ORIGINAL ARTICLE

Comparative Study between IV Paracetamol and IM Pethidine for Post Operative Analgesia in Laparoscopic Cholecystectomy

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ABSTRACT

Background: Effective analgesia is important after laparoscopic cholecystectomy. Paracetamol have been used extensively as alternatives, and it seems that they are more effective for mild to moderate pain control postoperatively. As laparoscopic Cholecystectomy poses moderate pain, in this study we compare the quality of analgesia and side effects of paracetamol versus pethidine for post-operative analgesia after laparoscopic cholecystectomy.

Objectives: This study was designed to observe the effect of I.V. paracetamol and I.M. pethidine for analgesic efficacy in post-operative analgesia with their side effects in laparoscopic cholecystectomy.

Material and method: Sixty (60) patients were selected in the pre anaesthetic check up room whose were going to be operated for laparoscopic cholecystectomy. Each patient in group A received intravenous paracetamol (1g/100ml)15mg/kg over 15minutes and group B received intramuscular pethidine (100mg)-2mg/kg postoperatively.

Results: In group A that was paracetamol group and group B that was pethidine group the visual analogue scale (VAS) almost similar but total analgesic consumption in pethidine group were slightly higher than paracetamol group and the respiratory rate were significantly lower in pethidine group.

Conclusion: Our results indicate that IV paracetamol 15mg / kg has better analgesic potency and less side effects than 2 mg / kg IM pethidine for postoperative analgesia after laparoscopic cholecystectomy.

Key Words: IV Paracetamol, IM Pethidine, laparoscopic cholecystectomy, postoperative analgesia.

Introduction

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage.[1] Postoperative pain, is typically associated with neuro-endocrine stress response that is proportional to pain intensity. Many patients, however, continues to experience inadequate pain relief.[2] Despite improvements in analgesic delivery, several recent surveys have found that up to 80% of patients report moderate to severe pain after surgery.[3,4,5]

After laparoscopic cholecystectomy parental opioid and NSAIDS are commonly used for postoperative analgesia.[6,7] Opioid remain the agents of choice for severe pain; however, this class of analgesics is associated with dose-dependent adverse effects such as nausea vomiting, ileus, sedation and respiratory depression and prolongs the time to readiness for discharge.[8,9]

In our institution it is general practice to administer pethidine for post laparoscopic cholecystectomy

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analgesia. Pethidine is a synthetic opioid, the onset of action is lightly more rapid than with morphine and the duration of action is slightly shorter.[10]

Nonopioid analgesics (acetaminophen and NSAIDS) are commonly used alone or as adjuncts to opioid-base analgesia to treat moderate to severe pain. Nonsteroidal anti-inflammatory drugs (NSAIDS) have been widely applied for postoperative pain management after laparoscopic surgery. NSAIDS is free from many of the adverse effects of opioids, such as respiratory depression, sedation, nausea and vomiting and gastrointestinal stasis.

Paracetamol has a well- established safety and analgesic profile. The onset of analgesia occurs within five to ten minutes after IV administration. The peak analgesic effects are obtained in one hour and its duration is approximately four to six hours.[11,12] The minimum plasma paracetamol label required for analgesia is thought to be 10 mcg / ml and the therapeutic range is usually considered to be 10 - 20 mcg / ml.[13]

Paracetamol has few contraindications and lacks significant drug interactions.[14,15] Injectable paracetamol solution in a unit-dose form, ready for infusion. Effective relief of postoperative pain is one of the primary targets as postoperative pain also affects the clinical outcomes of the surgeons.[16,17]

Our goal in this prospective, single blind, randomized study was to compare the effect of I.V. paracetamol and I.M. pethidine for analgesic efficacy in post-operative analgesia with their side effects in laparoscopic cholecystectomy.

Materials & Methods

This prospective randomized control study was conducted from 1st July '2014 to 31st December '2014 at the department of Anaesthesiology and Surgical ICU, BIRDEM General Hospital, Dhaka, Bangladesh. After institutional ethical committee approval and informed written consent, a total number of 60 adult patients with Cholelithiasis with ASA physical status I & II scheduled for Laparoscopic cholecystectomy surgery under general anaesthesia were enrolled in this study. Patients were randomly allocated equally 30 in each group, into two groups A and B. Patients of Group A (n=30) received intravenous paracetamol (1g/100 ml)-15mg/kg, over 15 minutes and Group B (n=30) received intramuscular pethidine (100 mg)-2 mg/kg postoperatively. Rescue analgesic was given inj. Ketorolac 30 mg IV according to patient's demand in both groups. All patients were kept nil per oral for 6 hours before the scheduled time of surgery. All patients were premedicated with Tab. Midazolam 7.5 mg & Tab. Ranitidine 150 mg orally. On the arrival of the patient in the operating room, 18 gauge /20-gauge Intravenous cannula was inserted and an infusion of dextrose with normal saline was started. The patient was connected to multi-channel monitor which records heart rate, non-invasive blood pressure (NIBP), continuous ECG monitoring and oxygen saturation.

Each patient was received general anaesthesia with induction dose of inj. Fentanyl 2microgram/kg, inj. Propofol 2mg/kg and muscle relaxant inj. Atracurium 0.5mg/kg. After induction, general anaesthesia maintained by 60% N2O and 40% O2 and continuous infusion of Propofol @ 5mg/kg/hr. An incremental dose of muscle relaxant inj. Atracurium 1/4th of initial dose was given every 20 minutes interval. The base line blood pressure and heart rate were recorded from the same noninvasive monitor and cardiac rate and rhythm were also monitored from a continuous display of electrocardiogram from lead II.

After extubation patients were transferred to recovery room and analgesia was given in the immediate postoperative period (0 hr.). Visual analogue score (VAS), noninvasive blood pressure, heart rate, oxygen saturation, respiratory rate was recorded in every patient. All parameters were recorded at 0 hour, 1 hour, 2 hour, 4 hour, 6 hour, 8 hour and 24 hour after surgery.

Post-operative pain was assessed by visual analogue scale (VAS) which is a simple and often used method for evaluating variations in pain intensity. Subjects are instructed to indicate the intensity of the pain by marking a 10 cm line anchored with terms describing the extremes of pain intensity. VAS pain scale was 10 cm vertical lines anchored with "no pain" at the bottom and "worst imaginable

pain" at the top. Visual analogue score (VAS) was recorded at 0 hour, 1hour, 2 hour, 4 hour, 6 hour, 8 hour and 24 hour after surgery (VAS; 0 - 10 cm; 0= no pain and 10 = worst possible pain). Ramsay sedation score (1= anxious, agitated, and restless; 2=cooperative, oriented and tranquil; 3=responds to commands only; 4=asleep, brisk response to light glabellar tap or loud auditory stimulus; 5= asleep, sluggish response to light glabellar tap or loud auditory stimulus; 6= asleep, no response) was recorded at 0 hour, 1hour, 2 hour, 4 hour, 6 hour, 8 hour and 24 hour after surgery. Side effects including nausea, vomiting, respiratory depression (respiratory rate < 10 breaths/ min or oxygen saturation < 90 % without oxygen supplementation) were recorded throughout the postoperative period. If indicated, side effects were treated as required (oxygen saturation < 90%, two or greater than two episodes of vomiting). When the patient's pain was greater than three according to VAS rescue analgesic was used.

Data Processing

All data presented as mean (standard deviation) unless otherwise indicated. Analysis of variance unpaired student t test and chi-square test used to detect the demographic data among the two groups. Chi-square test, with any correction needed (e.g., Yates's continuity correction) used to analyze the collected data. Data collected on a predesigned data collection sheet and later on compiled on a master chart. A p value of <0.05 accepted as statistically significant. Statistical analysis carried out using Statistical Package for Social Science (SPSS) for Windows version 17.0.

Results

Sixty patients who underwent laparoscopic cholecystectomy surgery were enrolled in this study. Among them 41 male and 19 female. Demographic data for each group was similar (Table 1, Table 2 & Table 3). Postoperative satisfaction with the intravenous paracetamol and intramuscular pethidine analgesia was similar with median scores of 71 (IV Paracetamol) and 73(IM pethidine) (VAS; 100 mm= extremely satisfied) in the first 24 hour after operation. There was no significant difference between groups for heart rate (Figure 1), systolic blood pressure (Figure 2), diastolic blood pressure (Figure 3) and postoperative analgesic requirements (Figure 4). Total drug consumption of group A that is paracetamol group was 30 gram and for group B that is pethidine group was 4000 mg. When VAS score was more than three rescue doses of 30 mg IV ketorolac was given in both groups. Patients demand for rescue dose for group A on an average 8 hrs. and for group B 7 hrs. (Table 4) after operation. Post-operative nausea, vomiting was found in nine patients of group B and they were treated with antiemetic like inj. Ondansetron 4 mg IV.

Our postoperative repeated visits for sedation score and respiratory rate monitorization were a precaution for early detection of respiratory depression and provide increased patient satisfaction. In postoperative 2nd hour there was significantly decrease in respiratory rate in group B and sedation score also significantly changes in between groups (p value <0.05). None of the patients had a respiratory rate less than 10. But oxygen saturation was maintained in both groups.

Table 1: Age distribution of the study respondents (n=60)

Age (in years)	Group-A	Group-B	p value
20-30 yrs	2(6.7%)	2(6.7%)	
31-40 yrs	9(30.0%)	13(43.3%)	
41-50 yrs	13(43.3%)	10(33.3%)	0.56^{ns}
51-60 yrs	6(20.0%)	5(16.7%)	
Total	30(100.0%	30(100.0%)	
Mean±SD	48.40±11.12	50.20±12.55	

Mean±SD
ns = Not significant (p>0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by unpaired student t-test

Table shows the age distribution of the patients of all treatment groups. Out of all patients of group A 6.7% were belonged up to 30 years age group, 30.0 % within 31 to 40 years, 43.3 % within 41 to 50 years

and 20.0 % within 51 to 60 years age group. In group B maximum 43.3 % patients were 31 to 40 years age group, 33.3 % patients were 41 to 50 years age group and 16.7 % were 51 to 60 years age group followed by 6.7 % belonged up to 30 years age group. Mean ages of the patients of group A & group B were 48.40±11.12 and 50.20±12.55 years respectively. No statistically significant difference was observed among groups in term of age (p value>0.05).

Table 2: Sex distribution of the study respondents (n=60)

Sex	Group-A	Group-B	p value
Male	9(30.0%)	10(33.3%)	0.78ns
Female	21(70.0%)	20(66.7%)	
Total	30(100.0%)	30(100.0%)	

Data were expressed as number and percentage
ns = Not significant (p > 0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by Chi-square test

In group A 70.0% patients were female and 30.0% were male and in group B 33.3% were male and 66.7% were female. No statistical significance difference was observed in term of sex distribution among groups (p value>0.05).

Table 3: Comparison of weight (kg) of the two groups (n=60)

Weight (kg)	Group-A	Group-B	p value
Mean±SD	67.67±8.13	66.30±9.44	0.55ns

Data were expressed as number, percentage and Mean±SD
ns = Not significant (p>0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by unpaired student t-test

Mean weights of the patients of group A was 67.67±8.13 and group B was 66.30±9.44 respectively. No statistically significant difference was observed among groups in term of body weight (p value>0.05)

Table 4: Comparison of first analgesic demand of the two groups (n=60)

	Group-A	Group-B	p value
Mean±SD (hour)	8.07±8.13	7.03±9.44	0.63ns

Data were expressed as number, percentage and Mean ± SD
ns = Not significant (p > 0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by unpaired student t-test

Mean analgesic demand for group A was 8.07±8.13 hrs. and group B was 7.03±9.44 hrs. No statistically significant difference was observed among groups in term of analgesic demand (p value>0.05)

Table 5: Comparison of pain complain four hours after operation in two groups (n=60)

	Group-A: Case (n=30)	Group-B: Control (n=30)	p value
No pain	28	29	0.78ns
pain	2	1	

Data were expressed as number and percentage
ns = Not significant (p>0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by Chi-square test

No statistically significant difference was observed among groups in term of pain (P value>0.05).

Table 6: Comparison of pain complain eight hours after operation in two groups (n=60)

	Group-A: Case (n=30)	Group-B: Control (n=30)	p value
No pain	15	13	0.26ns
pain	15	17	

Data were expressed as number and percentage
ns = Not significant (p>0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis were done by Chi-square test

No statistically significant difference was observed among groups in term of pain (P value > 0.05).

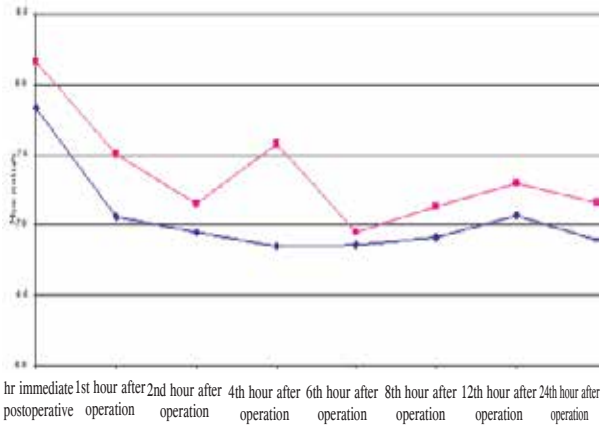

Figure-1: Line diagram showing postoperative heart rate in two groups

The mean heart rate at immediate postoperative & 4th hour were significantly higher in group B where as other period were non significant in between groups (p > 0.05).

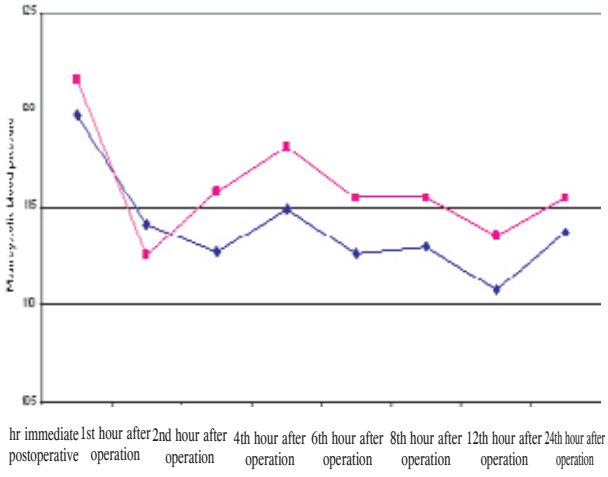

Figure-2: Line diagram showing postoperative mean systolic blood pressure in two groups

The mean systolic blood pressure at different time in postoperative period compared between two groups. No statistically significant were observed in between groups (p > 0.05)

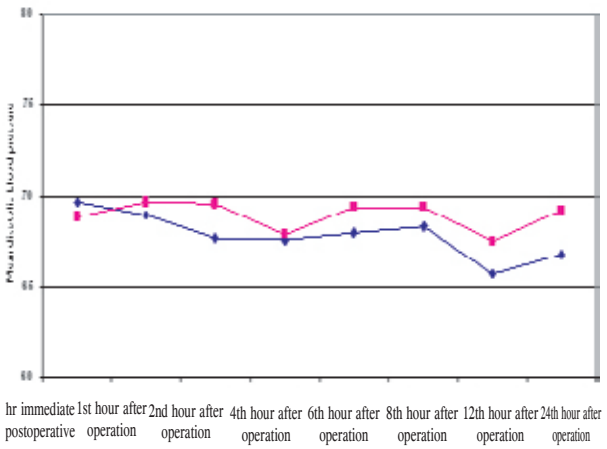

Figure-3: Line diagram showing postoperative mean diastolic blood pressure in two groups

The mean diastolic blood pressure at different time in postoperative period compared between two groups. No statistically significant were observed in between groups (p > 0.05)

Table 7: Comparison of respiratory rate at postoperative monitoring of the study respondents (n = 60).

Respiratory rate	Group-A Case (n=30) (Mean±SD	Group-B Control (n=30) (Mean±SD	p value
0 hr immediate postoperative	13.5±0.9	13.0±1.0	0.06^{ns}
1st hour after operation	12.1±0.4	12.1±0.5	0.56^{ns}
2nd hour after operation	13.1±0.5	10.5±0.4	<0.001^{s}
4th hour after operation	12.3±0.7	12.1±0.5	0.39^{ns}
6th hour after operation	12.3±0.8	12.1±0.4	0.09^{ns}
8th hour after operation	12.3±0.7	12.2±0.6	0.69^{ns}
12th hour after operation	12.1±0.5	12.3±0.8	0.24^{ns}
24th hour after operation	12.2±0.5	12.4±0.8	0.18^{ns}

Data were expressed as number, percentage and Mean±SD
ns = Not significant (p > 0.05)
s = Significant
n = Number of subjects.
SD = Standard Deviation.
Statistical analysis was done by unpaired student t-test

The mean respiratory rate at postoperative period compared between two groups. There was statistically significant decrease in respiratory rate in group B in 2nd hour postoperatively ($p<0.05$). No statistically significant were observed in other times ($p>0.05$).

Table 8: Comparison of SPO2 at postoperative monitoring of the study respondents (n=60)

SPO_2	Group-A (n=30) (Mean±SD	Group-B (n=30) (Mean±SD	p value
0 hr immediate postoperative	100.0±.00	100.0±.00	-
1st hour after operation	98.4±0.9	95.5±16.2	0.33ns
2nd hour after operation	98.8±1.0	98.6±1.1	0.62ns
4th hour after operation	98.8±0.8	99.0±1.0	0.48ns
6th hour after operation	94.2±15.8	98.0±0.9	0.19ns
8th hour after operation	98.1±1.0	98.2±1.2	0.91ns
12th hour after operation	94.2±15.8	98.1±1.2	0.18ns
24th hour after operation	98.7±2.3	98.3±1.3	0.49ns

Data were expressed as number, percentage and Mean±SD

ns = Not significant (p>0.05)

s = Significant

n = Number of subjects.

SD = Standard Deviation.

Statistical analysis was done by unpaired student t-test

The mean SPO_2 at different time in postoperative period compared between two groups. No statistically significant were observed in between groups ($p>0.05$).

Table 9: Comparison of sedation score at postoperative monitoring of the study respondents (n=60)

Sedation score	Group-A Case (n=30) (Mean±SD	Group-B Control (n=30) (Mean±SD	p value
0 hr immediate postoperative	2.1±0.3	2.0±0.1	0.06ns
1st hour after operation	3.0±0.5	3.1±0.2	0.51ns
2nd hour after operation	2.2±0.3	3.8±0.1	<0.047s
4th hour after operation	2.8±0.4	2.9±0.1	0.22ns
6th hour after operation	2.3±0.5	2.4±0.2	0.52ns
8th hour after operation	2.3±0.5	2.1±0.5	0.25ns
12th hour after operation	2.1±0.4	2.2±0.1	0.13ns
24th hour after operation	2.2±0.5	2.4±0.5	0.25ns

Data were expressed as number, percentage and Mean±SD

ns = Not significant (p>0.05); s = Significant

n = Number of subjects; SD = Standard Deviation.

Statistical analysis was done by unpaired student t-test

The mean sedation score at postoperative period compared between two groups. There was statistically significant in sedation score in group B in 2nd hour postoperatively ($p<0.05$). No statistically significant were observed in other times ($p>0.05$).

Discussion

Postoperative pain is multifactorial, and predominantly of inflammatory nature from skin incision and tissue damage. Ischemia from retraction of tissue, as well as disrupted blood supplies, contributes to pain significantly, characterized by low tissue pH and high lactate levels at the site of incision.[18,19]

After laparoscopic cholecystectomy, parentral acetaminophen, opioid and NSAIDS are commonly used for postoperative analgesia. Besides showing individual variation in intensity and duration, the pain is often unpredictable. It may even remain severe throughout the first week in 18% of the patients.[20] Although laparoscopic cholecystectomy is less invasive procedure than classical open surgical approach, many laparoscopic patients suffer considerable postoperative pain.[21]

In a study by Brodner and colleagues on patients undergoing mild to moderate surgery with general anesthesia, it was concluded that Paracetamol and other nonopioid analgesics have a similar effect.[22] Furthermore, in our study, the effects of Paracetamol were significant in the pain control.

I.V administration of paracetamol has already demonstrated its analgesic efficacy in patients with postoperative pain following gynecologic surgery[23,24], retinal surgery[25], dental surgery[26], hand surgery[27], spinal fusion surgery[28] and orthopedic surgery.[29] Clinical studies have also found that 1 gm intravenous paracetamol employed alone is just as effective as 30 mg ketorolac, 75 mg diclofenac or 10 mg morphine.[30,31]

Rawal *et al.*[32] Compared oral metamizol, oral tramadol and IV paracetamol for the postoperative analgesia at home after ambulatory hand surgery. This study showed that tramadol provided the most effective analgesia as compared with the other group. But in this study, side effects were higher in tramadol group.

In our study there were no significant differences in heart rate, mean systolic blood pressure and diastolic blood pressure and in the postoperative period.

This study revealed that there was no significant difference in behavioral pain score between patients treated with paracetamol and those treated with pethidine at post operative period. The respiratory rate and sedation score in pethidine group were significantly changes in 2nd hour at postoperative period. In a study, opioids are associated with respiratory depression and prolong the time to readiness for discharge.[33,34]

In our study Postoperative complications like nausea, vomiting was more common in pethidine group. In a study conducted in 2010 by Memis and colleagues, they reviewed the effect of intravenous Paracetamol in reducing opioid consumption and opioid side effects in intubated patients admitted to the ICU. Ultimately, they concluded that intravenous Paracetamol reduces opioid consumption and opioid side effects, such as nausea, vomiting, and itching.[35]

However, our study had a few limitations. First, the route of administration of two drugs was different; secondly, the group of drugs also different and finally the total consumption of rescue drug was not recorded. But traditionally we commonly practiced postoperatively these drugs for analgesia after laparoscopic cholecystectomy.

Conclusion

Our study was the first study conducted in Bangladesh population. It demonstrated the usefulness of intravenous paracetamol for the postoperative pain management after laparoscopic cholecystectomy which may be beneficial in patients prone to opioid-related complications.

Conflict of interest: none.

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