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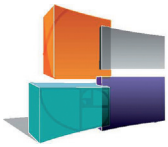

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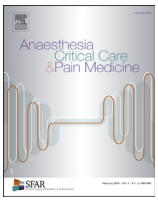

Letter to the Editor

Prolonged continuous wound infiltration with a local anaesthetic after total mastectomy: pharmacokinetics and preliminary results on postoperative pain

Continuous wound infiltration (CWI) of long acting local anesthetics into the surgical wound is an interesting pain-relief strategy which proven effective immediate postoperative pain, reducing opioid use and side effects incidence in various surgical procedures.

We report ropivacaine continuous wound infiltration in ten women undergoing unilateral breast cancer surgery (median [range] age: 67 [44–83], BMI: 23.9 [20.6–30.0]), nine with axillary lymph node dissection and one with sentinel lymph node dissection. The research was approved by the local ethics committee and the French Agency for the Safety of Medicines and Health Products (http://www.clinicaltrials.gov; NCT02525211). Written informed consent was obtained from each patient.

A 150 mm multiperforated CWI catheter (Painfusor catheter™, Baxter) was positioned by the surgeon at the end of the procedure on the pectoralis major muscle with the distal end directed towards the axilla before wound closure. A loading dose of 10 mL of ropivacaine 7.5 mg/mL (75 mg) was administered via the catheter during wound closure. This injection was followed by continuous infiltration of 400 mL of ropivacaine 2 mg/mL for 40 hours using an elastomeric pump at a fixed continuous flow rate of 10 mL/hour. Total amount of ropivacaine was 850 mg, except one patient who mistakenly received the loading dose twice (20 mL ropivacaine 7.5 mg/L, i.e. 150 mg). The catheter was kept in place until the patient was discharged. At the end of the procedure, one or two suction drains, respectively in 2 and 8 out of the ten patients, were positioned by the surgeon and left to aspirate throughout the study.

Standardised general anaesthesia included AIVOC propofol (2 to 5 mcg/mL) and remifentanil (2 to 4 ng/mL). Ventilation was controlled using a laryngeal mask airway or orotracheal intubation. The bispectral index (BIS) was maintained between 40 and 60. Ketamine was used at the induction of anaesthesia at a single dose of 0.5 mg/kg for opioid sparing.

Intraoperative analgesia included 1 g of acetaminophen, 100 mg of ketoprofen and 20 mg of nefopam intravenously 1 hour before the end of surgery. Post-operative analgesia included oral acetaminophen on request (up to 3 g/day), 100 mg of oral ketoprofen (up to 200 mg/day) or 100 mg of tramadol SR (up to 200 mg/day) during the first 48 hours. An IV bolus of 3 mg morphine was required in one patient in the recovery room, who experienced an episode of nausea treated with IV ondansetron. In three patients with a pain Score $>$ 3 for more than 48 hours after surgery, oral acetaminophen and ketoprofen were continued.

Mean pain Score assessed by a numerical Scale on arrival and on exit in the recovery room, 24 and 48 hours after surgery at rest and with standardized arm movements. Active arm movements, defined as hand positioned behind the neck, with the elbow away from the body on the wound side; the ability to drink from a glass; the ability to insert the arm on the wound side into the sleeve of a garment, were possible in all patients before leaving the recovery room (Table 1).

Two cohorts of five patients were included. In the first group, venous blood samples were collected, before the wound infusion bolus, at the start of surgery and 1, 12, 24, 36 and 48 hours later. For the next five patients, the samples were taken before the bolus and then 6, 30, 42, 54, 68 and 75 hours later. Total and unbound (obtained by the ultrafiltration method, Centrifree™ Millipore™) ropivacaine concentrations were determined using gas chromatography coupled to nitrogen-phosphorus detector. The maximum concentration (Cmax) could not be observed in four of the first five patients included. The blood collection period was therefore extended for the second cohort of patients. The median Cmax of ropivacaine was 1.16 mg/L (0.52–2.14 mg/L) (n = 6) was reached at 42 hours f(30–54 hours) and corresponds to a maximum free ropivacaine concentration of 0.09 mg/L (0.007–0.09 mg/L). Total and free serum ropivacaine concentrations remained relatively stable between 24 and 54 hours (Fig. 1).

There was no evidence of local anaesthetic toxicity or adverse reactions. No infectious complications, haematomas or accidental wound catheter removal were observed.

The continuous administration of ropivacaine into the wound in the context of multimodal intra- and postoperative analgesia appears to control effectively pain at rest and with movement after breast cancer surgery. In our study, standardised rapid movements of the arm on the side of the wound were possible in all patients, a short time after surgery in recovery room without increased pain. IV morphine was required in only one patient, which confirms that ropivacaine CWI resulted in limited use of intravenous opioids in the recovery room after mastectomy with or without axillary lymph node dissection. This finding confirms the results of two previous studies in young women undergoing plastic breast surgery, which showed that a continuous wound infusion of 0.25% bupivacaine at 5 mL/hour combined with IV pain relief resulted in a significant reduction in postoperative pain and in the use of intravenous opioids during the infusion[1].

No patients experienced any adverse reactions to prolonged administration of ropivacaine or the presence of the continuous infiltration catheter. To date, there are no factors suggesting that this technique leads to a risk of local wound infection, delayed healing or delayed bleeding [1] and the multiperforated catheter positioned during surgery appears to expose patients to a lower risk of a direct vascular injection compared to a single needle injection for infiltration [2]. Total and free serum concentrations of ropivacaine determined over 75 hours after catheter insertion, were below the neurological toxic threshold (Ctotal = 4.3 mg/L; Cfree = 0.56 mg/L) [3] although doses of ropivacaine well above the maximum recommended dose (3 mg/kg) for single infiltration

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Table 1
Mean pain Score assessed by a numerical Scale (NS) (from 0 = no pain to 10 = worst pain imaginable); standardised movement: hand positioned behind the neck, with the elbow away from the body on the wound side; the ability to drink from a glass; the ability to insert the arm on the wound side into the sleeve of a garment.

	Arrival on recovery room	Exit from recovery room		Surgery H + 24		Surgery H + 48	
		rest	movement	rest	movement	rest	movement
NS Score mean [range]	4.1 [0–5]	‘2.3 [1–4]	3.2 [1–4]	2.2 [0–4]	3.1 [0–4]	2.5 [0–4]	3.2 [0–4]

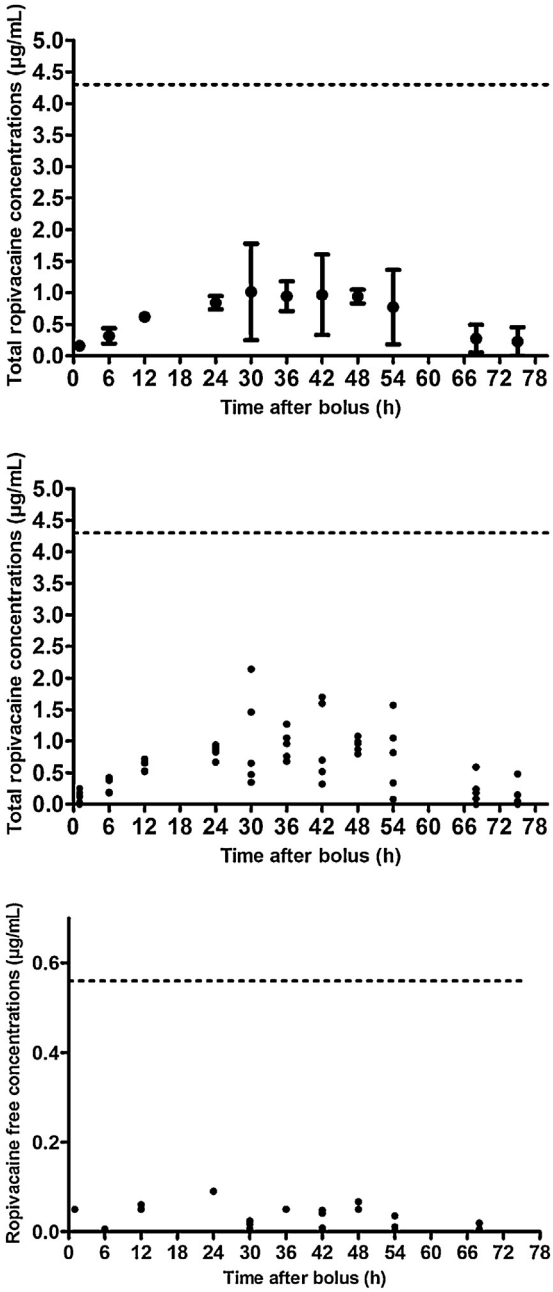

Fig. 1. Ropivacaine concentration profile over time. A: mean total ropivacaine concentration; B: individual ropivacaine concentrations; dotted line = 4.3 µg/mL; C: individual free ropivacaine concentrations; dotted line = 0.56 µg/mL.

were infused. We observed comparable total ropivacaine concentrations to those previously reported during CWI in colorectal and abdominal surgery, where respective mean maximum concentrations of 2.3 ± 0.9 and 2.32 ± 0.21 mcg/mL were found [4,5]. These results show that the suction drains do not prevent the absorption of the local anaesthetic in the pectoralis major muscle.

CWI appears to be a good alternative to paravertebral blocks, enabling effective intra- and postoperative pain management after mastectomy. Its potential role in the prevention of chronic postoperative pain is possible but it shall be demonstrated. This analgesia technique can be envisaged for enhancing recovery after breast surgery in both hospital and outpatients settings. Further studies should be conducted to confirm this possibility.

Disclosure of interest

The authors declare that they have no competing interest.

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