in our study.

An influence of PVB on the incidence and severity of symptoms related to chemotherapy and radiotherapy, such as fatigue, nausea and vomiting, and inflammation of the skin (20), could not be demonstrated because in the one-year interview, the prevalence of these symptoms was already low. PVB seemed to prevent the aggravation of pain in the breast area occurring after radiotherapy in patients who did not need axillary dissection. In almost all of the patients (21 of 22) who had axillary dissection and chemotherapy and radiotherapy, the latter was commenced after the 6-month interview. Therefore, the impact of radiotherapy on their symptoms could not be evaluated until the 12-month interview.

The prevalence of chronic pain symptoms (Table 2) is comparable to that reported earlier in our hospital (1,3). Importantly, however, the incidence of neuropathic pain (8.3%) in our patients was less frequent than in several earlier studies (17%–50%) (1–3,11), and the favorable results, independent of the PVB, may be ascribed to the nerve-sparing surgical technique of axillary dissection (3,11,19).

The development of chronic pain in patients undergoing surgery for breast cancer is associated with depression (11). However, in our study, we did not detect any difference in the POMS scores for depression or anxiety between the PVB and sham groups during the 12-month study period. However, higher depression scores had been detected one month after surgery in patients who required axillary dissection and in the five patients who developed neuropathic pain approximately six months after surgery. Several studies have, in fact, confirmed that the presence of depression predisposes to the development of chronic pain (21,22).

Preincisional PVB was found to reduce motion-related pain and chronic pain symptoms 12 months after surgery independently of whether or not axillary dissection had been performed (Tables 1, 2, and 4).
Radiotherapy was related to pain at rest 12 months after surgery (Table 4), and in addition, all five patients who were diagnosed with neuropathic pain received radiotherapy. This confirms radiotherapy as a predisposing factor for chronic pain (4). Pain (VAS) at home (1–14 days) was related to motion-related pain and chronic pain symptoms 12 months after surgery (Table 4). The consumption of acetaminophen + codeine in addition to standard ibuprofen and acetaminophen alone during the first 14 days was related to axillary pain, pain at rest, and neuropathic pain 12 months after surgery. The patients, with or without axillary dissection, who experience prolonged acute postoperative pain and require opioids in addition to ibuprofen during the first 14 postoperative days are predisposed to development of chronic pain and require special attention to prevent chronic postoperative pain (4).

In addition to providing good acute postoperative pain relief, preoperative PVB prevented pain conditions for up to one year after breast cancer surgery. These extended benefits should encourage the use of PVB in connection with breast cancer surgery. However, it is also important for the surgeon to spare the intercostobrachial nerves in the axillary dissection.

REFERENCES