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Research Article

Comparative Study of Butorphanol and Pethidine in Post Operative Nausea Vomiting When Used as Pre-Medicant for Laparoscopic Cholecystectomy

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Abstract: The aims and objective of the study were to compare the efficacy of inj. Pethidine and inj. Butorphanol in preventing post-operative nausea and vomiting and to compare better analgesic as premedicant in patients undergoing laparoscopic cholecystectomy.50 patients aged from 20 – 70 years of ASA –I &II physical status under going laparoscopic cholecystectomy were included and were divided into two groups; group I (25 patients) received Pethidine 0.5 mg/Kg body weight and group II (25 patients) received Butorphanol20 mcg/Kg intravenously 10 minutes before the induction of anaesthesia. Postoperatively the patients were assessed for vital signs, pain, nausea, vomiting. The patients selected in both the groups are comparable, in terms of age, weight, technique of anaesthesia, and surgical procedure. Post operatively there was no significant difference in the pulse rate, BP, RR, VAS between the two groups. The incidence of nausea was significantly higher in patients who received Pethidineas compared to Butorphanol ($p < 0.05$). Similarly the incidence of vomiting was high in Pethidine group that is seven patients experienced vomiting compared to two patients in Butorphanol group which is statistically significant ($p < 0.05$). The time of first rescue analgesic was longer in patients of Butorphanol (205 $\pm$ 60 mins.) as the pre-medication drug compared to the Pethidine (170 $\pm$ 40 mins.) and it was supplemented with inj. Tramadol (0.5 mg / kg body wt.). Eight patients in Butorphanol group had more drowsiness than four in Pethidine group, one hour after the admission to recovery room. However there was no episode of Hypoxemia (SPO2 < 90%), respiratory depression (RR< 8 / min.) in any of the patient. In conclusion, Butorphanol decreased the nausea, vomiting episodes, and provided a better control of pain in the postoperative period than Pethidine.
Keywords: Butorphanol, Pethidine, Post-operative nausea, Vomiting, Laparoscopic cholecystectomy.

INTRODUCTION

It was in 1882 that Carl Langen back performed the first successful removal of the gall bladder for the treatment of gall-stone disease. Over the years, both the mortality and morbidity for cholecystectomy have decreased because of the improvement in the operating procedures and anaesthesia. Since the first laparoscopic cholecystectomy using keyhole approach by Mouret, Lyon France in 1987, laparoscopic cholecystectomy has rapidly become the standard approach for gall stone disease management. Patients undoubtedly benefit from less trauma, less pain, less postoperative ileus, less postoperative pulmonary dysfunction, quick recovery, short hospital stay and cosmetic acceptability but, life – threatening intraoperative complications are possible, because of intra-peritonealgas insufflations, patient positioning and the surgical technique.

Large surveys show that laparoscopic cholecystectomy is accompanied by postoperative pain of various types, the most frequent complaint following laparoscopic cholecystectomy are headache, sore throat, and, more particularly, nausea and vomiting. Nausea and vomiting is one of the most common and disturbing complication faced by the patient in post-operative period after general anesthesia with an overall incidence of 25 – 43% [1]. Laparoscopic surgeries have however, reported an incidence of 50 – 80% [2]. Persistent PONV can be very distressing to the patients and can cause complications like oesophageal tears, gastric herniation, muscle strain, fatigue and pulmonary aspirations [3]. Fluid and electrolyte loss accompanying vomiting may lead to dehydration and electrolyte imbalance [4] and 71% of the patients have the reason of dissatisfaction from anesthesia and surgery when they leave the hospital [2]. This problem is compounded in day care centers where delay in the discharge from the hospital, unanticipated admission and readmissions after day-care surgery and hence the very purpose of cost saving in day care surgery may be lost [5, 6].

Kenny [2] studied the anesthetic and non-anesthetic risk factors in the pathogenesis of post-operative nausea and vomiting. Age, sex, and duration of surgery, type of surgery, pre-medication, type of anesthesia and patients ambulatory status have all been variously implicated. A

better understanding of these multifactors has lead to decrease incidence of PONV from 70 – 80%to 20 – 30% [3].

Creating pneumoperitoneum by using carbon dioxide gas, positioning of the patient during surgery, multiple use of drugs of general anaesthesia and the anaesthetic technique are few of the pre – disposing factors for postoperative nausea and vomiting (PONV). Intraoperative opioids increase the incidence of nausea and vomiting, propofol induction can decrease it drastically and the role of nitrous oxide is controversial. Drainage of the gastric contents also reduces the incidence of PONV. Intraoperative administration of Droperidol and the use of Ondansetron appear to be helpful in the prevention and treatment of these side effects.

Prophylaxis against PONV does not work very well and there is finite risk of drug reaction with the use of most of the anti–emetic drugs like dopaminergic antagonist, $5HT_3$ antagonist, Butyrophenone, phenothiazenes etc. [7-9]. The common side effects like drowsiness, extra – pyramidal symptoms are, at times, more distressing.

Oxygen therapy an expensive and easily available medicine can be administered to reduce the incidence of PONV [10]. Use of balanced anaesthesia technique rather than a single drug therapy is worth, while approach for reducing the incidence of PONV [11, 12]. Gentleness while doing throat suction, shifting the patient to PACU and change of posture are other variables that helps to minimizes the unnecessarily increase in risk of PONV. The prolonged pre – operative fasting and early oral intake in the post – operative may increase the risk of PONV relatively [13].

Opioids are routinely used for control of intra- and post-operative pain. While pain may be adequately controlled, distressing side-effects like nausea and vomiting occur with greater frequency. Search is on for an opioid which has minimal nausea and vomiting while producing adequate analgesia.

AIMS AND OBJECTIVES

The study is done with the following aims and objectives

- To find the incidence of nausea and vomiting with the use of injection Pethidine and injection Butorphanol; when these drugs are used for pre-medication in patients undergoing laparoscopic cholecystectomy.
- To compare the efficacy of both drugs.
- To find out a better analgesic to be used in pre-medication that will cause lesser incidence of nausea and vomiting in the post-operative period.

MATERIALS AND METHODS

The study was conducted after the approval for the study protocol was taken from the Hospital Ethics Committee. Written and informed consent of the patients and their relatives were taken. The study is conducted in 50 patients with ASA – I & II who were planned for Laparoscopic Cholecystectomy.

All the patients in the study were divided into two double- blind cohorts of twenty five each. Patients with the following exclusion criteria were not included in the study:

- History of pre-operative nausea and vomiting (24 hours before surgery)
- Patients on anti-emetic drugs.
- Patient with history of motion sickness.
- Patient with history of hypersensitivity to the drugs to be used in study.
- Patient with history of liver and renal dysfunction.
- Patient with the diseases prolonging gastric emptying.
    - Diabetes Mellitus
    - Intestinal obstruction
    - Hiatus hernia
    - Raised intra cranial pressure
    - Pyloric stenosis
- Patient with difficult communication.

All patients were comparable for their age, weight, sex, duration of surgery, surgical procedure and technique of anaesthesia.

Grouping

This is a study conducted on 50 patients who were divided into two groups with 25 in each.

Group – I = Injection Pethidine 0.5 mg/kg body wt.

Group – II = Injection Butorphanol 20 mcg/kg body wt.

Each group received a single dose of the drugs intravenously 10 minutes before the surgery through two different syringes.

The duration of surgery was 60 – 90 mins and the patients followed up in the post-operative period for four hours by oral questionnaire method. The anaesthesia technique and the surgical procedure were same in all the patients in both the groups.

All the patients were shifted to the operation theater after the pre-medication in the pre-operative anaesthesia room. All were pre-oxygenated with 100% of oxygen for three minutes. Injection Thiopentone Sodium (2.5%) at a dose of 3-5mg / kg body wt. was the drug for induction of anaesthesia and the patients trachea intubated after giving injection Suxamethonium 1 – 1.5 mg / kg body wt. with cuffed endotracheal tube. All patients were put on controlled ventilation with

Mapelson – D breathing system and with Nitrous Oxide (66%) and Isoflurane (0.5% - 1.5%) in 33% of oxygen. Neuromuscular blockade achieved with injection Vecuronium Bromide (0.1mg / kg body wt.) and supplemented for maintenance of plane of anaesthesia with mixture of gases.

All the patients were monitored throughout the surgical procedure with heart rate (HR), NIBP, MAP (mean arterial pressure) SPO_2 with pulse oxymetry, ECG lead II, EtCO2 before, during and after the anesthesia at an interval of 10 mts. until patient became stable in recovery room.

Whenever there was any increase in the heart rate (HR), mean arterial pressure (MAP) intra operatively from the pre-operative value the concentration of Isoflurane was increased by0.1 - 0.2% to keep the HR & MAP within the 20% of the base line value.

Residual neuromuscular blockade reversed with injection Neostigmine .04 mg / kg and Atropine .02 mg / kg at the end of procedure.

The recovery time was recorded by two methods (i) time of orientation by asking the name, the place or the date of birth of the patient (ii) time of discharge from the recovery room to the surgical ward from the cessation of inhalation anaesthetic agents (Isoflurane, Nitrous Oxide). All the patients were monitored for nausea, vomiting, pain, vital signs and any other complaints by oral questionnaire method till 4 hours post operatively and pain was assessed by VAS. For discharge the standard discharge criteria (Wetchler Criteria) was used that includes:

- Full awake and alert
- No respiratory distress
- Gag and cough reflex present
- Stable vital signs.
- Minimum or no nausea
- No active bleeding

Statistical Analysis

All the patients were interviewed after the operation in the surgical ward to get the information regarding the experience in the peri-operative period and all these results were assessed statistically by students t-test and chi-square test. A p value of < 0.05 was considered significant.

RESULTS

The study included fifty patients ASA I & II scheduled for elective laparoscopic cholecystectomy for gall stone disease. The patients were randomly divided in to two groups. Twenty five patients received Pethidine 0.5 mg / kg IVas the opioid analgesic (Group I) and the remaining twenty five patients received Butorphanol 20 mcg/kg IV. The following observations were recorded and the results were statistically analysed.

The patients selected in both the groups are comparable, as shown in Table 1 in terms of age, weight, technique of anaesthesia, and surgical procedure.

The mean age group of the patient was 45 yrs. in group I and 46 yrs. in Group II. The weight of the patient ranges from 40 to 80 kgs. in both groups. The average surgery time was 60 – 70 minutes in group I and 65 – 75 minutes in group II. The duration of abdominal insufflation was 37 – 44 minutes in group I and 23 – 37 minutes in group II and these differences were not significant.

Intraoperative vital score (IVS)

Heart rate and mean arterial pressure were considered as the measures of intra operative vitals. A Score 1 if within 20% of the base line. Score 2 if within 20 – 40% of the base line and score 3 if more than 40% of the base line. Similarly postoperative vital score (PVS) was measured till 4 hrs. of the surgery.

All patients in group I had intra operative vital score of 1 except one patient who had a score of 2. The average score was 0.96. Similarly 24 patients out of 25 in group 2 had IVS of one and only 1 had IVS of 2. The mean IVS was 0.96 and the difference was not statistically significant as shown in Table 2. Similarly the post operative vital scores were nearly same in both the groups with an average score of 0.96 – 1.00.

During the intra operative period the mean concentration of Isoflurane required to keep heart rate and mean arterial pressure $\pm$ 20% of the base line values was significantly less in Butorphanol group compared to Pethidine group (0.5% - 0.7%). Three patients in Butorphanol group had sinus bradycardia which was managed with the cessation of Isoflurane for few minutes and injection of Atropine 20 mcg / kg.

The recovery time between the two groups was not statistically significant (p value > 0.05).

Post operatively there was no significant difference in the pulse rate, blood pressure, respiratory rate between the two groups. The side effects in the post-operative period were elicited by direct questioning of the patient. VAS was comparable in both the groups and was not significant as two patients in group 1 needed rescue analgesic where as only one patient in group 2 required rescue analgesic within the period of study that is till 4 hrs. as shown in Table 3.

The significant pain score was taken if more than 4 – 5 and rescue analgesic was given to the patient with injection Tramadol 0.5 – 1 mg intramuscularly.

The incidence of nausea was significantly higher in patients who received Pethidine as compared to

Butorphanol as shown in the Table 4 ($p < 0.05$).Only two patients had experienced nausea compared to five patients in Pethidine group. Similarly the incidence of vomiting was high in Pethidine group that is seven patients experienced vomiting compared to one patient in Butorphanol group which is statistically significant ($p<0.05$) as shown in Table 5.

The time of getting first rescue analgesic was longer in patients who received Butorphanol (205 $\pm$ 60 mts.) as the pre-medication drug compared to the Pethidine (170 $\pm$ 40 mts.) and it was supplemented with injection Tramadol (0.5 – mg / kg body wt.).

Eight patients in Butorphanol group had more drowsiness than four in Pethidine group, as observed one hour after the admission to recovery room. However there was no episode of Hypoxemia (SPO2 < 90%), respiratory depression (RR< 8 / min.) in any of the patient.

Table 1: Demographic Profile of Patients

	Group I (n-25)	**Group II(n-25)**
Age(yrs)	45±2.50	46±2.6
Weight (kgs)	40-80	40-80
Surgery time(mins)	60±11	65±15
Anaesthesia time(mins)	85±19	80±11
Duration of abdominal insufflations(mins)	37-44	23-37

Table 2: Mean of average of vitals at different time intervals during the study

	Group I (n-25)	**Group II(n-25)**
IVS	0.96± 0.2	0.86± 0.2
PVS-0 hr.	0.96± 0.2	0.96 ±0.2
PVS-1 hr.	1.00± 0	1.00± 0
PVS-2 hr.	0.96 ±0.2	1.00± 0
PVS-3 hr.	1.00± 0	1.00± 0
PVS-4 hr.	1.00 ±0	1.00± 0

Table 3: Patients with VAS ≥ 4 at different time intervals during the study

VAS at	**Group I (n-25)**	**Group II (n-25)**
0 hr.	0	0
1 hr.	0	0
2 hr.	0	0
3 hr.	1	0
4 hr.	1	1

Table 4:Incidence Of Nauseaduring post-Operative Period

	Group I (n-25)	**Group II(n-25)**
Nausea	5(20%)	2(8%)

$p<0.05$

Table 5:Incidence Of vomiting during post-Operative Period

	GroupI (n-25)	**GroupII(n-25)**
Vomiting	7(28%)	1(4%)

$p<0.05$

DISCUSSION

PONV are among the most common postoperative complications after laparoscopic surgery [2]. Though multifactorial like patients characteristics, age, gender, obesity, gastroparesis, anxiety, previous history of PONV, type of anaesthesia and surgery or environmental factors [2] contribute to it, many of them are excluded from our study. Use of opioids in premedication via any route has been associated with increased PONV [14, 15] but the avoidance of opioids can also result in PONV secondary to visceral pain [16]. In this study we compared two opioids Pethidine and Butorphanol that cause less nausea and vomiting in post-operative period. The anaesthetic drugs and the procedures used in both the groups under this study were same. Gastric distension from vigorous IPPV via face mask, repeated suctioning or presence of Ryles tube can increase PONV [3, 17] which were avoided during anaesthesia in both groups.

The peak incidence of vomiting is seen in 6 to 16 years [4] and in this study the patient age ranged from 20 to 80 years. Incidence of PONV increased during long duration of surgery [3, 18]. In this study the duration of study was average that is from 70 to 80 minutes and duration of abdominal insufflation was also

the same in both the groups that is in group I it was 35 – 40 minutes, in group II 30 – 35 minutes.

Thus there was no significant difference in any of the patient's characteristics in between two groups and both were comparable.

Hypotension [19], Hypoxemia [19], Tachycardia and Hypertension [3], can influence the incidence of emesis in early post operative period which can be alleviated by Oxygen, Atropine, Ephedrine.

Verbal questionnaire and analysis of the variations in the recorded haemodynamic data was done to see if the episodes of nausea and vomiting were due to pain. There was a lower incidence of nausea (8%) and vomiting (4%) in patients receiving Butorphanol (Group II) which was statistically significant from Group I ($p<0.05$). Also, there was <20% variation in the haemodynamic parameters. This indicates that the lower incidence of nausea and vomiting was not due to any intraoperative haemodynamic disturbances like hypertension, hypotension or tachycardia. This correlates well with the multicenter study of Forrest el al in 1990 [20]. They studied a population of 16,000 and compared the incidence of postoperative nausea and vomiting using Halothane, Enflurane and Isoflurane. They reported an overall incidence of 18-25% with 0.15% reporting severe emesis following wide variations in intraoperative blood pressure and pulse. Cohen et al [21] studied a population size of 29, 220 children and reported a 11% incidence of postoperative nausea and vomiting in children having an intraoperative episode of fall in oxygen saturation of <90%. In this study, there was no documented fall in oxygen saturation of <90%.

Various methods have been used to quantify post operative nausea and vomiting. Verbal questionnaires in which patients were asked to rate the degree of nausea and number of vomiting on a two-point scale [2], three-point scale [22], four-point scale [23], or a eleven-point scale [10] have been variously used. Time for first antiemetic has also been used [24]. In this study we used a verbal questionnaire method using a two-point scale to analyze the result.

Stelhing et al demonstrated that 0.5 – 2 mg Butorphanol when given intravenously causes less nausea compared to 80 mg of Pethidine in group of 80 patients in their study. Two patients experienced nausea in the group of patients receiving Butorphanol while 10 patients experienced nausea in the group receiving Pethidine [25]. Sung *et al*. [26] in their study observed a significantly less incidence of nausea in patients who received Butorphanol as compared to Morphine. They documented that only 8.3% of the patients experienced nausea compared to 40.4% in Morphine group.

In a study done by Hodgkin and colleagues [27] in 10 patients for maternal analgesia and neonatal behavior, they reported that none of the patients experienced nausea when given 1 – 2 mg Butorphanol by intravenous route. This is in contrast with this study where 8% patients complained of nausea with the use of Butorphanol. Laparoscopic surgery is associated with a high rate of PONV [2, 3, 13], ranging from 20-51%. The reason for this high rate is not clear. Various factors have been postulated which include mechanical factors, such as pressure on the stomach and the gut caused by the pneumoperitoneum; neural factors, such as vagal reflexes elicted by irritation of parasympathetic nerve endings in the abdomen, and chemical factors which include speculative considerations regarding a possible influence of carbon dioxide on PONV, A study done by Madhusuka and Hajghassemalli [28] recorded no nausea with 2 mg of Butorphanol intravenously when used in a double blind manner for labour analgesia.

Pandit and Wetchler [29, 30] in their study found a high incidence of nausea and vomiting in patients who received Butorphanol in pre medication (55%). This is in contrast with this study. However, the dosage used in their study was higher, 40 – 60 mcg / kg as compared with this study where we used 20 mcg / kg of Butorphanol. The authors also mentioned a significant delay in discharge from the hospital in those patients who received Butorphanol as compared with those who received 2 mcg/kg Fentanyl. In this study there is no comment about any delay in discharge since the cases were observed only till four hours postoperative.

In the present study the complaint regarding the nausea was less in Butorphanol than Pethidine group which is similar to the study done by Madhusuka [28] and Hodgkin *et al*. [27]. A major difficulty found in our study was limited number of references available for Butorphanol for comparison.

Stelhing *et al*. [25] observed a high incidence of vomiting in patients who received intravenous Pethidine in a balanced anaesthesia technique. In his study of 80 patients, 10 patients experienced vomiting in comparison to only 2 patients receiving Butorphanol. Similarly, Dundee *et al*. [15] demonstrated a significant higher incidence of vomiting when Pethidine was given to the patients for pre medication. In their study, the intra muscular route was used for pre medication. Pandit *et al*. [29] also reported an incidence of 32% when patients received Pethidine as pre medication by intravenous route. In our study we also found a 28% incidence of vomiting in Pethidine group which correlates well with the above findings.

In another study done by Hodgkin *et al*. [27] in 100 patients they found no incidence of vomiting with 1 – 2mg intravenously of Butorphanol and this too is supported by Madhusuka and Hajghssemali [28] where only one patient who received 2 mg intravenously of

Butorphanol had vomiting. This is in agreement with this study where we found a 4% incidence (1 patient out of 25 patients) of vomiting. The number of patients in both Hodgkin *et al*. [27] and Madhusuka and Hajghssemali [28] studies were comparatively more than that in this study, that is, 100 as compared to 25. Kilmen *et al*. [31] found a high rate with the use of Butorphanol (2 mg.) for long term pain relief of malignancy by intramuscular route. They postulated that repeated and prolonged use (3 – 4 hrs. for 30 – 34 weeks) of painful intramuscular injections of Butorphanol in these patients increased the incidence. He mentioned 18 out of 63 patients had repeated episodes of vomiting who received Butorphanol for the pain relief. Hew *et al*. [32] documented a 22% incidence of vomiting in 150 patients given Pethidine for post-operative pain relief as compared to Nalbuphine.

Burtle and Peckett *et al*. [33] suggested a lesser incidence of PONV with the use of Pethidine than Morphine in contrast Bellville, Bros and Howland [34] demonstrated a high rate PONV with Pethidine in their study. Nimmon MS [35] suggested that a delay in gastric emptying leads to accumulation of gastric secretions and saliva following the use of Pethidine which can be the one of the reason for increased incidence of post operative nausea and vomiting. These studies support our findings that a comparatively high incidence of nausea and vomiting occur with the use of Pethidine.

Pandit and Kotharay [14] in a study of 100 patients for gynecological laparoscopic out patients surgery documented 20% of the patients had vomiting when Pethidine is used as the drug for pre medication by intravenous route which too supports high rate of vomiting with Pethidine as observed in our study.

Del pizzo [36] in a study on 63 patients demonstrated a higher incidence of sedation with 2-4 mg of Butorphanol by the intramuscular route. He noted 23 – 25% patients experienced sedation with this dosage, which supports our findings that some patients were drowsier in the first hour of post operative period while he mentioned that sedation reduces when lower dose (0.5 – 2 mg) of Butorphanol is used intravenously to 16%.

There was no significant difference in the side effects between two groups. Though three patients in each group had side effects but were mild and not worth considering. Thus the observations of this study confirmed the safety and the benefit of Butorphanol in pre medication.

Thus the present study showed that though the incidence of post operative nausea and vomiting were less with Butorphanol but still more studies are required to determine the regular use of Butorphanol in pre medication for laparoscopic surgeries. There was no significant difference in the time taken to attain discharge criteria.

CONCLUSION

From the study we conclude that postoperative nausea was significantly less with Butorphanol compared to Pethidine. Butrophanol decreased the nausea, vomiting episodes better than Pethidine group. Butorphanol provides a better control of pain in the post-operative period than Pethidine. Use of Butorphanol does not increase the hospital stay of the patients. No symptoms and signs of toxicity seen with the use of these drugs.

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