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EFFECTS OF PREINCISIONAL ANALGESIA WITH SURGICAL SITE INFILTRATION WITH KETAMINE OR LEVOBUPIVACAINE IN PATIENTS UNDERGOING ABDOMINAL HYSTERECTOMY UNDER GENERAL ANAESTHESIA; A RANDOMISED DOUBLE BLIND STUDY

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ABSTRACT

Objectives: This study was aimed at comparing the analgesic effects of local wound infiltration preincisionally with Ketamine or Levobupivacaine in elective total abdominal hysterectomy cases done under general anaesthesia.

Methods: This randomized, double blinded, group allocation concealed study of patients was carried out after ethical committee clearance. Eighty patients scheduled for total abdominal hysterectomy, were assigned randomly into two groups to preoperatively receive local subcutaneous wound infiltration with either 20 ml of 2mg/kg Ketamine (Group K) or 20 ml of 0.25% Levobupivacaine (Group L) along the surgical incision 15 minutes before incision. Postoperative pain was assessed using Visual Analogue Scale at predefined time points post operatively. Duration of analgesia and amount of rescue analgesic requirement was evaluated.

Results: The demographic parameters and the duration of surgery were comparable. VAS scores decreased significantly in Group K at 8, 12 and 24 hours post operatively compared to Group L. First request for rescue analgesic was significantly delayed in group K (165.45 ± 9.38 vs 133.07 ± 8.00 mins, p= <0.001) and the total amount of rescue analgesic consumption in 24 hours postoperatively was significantly less in group K (128.57 ± 45.83 vs 155 ± 50.38 mg, p= 0.02).

Conclusion: Surgical site infiltration with Ketamine provides better postoperative analgesia in lower abdominal surgeries compared to Levobupivacaine without any significant changes in haemodynamics or associated side effects.

KEYWORDS :

INTRODUCTION

Wound infiltration is a method of postoperative analgesia, commonly used alone or with other analgesic regimens . Several methods have been followed to provide effective postoperative analgesia by systemic route, various neuraxial and peripheral regional analgesic techniques. Pre-incisional and post-incisional surgical wound infiltration has several advantages over systemic analgesics and neuraxial techniques by reducing their adverse effects.(1) (2) . A wound infiltration is a method of postoperative analgesia commonly used alone or with other analgesic regimens. It was developed to improve postoperative analgesia, reduce opioid consumption and hasten the patient recovery.(3) The advantages of wound infiltration analgesia over neuraxial analgesia are, side effects like motor blockade, hypotension, nausea and vomiting are avoided. Analgesic requirements are reduced, with fewer opioid-related side-effects . (2)(4) Advantage of wound infiltration analgesia over nerve block is the control of pain over the surgical areas without interfering with the nerve function.(4)(5)

Preemptive analgesia has been used in different surgeries including cesarean delivery, abdominal hysterectomy, and open cholecys tectomy.(4) Various parameters have been seen to effect the type and duration of pain and its optimization including age, sensitivity to pain, type and duration of surgery, and type of analgesia used (6)

Ketamine is an antagonist of n-methyl-d-aspartate (NMDA) receptor which has an important role in pain modulation.(7) It has been seen) that ketamine reduces acute postoperative pain by inhibiting C-fiber activity (8). Preincisional infiltration of ketamine prolongs the time to first analgesic requirement and also decreases the total amount of analgesics used postoperatively.(9) Levobupivacaine, the pure S (−) enantiomer of bupivacaine, has strongly emerged as a safer alternative for regional anaesthesia than its racemic sibling, bupivacaine. Levobupivacaine has been found to be equally efficacious as bupivacaine, with its superior pharmacokinetic profile. It is well-tolerated in regional anaesthesia techniques after bolus administration as well as continuous post-operative infusion (10)

We intend to evaluate and compare the preemptive analgesic effect of surgical site infiltration with Levobupivacaine or Ketamine in patients undergoing abdominal hysterectomy. We are doing the study in the population of patients in gauhati medical college.

AIMS AND OBJECTIVES

The aim of this study is to study was to compare the primary and secondary outcomes in two groups . GROUP Ketamine (K) : 20 ml of 2mg/kg ketamine diluted to 20 ml with 0.9% saline solution and GROUP Levobupivacaine (L) : 20 ml of 0.25% Levobupivacaine in wound site infiltration for abdominal hysterectomy cases under general anaesthesia for patients aged between 18 to 65 years :

PRIMARY OBJECTIVES

To assess the effectiveness of preincisional infiltration of Ketamine with Levobupivacaine for attenuation of postoperative pain following elective abdominal hysterectomy .

To evaluate the requirement of post operative analgesia.

SECONDARY OBJECTIVES

To evaluate any other relevant observations , if they arise .

This prospective, double blind, randomized clinical study was conducted on 88 patients, scheduled for total abdominal hysterectomy surgeries under general anaesthesia at Gauhati Medical College ,Guwahati under the Deptt of Anaesthesiology and Critical Care . The approval of institutional ethical committee and informed written consent from the participants was obtained. The study was conducted for a period of one year commencing from 1st June 2018 to 31st May 2019 and was conducted in the Gynaecology operation theatre and respective wards.

INCLUSION CRITERIA:

1) ASA grades I & II scheduled for elective hysterectomy.
2) age between 18-65 years.
3) Patients who have given valid informed written consent.
4) No known allergy to study drugs.

EXCLUSION CRITERIA

1) Unwilling patients.
2) Allergy to the study drugs.
3) Patients with hypertension (history of hypertension or blood pressure more than 140/90 mm of Hg on examination).
4) Cardiovascular diseases (hypertension, tachycardia, congestive heart failure, and coronary artery disease).
5) Chronic obstructive pulmonary disease.
6) Other major systemic illness.
7) Renal insufficiency.
8) Liver dysfunction.

Participats in the study were divided into two groups K and L, by a computer generated random selection using block randomization with 4 patients in each block . Concealment of allocation was done by opaque sealed envelope technique. Patients received either

subcutaneous infiltration of Ketamine 2 mg/kg or receive subcutaneous infiltration of 20 ml of levobupivacaine 0.25%. All medications were diluted with sterile 0.9% saline solution to 20 ml volume in similar syringes and were infiltrated subcutaneously along the skin wound edges 15 min before skin incision. In the operating room, monitors like electrocardiogram (ECG), non-invasive blood pressure (NIBP) and pulse oximetry (SPO2) were connected. Peripheral 18 gauge intravenous line was secured, Ringer lactate solution was started and inj. Ondansetron 4mg intravenously was given. Patients were premedicated with intravenous inj. Glycopyrrolate 0.004 mg/kg, and inj. Tramadol 1 mg/kg. Preoxygenated with 100% Oxygen for 3 minutes. Patient was induced with Inj. Propofol 1.5-2.5 mg/kg IV . Patient were intubated using appropriate size endotracheal tube, by direct laryngoscopy, under inj. succinylcholine 1mg/kg IV.

Anaesthesia was maintained with N2O:O2 4:2, inhalational isoflurane 0.8% dial settings , inj. Atracurium 0.1mg/kg IV and repeated accordingly. Intra-operatively ECG, NIBP, SPO2, and pulse rate were monitored. Patient lungs were ventilated to maintain normocapnia. The study drugs were infiltrated subcutaneously by a designated resident who was not involved in group assignment into the incisional site region after induction of anesthesia. Under all aseptic and antiseptic precautions, the area around the proposed incision site of the abdomen was prepared with povidone iodine and spirit. Two 10 ml syringes filled with the study drugs were used for all the blocks. Pfannenstiel incision was given in all cases. All surgical incisions were done only after 15 min from the study drug administration. At the end of surgery, volatile anesthetics were discontinued, neuromuscular blockade was reversed by intravenous (IV) neostigmine 0.05mg /kg and IV glyccopyrolate 0.01 mg/kg, and extubation was performed when airway reflexes had returned. The post operative analgesic effect of each patient were assessed at the time of 0 hr 1hr, 2hr, 4hr , 8hr, 12 hr and 24 hr after surgery using VAS score (0-10). In addition, the patients were assessed for HR, SBP and DBP .. The time from induction of anesthesia to discontinuation of anesthesia was considered as the anesthetic time and the time from the first surgical incision till the last skin suture was considered to be the operative time. Rescue analgesia was given with inj. tramadol 100mg intravenously (IV), whenever VAS >4.

The following were noted in all the patients

1. Total duration of analgesia and time to rescue analgesia
2. Amount of rescue analgesics required in each group.
3. Number of patients requiring rescue analgesics in each group
4. Baseline, induction , infiltration , intraoperative, postoperative hemodynamic parameters pulse rate (PR), systolic blood pressure (SBP) and diastolic blood pressure (DBP) .
5. Postoperative analgesic effect of locally infiltrated drugs at 0 hr 1hr, 2hr, 4hr , 8hr, 12 hr and 24 hr according to visual analogue scale (0-10).

6. Systemic side effects of the locally infiltrated drugs .

The assessment of analgesia was done using 10 cm Visual Analogue Scale score (VAS score) 0-10. Patient was given a scale marked from 0 – 10 and were asked to mark on a scale, the degree of pain he or she experienced ranging from No pain at 0 to Maximum pain at 10 point. When patient complained of pain with VAS>4, rescue analgesic was given with inj. Tramadol 100 mg IV and assessed how many times rescue analgesic was taken by the patient for 24 hours after surgery.

STATISTICAL ANALYSIS OF DATA

The data were entered into MS Excel spread sheets and analysis were carried out. Student T tests, Fischer's exact test , Mann Whitney test, chi-square test and Analysis of Variance were employed using the computer program Graph Pad Instat for analyzing of data. Block randomization was done using computer generated randomization table. The results were tabulated and statistically analysed using SPSS version 21.0

RESULTS

The demographic characteristics of the study groups in terms of age , ASA category , height , weight , the duration of surgery were comparable and did not show any difference.

Table 1 : Demographic Variables

	Group K	Group L	P value
Duration of analgesia (minutes)	165±9.38	133.07±8.00	<0.001
Amount of rescue analgesic (mg)	128.57±45.83	155±0.38	0.02

The duration of analgesia observed in the Ketamine infiltration group was found to be 165.45 ± 9.38 minutes which was longer than in Levobupivacaine group where it was 133.07 ± 8.00 minutes which was statistically significant .

The amount of rescue analgesics consumed by both the groups in the 24 hour postop period was compared statistically and was found to be significantly less in group K (128.57±45.83 mg) than in group L (155±50.38 mg).

Table 2 :amount And Duration Of Rescue Analgesics

Time	Group K	Group L	P value
0 HOUR	2(0-2)	2(0-2)	0.14
1 HOUR	2(1-3)	3(1-3)	0.06
2 HOUR	3(2-4)	3(2-4)	0.06
4HOUR	3(2-4)	3(2-4)	0.12
8 HOUR	3(1-4)	3(1-4)	0.02*
12 HOUR	3(0-4)	3(0-4)	0.02*
24 HOUR	2.5(0-3)	3(0-3)	0.01*

The VAS scores of the 2 groups were measured in the postop period at 0 , 1 , 2 , 4 , 8 , 12 and 24 hours . In Ketamine group VAS score decreased significantly from 8 to 24 h as compared to the immediate postoperative reading .

Table 3 : Postop Vas Scores

Variable	Group K	Group L	P value
Age (years)	52.17±9.2	53.08±9.4	0.67
Weight(kgs)	60.09±9.47	59.66±10.34	0.97
Height(cms)	156±207.02	155.03±7.64	0.86
ASA 1:2	30:10	32:8	0.183
Duration of surgery (minutes)	103.21±10.71	106.52±10.66	0.15

The percentage of patients requiring 0 doses of rescue analgesics in group K was 12.5% while there were no such patients in group L .

In group K 62.5% patients required 1 dose of rescue analgesic while in group L 45% patients required 1 dose . 25% patients in group K required 2 doses of rescue analgesics while in group L 55 % patients needed 2 doses.

Baseline and intraop haemodynamic parameters were not found to be statistically significant on comparison .

Patients in both groups did not show statistically significant difference in the incidence of side effects .

DISCUSSION

The duration of analgesia in the Ketamine group observed in our study was highly significant . This finding of our study is consistent with the findings of Abdallah N et al (12) who also studied the effect of subcutaneous infiltration of Ketamine 2mg/kg (diluted to 20 ml) and subcutaneous Levobupivacaine 0.25% 20 ml in patients undergoing total abdominal hysterectomy and found significantly prolongation in the Ketamine group compared to the Levobupivacaine group .

Similarly Safavi M et al (13) in 2014, comparing different doses of subcutaneous ketamine in open cholecystectomy cases found that the time for 1st analgesic requirement in patients receiving Ketamine subcutaneously was 170.0±14.1 min which was comparable with our study wherein we have observed that patients infiltrated with ketamine 2mg/kg showed good pain relief till 24 hours post surgery.

Similarly Pouliou A et al (11) found prolonged time for first analgesic in the incision site infiltration ketamine group in hernia repair cases .

Ketamine binding to the NMDA receptors may prevent glutamate induced activation of NMDA receptors on the primary afferent axons in the skin which subsequently reduces peripheral nociceptive input into the spinal cord and central sensitization of dorsal horn. Long lasting decrease of the wound pain can be explained by the long duration of ketamine's direct peripheral pharmacologic action or by its preemptive effect on the inflammatory response to surgery The preemptive analgesic effects of Ketamine have been well established by various studies(14)(15) . Yang L et al (16) and Safavi M et al (13)

conducted studies supporting the analgesic efficacy of subcutaneous Ketamine .Intraperitoneal postsurgical installation of Ketamine has also been done in various studies with effective postop analgesia and low VAS score till 24 hours of surgery (17)(18)(19)

In our study, we also compared the VAS scores of the patients in the postop period and significant difference in the VAS scores of the two groups were found from 8 hours till 24 hours. There was no significant difference between the two groups till 8th postoperative hour. The findings of our study are similar to the findings by Abdallah N et al (12)

Similarly in the study by Safavi M et al (13) postop VAS was assessed and it was found that Ketamine provided analgesia upto 24 hours postoperatively .

On comparing the dose of rescue analgesics, we found that the requirement of tramadol was significantly lower in the group receiving Ketamine as compared to patients receiving levobupivacaine. In the study conducted by Abdallah N et al (12) rescue analgesic and the amount required was significantly lower in the ketamine group which is comparable to our study. Similarly Safavi M et al (13) in 2014 , the amount of rescue analgesic consumption was seen to be the least in the Ketamine infiltration group. Similar results were also found by Jha AK et al (20) where least rescue analgesic consumption was seen in the Ketamine group.

The strength of our study lies in the fact that it is a randomized, observer and patient blinded study. The hemodynamic parameters were also compared in our study and no significant difference was found between the two groups. These findings are similar to the findings of by Abdallah N et al (12) who found no significant difference between the hemodynamic parameters of patients receiving Ketamine and those receiving Levobupivacaine alone.

The incidence of adverse effects in both groups of our study was low. No significance was found between the two groups with respect to any of the side effects noted.

CONCLUSION

From our clinical study it can be concluded that wound infiltration technique with Ketamine in patients undergoing total abdominal hysterectomy resulted in enhanced postoperative analgesia with decreased need for rescue analgesics compared to levobupivacaine with minimal side-effects . Thus Ketamine appears to be a promising pre emptive analgesic in lower abdominal surgeries providing better pain relief and patient recovery .

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