Mohammed *et al.*
Ain-Shams Journal of Anesthesiology (2022) 14:41
https://doi.org/10.1186/s42077-022-00240-3

Ain-Shams Journal of Anesthesiology

ORIGINAL ARTICLE Open Access

A comparative study between the efficacy of bupivacaine plus nalbuphine versus bupivacaine alone in pectoral nerve block for management of postoperative pain in patients undergoing breast fibroadenoma excision

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Abstract

Background: Breast surgeries, even the relatively minor ones, can be associated with significant postoperative pain affecting patients' physical and psychological well-being. As a result, regional anaesthetic approaches have been used for breast surgery anaesthesia and analgesia. PECS I and II blocks have been proven to be relatively easy and safe in such regards. Moreover, using adjuvants, such as nalbuphine, have been proposed by many studies to intensify the block and decrease postoperative analgesic intake.

This current study aims to assess the effects of using nalbuphine (20 mg) as a bupivacaine 0.25% (10 ml) adjuvant in PECS I block compared to injecting bupivacaine 0.25% (10 ml) alone in fibroadenoma excision patients.

This trial enrolled 60 patients, 30 of whom received bupivacaine plus nalbuphine (group BN) and 30 in the bupivacaine only (group B). Postoperative VAS, SpO_2 and vital signs at 0, 1, 2, 4, 6, 12 and 24 h as well as the amount of morphine consumed, the time it took for the first analgesic to be administered and adverse effects were both recorded and compared.

Results: Regarding postoperative outcomes, a statistically significant difference between the two groups was not detected regarding VAS, SpO_2, vital signs and adverse effects. Similarly, there was no statistically significant difference in total morphine intake in the 24 h following surgery between the two groups (p-value = 0.65). Only 9 out of 60 patients needed analgesia, 5 in the BN group and 4 in the B group, and time to the first analgesic was not of statistically significant difference between BN and B groups (211.8 ± 71.29 and 183.5 ± 29.872 min respectively) (p-value = 0.73). In terms of postoperative complications, there was no statistically significant difference between the two groups.

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Conclusions: Adding nalbuphine (20 mg) to bupivacaine in PECS I block in fibroadenoma patients undergoing excision is not accompanied by a difference with statistical significance in postoperative VAS, morphine consumption and duration to the first analgesia when compared to bupivacaine alone.

Keywords: PECS I block, Nalbuphine, Fibroadenoma, Breast surgery, Pectoral nerve block, Regional anaesthesia

Background

Surgeries involving breast tissue is one of the most prevalent types of procedures performed in hospitals, and even modest procedures can result in substantial postoperative pain that might have physiological and psychological repercussions if poorly managed. Also, acute postoperative pain is a major contributor to the onset of persistent post-mastectomy pain. Breast surgery anaesthesia and/or analgesia have been achieved using regional anaesthesia procedures such as thoracic epidural, thoracic paravertebral block and intercostal nerve blocks (Sittl et al. 2013; Gärtner et al. 2012).

The pectoral nerve blocks, namely PECS I and II, are less invasive, have fewer complications and provide excellent analgesia for surgical procedures involving the breast and the chest wall. The PECS I block is originally intended to inject a local anaesthetic into the space between the pectoralis major and minor muscles blocking the medial and the lateral pectoral nerve to provide analgesia during breast surgery (Blanco 2011).

Many adjuvants, such as opioids, dexamethasone and clonidine, have been administered with local anaesthetics aiming to increase the longevity of the block and reduce its toxic effects (Saryazdi et al. 2015).

Nalbuphine has been administered as an adjuvant to local anaesthetics in spinal, epidural and regional anaesthetic blocks since it has been shown to extend the block's duration considerably. Also, it is a powerful analgesic and kappa-opioid receptor agonist and mu-opioid receptor antagonist. Pain relief achieved using nalbuphine is roughly like that of morphine; however, unlike morphine, it has a ceiling effect on respiratory depression (Abdelhamid and Omar 2018).

The primary outcome was VAS postoperatively. Secondary outcomes were postoperative total morphine consumption, time to first analgesic, heart rate, non-invasive blood pressure, respiratory rate, peripheral oxygen saturation (SpO_2), adverse effects such as nausea, vomiting and sedation as well as sedation score.

This current study aims to assess the effects of using nalbuphine (20 mg) as a bupivacaine 0.25% (10 ml) adjuvant in PECS I block compared to injecting bupivacaine 0.25% (10 ml) alone in fibroadenoma excision patients.

Methods

Following the acceptance of the scientific and the research ethical committee of the Ain-Shams University Hospitals number FMASU M D 02/2018, sixty ASA I and II female patients, 18–60 years old, 50–90 kg, who underwent elective fibroadenoma excision surgery were allocated to this prospective randomised double-blind clinical trial, between April and October 2021. The exclusion criteria were as follows: patients' declination, patients with bleeding diathesis, drug hypersensitivity, infection at the needle insertion site, pregnancy and lactation, patients with advanced cardiovascular and psychiatric diseases. The Pan African Clinical Trial Registry database was also used to register this trial (clinical trial ID: PACTR202112778684666).

Participants were divided into two equal groups using computer-generated random numbers stored in opaque sealed envelopes by a senior anaesthetist. After obtaining the patient's written informed approval to participate, a randomly picked envelope was opened on the patient's arrival at the operating room to determine which intervention will be pursued.

Group-BN is as follows: bupivacaine and nalbuphine group, ultrasound-guided PECS I block with 10 ml of 0.25% bupivacaine hydrochloride plus nalbuphine 1 ml (20 mg) administered in the interfascial plane between the two pectoral muscles.

Group-B is as follows: bupivacaine only group, ultrasound-guided PECS I block with 10 mL of 0.25% bupivacaine hydrochloride administered in the interfascial plane between the two pectoral muscles.

The primary outcome was VAS postoperatively. Secondary outcomes were postoperative total morphine consumption, time to first analgesic, heart rate, non-invasive blood pressure, respiratory rate, peripheral oxygen saturation (SpO_2), adverse effects such as nausea, vomiting and sedation as well as sedation score.

Full history was taken, patients were fully examined, and vital data was measured and recorded.

Patients were instructed on how to utilise the visual analogue scale (VAS) before the procedure on a scale from zero to ten (where zero means pain-free and ten means worst experienced pain).

IV access was placed in the contralateral upper limb to the side of the operation upon arrival in the operating theatre, and all patients received 2 mg of IV midazolam as a premedication. ECG, non-invasive blood pressure, peripheral oxygen saturation, and end-tidal carbon dioxide were all monitored intraoperatively.

Anaesthesia was induced using 2–3 mg/kg propofol, 2 µg/kg fentanyl and 0.5 mg/kg atracurium to facilitate endotracheal intubation. The PECS I block was administered with the patient supine and the ipsilateral upper limb abducted 90° using (Sonosite® M-Turbo C U.S.A) linear array ultrasound probe with 6–13 MHz frequency placed medial to the coracoid process; the probe is then tilted medially and moved distally and laterally until the 3rd rib is visualised. Quincke's spinal needle, 22 gauge, was placed in-plane targeting the plane between the pectoralis major and minor muscles, and 10 mL of bupivacaine 0.25%, with or without nalbuphine, was injected after negative aspiration, preferably in the vicinity of the thoracoacromial artery. Surgery was started 15 min after the regional anaesthetic was administered. Anaesthesia was maintained using isoflurane (1–1.5 MAC) in a 50/50 oxygen/air mixture. Muscle paralysis was maintained with 0.1 mg/kg atracurium every 20 min, and ventilation settings that maintained $EtCO_2$ 35-40 mmHg.

Muscle paralysis was reversed with neostigmine (0.04 mg/kg) and atropine (0.01 mg/kg) when surgery was finished. All patients were transferred to the post-anaesthesia care unit after being extubated (PACU). Postoperative analgesia using morphine of 0.1 mg/kg once a VAS ≥ 3 was achieved; then, 1 mg on-demand bolus every 15 min was given if the patient is still in pain, and no background infusion was permitted.

Patients' VAS, SpO_2 and vital signs (patients' heart rate, non-invasive arterial blood pressure and respiratory rate) were monitored and recorded upon arrival to PACU and at 1, 2, 4, 6, 12 and 24 h postoperatively. Moreover, time to the first analgesic and total morphine consumption in the 24 h post-surgery were also documented.

Sedation was assessed using a score from zero to four (zero means patient is fully awake; one means the patient is sleepy, yet responsive to verbal orders; two means patient is sleepy, yet responsive to touch; three means patient is asleep and responsive to painful stimulation; four means the patient is deeply sedated not responding

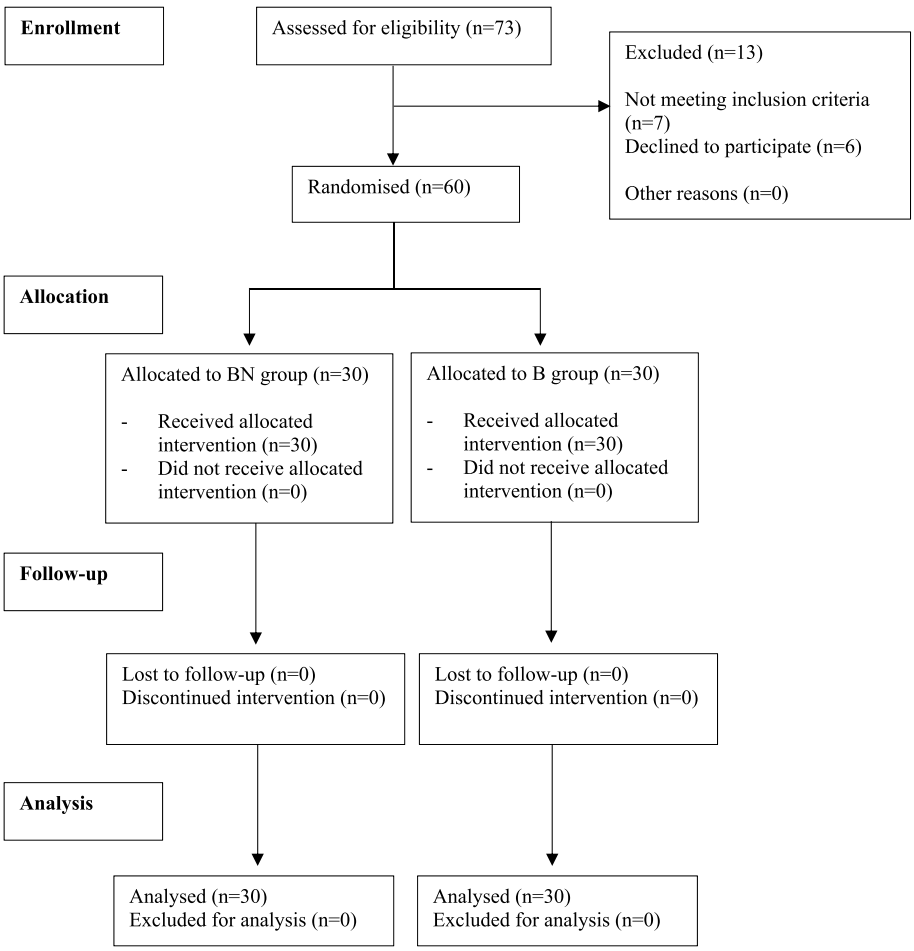

Fig. 1 CONSORT flow chart of participants at each stage of the randomised study

Table 1 Demographic data

	BN group ($n=30$)	B group ($n=30$)	*P*-value
Age (years)	24.97 ± 5.487	27.87 ± 6.334	0.063
Weight (kg)	61.97 ± 7.797	59.10 ± 7.227	0.145
Duration (min)	57.00 ± 25.951	54.00 ± 17.44	0.601
ASA			
I	23 (76.7%)	26 (86.7%)	0.317
II	7 (23.3%)	4 (13.3%)	

Data are presented as mean ± SD, number (%)

P-value > 0.05 is considered statistically non-significant

to any stimuli including painful one). Nausea and vomiting (managed with an IV bolus of metoclopramide 10 mg) were also reported as possible side effects.

Statistical analysis

The sample size was determined with the help of the PASS 11.0 sample size calculator setting power at 80% and alpha error at 0.05. Results from a previous study (Othman et al. 2016) showed that a sample size of 60 patients (30 in each group) can detect a significant difference between the two groups. The collected data were revised, coded, and introduced to a computer using a statistical package for social science (SPSS 23.0.1 for windows; SPSS Inc., Chicago, IL). Quantitative parametric data were analysed by Student *t*-test and were presented as mean (± SD); non-parametric data were analysed using the Mann-Whitney test and were presented as median (IQR). Qualitative data were analysed using the chi-square test and will be presented as number of patients. $P < 0.05$ was considered significant.

Results

Seventy-three patients were evaluated for their suitability for the trial. Six patients declined participation in the study. All inclusion criteria were not met in seven patients, and the remaining sixty patients were followed up. Thirty patients were allocated to each group (Fig. 1).

All of the randomised patients completed the trial. In terms of demographic statistics, the difference between the two groups was statistically insignificant (Table 1).

Heart rate, blood pressure, respiratory rate, and peripheral oxygen saturation on PACU admission and at 1, 2, 4, 6, 12 and 24 h postoperatively did not demonstrate a statistically significant difference between the two groups (Figs. 2, 3 and 4).

On admission to PACU and at 1, 2, 4, 6, 12 and 24 h postoperatively, the disparity between the two groups was insignificant statistically regarding the visual analogue scale (VAS) (Fig. 5).

During the first 24 h following surgery, there was no statistically significant difference in the total amount of morphine given to the two groups (Table 2).

Only nine out of sixty patients needed analgesia, five in the BN group and four in the B group. Regarding those who needed analgesia, there was no statistically significant difference in the time to the first analgesic between the two groups (Table 2).

In terms of sedation, 7 patients experienced sedation in group BN and 6 in the B group, all with a sedation score of one. Regarding adverse effects, 3 patients experienced nausea and 1 patient experienced vomiting in group BN. Comparing the aforementioned parameters, the difference between the two groups was insignificant statistically (Fig. 6).

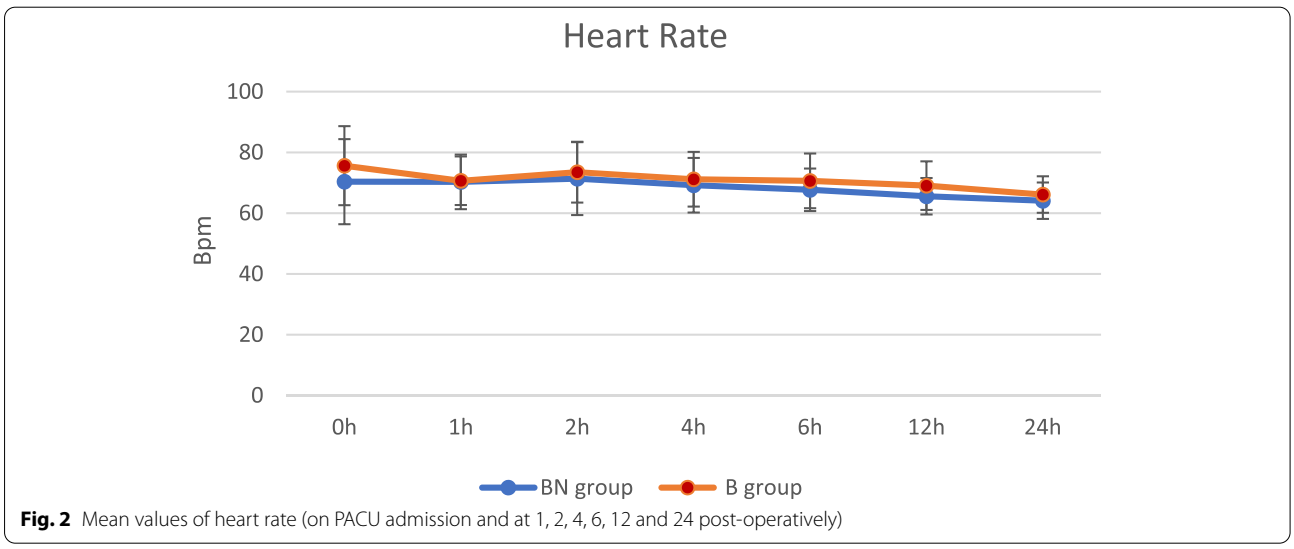

Fig. 2 Mean values of heart rate (on PACU admission and at 1, 2, 4, 6, 12 and 24 post-operatively)

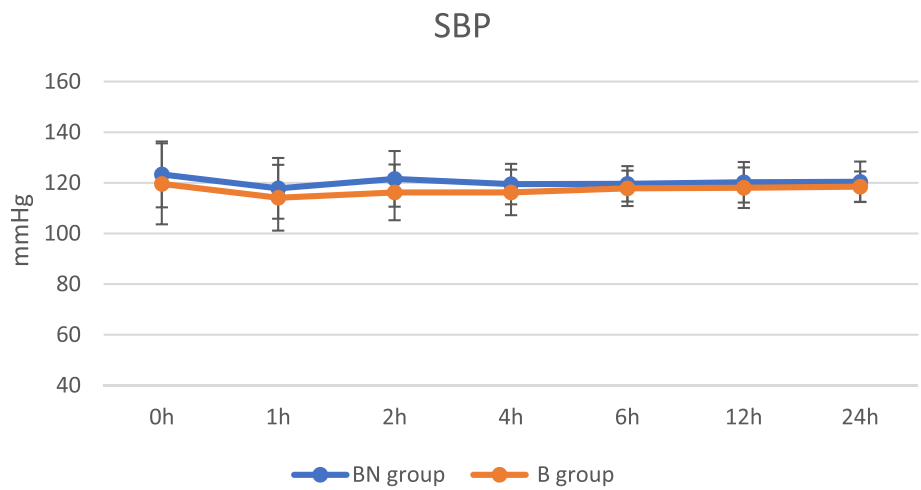

Fig. 3 Mean values of systolic blood pressure (on PACU admission and at 1, 2, 4, 6, 12 and 24 post-operatively). The lines represent mean values, and the error bars represent SD

Discussion

The current study did not find differences that are statistically significant when it came to postoperative VAS, peripheral O_2 saturation, vital signs, duration to the first analgesia and morphine use in the 24 h post-surgery when 20 mg nalbuphine was added to 0.25% bupivacaine in PECS I block compared to 0.25% bupivacaine alone. Moreover, there was no evident difference between the two groups in terms of complications like nausea, vomiting or sedation.

Regarding pain management for breast surgeries, a variety of regional approaches have been used, such as thoracic paravertebral nerve block, thoracic epidural, intercostal nerve block and PECS blocks. However, PECS I block is of lesser complications and is more time-efficient when compared to the previously mentioned techniques (Hamed et al. 2020). Adjuvants added to nerve blocks are effective means of controlling pain after breast surgeries. Previous studies have attested nalbuphine as an adjunct to local anaesthetics in epidural, caudal, intrathecal anaesthesia and peripheral nerve blocks. When compared to morphine, nalbuphine is both a kappa-opioid receptor agonist and an antagonist to mu-opioid receptors with a less potent analgesic effect. Because of its kappa-receptor agonism, it provides pain relief and sedation but has lesser respiratory depressive effects than other opioids (Das et al. 2017).

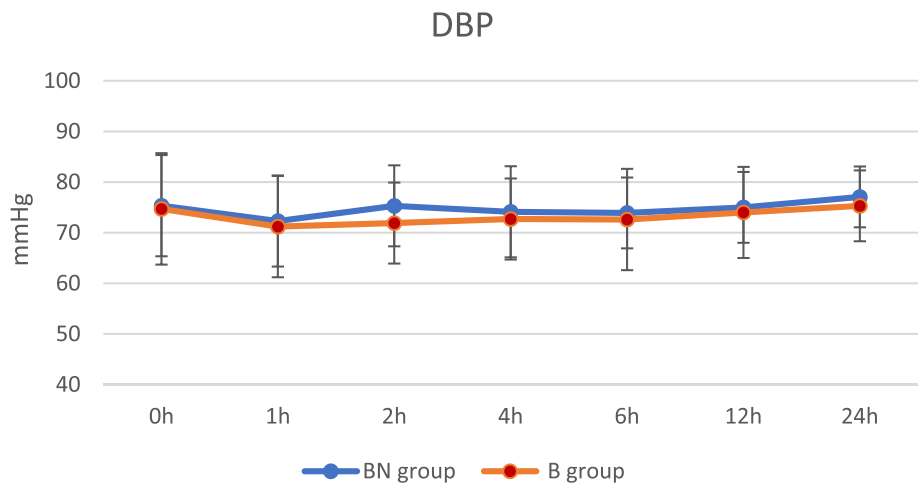

Fig. 4 Mean values of diastolic blood pressure (on PACU admission and at 1, 2, 4, 6, 12 and 24 post-operatively). The lines represent mean values, and the error bars represent SD

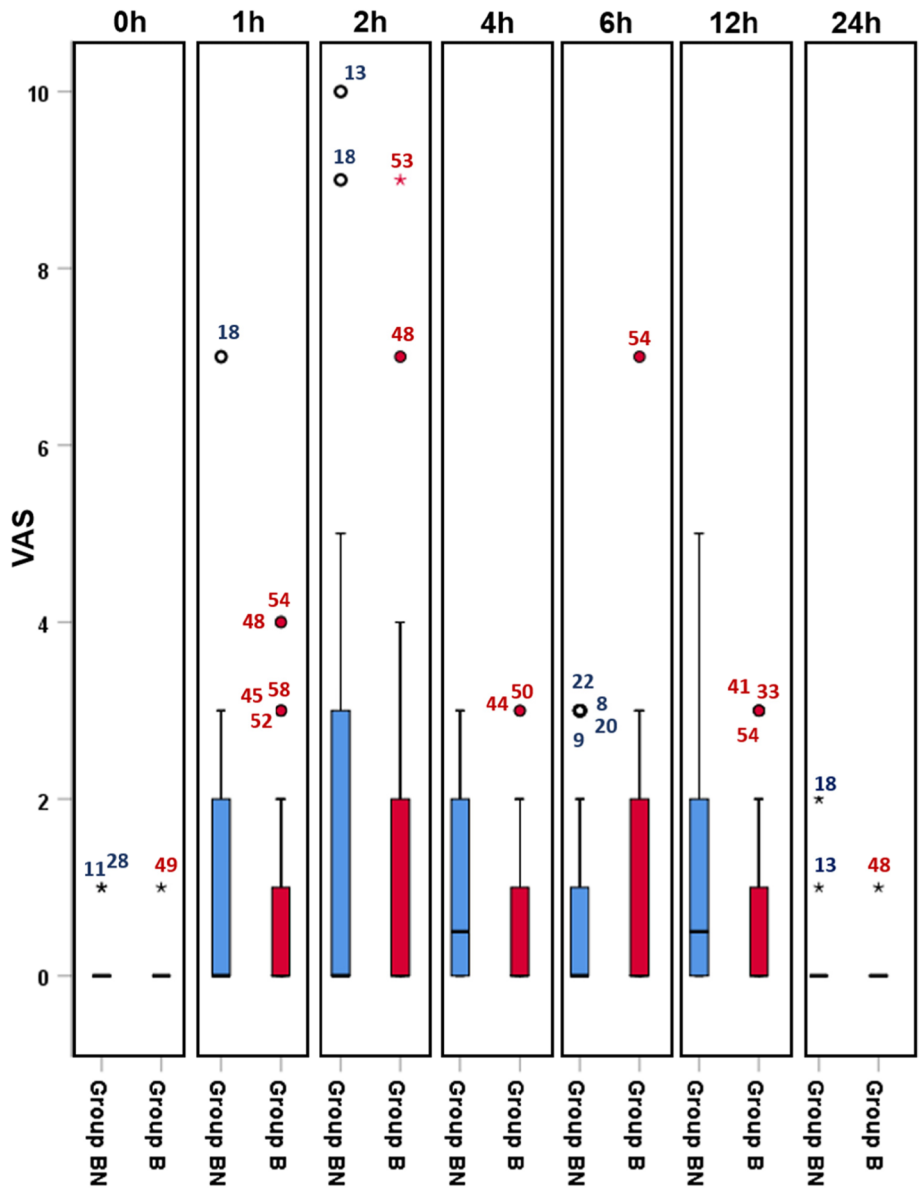

Fig. 5 Boxplots of VAS. The median is represented by the middle black solid line, the upper and lower margins of each box are the IQR, and the whiskers are the maximum and minimum values. The number of patients with outlier data is represented by dots

Table 2 Morphine total dose and time to analgesia

	BN group ($n=30$)	B group ($n=30$)	*P*-value
Morphine total dose (mg)			
6	3	4	0.650
8	1		
10	1		
Time to analgesia (min)	**($n=5$)** 211.8 ± 71.29	**($n=4$)** 183.5 ± 29.872	0.730

Data are presented as mean ± SD

P-value > 0.05 is considered statistically non-significant

To the recent knowledge, there have been no studies on the usefulness of nalbuphine as an adjuvant in PECS I block. Other adjuvants, however, have been added to PECS as adenosine, magnesium sulphate (Ibrahim and Sultan 2018) and ketamine (Othman et al. 2016).

As no studies have previously examined adding nalbuphine to the PECS block, the current discussion will enumerate studies using nalbuphine in other different blocks such as the supraclavicular block.

Gupta et al. (2016) added nalbuphine to bupivacaine 0.5% in supraclavicular nerve block versus bupivacaine

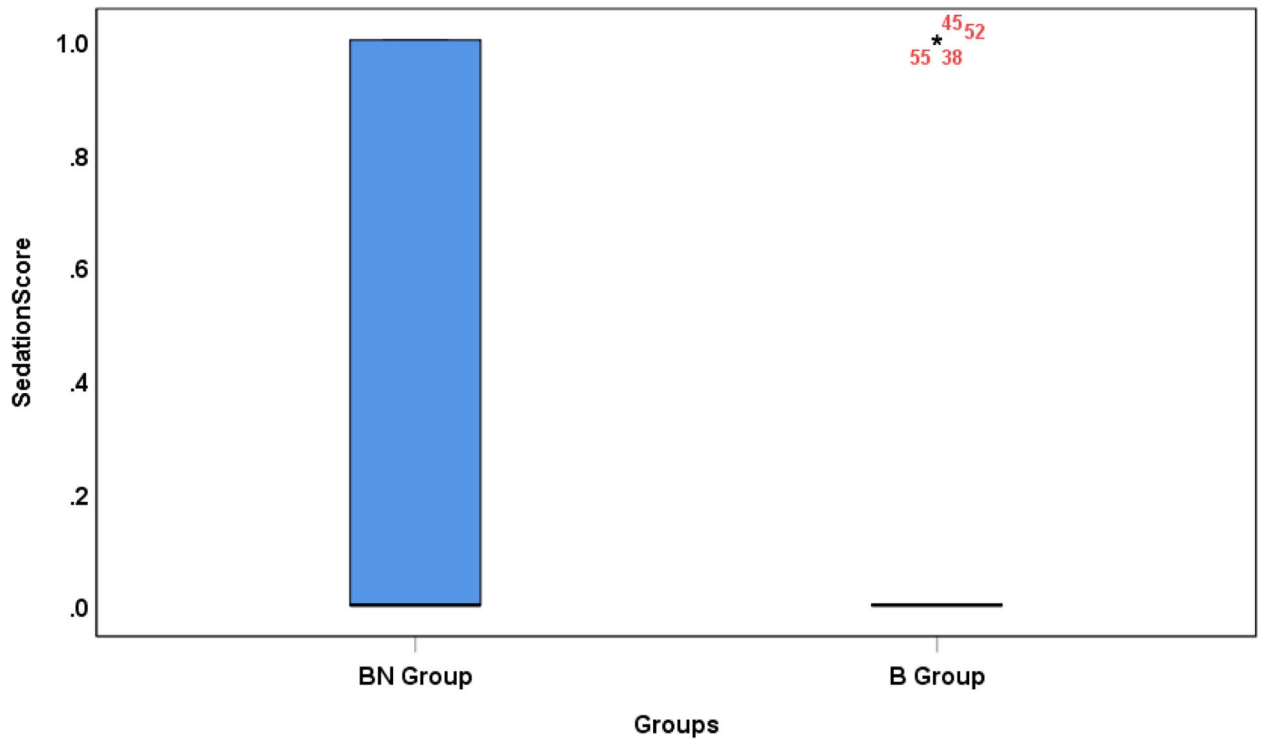

Fig. 6 Boxplots of sedation score

0.5% alone. The study showed a significantly lower VAS in the nalbuphine group (mean 1.44) when compared to the bupivacaine group (mean 5.6) at 6 h postoperatively and significantly longer duration of analgesia 481.53 ± 42.45 min in the nalbuphine group and 341.31 ± 21.42 min in the other group (Gupta et al. 2016).

Abdelhaq and Adly Elramely (2016) in a trial comparing the effectiveness of nalbuphine as an adjuvant to 0.5% bupivacaine in supraclavicular brachial plexus block showed a greater duration of analgesia in the nalbuphine group (835.18 ± 42.45 min) compared to a control group (708.14 ± 54.57 min) that only received plain 0.5% bupivacaine. Nazir and Jain (2017) also concluded that adding nalbuphine 10 mg to bupivacaine 0.375% increased longevity of analgesia of the supraclavicular nerve block (389.33 ± 14.52 min vs. 171.65 ± 19.79 min). Abdelhamid and Omar (2018) concluded a very similar result after studying nalbuphine's effectiveness as an adjuvant to 0.25% levobupivacaine in ultrasound-guided supraclavicular brachial plexus blocks compared to 0.5% levobupivacaine without adjuvants; the nalbuphine group had a greater duration of analgesia and a longer duration to first analgesic dose compared to the other group, 649.78 ± 114.76 and 575.56 ± 96.85 min respectively. The results of the latter mentioned study differ from that of this study, where the difference in time to first analgesic dose between the two groups was insignificant statistically.

Rashwan et al. (2020) carried out a study comparing the efficacy of using magnesium sulphate and nalbuphine as adjuvants to bupivacaine in the serratus anterior plane block (SABP) in mastectomy patients, which is a close block to PECS in terms of the targeted pectoral nerves; yet, the former provides a denser block. The study showed that the nalbuphine group was superior in terms of sensory block, postoperative VAS, pain control and analgesic consumption compared to the magnesium sulphate group (Rashwan et al. 2020).

This study showed different results regarding VAS compared to the previously mentioned studies. This could be attributed to the short follow-up duration of only 24 h compared to the 48 h follow-up period of most studies, as fibroadenoma excision is usually less painful and considered to be minor surgery. Thus, hospital stay usually does not exceed 24 h compared to mastectomy which is a major surgery that was investigated in other studies. The absence of significant difference when it came to the duration to the first analgesia and total postoperative morphine consumption in the first 24 h post-surgery shown in this study could also be a result of the small sample size. Although most of the literature showed that patients who receive regional blocks with adjuvant

usually require less postoperative analgesia compared to patients who did not receive regional block, it could not be said from the current study, because no control group receiving no peripheral nerve block was included.

Bouzinac et al. (2015) reported a case where PECS I and serratus plane blocks were used for bilateral breast surgery. According to the author, postoperative morphine was not needed, and further studies were recommended to test pectoral nerve blocks (PECS I and II) in surgeries involving the breasts (Bouzinac et al. 2015). Similarly, Bashandy and Abbas (2015) investigated the analgesic properties of PECS I and II in breast cancer operations without adjuvants and noticed the reduction in the total analgesic requirements when compared to patients who received general anaesthetic without regional block.

Further studies are recommended to attest nalbuphine's efficacy as an adjuvant in fascial plane blocks of the chest wall with denser analgesic and anaesthetic effects such as PECS II block.

Conclusions

According to this study, adding 20 mg nalbuphine to bupivacaine to PECS I block in fibroadenoma patients having excision surgery is not accompanied by a significant difference in postoperative VAS, total morphine consumed and duration to the first analgesic when compared to bupivacaine alone.

Limitations of the study are the small number of patients, insulated short-bevel needles were not available, and a lack of no block group as a control.

Abbreviations

ASA: American Society of Anesthesiologists; ECG: Electrocardiogram; IQR: Interquartile range; IV: Intravenous; NIBP: Non-invasive blood pressure; PACU: Post-anaesthesia care unit; PECS I: Pectoral block type 1; PECS II: Pectoral block type 2; VAS: Visual analogue score; SABP: Serratus anterior plane block; SpO_2: Oxygen saturation; $ETCO_2$: End-tidal carbon dioxide.

Acknowledgements

Not applicable.

Authors' contributions

SA designed the study, revised literature, followed up the patients and critically reviewed the manuscript. DN designed the study, analysed the data and wrote and critically revised the manuscript. MS revised the literature and followed up the patients. MM collected the data, performed the analysis and wrote the manuscript. All authors approved the final version of the manuscript.

Funding

Self-funded.

Availability of data and materials

The datasets generated and/or analysed during the current study are not publicly available due [publishing the clinical data about any study conducted in our hospitals and approved by the institutional ethical committee is against the policy of the Faculty of Medicine, Ain Shams University, unless there is a reasonable request] but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the ethical committee of the Ain Shams University with approval number (FMASU M D 02/2018); the participants provided writing consent. This clinical trial is retrospectively registered by PACTR, PACTR202112778684666. Registered 17 December 2021—http://www.pactr.org/PACTR202112778684666.

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

Received: 22 December 2021 Accepted: 4 April 2022
Published online: 21 April 2022

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