

# Effects of Preincisional Analgesia with Surgical Site Infiltration with 0.25% Bupivacaine or with Ketamine in Patients Undergoing Open Cholecystectomy and Pyelolithotomy Surgery Under General Anaesthesia

Sweety Bhola<sup>1</sup>, Ranjeeta Aske<sup>2</sup>

## ABSTRACT

**Introduction:** Postoperative pain management remains very important in patient's management to ensure a better quality of life. Unfortunately, adequate postoperative analgesia is achieved in a very less number of patients. Delayed postoperative mobilization because of pain reduces quality of life and delays return to normal daily activities. Preemptive analgesia is reported to inhibit the persistence of postoperative pain after surgery. The aim of this study was to assess the analgesic effectiveness of preincisional infiltration of ketamine following elective open cholecystectomy and pyelolithotomy surgery as compared to 0.25% bupivacaine.

**Material and methods:** In this study, 60 patients, age (16 – 50yrs) ASA grade I and II are posted for open cholecystectomy and pyelolithotomy surgery, randomly assigned with informed consent, into 2 groups (n=30), as; Group K: Received subcutaneous infiltration of 10 ml containing ketamine 2 mg/kg. Group B: Received subcutaneous infiltration of 10 ml 0.25% of bupivacaine, Skin infiltration was given along the incision 5 min before incision. Postoperative pain was assessed using visual analogue scale (VAS) at rest and with evaluation of additional opioid analgesic requirements.

**Results:** Results will be analysed by using the independent-sample Student's *t*-test or Mann-Whitney test for numerical variables and  $P < 0.005$  will be considered significant. We can conclude that ketamine appears to be a promising preemptive analgesic through surgical site infiltration. VAS score in ketamine group was significantly lower than that in the bupivacaine group 8, 10, and 24 h postoperatively.

**Conclusion:** Ketamine group showed delayed request of additional opioid analgesia ( $P < 0.001$ ) with significantly less opioid consumption ( $P < 0.001$ ) as compared to bupivacaine. Ketamine has comparable effect to bupivacaine with longer duration of action and minimal adverse effects.

**Keywords:** Open Cholecystectomy and Pyelolithotomy Surgery, Postoperative Pain, Bupivacaine, Ketamine

## INTRODUCTION

Postoperative pain management remains very important in patient's management to ensure a better quality of life.<sup>1</sup> Unfortunately, adequate postoperative analgesia is achieved in less number of patients. Adverse physiological alterations due to insufficient postoperative analgesia may eventually lead to increased morbidity and mortality after surgery.<sup>2</sup> Delayed postoperative mobilization caused by pain reduces quality of life and delays return to normal daily activities in many patients after surgery.<sup>3,4</sup> Preemptive analgesia is

reported to inhibit the persistence of postoperative pain after surgery.

**Preemptive analgesia**(treating pain before its onset):

The concept of providing analgesia to the patient before surgical incision, resulting in less postoperative pain.<sup>5</sup>

Application of analgesic agents in the area of the surgical incision

↓

Reduces the number of signals generated by pain receptors (nociceptors)

↓

preventing central hypersensitivity of the CNS

↓

reduces the incidence of pain sensation in the perioperative period

↓

Inhibit the persistence of postoperative pain  
Postoperative pain varies according to many variables which may be age, sensitivity to pain, type and duration of surgery, and type of analgesia used, judge the severity of pain and its management, other complications, etc.

The aim of this study was to assess the analgesic effectiveness of preincisional infiltration of ketamine following elective open cholecystectomy and pyelolithotomy surgery as compared to 0.25% bupivacaine.

## MATERIAL AND METHODS

In this study, 60 patients, age (16 – 50yrs) ASA grade I and II are posted for open cholecystectomy and pyelolithotomy surgery, randomly assigned with informed consent, into 2 groups; (n=30), as;

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Group K: received subcutaneous infiltration of 10 ml containing ketamine 2 mg/kg.

Group B: received subcutaneous infiltration of 10 ml 0.25% of bupivacaine,

The prospective, randomized study was conducted in dept. of anaesthesiology at Hamidia Hospital, bhopal, over a period of 6 months. With the help of a computer-generated table of random numbers, patients were randomized into 2 groups; all patients had an equal probability of assignment to the groups.

#### Inclusion criteria:-

- 1) Patients age (16 – 50yrs),
- 2) ASA grade I and II patients,
- 3) All patients going for elective open cholecystectomy and pyelolithotomy surgeries.

#### Exclusion criteria:-

- 1) ASA grade III,IV,V and (E),
- 2) Patients with allergy to study drugs,
- 3) Cardiovascular disease (hypertension, tachycardia, congestive heart failure, and coronary artery disease), decompensated liver, renal failure,
- 4) History of treatment of chronic pain condition.

#### All patients underwent a standardized anaesthesia protocol which included:-

- IV 0.04 mg/kg midazolam and glycopyrrolate 0.01mg/kg.
- Induction with propofol (2 mg/kg) and fentanyl (2 µg/kg).
- Succinylcholine(1mg/kg) was given and tracheal intubation performed.
- Atracurium was used as a muscle relaxant.
- Maintenance: 66% nitrous oxide and 33% O<sub>2</sub> mixture along with isoflurane (1-2%).
- The study drugs were infiltrated subcutaneously into the incisional site region after induction of anaesthesia and surgical incisions was given only after 15 mins from the study drug administration.
- I/V fentanyl infusion 0.5µg/kg/hr in 50 ml NS was given.
- At the end of surgery, IV glycopyrrolate 0.01mg/kg and neostigmine 0.05mg/kg. Under direct vision oropharyngeal suction was done and all patient's were carefully extubated when they were able to obey commands and lung ventilation was deemed adequate. On arrival in the post-anaesthesia care unit at 0 hr, 1 hr, 3hrs, 6hrs, 12 hrs and 24 hrs, Postop VAS Score and Sedation were recorded, thereafter,

**Visual Analogue Scale (VAS):** (Duration of Effective analgesia)

0: no pain, and 10: Worst pain

Sedation was assessed by RAMSAY Sedation score:

- 1 - Anxious agitated
- 2 - Cooperative, oriented and serene
- 3 - Sleeping, drowsy and responding easily to commands
- 4 - Sleeping and responding to stimuli on glabella
- 5 - Sleeping and responding slowly to stimuli on glabella
- 6 - Sleeping without response to pressure on glabella.

**Monitoring:-** ECG, Pulse rate, BP (SBP, DBP, MEAN arterial pressure), Respiratory Rate, Et-CO<sub>2</sub> and SpO<sub>2</sub> were recorded intraoperatively at 0, 5, 10, 20 mins and after that every 20 mins till the end of surgery. All the parameters were compared with baseline (pre-operative) value. Recovery room complications such as nausea/vomiting, dizziness, hallucination and any allergic reaction and other side effects, if any, were also noted.

#### STATISTICAL ANALYSIS

SPSS 16 for windows (SPSS Inc.,Chicago, IL,USA) was used for statistical analysis. Numerical variables were presented as mean and SD. The intergroup differences were compared using the independent-sample Student's *t*-test or Mann-Whitney test for numerical variables, Chi-square test (Fisher's exact test) for qualitative variables. *P* < 0.05 was considered statistically significant.

#### RESULT

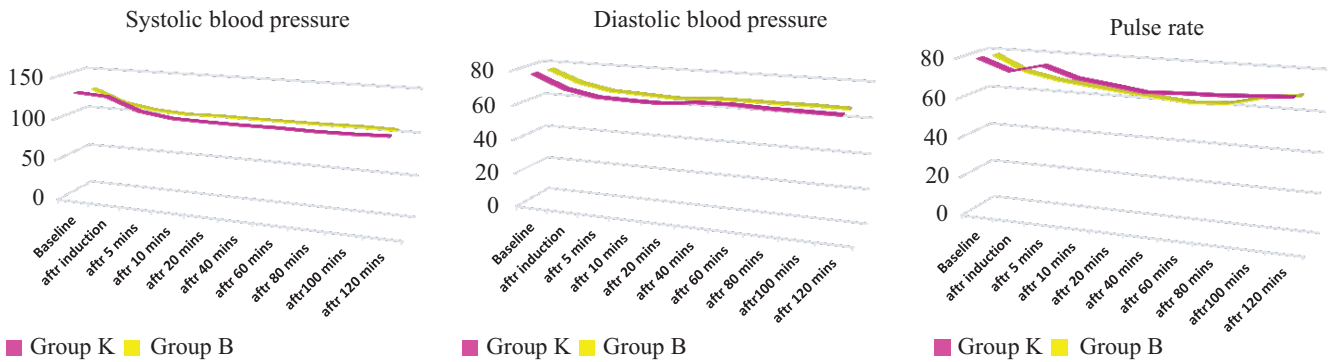
No patients were excluded from the study after enrollment. The two groups were comparable regarding age, weight, ASA class, and duration of anaesthesia and surgery [Table 1]. There were no clinically significant changes in blood pressure and HR throughout the 24 postoperative h in the two groups [graph 1,2]. Table 2 shows that the VAS score at rest decreased significantly in Group B starting from 10 h postoperatively up to 24 h and in Group K, from 8 to 24 h as compared to the immediate postoperative reading. VAS score in ketamine group was significantly lower than that in the bupivacaine group 8, 10, and 24 h post-operatively.

Ketamine group showed delayed request of additional opioid analgesia (*P* < 0.001) with significantly less opioid consumption (*P* < 0.001) as compared to bupivacaine. The total dose of Tramadol consumed during the 24 postoperative h was significantly smaller in ketamine group (*P* < 0.001). Table 4 shows sedation score was maximally upto 5 in the

Variables	Group K (n=30)	Group B (n=30)	P value
Age (years)	33.8 ± 7.87	34.9 ± 5.97	0.27
Weight (kg)	57.10 ± 8.99	55.23 ± 7.90	0.19
ASA Class I/II	1.4 ± 0.56	1.3 ± 0.47	0.24
Duration of surgery (min)	109.17 ± 10.00	107.33 ± 9.44	0.234
Anaesthetic time (min)	125.17 ± 9.19	123.4 ± 8.36	0.219

Data are expressed as mean and SD. SD: Standard deviation, ASA: American Society of Anesthesiologists

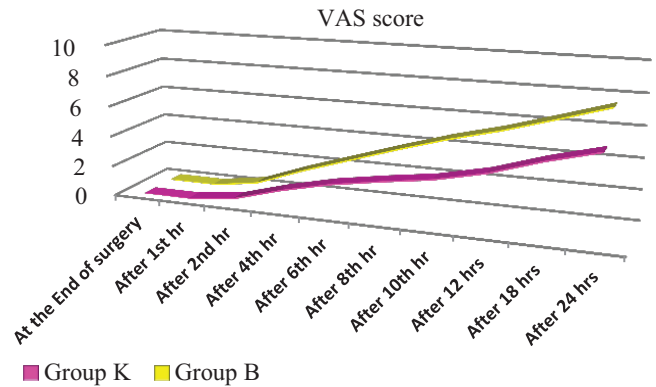
**Table-1:** Baseline patient's characteristics of the two studied groups



Graph-1: Intraoperative hemodynamic changes (a. systolic blood pressure, b. diastolic blood pressure, c. pulse rate)

VAS Score	Group K (n=30)	Group B (n=30)	P value
At the End of surgery	0	0	NA
After 1 <sup>st</sup> hr	0	0	NA
After 2nd hr	0.37±0.49	0.47±0.63	.247
After 4th hr	1.27±0.58	1.63±0.76	.020
After 6th hr	2±0.52	2.67±0.84	.0002
After 8th hr	2.53±0.50	3.7±0.83	<.00001
After 10th hr	3 ± 0.52	4.67±0.84	<.00001
After 12 hrs	3.73±0.58	5.5±0.82	<.00001
After 18 hrs	4.77±0.57	6.47±0.75	<.00001
After 24 hrs	5.63±0.67	7.47±0.68	<.00001

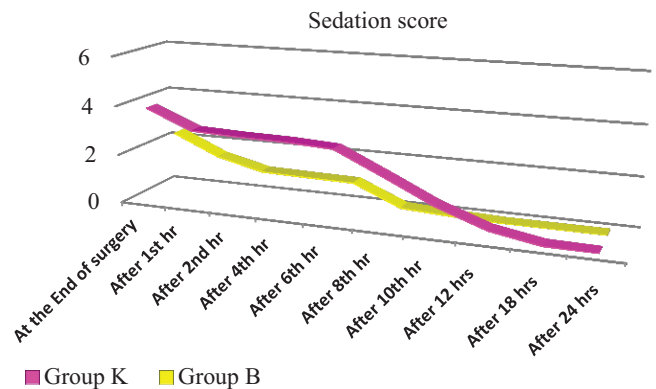
Table-2: Visual analogue score postoperatively in the two studied groups



Graph-2: Visual analogue score postoperatively in the two studied groups

Sedation score	Group K(n=30)	Group B(n=30)	P value
At the End of surgery	3.87±0.51	2.37±0.49	<0.00001
After 1 <sup>st</sup> hr	3.1±0.30	1.53±0.57	<0.00001
After 2nd hr	3.03±0.18	1.07±0.25	<0.00001
After 4th hr	3±0	1.03±0.18	<0.00001
After 6th hr	2.9±0.30	1±0	<0.00001
After 8th hr	2±0	0.17±0.38	<0.00001
After 10th hr	1.07±0.25	0.07±0.25	<0.00001
After 12 hrs	0.37±0.49	0	0.00006
After 18 hrs	0.03±0.18	0	0.164
After 24 hrs	0	0	NA

Table-3: Sedation score postoperatively in the two studied groups



Graph-3: Sedation score postoperatively in the two studied groups

	Group K (n=30)	Group B (n=30)	P value
Time of first analgesic demand (min)	155.8 ± 5.13	130.8 ± 8.08	<.00001
Total Tramadol consumption (mg)	185 ± 39.71	236 ± 40.01	.000017

Table-4: Pattern of additional analgesic requirements during the postoperative period in the two studied groups

two groups up to 8 h postoperatively, which is significantly more with group K. Afterward, sedation score was zero in all patients. Postoperative adverse effects of bupivacaine were limited to only one case of nausea. Ketamine-related adverse effects were two cases of nausea, one case of vomiting and one case of dizziness.

## DISCUSSION

The results of this study indicate that preincisional surgical site infiltration using both ketamine and bupivacaine can provide adequate postoperative pain relief up to 24 h postoperatively following open cholecystectomy and pyelolithotomy surgery under general anaesthesia. Both drugs were safe with minimal sedation and limited adverse events. Ketamine appeared to have a longer analgesic duration compared to bupivacaine. It delayed requesting and decreased consumption of additional analgesia.

### Ketamine

Noncompetitive antagonist of NMDA receptor that can reverse central sensitization and reduce wind-up and consequently decreases postoperative pain, which plays an important role in pain modulation. Ketamine has a local anaesthetic effect mediated by a depression of sodium-channel function. The

analgesic effect of ketamine may be increased due to its anti-proinflammatory effect. It interacts with inflammatory cells recruitment, cytokines production, and inflammatory mediator regulation. Stubhaug *et al.*<sup>15</sup> showed that ketamine decreases acute postop pain by inhibiting C-fiber activity. Preincisional infiltration of ketamine prolongs the time to first analgesic requirement and also decreases the total amount of analgesics used postoperatively.

In the current study, we tested the hypothesis that ketamine, having multiple mechanisms of action, may be effective when administered by subcutaneous injection at the surgical site prior to incision.

### Bupivacaine

In the case of local anaesthetic agents such as bupivacaine or ropivacaine, pain evaluation is particularly important during the period of drug action (ie, the first 12 hours after their administration). Decreasing number of stimuli reaching the CNS from the nociceptors achieved through administration of local anaesthetic agents limits the development of peripheral and central sensitization.

However, earlier studies found less or no beneficial postoperative analgesic effects of preemptive ketamine administered intravenously in small doses in adults undergoing abdominal hysterectomy,<sup>6</sup> total mastectomy,<sup>7</sup> cruciate ligament repair and other surgeries.<sup>9,10,11,12</sup> Several previous studies demonstrated postoperative analgesic efficacy of local anesthetic infiltration of surgical site including laparoscopic gynecology, orthopedic surgery, and hernia repair.<sup>13,14</sup>

In the present study we have shown that patients preemptively receiving bupivacaine along the line of the planned surgical incisions reported less pain intensity according to VAS.

### CONCLUSION

We can conclude that ketamine appears to be a promising preemptive analgesic through surgical site infiltration. Ketamine has comparable effect to bupivacaine with longer duration of action and minimal adverse effects.

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