Evaluation of pre-emptive mastectomy flap infiltration with bupivacaine adrenaline

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Objective
Postmastectomy pain is responsible for distress with subsequent organ dysfunction. Systemic analgesics such as opioids are not free of complications. The idea of preincisional mastectomy flap infiltration with bupivacaine and adrenaline was shown by many reports to decrease the postmastectomy pain and analgesic requirements. The aim of this study was to prove this with the assessment of the stress-response changes.

Patients and methods
A total of 120 females who were candidates for mastectomy were randomized into an equal two groups using computer-generated random numbers; first was the study group in which the mastectomy flap was infiltrated before skin incision with bupivacaine and adrenaline, whereas the second was a control. Assessment of patient and operative data was done.

Results
There was no statistical difference between both groups regarding the demographic data, the tumor pathological data, hospital stay, and overall complications. The mean operative time was significantly longer in the study group ($P = 0.01$). The mean blood loss was significantly less in the study group ($P = 0.001$). The mean postoperative arterial blood pressure and pulse were significantly less in the study group ($P = 0.004$ and 0.04, respectively). The mean intraoperative fentanyl and mean postoperative nalbuphine requirements were significantly less in the study group ($P = 0.007$ and 0.002, respectively). Visual analogue scale was significantly less in the study group ($P = 0.01$).

Conclusion
Pre-emptive mastectomy flap infiltration with bupivacaine adrenaline solution is a safe and effective method for reduction of postmastectomy pain and stress response with a significant reduction of the analgesic requirements.

Keywords:
adrenaline, bupivacaine, mastectomy, pain

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Introduction

Postoperative pain is responsible for the afferent stimuli that precipitate abnormal reflexes and result in stress response with subsequent organs dysfunction. Blockade of these stimuli is proposed to decrease the postoperative organs' dysfunctions [1]. The control of postoperative pain is a major concern to achieving a smooth postoperative recovery and to alleviating the stress response especially in patients with associated comorbidities and the elder group [2]. The noxious stimuli that are caused by the surgical incision are transmitted from the cutaneous nociceptors to the brain through the lateral spinothalamic tract in the spinal cord. Opioids can alleviate the incision pain through a central mechanism [3]. Their use is not free of complications, especially those related to the central nervous system depression and vomiting [4]. Local anesthetic techniques were found to be superior to systemic therapy whatever the type of operation or the method of delivery [5,6]. Although regional anesthesia and nerve block techniques are widely used in many situations, many anesthetists are still minded by the simplest way – the wound infiltration [2]. It is very important to mention that wound infiltration with long-standing local anesthetics decreases the anesthetic and analgesic doses during surgery. Moreover, it decreases the need for postoperative opioid-containing analgesics with subsequent decrease of the opioid hazards (opioid-sparing effects) [7]. Moreover, a comparison of different modes of delivery showed equal results of analgesia; for example, creams, patches, topical instillation, local wound infiltration, or regional block [8,9]. There was a debate: either to apply the anesthesia at the end of the procedure or at the start (pre-emptive anesthesia). The second one is more desirable as it was found to decrease both the intraoperative anesthetic requirement and opioid consumption [2,10]. The rate of wound infection was not increased using these techniques [10]. The main concern was the systemic toxicity of the local anesthesia, which was not recorded in a large number

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of studies [11]. The addition of adrenaline to the local anesthetic prolongs its duration of action; moreover, it decreases its systemic absorption, thus decreasing its toxicity [12]. This study aimed at evaluating the effects of pre-emptive mastectomy flaps infiltration with a cocktail including bupivacaine hydrochloride and adrenaline 1/200 000 over the postoperative stress response, pain score, and the opioid requirement.

Patients and methods

This study was conducted during the period from January 2014 to December 2014. It included 120 operable female patients who were candidates for total mastectomy and axillary clearance for breast carcinoma. A written consent was obtained from all patients prior to enrollment. Patients with a history of prior chemotherapy or breast irradiation, those with a history of previous breast surgery, those with morbid obesity, those with collagen disease, those with ASA (the American Society of Anesthesiologists) score poorer than 3, and those with a history of hypersensitivity for local anesthesia were excluded from this study. After obtaining an approval from the institutional review board, patients were randomized into an equal two groups using computer-generated random numbers. In all cases, induction of the general anesthesia was done using a standard technique including 1 μg/kg of fentanyl, 2.5 mg/kg of propofol, and 0.5 mg/kg of atracurium. Maintenance with isoflurane inhalational anesthesia (MAC 1.2) and atracurium at a dose of 0.1 mg/kg every 20 min was carried out. Intraoperative standard monitors were recorded as ECG, pulse oximeter, blood pressure, capnogram, and core body temperature. All these measures were recorded as baseline at skin incision and then every 15 min till the end of surgery. Intraoperative bolus of fentanyl at a dose of 1 μg/kg was administered if the pulse was more than 90/min or blood pressure was higher than 25% of baseline. In the first (study) group (n = 60), mastectomy was done with pre-emptive local infiltration with a cocktail of 120 ml of bupivacaine hydrochloride (0.125% concentration) and adrenaline 1/200 000. For infiltration, mastectomy was done using the classic horizontal Meyer's incision and this line was marked preoperatively, then while the patient was under the induction with propofol, four skin snips were made over angles of the diamond through which a 5-mm liposuction cannula was used to inject the cocktail (Fig. 1), whereas in the second (control) group (n = 60), mastectomy was done in the routine way without local infiltration. All patients received a postoperative 30 mg of intramuscular ketorolac and 1 mg of acetaminophen infusion.

Figure 1

Skin incision marking and method of infiltration.

Patients follow-up

All patients were monitored for pulse, blood pressure, respiratory rate, and pain score [using the visual analogue score (VAS)] every 2 h. Any patient expressing a VAS score more than 4 was offered a bolus of 5 mg intravenous nalbuphine. The amount of drainage of the wound was recorded during the first 12 h as well.

Statistical analysis

Data were presented as frequencies and percentages for categorical data and mean, SD, and range for continuous data. The association between categorical variables was examined using χ^2-test. The difference in mean values of continuous data was examined using independent-samples t-test. All P values were two-tailed. P value less than 0.05 was considered as significant. SPSS software (release 15.0; SPSS Inc., Chicago, Illinois, USA) was used for statistical analyses.

Results

Patients' demographic data are shown in Table 1 with no significant differences among both groups. Table 2 shows the operative data and postoperative outcome. There was no significant difference in between the two groups as regard the tumor size, the nodal status, the incidence of flap necrosis, hematoma, and seroma. There was a significantly longer mean operative time in the study group (127 ± 10.5 min with a range of 90–160 min vs. 105 ± 7.5 min with a range of 80–139 min with P = 0.01). On the other hand the mean blood loss was significantly less in the study group (290 ± 75 ml with a range of 210–370 ml vs. 370 ± 105 ml with a range of 250–480 ml). Meanwhile, the tumor sizes, the nodal status, the hospital stay, the incidence of hematoma, seroma, and flap necrosis

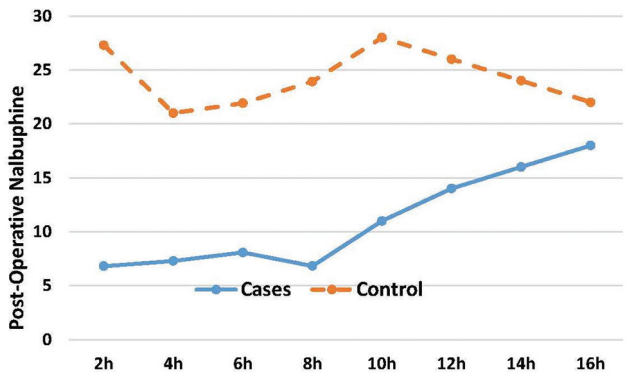
were not statistically different between the two groups (Table 2). By comparing the mean intraoperative fentanyl requirement between both groups, it was significantly less in the study group (1.4 ± 0.7 μg/kg with a range of 1–3 μg/kg vs. 3.4 ± 1.2 μg/kg with a range of 2–5 μg/kg with $P = 0.007$). By comparing the mean postoperative nalbuphine requirement between both groups, it was significantly less in the study group (9 ± 4 mg with a range 5–14 mg vs. 26 ± 7 mg with a range 16–35 mg with $P = 0.002$) (Fig 2). The mean postoperative arterial blood pressure in the study group was 75 ± 4 mmHg with a range of 70–80 mmHg, whereas in the control group it was 81 ± 5 mmHg with a range of 78–90 mmHg with a P value of 0.004 (highly significant). The same was found for the mean postoperative pulse (in beats/min). In the study group it was 82 ± 5 with a range of 74–88 versus 91 ± 7 with a range of 80–100 with a P value of 0.04 (significant). The mean postoperative VAS in the study group was 4 ± 2.6 with a range of 4–7 versus 7 ± 6.9 with a range of 5–8 in the control group with a significant P value of 0.01 (Fig 3).

Discussion

The concept of pre-emptive analgesia is the application of local anesthetic drug by regional nerve blockade, infiltration of the surgical wound, or by topical instillation into the operative bed before tissue trauma, thus preventing the noxious stimuli that result from the tissue damage [3,13].

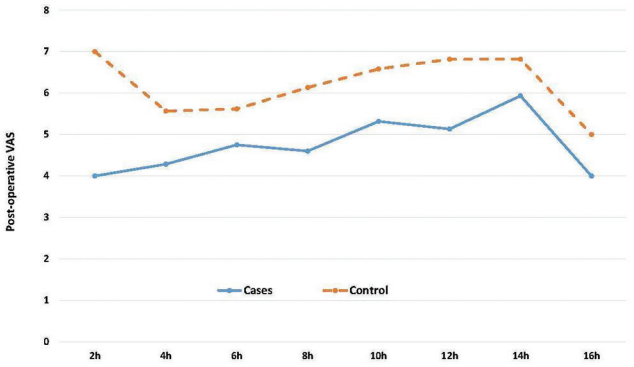
Some studies reported that the preincisional infiltration is more superior to the postincisional one [14]. This was documented by many reports including several

Figure 2



Postoperative mean nalbuphine requirement for cases and control groups.

Figure 3



Postoperative mean visual analogue scale among cases and control groups.

Table 1 Demographic data of the two study groups

Parameter	Study group (n = 60)	Control group (n = 60)	P value
Mean ± SD age (range) (years)	42 ± 7 (28–66)	44 ± 8 (37–66)	0.12
Mean ± SD BMI (range)	29.4 ± 1.8 (22–36)	30.1 ± 1.6 (21–35)	0.39
Mean ± SD BSA (range)	1.7 ± 0.7 (1.55–2.3)	1.65 ± 0.6 (1.51–2.2)	0.9
Hypertension [n (%)]	7 (11.7)	8 (13.3)	1
DM [n (%)]	7 (11.7)	9 (15)	0.82

BSA, Body surface area, DM, diabetes mellitus.

Table 2 Operative data and postoperative outcome

Parameter	Study group (n = 60)	Control group (n = 60)	P value
Mean ± SD operative time (range) (min)	127 ± 10.5 (90–160)	105 ± 7.5 (80–139)	0.01
Mean ± SD blood loss (range) (ml)	290 ± 75 (210–370)	370 ± 105 (250–480)	0.001
Mean ± SD hospital stay (range) (days)	2.1 ± 1.4 (1–4)	2.5 ± 1.1 (1–5)	0.09
Postoperative seroma [n (%)]	22 (36.7)	23 (38.3)	0.32
Postoperative hematoma [n (%)]	9 (15)	8 (13.3)	0.80
Partial flap necrosis [n (%)]	2 (3.3)	1 (1.7)	1.00
Tumor size (mm) ± SD (range)	36 ± 6 (23–69)	34 ± 8 (24–69)	0.51
Total number of lymph node ± SD (range)	11 ± 3 (8–23)	15 ± 3 (9–26)	0.12
Number of positive lymph node ± SD (range)	3.3 ± 1.5 (0–9)	3.6 ± 1.6 (0–10)	0.30

Table 3 Intraoperative and postoperative pain and stress response records

Parameter	Study group (n = 60)	Control group (n = 60)	P value
Mean ± SD intraoperative fentanyl (range)	1.4 ± 0.7 (1–3)	3.4 ± 1.2 (2–5)	0.007
Mean ± SD postoperative nalbuphine (range)	9 ± 4 (5–14)	26 ± 7 (16–35)	0.002
Mean ± SD postoperative ABP (range)	75 ± 4 (70–80)	81 ± 5 (78–90)	0.004
Mean ± SD postoperative pulse (range)	82 ± 5 (74–88)	91 ± 7 (80–100)	0.04
Mean ± SD postoperative VAS (range)	4 ± 2.6 (4–7)	7 ± 6.9 (5–8)	0.01

ABP, arterial blood pressure; VAS, visual analogue scale.

operative tasks [15]. In an important recent systematic review for 10 trials entailing the use of pre-emptive wound infiltration with bupivacaine adrenaline solution, three for mastectomy, four for segmental mastectomy, and three for reduction mammoplasty or excision of benign masses, six of them demonstrated a statistically significant reduction of postoperative pain score and four demonstrated a reduction of postoperative opioid use [16]. A recent trial demonstrated a significant reduction of the opioid requirement in mastectomy after local bupivacaine infiltration [17]. However, the intraoperative and postoperative assessment of the stress response in the form of pulse, blood pressure, and respiratory rate changes is an important issue to be investigated in any painful surgical maneuver. A significant reduction of the VAS and opioids consumption was reported by several studies [18]. A significant reduction of the postoperative pain score and postoperative opioid requirements was also reported with preincisional bupivacaine infiltration in cases of reduction mammoplasty [19]. Our work demonstrated that the postoperative VAS was significantly reduced in the study group. All stigmata of the stress response were reduced in the study group with a highly significant P value. The same was noticed in the doses of intraoperative fentanyl and postoperative nalbuphine. This copes with most of that recorded by the other studies [16]. This valuable benefit was at the cost of increased operative time (Table 2). An interesting finding in our results is the significant reduction of the mean blood loss and this is mostly due to the use of epinephrine in our cocktail (Table 3).

Conclusion

Pre-emptive mastectomy flap infiltration with bupivacaine adrenaline solution is a safe and effective method for reduction of postmastectomy pain and stress response with a significant reduction of the analgesic requirements.

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Conflicts of interest

There are no conflicts of interest.

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