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Original Contribution

Does the perioperative analgesic/anesthetic regimen influence the prevalence of long-term chronic pain after mastectomy?☆

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Abstract

Study Objective: To investigate if the anesthetic/analgesic regimen is associated with the risk of reporting long-term chronic postmastectomy pain (CPMP).

Design: Cross-sectional survey

Setting: Academic hospital

Patients: A total of 267 women having undergone mastectomy with axillary lymph node dissection between 2003 and 2008

Interventions: All patients were contacted between October and December 2012, with a questionnaire asking for persistent pain after surgery and its characteristics.

Measurements: Besides demographical data, tumor characteristics, and adjuvant treatment, we recorded type and doses of intraoperative anesthetics/analgesics (sufentanil, ketamine, clonidine, nonsteroidal anti-inflammatory drugs, $MgSO_4$, propofol, or halogenated agents).

Results: Of the 128 patients returning analyzable questionnaires, 43.8% reported chronic pain (48.2% with neuropathic characteristics). Multivariate logistic/linear regression model showed 4 factors independently associated with persistent pain: recall of preoperative pain (odds ratio [OR], 1.27; 95% confidence interval [CI], 1.09-1.48), chemotherapy (OR, 1.32; 95% CI, 1.13-1.55), need for strong opioids in postanesthesia care unit (OR, 1.30; 95% CI, 1.11-1.53), and halogenated agent anesthesia (OR, 0.81; 95% CI, 0.70-0.95).

Conclusion: In conclusion, our study confirms the high prevalence of CPMP, 4 to 9 years after surgery. Recall of preoperative pain, chemotherapy, and need for strong opioids in the postanesthesia care unit were all associated with the presence of chronic pain. Of the intraoperative analgesics/anesthetics studied, only use of halogenated agents was associated with a lower prevalence of CPMP.

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1. Introduction

Chronic postmastectomy pain (CPMP) is a common occurrence and a significant clinical problem, with prevalence as high as 50% reported in the literature. About 10% of

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patients experience severe pain and this is associated with a considerable impact on their quality of life [1,2].

As mastectomy is a frequent procedure, this syndrome affects a great number of women. Consequently, it is important to gain a better understanding of the factors associated with the development of persistent pain. Epidemiologic studies—both retrospective and prospective—have identified several of these risk factors, for example, younger age, chemotherapy and radiotherapy, and presence of preoperative pain or severe acute postoperative pain. Unfortunately, few of those studies have taken into account the possible role of the anesthesia/analgesia regimen [3]. This is possibly an important bias, as there is evidence to suggest that intraoperative anesthetics and analgesics can influence the risk of developing persistent pain after breast surgery [4–8].

The aims of our study were to determine the prevalence for CPMP 4 to 9 years after mastectomy with axillary dissection for breast cancer and investigate if the anesthetic/analgesic regimen our patients received was associated with the risk of reporting such persistent pain.

2. Methods

2.1. Patients and procedures

After approval from the Ethical Committee of the Université Catholique de Louvain (CEBHF, chairperson: Pr. J.-M. Maloteaux), Brussels, Belgium, we considered all patients previously included in a prospective listing of our center and in a previous study on the effect of perioperative analgesics on cancer recurrence [9]. These 323 consecutive patients underwent mastectomy with axillary dissection between February 2003 and September 2008. The same experienced surgeon performed all surgical procedures. Patients with previous surgery for breast cancer had been excluded. Other exclusion criteria for this study were death and cancer recurrence.

In all patients, general anesthesia was induced with either sodium thiopental (4 mg/kg) or propofol (2-3 mg/kg), associated or not with sufentanil (0-0.2 μg/kg). After insertion of a laryngeal mask airway, anesthesia was maintained with continuous infusion of propofol (target concentration total intravenous anesthesia (TIVA)) or a halogenated agent (sevoflurane or desflurane) in an oxygen/air or an oxygen/nitrous oxide mixture. Possible intravenous adjuvants included clonidine (0-6 μg/kg), ketamine (0-0.5 mg/kg), $MgSO_4$ (0-3 g), and nonsteroidal anti-inflammatory drugs (NSAIDs), diclofenac (0-75 mg), or ketorolac (if administered: 20 mg in patients <60 kg body weight and 30 mg in patients >60 kg). Anesthetic management was left to the discretion of the senior anesthesiologist in charge of the patient.

In the postanesthesia care unit (PACU), postoperative analgesia consisted of intravenous piritramide titrated until the visual analog scale score was lower than 4 on a scale anchored with 0 as "no pain" and 10 as "the worst pain ever experienced." During the first 48 postoperative hours, all patients received acetaminophen (paracetamol), 3 to 4 g/d. Oral diclofenac 50 mg was administered 3 times a day for 3 days as necessary in the absence of contraindication (gastric, renal, or advanced age). No additional opioids were needed during the postoperative period.

2.2. Data collection

The following data were obtained from the prospectively computed medical records: perioperative (demographic) characteristics, tumor size, histologic tumor grade, histopathologic type, estrogen and progesterone receptor status, epidermal growth factor receptor type 2 expression, extent of axillary node disease, and administration of perioperative or postoperative adjuvant chemotherapy, radiotherapy, or endocrine therapy. Duration of the surgical procedure as well as type and total dose of the hypnotics and analgesics administered intraoperatively were obtained by reviewing the electronic intraoperative and postoperative records.

All patients received an informed consent form and a questionnaire by mail in October 2012. A reminder was sent in December 2012 to the patients who had not responded. Our questionnaire was based on the one used by Gärtner et al [1] and the one used by Li and Kong [10], in 2 recent studies on prevalence of chronic pain after breast cancer treatment. We inquired about recall of preoperative breast pain and about the presence of pain at the time of questioning. If the answer was positive to the second question, we asked for additional information: localization, frequency, and intensity of the pain (on a Numerical Rating Scale (NRS) of 0 to 10, with 0 being no pain and 10 the worst pain imaginable); whether the patient had contacted a doctor; and whether she took analgesics for the pain. To assess the type of pain, we used the ID Pain questionnaire, a tool validated for the detection of neuropathic pain after breast cancer treatment [11]. Finally, we asked questions about abnormal sensations (eg, phantom breast sensations) and whether the patients had pain elsewhere in the body, for example, low back pain or migraine.

2.3. Primary end point

The main objective of our study was to determine the effect, if any, of the intraoperative and postoperative analgesics and anesthetics (propofol or halogenated agent, nitrous oxide, sufentanil, ketamine, clonidine, $MgSO_4$, piritramide, and NSAIDs) on prevalence of chronic pain after breast cancer surgery. Therefore, our primary end point was the presence or absence of pain at the time of questioning, 4 to 9 years after the surgical procedure.

2.4. Statistical analysis

Patient characteristics are presented as mean ± SD, median (interquartile 25th-75th), or numbers (percentage).

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