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Effect of Ketamine as an Adjuvant to Bupivacaine in Ilioinguinal and Iliohypogastric Nerve Block for Postoperative Analgesia after Inguinal Hernia Repair

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Abstract

Ilioinguinal and Iliohypogastric nerve block is one of the methods exercised widely to reduce postoperative pain after inguinal hernia repair. Several initiatives are ongoing to prolong the duration of postoperative analgesia by adding various adjuvants to the local anaesthetic agents in different nerve blocks. In this study ketamine has been added as an adjuvant to local anaesthetic bupivacaine in Ilioinguinal and Iliohypogastric nerve blocks. Our study aims to evaluate the effect of adding ketamine to local anaesthetic bupivacaine in ultrasound guided Ilioinguinal and Iliohypogastric nerve block in patient scheduled for inguinal hernia repair under subarachnoid block. This randomized control trial was carried out among 94 patients scheduled for elective inguinal hernia repair under subarachnoid block in Dhaka Medical College Hospital, Dhaka, Bangladesh. Two nerves, Ilioinguinal and Iliohypogastric were blocked by 0.25% bupivacaine under ultrasound guidance after the completion of surgery for postoperative analgesia. The study population was divided equally into two groups having 47 patients in each. Patients of group-A was received 20 ml of 0.25% bupivacaine and 2ml normal saline in the block procedure. Another group, group B patients received 20ml of 0.25% bupivacaine and 1mg/kg of ketamine in the same nerve block. Demographic profiles had no significant differences between two groups ($p>0.05$). Mean duration of the analgesia or the time of first rescue analgesic requirement were significantly higher in ketamine group (595.24±15.90 minutes) than normal saline group (226.4±20.6 minutes). ($p<0.05$); Postoperative total analgesic (pethidine) requirement within first 24 hours (178.3±18.3 vs. 92.3±15.3) milligrams, ($p<0.05$) was higher in normal saline group. Our data suggests that ketamine when used as an adjuvant to bupivacaine for ilioinguinal and iliohypogastric nerve block prolongs the time to first analgesic request as well as decreases the analgesic requirement during postoperative period.

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Introduction

The goal of postoperative pain management is to reduce or eliminate pain and discomfort with least side effects and minimal cost. Opioid based patient-controlled analgesia is an effective approach for postoperative pain management but limited by the availability of this system in low income countries.[1] Again, opioids have their characteristic adverse effects like pruritus, respiratory depression, gastrointestinal hypomotility, nausea-vomiting and urinary retention.[2]

The use of ilioinguinal iliohypogastric nerve (IIN & IHN) block may be the most convenient method for patients after inguinal hernia repair. During the last decade, the use of ultrasound-guided regional anaesthesia has been increased, and developments in ultrasound technology have enabled direct visualization of peripheral nerves. A technique for ultrasound-guided ilioinguinal and iliohypogastric nerve blocks has been described in adults.[3] In paediatric patients, ultrasound-guided blocks have been associated with a higher success rate and a lower volume of local anaesthetic needed, compared with the conventional landmark based techniques.[4]

Ilioinguinal and iliohypogastric blocks have been routinely used as anesthetic technique for surgeries at the inguinal region and these blocks also improves the postoperative analgesia for cesarean section and other lower abdominal surgeries.[1,4] This nerve block involves the blocking of ilioinguinal and iliohypogastric nerves in the plane between the transverses abdominis and internal oblique muscles.

To prolong the duration of sensory-motor block and limiting the cumulative dose requirement of local anaesthetics, co-administration of adjuvants has the potential to improve efficacy of perineural blocks and decrease the chance of local anaesthetic toxicity. The terms, local anaesthetic “adjuvants” or “additives”, have often been used interchangeably. They contribute in their own special manner to potentiate the analgesic effect of the local anaesthetics.[5] Adjuvants are usually added to local anaesthetic so as to enhance the quality as well as to prolong the period of peripheral nerve blockade, without producing adverse effects associated with the systemic use of these additives, such as hypotension, bradycardia, respiratory depression, sedation, hallucinations, nausea, vomiting, itching, or urinary retention.

Ketamine has been considered to be mainly a non-competitive antagonist of the NMDA receptors.[6] Some authors proposed that, ketamine can also enhance the local anaesthetic action via peripheral mechanisms and ketamine has also some local anaesthetic properties.[7] Ketamine also directly inhibits Na^+ channel and also potentiate the blocking of Na^+ channel by the local anaesthetic bupivacaine.[8] Ketamine has also some secondary effects on opioid receptors that can enhance its analgesic effect.[9]

Various studies assessed the effect of ketamine as adjuvant to peripheral nerve block concluded that, addition of ketamine in peripheral nerve block results in decreasing the postoperative pain and need for rescue analgesics.[7,10-13] The results indicate that ketamine acting by a peripheral mechanism can profoundly enhance anaesthetic and analgesic actions of a local anaesthetic administered. But still there are scope to study more regarding the additive effects of ketamine with local anaesthetics in peripheral nerve blocks

like ilioinguinal and iliohypogastric as revealed by paucity of relevant studies.

Therefore, in this study, we proposed to use ketamine 1mg/kg in USG-guided IIN & IHN block as an adjuvant to bupivacaine in patients scheduled for inguinal hernia repair under subarachnoid block, as it is a very cheap drug and available throughout Bangladesh. This study aims to evaluate the effect of adding ketamine to bupivacaine for ultrasound-guided ilioinguinal and iliohypogastric nerve block for postoperative analgesia in patients undergoing inguinal hernia repair.

Methods

This randomized control trial was carried out in 94 adult male patients (Age 18 years and above) belonging to American Society of Anesthesiologists (ASA) physical status I and II scheduled for elective inguinal hernia repair under SAB. The study was conducted between March 2018 and September 2020 in Dhaka Medical College Hospital, Dhaka, Bangladesh. A total of 120 patients were screened during pre-anaesthetic checkup for the study. Among them 94 patients were finally selected according to inclusion criteria and rest of all were excluded in aspect of exclusion criteria and who did not give consent. They were randomly allocated into two groups. Randomization was achieved by computer-generated random number table. The principal investigator performed the IIN & IHN block at the end of the surgery. The trained observer who was the on-duty anaesthesiologist in the post anaesthesia care unit collected the data in the postoperative period. The observers as well as the patient were blinded to the drug solution administered.

During pre-anaesthetic visit, the patients were explained about the study purpose, advantages and risks of procedure and after that informed written consent were obtained. The patients were excluded as they had history of chronic pain or opioid use, Neuropathy, Hypertension or Ischemic heart disease, Known allergy to bupivacaine, ketamine or pethidine and mentally impaired adults. Patients were educated about the visual analogue scale (VAS) during the preoperative assessment.

All the patients were kept nil orally for 8 hours before surgery. In the operation theatre, after securing an 18-gauge intravenous (IV) cannula, Ringer's lactate solution (Hartmann solution) infusion was commenced. After established standard anaesthesia monitoring, baseline measurements such as pulse, non-invasive blood pressure and peripheral oxygen saturation were recorded. Under all aseptic conditions, patients undergoing elective inguinal hernia repair was given sub arachnoid block (SAB) in the sitting position using a 25-gauge Quincke spinal needle at L3–L4 inter-spinous space and 3ml (15 mg) of 0.5% hyperbaric bupivacaine was injected after confirming free flow of cerebrospinal fluid (CSF). After confirmation of adequate level (T8) of anaesthesia, surgery began. When the surgery was over, with all aseptic precautions, the USG-guided IIN & IHN block (using SonoSite™ Micromax machine, linear high-frequency probe, 6–12 MHz) was performed with respective drug solutions according to Group distribution.

After proper draping over area, with the patient supine, the ultrasound transducer was placed medial to the anterior superior iliac spine oriented on spino-umbilical line; the needle was inserted by a USG-guided in-plane technique at the area

just medial to the medial end of the transducer which is placed perpendicular to the inguinal ligament and its lateral end was contacted to the anterior superior iliac spine. After checking the exact location of the needle tip, 1-2 ml of normal saline was injected to open the plane and after confirmation of hypoechoic area on USG image, the study solution of 22ml (20+2) was injected. The patients in Group A received 20 ml 0.25% bupivacaine (50 mg) with 2 ml of normal saline, whereas the patients in Group B received 20 ml 0.25% bupivacaine (50 mg) with 1mg/kg of 5% ketamine in 2ml volume by adding normal saline if required.

Postoperatively, the patients were evaluated for pain in the post-anaesthesia care unit using Visual analogue scale (VAS) at time 0 to 1hour (after the time of completion of IIN & IHN block), 1-2 hour, 2-3 hours, 3-4 hours, 4-6 hours, 6-8 hours, 8-10 hours, 10-12 hours, 12-14 hours, 14-16 hours, 16-18 hours, and 18-24 hours by VAS scoring by the observer blinded to the group assignment. Duration of analgesia was measured according to time elapsed from the nerve block to the time when VAS score was >4. Total opioid analgesic (pethidine) consumption was calculated and recorded at the end of 24th post-operative hour.

The outcome measures in this study were, the post-operative pain score by VAS, duration of post-operative analgesia that is the time to VAS >4 from the time of giving nerve block, the amount of supplemental opioid analgesic requirements in first 24 hours. All the patients have monitored in the post-operative period for any side effects (nausea vomiting, hypotension, respiratory depression) including sedation according to Ramsay sedation assessment scale. On demand rescue analgesic was inj. Pethidine 1.5 mg/kg intramuscularly with an antiemetic Inj. Ondansetron 8mg IV if required. The dose of intramuscular pethidine was calculated according to a study of Banik *et al.*[14]

Every patient's data was collected and recorded on a separate data sheet. Demographic information was collected from the patients. Following collection of all necessary data, all of them were entered into SPSS 26.0 (IBM SPSS, Chicago, IL, USA). Numerical data such as pulse, mean arterial pressure, oxygen saturation, sedation score, duration of analgesia and total supplemental analgesic consumption in first 24 hours was expressed as mean±SD and was analyzed by independent samples t-test and mean pain scores by VAS at different points of time was analyzed by repeated measures ANOVA. Categorical data was analyzed with Chi-square test. All analysis was conducted with intent-to-treat approach to minimize the potential effects of dropout. All P values were two tailed, and P values ≤0.05 was considered significant. The study was approved by the Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh.

Results

A total of 94 patients participated in this study, i.e. 47 in each group. The patients of two groups were comparable with each other in respect to demographic criteria and duration of surgery (min). No significant statistical difference was found in aspect of age, ASA physical status classification and weight on patients between two groups (p>0.05). The mean duration of surgery (min) for both groups was also not significant (p>0.05) (Table-I). Mean value of pulse rate was

higher at 180 min after nerve block in Group A (p value was significant<0.05). In Group A pulse rate was decreased at 240min after giving parenteral analgesic. In case of Group B, mean pulse rate was relatively constant throughout the first 300 min after the nerve block during postoperative period (Fig. 1). Mean arterial pressure (MAP) in mmHg of patients had no significant difference between the groups. In Group A, MAP was decreased at 240min after giving parenteral analgesic. In case of Group B mean MAP was stable in first 300 min during postoperative period. In both groups, MAP (mmHg) was decreased after SAB but at the end of the surgery the MAP of two groups was restored to preoperative baseline value (Fig. 2). There was no significant statistical difference (p>0.05) in perioperative oxygen saturations between the groups (Fig. 3). Mean value of VAS score was higher at 3-4 hours interval and 10-12 hours interval in Group A. In case of Group B mean value of VAS score was highest at 8-10 hours interval. In both groups VAS score was decreased after giving parenteral opioid analgesic (Table-II). Post nerve block sedation score of two groups were analyzed and there was no significant statistical difference (p>0.05) in sedation score between the groups (Fig. 4). Mean duration of analgesia for group A was 226.4±20.6 minutes and for group B, it was 595.24±15.90 minutes. Mean values of post-operative pethidine requirements were 178.3±18.3 mg and 92.3±15.3 mg respectively for group A and group B. Significant statistical difference was found (p<0.05) in duration of analgesia and post-operative pethidine consumption between the groups (Table-III). Significant statistical difference was found in side effects between two groups and side effects were significantly higher in group A (P value <0.05). Side effects are partly due to increased consumption of opioid analgesic (pethidine) in group A in respect to group B (Table-IV).

Table-I: Demographic criteria and duration of surgery for the patients

Criteria	Group A (n=47)	Group B (n=47)	p-value
Age (years)	51.35± 15.73	53.41± 16.73	0.257
ASA classification (I/II)	23/24	25/22	0.587
Weight (kg)	60.34± 4.68	58.52± 5.53	0.342
Duration of surgery (minutes)	75.42± 15.43	69.22± 15.73	0.428

Values were described as Mean±SD. P values were reached from Unpaired student t test.

Fig. 1: Perioperative pulse rate of the patients

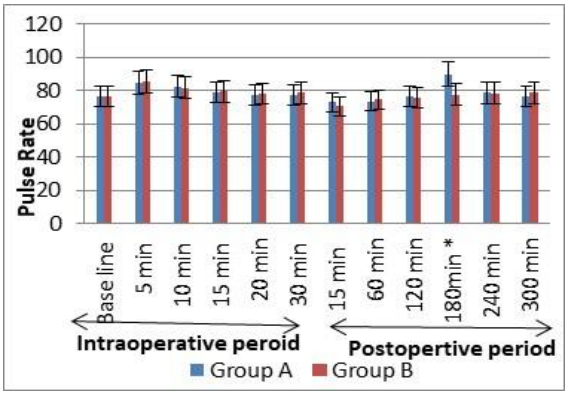

Fig. 2: Perioperative mean arterial pressure (MAP) of the patients

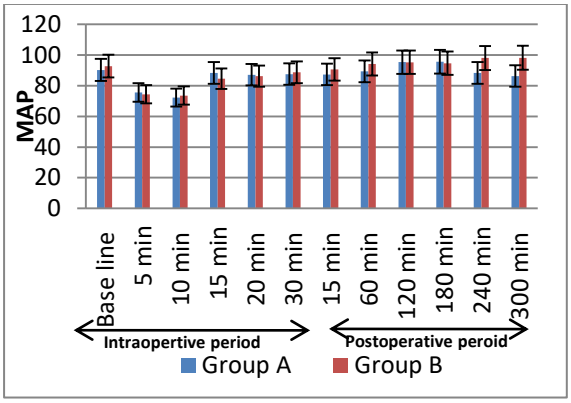

Fig. 3: Perioperative oxygen saturation of the patients

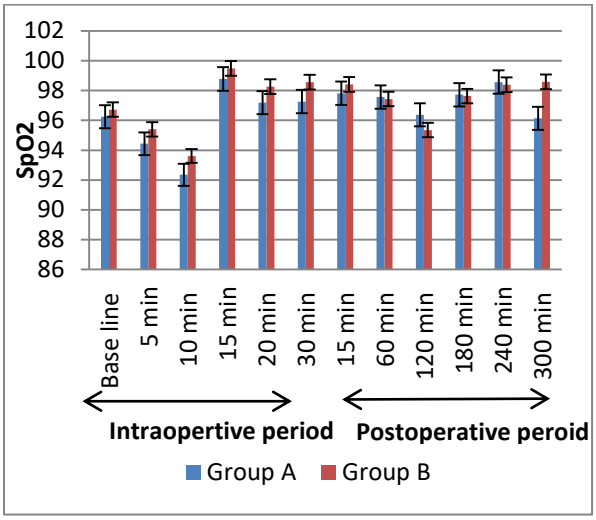

Table-II: Variations in Visual analogue scale (VAS) score with time intervals

VAS score	Group A (n=47)	Group B (n=47)	p-value
0-1 hour	1.20±0.43	1.00±0.53	0.440
1-2 hour	1.28±0.52	1.06±0.69	0.230
2-3 hour	3.20±0.98	1.30±0.78	0.321
3-4 hour	5.20±1.00	1.80±0.39	<0.001**
4-6 hour	1.80±0.65	2.20±0.72	0.270
6-8 hour	2.00±0.81	3.50±0.88	0.084
8-10 hour	3.20±0.94	5.10±1.20	<0.001**
10-12 hour	5.20±1.54	1.20±0.67	<0.001**
12-14 hour	2.20±0.49	1.30±0.58	0.470
14-16 hour	2.80±0.78	1.50±0.34	0.231
16-18 hour	3.20±0.37	1.60±0.56	0.561
18-24 hour	3.50±0.47	1.80±0.52	0.841

Values are described as Mean±SD. p value was determined by ANOVA.

Fig. 4: Post block sedation scoring by Ramsay sedation assessment scale

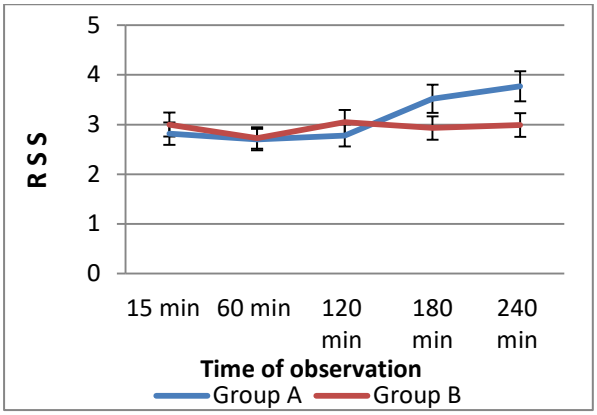

Table III: Mean duration of analgesia and total requirement of pethidine in 24 hours

Variable	Group A (n=47)	Group B (n=47)	p-value
Duration of analgesia (min.)	226.4± 20.6	595.24± 15.90	0.0021*
Postoperative pethidine (mg)	178.3± 18.3	92.3± 15.3	0.0018*

Values were described as Mean±SD. P values were reached from Unpaired student t test.

Table-IV: Comparison between side effects of patients in two groups

Side effects	Group A (n=47)	Group B (n=47)	p-value
PONV[#]	5 (11%)	2(4%)	
Hypotension	2 (4%)	0	
Respiratory depression	3 (6%)	0	
Total	10 (21%)	2 (4%)	0.02*

Values were described as frequency and percentage. [#]PONV= Post-operative nausea vomiting. Chi square test was done to reach the P value.

Discussion

Demographic variables of current study were statistically comparable between two groups in aspect of age, weight, ASA status and duration of surgery (p values are 0.257, 0.342, 0.587, & 0.428 respectively) as p values were not significant. Perioperative hemodynamic parameters such as pulse rate and mean arterial pressure as well as arterial oxygen saturation was also recorded and analyzed. Except at 180min after block when mean pulse rate of group A was raised and was statistically significant to group B, all the mean values of hemodynamic parameter and oxygen saturation were comparable between two group as revealed by there was no significant statistical difference (p>0.05). This statistical rise of pulse rate at 180min post nerve block might be due early appearance of postoperative pain in group A as it is known that the VAS score at 3-4 hour interval in group A was higher (>4) and required a dose of rescue analgesic.

As ketamine can cause sedation when given in intravenous route, post nerve block sedation was assessed by Ramsay sedation assessment scoring, and it was found that no rise of sedation scores in group of patients (group B) who received ketamine admixed bupivacaine in nerve block. Sedation scores were also comparable with that of patients of group A and found no significant differences between the groups. This result was similar with the result found in Othman *et al.*[15] study where no significant difference is found in sedation scoring between ketamine group and control (local anaesthetics only) group.

In this study the VAS score was recorded at various time interval after doing the nerve block and it showed that, VAS score >4 was found at about 8-10 hours after the block in ketamine group in comparison to 3-4 hours after the block in control group (p<0.001) that was similar with the result found by Lashgarinia *et al.*[10] and the total amount of required analgesic (pethidine) was also significantly lesser in the ketamine group than control group (p=0.0018) which is also comparable with the result (p<0.001) of Lashgarinia *et al.*[10] where they studied to see the effect of ketamine as an adjuvant in ultrasound guided supraclavicular brachial plexus block. Result of this study was also consistent to another study done by Noha *et al.*[16] that showed that pain began earlier and more severe in patients who did not receive ketamine added to local anaesthetic than the patients who received that as an adjuvant. Their study also revealed that significant reduction (p-value< 0.05) in cumulative morphine consumption in first 24 hours by adding ketamine with local anaesthetic bupivacaine in IIN & IHN block to prolong postoperative analgesia after inguinal hernia repair.

Gamil and Fathy[17] had done spermatic cord block with 0.5% bupivacaine and 20mg ketamine in patient undergoing testicular sperm extraction surgery under general anaesthesia to compare the postoperative analgesic effect of ketamine adjuvant with local anaesthetic bupivacaine. They found results consistent with current study that VAS score was significantly lower at 6, 9, 12, 24 hours in ketamine group. The mean pain free time (time from regaining consciousness to onset of testicular pain) that corresponds to the duration of analgesia was significantly higher in ketamine group. 302 min vs 225 min (p<0.05). This result is also consistent with this current study.

Another study done by Cook *et al.*[18], where they investigate the comparison of 3 different adjuvant adrenaline (5mcg/ml), clonidine (2mcg/kg), and ketamine (0.5mg/kg) with 0.25% bupivacaine in caudal epidural block for orchidopexy in children. Their result found that the mean duration of analgesia in ketamine group was 12.5 hour compared with 5.8 hr. in clonidine group and 3.2 hr. in adrenaline group. Here significant prolongation of duration of analgesia is seen by adding ketamine with local anaesthetic 0.25% bupivacaine that is also consistent with current study as here duration of analgesia is prolonged significantly by adding ketamine.

In another study, patients who received transverses abdominis plane (TAP) block for inguinal hernioplasty with bupivacaine-ketamine had comparable postoperative 24 h cumulative morphine consumption, time of first request for morphine, pain and sedation scores, and postoperative nausea and vomiting with the patients who received bupivacaine only. The possible cause of this negative result may be either due to type of nerve block (TAP) as there are several studies that recommend, IIN and IHN block provides better postoperative analgesia than TAP block[19,20,21] or due to lower dose of ketamine (0.5mg/kg) in their study. So here ketamine 1mg/kg is used in current study. No patient reported any postoperative complications related to ketamine in their study as in our study.[22]

Ketamine plus bupivacaine was compared to bupivacaine alone in pectoral block, prolonged the mean time of first request of analgesia (18.25±1.98 hrs), (12.56±2.64 hrs), respectively (p<0.001), reduced total morphine consumption (12.50±4.63 mg), (18.86 ± 6.28 mg), respectively (p=0.016). The result of current study is consistent with the result of them. Moreover, as current study there was no significant difference in hemodynamics, oxygen saturation, sedation scores, and side effects observed between the two groups.[15] In this study pectoral block was given with 30ml of 0.25% bupivacaine plus ketamine hydrochloride (1 mg/kg) as in current study.

Shaheen *et al*.[23] studied the effect of ketamine as an adjuvant to bupivacaine in spermatic cord block for scrotal surgery. They observed that there was significantly rapid onset and prolonged duration (735.00±420.27 min.) of blockade in ketamine group and significant increase in visual analogue scale score in control group at 6 h postoperatively, whereas a significant increase occurred in ketamine group at 12 h, postoperatively. In current study it was 3-4 hour and 8-10 hour respectively. There was significant increase amount of rescue morphine analgesic (3.91±1.41mg vs 2.38±1.53mg) in control group than ketamine group. Result is similar with current study in case of total opioid requirement that it was significantly high (178.3±18.8mg vs 92.3±15.3mg) in control group than ketamine group.

It is expected that results of this study highlight the value of adding ketamine to local anesthetics in peripheral nerve block, especially in this technique of Ilioinguinal and Iliohypogastric nerve block, where postoperative analgesia lasted for a long period of time. However, our study had some limitations, too. The analgesic effect of ketamine might be in part due to its systemic absorption; Serum levels of ketamine (if present)

could have measured or declared the analgesic efficacy is solely due to of perineural ketamine. Moreover, onset of sensory block in the lower abdominal wall after IIN & IHN block could not be assessed because patients were under the effect of subarachnoid block while giving these nerve blocks at the end of the surgery.

Conclusion

Our data suggests that an addition of ketamine to bupivacaine in IIN & IHN block prolonged the duration of postoperative analgesia as time to first rescue analgesic requirement was increased and total opioid consumption was reduced without serious side effects in patients undergoing inguinal hernia repair.

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