

Comparison between Intravenous Ibuprofen and Ketorolac for Intraoperative and Postoperative Analgesia in Breast Surgeries

Original Article

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ABSTRACT

Background: Effective postoperative pain management is essential, but concerns over opioid overprescription have increased interest in non-opioid alternatives like NSAIDs. This study compares the analgesic effects of intravenous (IV) ketorolac and ibuprofen in women undergoing breast excisional biopsy or mastectomy.

Methods: A total of 54 patients at Maadi Military Hospital, Cairo, Egypt, were randomized into two groups: 27 received IV ibuprofen (400–800 mg every 20 minutes, up to 3200 mg/day), and 27 received IV ketorolac (30 mg every hour, up to 120 mg/day). Pain was assessed using the Visual Analogue Scale (VAS), opioid consumption, and hemodynamic stability.

Results: The ketorolac group had a significantly shorter early recovery time and lower pain scores at multiple time points (4, 12, 16, 20, and 24 hours; $p < 0.05$). Baseline VAS scores were also lower in this group. Patients receiving ketorolac spent less time in the post-anesthesia care unit (PACU), though hospital stays were similar. Both groups maintained hemodynamic stability, but ketorolac was associated with fewer adverse events.

Conclusion: IV ketorolac provides superior postoperative analgesia compared to IV ibuprofen in women undergoing breast surgeries, with faster recovery, lower pain scores, and fewer side effects.

Key Words: Breast surgeries, ibuprofen, ketorolac, postoperative pain.

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INTRODUCTION

Perioperative pain is impairing quality of life of many patients, causes many adverse outcomes, this can result in further interventions which exhausts time and healthcare costs^[1].

Postoperative pain management is a key concern for surgeons and anesthesiologists. A multimodal analgesic approach composed of NSAIDs and opioids has been shown to effectively control pain and reduce opioid use, minimizing associated side effects such as delayed discharge and potential addiction. The use of such a regimen is highly beneficial and supported by research, as it helps manage pain and decrease opioid consumption and its adverse effects and associated addiction^[2].

NSAIDs act centrally and peripherally; they can inhibit prostaglandin synthesis through obstruction of cyclooxygenase (COX) enzyme in the peripheral nociceptors, so decreasing to a great extent the sensitization of pain receptors NSAIDs also act centrally by blocking COX-2 inhibiting the production of prostaglandin E2 in the spinal dorsal horn, thereby activating medullary and

cortical regions which cause central sensitization which reduces the pain threshold around unharmed tissue^[3].

Ibuprofen and ketorolac have different COX 1 to COX 2 inhibition ratios which accounts for their distinction in both safety and efficacy. Ketorolac strongly inhibits COX-1 compared to COX 2 (330:1 ratio) while ibuprofen inhibits them by a much lower ratio (2.5:1 ratio), the higher ketorolac associated COX 1 inhibition increases the risk of, intraoperative blood loss, and postoperative bleeding. Therefore, its use for pre- or intraoperative pain management is controversial.

This study is the first to apply a multimodal analgesic approach to breast surgery, a painful procedure with high opioid use. The findings may support opioid-free analgesia in this high-risk population.

PATIENTS AND METHODS

Study Design

Double blinded randomized controlled clinical trial.

Population of study

54 adult female patients with breast mass or lesion undergoing breast excisional biopsy or mastectomy from January 2023 to September 2023 in Egypt, Cairo, Maadi military hospital,

Inclusion criteria

1. Patients with physical status according to American society of anesthesiologists (ASA) classification class I and II.
2. Adult female patient over 18 years of age.

Exclusion criteria

1. Patient refusal.
2. Severe cardiac co morbidity (impaired contractility with ejection fraction < 50%, significant arrhythmias, tight valvular lesions).
3. Patients below 18 years of age.
4. Patients with renal impairment.
5. Allergy to any of the compared drugs.
6. ASA III and IV.
7. Patients with increased bleeding tendency.

Sampling

Sample size: As mentioned in Uribe *et al* 2018^[2], VAS pain score at movement upon PACU arrival is lower in Ibuprofen group by 23 points than Ketorolac group with standard deviation 18.5 and 30.4 respectively, to obtain this difference at power of 90% and 95% confidence level, the minimum required sample size is 27 subjects in each group separately which was implemented by the study. block randomization was used to achieve equal groups. using a computer-generated random numbers table (Figure 1).

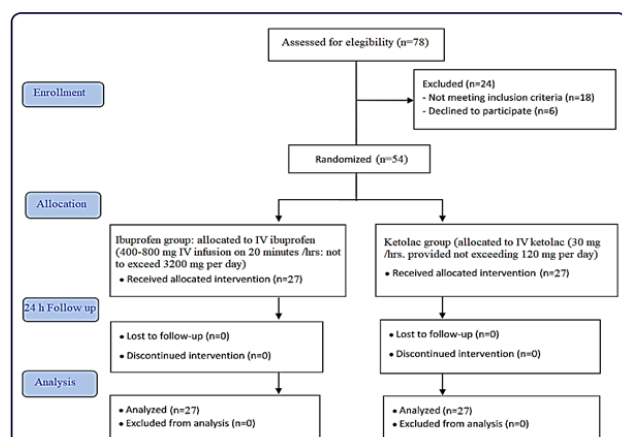


Fig. 1: The trial follow chart

Instruments

Anesthetic machine and vital signs monitor, Syringes 5 cm and 10 cm, 500 cm normal saline, the drugs compared.

Procedure

The night before the operation, patients were evaluated for study eligibility, and informed consent was obtained. Baseline heart rate (HR) and mean arterial blood pressure (MABP) were measured, and continuous monitoring of blood pressure, HR, rhythm, and oxygen saturation was done during the operation.

Anesthesia induction included 2 mg/kg propofol, 0.5 mg/kg atracurium for intubation, 1 mcg/kg fentanyl initially, and then 1 mcg/kg as needed based on hemodynamics. Anesthesia was maintained with 2% sevoflurane.

Intraoperative and postoperative analgesia included ketorolac (30 mg/hr, max 120 mg/day) or ibuprofen (400-800 mg IV infusion every 20 minutes, max 3200 mg/day). Effectiveness was monitored via blood pressure and HR every 10 minutes, with opioid use indicated by a >10% increase in either. Postoperative pain was assessed using the surgical pain Visual Analogue Scale (VAS) at recovery and every 4 hours for 24 hours. If VAS >4, 2 mg morphine was administered IV, repeated after 30 minutes if pain persisted (Figure 2).

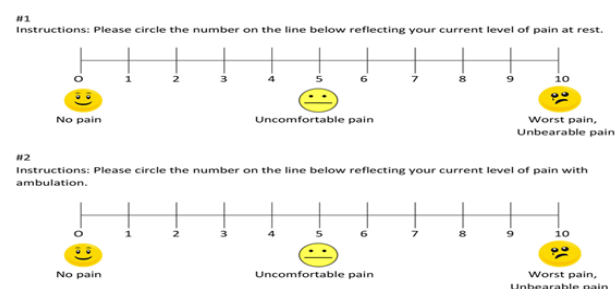


Fig. 2: Visual Analogue Scale (Uribe *et al* 2018)

Primary outcomes

- Measuring the mean post-operative static and dynamic VAS every 4 hours during the first 24 hours after surgery.

Secondary outcome

- total amount of opioid consumption during surgery and for the first 24 hours after surgery
- mean arterial blood pressure and heart rate every 4 hours postoperative
- Measuring recovery time and time to first analgesic requirement.
- Assessments of the complications such as increased blood loss perioperative, renal impairment and opioid-related complications (nausea, vomiting, itching, sedation and respiratory depression) with each drug.

Statistical analysis

Data coded and entered using the statistical package for the Social Sciences (SPSS) version 26 (IBM Corp., Armonk, NY, USA). Data summarized using mean and standard deviation for quantitative variables and frequencies (number of cases) and relative frequencies (percentages) for categorical variables. Comparisons between groups done using unpaired t test in normally distributed quantitative variables (Chan, 2003a). For comparing categorical data, Chi-square test performed. Fischer Exact test used instead when the expected frequency is less than 5 (Chan, 2003b). *P-values* less than 0.05 are considered statistically significant.

RESULTS

Demographic data of studied groups

The mean $\pm$ SD of age of studied patients was 50.33 ± 9.92 and 51.33 ± 10.42 in ibuprofen and ketorolac group respectively. BMI was 27.47 ± 2.07 and 26.69 ± 2.46 in ibuprofen and ketorolac group respectively with no significant differences between studied groups regard to age and BMI ($p > 0.05$) (Tables 1,2).

Table 1: Demographic data of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	t test	P value
Age (year)	50.33 ± 9.56 27-68	51.33 ± 10.42 33-73	0.367	0.714
BMI (kg/m ²)	27.47 ± 2.07 24.3-33	26.69 ± 2.46 23-32	1.261	0.213

There were similar levels of diastolic and systolic blood pressure among studied group (ibuprofen and ketorolac). Based on ASA classification, 66.7% and 33.3% were in ASA I and ASA II in ibuprofen group while 70.4% and 29.6% were in ASA I and ASA II in ketorolac group with no statistically significant differences between them ($p > 0.05$)

Table 2: Baseline clinical data of studied groups * t test # Chi-square test

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
DBP	79.33 ± 7.51	78.59 ± 10.55	0.297*	0.767
SBP	133.85 ± 18.01	130.66 ± 16.57	0.677*	0.501
ASA I	18 (66.7%)	19 (70.4%)	0.093#	0.760
II	9 (33.3%)	8 (29.6%)		

There was an insignificant lesser consumption of intraoperative fentanyl in patients receiving IV ketorolac (112.40 ± 30.61 ug) compared to those receiving IV ibuprofen (114.44 ± 31.54 ug) ($p = 0.810$), with significantly early recovery time (15.96 ± 2.13 minutes) compared to those receiving IV ibuprofen (17.29 ± 1.95 minutes) ($p = 0.020$) and insignificant later time to first rescue of excess fentanyl (5.66 ± 12.20 minutes) compared to those

receiving IV ibuprofen (4.48 ± 11.06 minutes) ($p = 0.020$). moreover, one patient from Ibuprofen group was in need of 2 mg morphine during early postoperative period compared to non-cases in Ketorolac group (Table 3).

Table 3: Intraoperative data of studied groups IT: invalid test

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
Intraoperative fentanyl (ug)	114.44 ± 31.54 100-200	112.40 ± 30.61 100-200	0.241	0.810
Recovery time (min)	17.29 ± 1.95 15-22	15.96 ± 2.13 12-22	2.393*	0.020
Time to first administration of excess fentanyl (min)	4.48 ± 11.06 0-35	5.66 ± 12.20 0-35	0.372	0.711
Usage of post-operative morphine (mg)	1 (3.7%)	0		IT

Results showed that in breast surgeries the mean $\pm$ SD duration of anesthesia was insignificantly shorter in Ketorolac group (140.11 ± 21.46 minutes) compared to Ibuprofen group (145.96 ± 24.05 minutes) ($p = 0.350$). Duration of operation was insignificantly shorter in Ketorolac group (111.96 ± 9.61 minutes) compared to Ibuprofen group (121.07 ± 23.69 minutes) ($p = 0.069$). Insignificant lesser amount of intraoperative blood loss in Ketorolac group (111.03 ± 15.10 mL) compared to Ibuprofen group (134.37 ± 77.94 mL) ($p = 0.133$). The most common surgical procedure done in studied cases was tumor excision with safety margin (92.6% and 96.3% in Ibuprofen and ketorolac group respectively), radical mastectomy was done in one case of Ibuprofen group while modified radical mastectomy was done in one case of Ibuprofen group and one case of Ketorolac group with no statistically significant differences between both groups ($p > 0.05$) (Tables 4,5,6).

Table 4: Operative data of studied groups * t test # Chi-square test

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
Duration of anesthesia (minutes)	145.96 ± 24.05 120-250	112.40 ± 30.61 100-200	0.943*	0.350
Duration of operation (minutes)	121.07 ± 23.69 100-225	15.96 ± 2.13 12-22	1.852*	0.069
Intraoperative blood loss (mL)	134.37 ± 77.94 85-420		1.528*	0.133
Type of surgery				
Tumor excision with safety margin	25 (92.6%)	26 (96.3%)		
Radical mastectomy	1 (3.7%)	0	1.020#	0.601
Modified radical mastectomy	1 (3.7%)	1 (3.7%)		

Patients receiving IV ketorolac stayed significantly longer in PACU unit (19.55 ± 3.57 minutes) compared to those receiving IV Ibuprofen (22.03 ± 4.5 minutes) ($P=0.029$) while the hospital stays were similar to both groups (42.74 ± 3.91 hours' vs 42.55 ± 2.36 hours in Ibuprofen and Ketorolac groups respectively) ($P>0.05$).

Table 5: Post-operative data of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	t test	P value
PACU time (min)	22.03 ± 4.53 15-30	19.55 ± 3.57 14-30	2.234	0.029
Hospital stays (hours)	42.74 ± 3.91 35-59	42.55 ± 2.36 39-48	0.216	0.829

The mean + SD of baseline pain VAS score at rest was similar among patients receiving IV Ibuprofen (2.63 ± 0.83) or IV ketorolac (2.59 ± 0.50) ($p=0.831$). At 4 hours postoperative, pain VAS score was significantly lower in patients receiving IV ketorolac (2.33 ± 0.48) than those receiving IV Ibuprofen (2.81 ± 0.55) ($p=0.001$). At 8 hours postoperative, pain VAS score was insignificantly lower in patients receiving IV ketorolac (1.55 ± 0.50) than those receiving IV Ibuprofen (2.07 ± 1.26) ($p=0.051$). At 12 hours postoperative, pain VAS score was significantly lower in patients receiving IV ketorolac (1.55 ± 0.50) than those receiving IV Ibuprofen (2.11 ± 1.06) ($p=0.016$).

At 16 hours postoperative, pain VAS score was insignificantly lower in patients receiving IV ketorolac (1.55 ± 0.64) than those receiving IV Ibuprofen (2.25 ± 1.79) ($p=0.051$). At 20 hours postoperative, pain VAS score was significantly lower in patients receiving IV ketorolac (1.03 ± 0.19) than those receiving IV Ibuprofen (1.92 ± 1.63) ($p=0.006$). At 24 hours postoperative, pain VAS score was significantly lower in patients receiving IV ketorolac (1.07 ± 0.27) than those receiving IV Ibuprofen (1.85 ± 1.42) ($p=0.007$).

Table 6: Static VAS score of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
Baseline	2.63 ± 0.83	2.59 ± 0.50	0.215	0.831
VAS 4 hours	2.81 ± 0.55	2.33 ± 0.48	3.417	0.001
VAS 8 hours	2.07 ± 1.26	1.55 ± 0.50	1.993	0.051
VAS 12 hours	2.11 ± 1.06	1.55 ± 0.50	2.483	0.016
VAS 16 hours	2.25 ± 1.79	1.55 ± 0.64	1.913	0.061
VAS 20 hours	1.92 ± 1.63	1.03 ± 0.19	2.818	0.006
VAS 24 hours	1.85 ± 1.42	1.07 ± 0.27	2.804	0.007

Mean +SD of baseline pain VAS score at ambulation was similar among patients receiving IV Ibuprofen (3.03 ± 0.70) or IV ketorolac (3.00 ± 0.67) ($p=0.872$). at 4 hours postoperative, dynamic VAS score was insignificantly lower in patients receiving IV ketorolac

(3.00 ± 0.55) than those receiving IV Ibuprofen (3.29 ± 0.60) ($p=0.069$). at 8 hours postoperative, dynamic VAS score was insignificantly lower in patients receiving IV ketorolac (2.03 ± 0.43) than those receiving IV Ibuprofen (2.22 ± 0.42) ($p=0.106$). at 12 hours postoperative, dynamic VAS score was significantly lower in patients receiving IV ketorolac (1.81 ± 0.55) than those receiving IV Ibuprofen (2.25 ± 0.44) ($p=0.002$). at 16 hours postoperative, dynamic VAS score was significantly lower in patients receiving IV ketorolac (1.87 ± 0.67) than those receiving IV Ibuprofen (2.25 ± 0.65) ($p=0.039$). at 20 hours postoperative, dynamic VAS score was significantly lower in patients receiving IV ketorolac (1.25 ± 0.44) than those receiving IV Ibuprofen (1.51 ± 0.50) ($p=0.047$). at 24 hours postoperative, dynamic VAS score was insignificantly lower in patients receiving IV ketorolac (1.03 ± 0.19) than those receiving IV Ibuprofen (1.00 ± 0.01) ($p=0.416$) (Tables 7-10).

Table 7: Dynamic VAS score of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
Baseline	3.03 ± 0.70	3.00 ± 0.67	0.161	0.872
VAS 4 hours	3.29 ± 0.60	3.00 ± 0.55	1.851	0.069
VAS 8 hours	2.22 ± 0.42	2.03 ± 0.43	1.642	0.106
VAS 12 hours	2.25 ± 0.44	1.81 ± 0.55	3.246	0.002
VAS 16 hours	2.25 ± 0.65	1.87 ± 0.67	2.115	0.039
VAS 20 hours	1.51 ± 0.50	1.25 ± 0.44	2.028	0.047
VAS 24 hours	1.00 ± 0.01	1.03 ± 0.19	0.819	0.416

Hemodynamic stability among studied groups with no significant differences between patients receiving IV Ibuprofen and those receiving IV Ketorolac regard to baseline heart rate (HR) up to 24 hours postoperatively follow up ($p>0.05$).

Table 8: Heart rate of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	test	P value
Baseline	77.81 ± 9.49	75.48 ± 8.03	0.974	0.334
HR 4 hours	76.25 ± 8.38	75.07 ± 7.25	0.553	0.582
HR 8 hours	75.74 ± 7.93	74.29 ± 7.17	0.705	0.484
HR 12 hours	75.37 ± 9.12	75.70 ± 7.22	0.147	0.883
HR 16 hours	76.70 ± 7.69	74.59 ± 6.42	1.094	0.278
HR 20 hours	76.03 ± 8.01	74.29 ± 6.37	0.883	0.381
HR 24 hours	75.59 ± 6.74	73.92 ± 6.27	0.943	0.350

Hemodynamic stability among studied groups with no significant differences between patients receiving IV Ibuprofen and those receiving IV Ketorolac regard to mean arterial blood pressure (MAP) levels and up to 24 hours postoperatively follow up ($p>0.05$).

Table 9: Mean arterial blood pressure of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	test	<i>P</i> value
Baseline	91.29±8.35	89.22±9.51	0.850	0.399
MAP 4 hours	89.48±8.40	88.29±9.02	0.502	0.618
MAP 8 hours	87.40±6.87	86.88±8.35	0.250	0.803
MAP 12 hours	88.11±7.87	87.22±8.40	0.402	0.689
MAP 16 hours	87.22±6.83	85.55±12.10	0.625	0.535
MAP 20 hours	88.92±5.86	86.14±7.87	1.472	0.147
MAP 24 hours	86.63±6.20	86.14±7.37	0.792	0.792

MAP: mean arterial blood pressure

Patients receiving IV Ketorolac have lower incidence of adverse events (3 cases of nausea and one case of vomiting) compared to those receiving IV Ibuprofen (5 cases of nausea, two cases of vomiting and one case of itching), with no statistically significant differences between them regard to documented adverse events during postoperative 24 hour period ($p>0.05$).

Table 10: Adverse events of studied groups

Parameters	Ibuprofen No=27	Ketorolac No=27	Chi-square test	<i>P</i> value
Nausea	5 (18.5%)	3 (11.1%)	0.562	$P=$ 0.755
Vomiting	2 (7.4%)	1 (3.7%)		
Itching	1 (3.7%)	0 (0.0%)		
Renal impairment	0 (0.0%)	0 (0.0%)		
Respiratory depression	0 (0.0%)	0 (0.0%)		
Surgical infection	0 (0.0%)	0 (0.0%)		

DISCUSSION

Uncontrolled postoperative pain is a significant issue, leading to adverse outcomes such as increased interventions, prolonged recovery, and greater healthcare costs^[4]. Nonsteroidal anti-inflammatory drugs (NSAIDs) like ibuprofen and ketorolac have been increasingly used as alternatives to opioids for pain management after surgeries due to their ability to reduce inflammation and lower opioid consumption, which can cause side effects like nausea, sedation, and respiratory depression^[5,6].

This study aimed to compare the postoperative analgesic effects of IV ketorolac and IV ibuprofen in 54 women undergoing breast surgeries. After anesthesia induction, patients were administered either IV ibuprofen (800 mg) or IV ketorolac (30 mg). We assessed postoperative pain intensity, opioid consumption, and hemodynamic stability using the Visual Analog Scale (VAS) and monitored vital signs throughout the procedure.

The results showed no significant differences between the two groups regarding baseline characteristics, surgical procedures, or intraoperative variables like blood loss. However, the ketorolac group required less fentanyl during surgery and had a shorter recovery time in the post-

anesthesia care unit (PACU). Despite this, the need for rescue opioid medication was similar between the groups. These findings align with prior research, which generally indicates that both IV ketorolac and IV ibuprofen provide comparable analgesic effects in various surgical settings^[2,7].

Regarding pain control, patients who received ketorolac generally reported lower VAS scores at rest and during movement at several time points, particularly at 4-, 12-, 20-, and 24-hours post-surgery. These results support earlier findings by Lee *et al.* (2022)^[7] and Uribe *et al.* (2018), where ketorolac was more effective in managing pain compared to ibuprofen immediately postoperatively. However, the overall opioid consumption and the number of patients requiring rescue analgesics did not differ significantly between the two groups, as seen in other studies by Dwarica *et al.* (2020)^[8] and Abdelbaser *et al.* (2022)^[11].

A key difference between studies is the timing and dosage of drug administration, which may account for some of the conflicting findings. For instance, Uribe *et al.* (2018)^[2] administered ketorolac post-surgery, whereas ibuprofen was given preoperatively, and this may have influenced the outcomes. Furthermore, the type of surgery can also impact drug efficacy, as noted in studies with different patient populations^[9].

Concerning hemodynamic stability, there were no significant differences between the two drugs in heart rate or mean arterial pressure (MAP), similar to previous studies^[10,2]. Adverse events were minimal, with patients in the ketorolac group experiencing fewer nausea and vomiting cases compared to the ibuprofen group, though this difference was not statistically significant.

Overall, both IV ketorolac and IV ibuprofen appear to be effective for postoperative analgesia, with ketorolac showing some advantages in terms of early pain relief and recovery time. However, the choice between the two may depend on individual patient factors, such as the type of surgery, the timing of administration, and the side-effect profiles. Further studies should explore these variables, including different dosages and the long-term impact of pain management strategies, to determine the most optimal approach for postoperative care.

LIMITATIONS OF THE STUDY

1. Study did not consider preoperative medication use.
2. There was no follow them long-term to track the development of chronic pain.
3. we did not investigate the effects of different dosages of IV ibuprofen, as we only analyzed the 800 mg dosage due to surgeon preference, and no patients received the 400 mg dose. Additionally, the varying half-lives of the two drugs—IV ibuprofen (2-3 hours) and IV ketorolac (5-6 hours)—could

have influenced both postoperative pain levels and the need for additional opioid analgesics, potentially affecting the accuracy of pain and opioid consumption assessments.

4. Generalizability may be affected as study was carried out in a single center

CONCLUSION

This study highlights that intravenous (IV) Ketorolac provides better postoperative analgesia than IV ibuprofen, as measured by lower morphine consumption and improved pain scores in women undergoing breast surgeries. Both drugs were effective and safe, with IV Ketorolac showing a lower incidence of postoperative complications. Due to its lower cost, IV Ketorolac is recommended for postoperative pain management in breast surgery patients. Given the limited adverse events associated with NSAID use, future studies could explore preoperative administration of IV ibuprofen and IV Ketorolac for pain management, which would address the confounding factor of preemptive versus postoperative NSAID administration.

ABBREVIATIONS

ASA: Acetylsalicylic acid, **COX:** Cyclooxygenase, **ERPs:** Enhanced recovery programs, **FDA:** Food and Drug Administration, **HR:** Heart Rate, **IV:** Intravenous, **MAP:** Mean arterial blood pressure, **NSAIDs:** Non-steroidal anti-inflammatory drugs, **PACU:** Post anesthesia care unit, **PCA:** Patient-controlled analgesia, **PCEA:** Patient-controlled epidural analgesia, **VAS:** Visual analog scale.

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CONFLICT OF INTERESTS

There are no conflicts of interest.

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