

Prevention of Post-operative Nausea and Vomiting Following Laparoscopic Cholecystectomy

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Abstract

Background: Gallstone disease and its symptoms are frequently encountered in Indian population. Approximately, 80% of the gallstones are asymptomatic. Female sex, obesity, pregnancy, rapid weight loss, gallbladder stasis, and increasing age are a few risk factors for the development of gallstones.

Materials and Methods: This study, "A study on the role of levosulpiride in prevention of post-operative nausea and vomiting (PONV) following laparoscopic cholecystectomy," was conducted for 1 year (November 2014–October 2015), in the Department of Surgery, Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu. Patients admitted in the Department of Surgery for elective laparoscopic cholecystectomy were enrolled in the study after fulfilling the eligibility criteria. The patients were allocated to 2 groups of 30 patients each on the basis of random sampling method.

Result: Pre-operative administration of injection levosulpiride 25 mg in patients undergoing elective laparoscopic cholecystectomy surgeries under general anesthesia significantly reduces the incidence of PONV.

Conclusion: It was hence seen to improve the quality of life in early stage of post-operative rehabilitation and also decreases the duration of hospital stay.

Key words: Cholecystectomy, Levosulpiride, Nausea

INTRODUCTION

Gallstone disease and its symptoms are frequently encountered in Indian population. Approximately, 80% of the gallstones are asymptomatic. Female sex, obesity, pregnancy, rapid weight loss, gallbladder stasis, and increasing age are a few risk factors for the development of gallstones. They usually present with symptoms like pain, dyspepsia or also can rarely lead to complications such as acute cholecystitis, common bile duct stones, and acute pancreatitis. The diagnosis is primarily based on the patients' anamnesis of pain attacks and the presence of

gall stones. Since 1980, the presence of gallstones has been diagnosed by ultrasonography.¹⁻¹⁵

The main treatment of gallstones is surgery. To live with gallstone disease during the waiting time for surgery, involves prolonged period of decreased health during which patients' psychological and social life suffers in some degree. Delayed surgery puts patients at risk for developing acute complications, requiring hospital admission and urgent treatment.

There has been a reduction in morbidity, pain and fatigue postoperatively with laparoscopic surgery. Moreover, there is an obvious clinical advantage over the open surgery due to less metabolic stress response.¹⁶⁻²⁸

Laparoscopic cholecystectomy is one of the most common surgical procedures being performed in the world. The procedure is performed in steep head-up tilt, usually under general anaesthesia. To get access to abdominal cavity small

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incisions are made and working trochars are inserted. To get visibility and to dissect gall bladder, the abdominal cavity is inflated with gas (usually carbon dioxide [CO₂]) called pneumoperitoneum. In this procedure intra-abdominal instruments are used, other incisions are used for optics, suction, electrocautery, etc.

The most frequent symptoms reported after laparoscopic cholecystectomy are pain, inability to ambulate and a high incidence of dyspepsia in immediate post-operative period, mostly in the form of nausea and vomiting (PONV), abdominal fullness and bloating.^{26,29-35}

Almost 30% of all patients undergoing general anesthesia experience PONV. It is a major distress within 24 h of surgery in 40-70% of patients undergoing laparoscopic cholecystectomy. Although the precise mechanism of PONV is still unknown, we believe that high frequency of PONV in patients undergoing laparoscopic operation may be due to pneumoperitoneum.

The vomiting center is an indiscrete area located in the lateral reticular formation of the medulla, which is responsible for controlling and coordinating nausea and vomiting. The center receives a wide range of afferent inputs from receptors in the gastrointestinal tract, peripheral pain receptors, the nucleus solitarius, vestibular system, the cerebral cortex, and the chemoreceptor trigger zone.

PONV is a common unwanted effect in patients undergoing laparoscopic cholecystectomy. PONV can be very distressing to the patient, sometimes more than the surgery itself. Several factors have been implicated specifically in laparoscopic cholecystectomy such as CO₂ insufflation, distension of the abdomen and irritation of the diaphragm and other abdominal viscera. In addition, other factors have also been associated such as female gender, history of motion sickness, obesity, length of surgery, post-operative pain, use of opioids, and use of inhalational anesthetics like halothane.

PONV following laparoscopic cholecystectomy is a primary cause for delay in discharge from hospital. Furthermore, the nausea and vomiting may cause dehydration, electrolyte imbalance, disruption of surgical repair, and increase the perception of pain. These factors reduce the quality of life of the patients and interfere with continuation of curative therapy.

PONV complicates the lives of both patients and surgeons. A good outcome during surgery may be followed by a period of discomfort to patient in immediate post-operative period. The true incidence and specific etiology

of PONV is difficult to determine because of the lack of a single stimulus of onset as well as the range of possible etiologies (medical, surgical, patient and anesthesia associated).³⁶⁻⁴⁸

MATERIALS AND METHODS

The present study, "A study on the role of levosulpiride in prevention of PONV following Laparoscopic Cholecystectomy," was conducted for 1 year (November 2014-October 2015), in the Department of Surgery, Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu. Approval for study was obtained from Ethical Committee. Patients admitted in the department of surgery for elective laparoscopic cholecystectomy were enrolled in the study after fulfilling the eligibility criteria. The patients were allocated to 2 groups of 30 patients each on the basis of random sampling method.

Inclusion Criteria

1. Patients posted for elective laparoscopic cholecystectomy surgeries.
2. Patients of either sex, between the age group 20 and 50 years.
3. Patients weighing between 40 and 70 kg.

Exclusion Criteria

1. Patient refusal.
2. Patients with known hypersensitivity or contraindications to study drug.
3. Patients coming for any emergency surgeries.
4. Patient age >50 years and <20 years.
5. Patients with a history of motion sickness.

METHODOLOGY

The patients were randomly allocated into 2 groups:

- Group L: Received injection. Levosulpiride 25 mg IV, just before surgery.
- Group C: Did not receive any medication.

Postoperatively, patients were advised to take rest and remain in the bed at least for the first 24 h. Other emetogenic analgesics and drugs were avoided for 24 h.

The number of episodes of nausea and vomiting and side effects of levosulpiride if any were assessed postoperatively for 24 h. The above findings were recorded in the following intervals: 0-4 h, 4-8 h, 8-12 h 12-24 h in the post-operative period and statistical analysis was done accordingly. Rescue anti emetic consisting of injection metoclopramide 10 mg IV was given after vomiting.

RESULTS

The present study, "A study on the role of levosulpiride in prevention of PONV following laparoscopic cholecystectomy," was conducted for 1 year (November 2014-October 2015), in the Department of Surgery, Acharya Shri Chander College of Medical Sciences and Hospital, Sidhra, Jammu. Approval for study was obtained from ethical committee. Patients admitted in the Department of Surgery for elective laparoscopic cholecystectomy were enrolled in the study after fulfilling the eligibility criteria. The patients were allocated to 2 groups of 30 patients each on the basis of random sampling method.

- Group L: Received injection. Levosulpiride 25 mg IV, just before surgery.
- Group C: Did not receive any medication.

The outcome of 2 groups was assessed and observations were made.

The patients included in control group were in range of 23-50 years and in levosulpiride group were in range of 21-50 years. The youngest patient in the study was 21 years, and the oldest was 50 (Table 1a and b).

The majority of patients in each group were males. The number of males and females in control group were 17 and 13, respectively, and in levosulpiride group were 18 and 12, respectively (Table 2).

The mean weight of patients in control group was 58.27 ± 8.14 and that of patients in levosulpiride group was 59.67 ± 6.91 (Table 3).

The most common clinical presentation in both the groups was pain in the right hypochondrium (RHC) (Table 4).

The most common comorbidity in both the groups was type 2 diabetes mellitus (Table 5).

The ultrasonography findings of 18 patients in control group consisted of multiple calculi, 11 had a solitary stone and 1 had sludge. In levosulpiride group, 21 patients had multiple calculi and 9 had a solitary stone (Table 6).

In control group, 17 patients experienced nausea or vomiting while as only 6 patients in levosulpiride group complained of same. None of the patients in levosulpiride group had nausea or vomiting within first 4 h (Table 7).

In control group, 16 patients were given rescue antiemetic whereas in levosulpiride group only 7 were given antiemetic (Table 8).

Table 1a: Group comparison for age of patients (years)

Age (years)	Number of patients (%)	
	Group L	Group C
<30	4 (13.33)	5 (16.67)
30-39	10 (33.33)	10 (33.33)
40-49	13 (43.33)	11 (36.67)
≥50	3 (10.00)	4 (13.33)
P value	0.712	
Remarks	NS	

NS: Non-significant

Table 1b: Mean age

Groups	Age of patients (years)
	Mean±SD
Group L	39.03±7.55
Group C	37.93±8.73
P value	0.604
Remarks	NS

NS: Non-significant, SD: Standard deviation

Table 2: Gender distribution

Gender	Number of patients (%)	
	Group L	Group C
Male	18 (60.00)	17 (56.67)
Female	12 (40.00)	13 (43.33)
P value	0.631	
Remarks	NS	

NS: Non-significant

Table 3: Weight

Groups	Weight of patients (kg's)
	Mean±SD
Group L	59.67±6.91
Group C	58.27±8.14
P value	0.476
Remarks	NS

NS: Non-significant, SD: Standard deviation

The mean hospital stay of patients in control group was 2.33 ± 0.48 and of those in levosulpiride group was 2.20 ± 0.41 (Table 9).

DISCUSSION

PONV following laparoscopic cholecystectomy is of multifactorial origin. The incidence of PONV, despite the advances in antiemetic therapy in the past decades is still found to be relatively high.

Factors affecting PONV include patient-related factors such as age, sex, phase of the menstrual cycle, anesthesia-

Table 4: Group comparison for clinical features of patients

Clinical features	Number of patients (%)	
	Group L	Group C
Pain RHC	21 (70.00)	20 (66.67)
Pain epigastrium	1 (3.33)	1 (3.33)
Incidental finding	3 (10.00)	5 (16.67)
Flatulent dyspepsia	5 (16.67)	4 (13.33)
P value	0.552	
Remarks	NS	

NS: Non-significant, RHC: Right hypochondrium

Table 5: Group comparison for comorbidity

Comorbidity	Number of patients (%)	
	Group L	Group C
T2DM	4 (13.33)	3 (10.00)
HTN	1 (3.33)	2 (6.67)
T2DM HTN	1 (3.33)	0 (0.00)
None	24 (80.00)	25 (83.33)
P value	0.174	
Remarks	NS	

NS: Non-significant, T2DM: Type 2 diabetes mellitus, HTN: Hypertension

Table 6: Group comparison for USG findings

USG findings	Number of patients (%)	
	Group L	Group C
GB Sluge	0 (0.00)	1 (3.33)
Multiple calculi	21 (70.00)	18 (60.00)
Solitary calculus	9 (30.00)	11 (36.67)
P value	0.091	
Remarks	NS	

NS: Non-significant, USG: Ultrasonography

related factors such as use of volatile anesthetic agents, N₂O, opioids and surgery-related factors (Bonder, 1991). Female gender has been associated with higher incidence of PONV compared to male patients. On an average, female patients suffer three times more often from PONV than men.

Our study was aimed at evaluating the antiemetic efficacy of levosulpiride in preventing PONV in patients undergoing laparoscopic cholecystectomy. Laparoscopic surgery was chosen because of high incidence of PONV associated with it. Naguib *et al.* demonstrated that the incidence of PONV after laparoscopic surgeries in their placebo group was remarkably high (72%) which is consistent with the findings of our study where the incidence of PONV in control group was about 57%. PONV is also one of most common reasons for patient's poor satisfaction during post-operative period.

Despite advances in antiemetic therapy in the last decade, incidence of PONV is still found to be relatively high.

Table 7: Group comparison for PONV

Time interval (h)	Number of patients (%)		P value	Remarks
	Group L (n=30)	Group C (n=30)		
0-4	0 (0.00)	17 (56.67)	<0.0001	S
4-8	1 (3.33)	16 (53.33)	<0.001	S
8-12	6 (20.00)	17 (56.67)	0.001	S
12-24	5 (16.67)	14 (46.67)	0.001	S

S: Significant, PONV: Post-operative nausea and vomiting

Table 8: Group comparison for rescue antiemetic

Groups	Rescue antiemetic
	Number of patients (%)
Group L (n=30)	7 (23.33)
Group C (n=30)	16 (53.33)
P value	0.002
Remarks	S

S: Significant

Table 9: Group comparison for hospital stay

Groups	Duration of hospital stay (days)
	Mean±SD
Group L	2.20±0.41
Group C	2.33±0.48
P value	0.251
Remarks	S

S: Significant, SD: Standard deviation

A wide variety of antiemetic drugs (e.g, anticholinergics, antihistaminics, dopamine receptor antagonists, glucocorticosteroids, neurokinin-1 antagonists, etc.) are available to prevent post-operative emetic symptoms. Although phenothiazines, butyrophenones (droperidol), and metoclopramide are also antiemetic, they are associated with extrapyramidal side effects (Islam, 2004).

In our study, the males outnumbered the females in both the control and levosulpiride group. The mean age in of control group was 37.93 ± 8.73 years (range 20-50 years) and that in levosulpiride group it was from 39.03 ± 7.55 years (range 21-50 years). The mean weight of the control group was 58.27 ± 8.14, whereas that of the levosulpiride group was 59.67 ± 6.91. A number of factors including sex, obesity and surgical procedure affect the incidence of emetic symptoms (Watcha 1992).

The majority of patients studied, presented with pain in the RHC followed by flatulent dyspepsia.

Preoperatively, ultrasound was done in all cases, showing multiple calculi predominantly followed by solitary stone.

Injection levosulpiride was administered 5 min before the induction of anaesthesia. Postoperatively, patients were

observed for 24 h. Metoclopramide 10 mg was given as a rescue antiemetic (based on the study conducted by Watcha who found and then suggested that administering a repeat dose of same antiemetic failed to control emetic symptoms). During first 24 h after surgery, all episodes of nausea and vomiting and complete response at various time intervals, i. e., 0-4, 4-12, 12-24 h, were analyzed statistically.

The study followed a well-established and robust methodology (Apfel, 2002). The incidence of PONV seen in the control group was observed to be highly consistent with that seen in many other recent studies, suggesting good comparability of these data with the latest literature (Kovac *et al.* 2008).

In the control group, the incidence of PONV was 56.67% within 0-4 h, 53.33% from 4 to 8 h, 56.67% from 8 to 12 h and 46.67% from 12 to 24 h, compared to the levosulpiride group, in which the incidence of PONV was 0.00%, 3.33%, 20.00% and 16.67% within the corresponding time intervals. This reflected the efficacy of pre-operative use of levosulpiride in consideration of studies by Pueyo *et al.* (1995) and Fuji *et al.*

Statistically significant improvement was also seen in terms of usage of the rescue anti-emetic, wherein 7 out of 30 patients were administered a rescue antiemetic in levosulpiride group, in control group the need for rescue antiemetic was more, with 16 patients being administered the same, showing a 30% lesser usage in the levosulpiride group. Furthermore, a lesser duration of hospital stay was seen in the levosulpiride group.

The incidence and profile of treatment-emergent adverse events were similar across both the study groups, i. e., control as well as the levosulpiride group, and there was no evidence of any of the toxicities of concern commonly associated with levosulpiride, such as extrapyramidal signs and symptoms, cardiotoxicity and psychological disturbances (Rossi, 1995).

In a study of over 200 patients Kranke *et al.* showed that administration of amisulpride preoperatively reduced the incidence of PONV in adult surgical patients. The observations made were consistent with the reduced rates of PONV seen with the usage of the drug levosulpiride in present study, wherein the incidence of PONV in control group was 17/30 (56.66%) and in the levosulpiride group was 7/30 (23.33%).

Singh (2015) in a series of 113 patients divided into three groups (Group 1 levosulpiride 40 patients, Group 2 domperidone 35 patients, and Group 3 metoclopramide 38 patients) found a highly significant improvement in

symptoms scale in Group 1 levosulpiride 40 patients' group, overall dyspeptic symptom relief rates were significantly high in the levosulpiride group ($P < 0.004$) as compared to domperidone and metoclopramide groups. Similarly in our study, a decreased incidence of nausea and vomiting was seen in the levosulpiride group ($P < 0.001$).

Apfel *et al.* (2004) in a large series of >5000 patients demonstrated that the benefit of a range of antiemetic interventions, including ondansetron, dexamethasone, and droperidol, was similar, with a relative risk reduction of ~25% compared with the absence of that intervention, equating to an absolute reduction of 15-20% points on a typical baseline PONV rate in the range 65-75%. This magnitude of benefit has been seen with many antiemetics in separate, placebo-controlled trials, including ondansetron (Fortney *et al.*) and palonosetron (Kovac *et al.*, 2008). A cochrane collaboration meta-analysis of 737 studies involving 103, 237 patients found that eight agents tested were effective antiemetics, with relative risk reductions in the range 20-40% Carlisle *et al.* The benefit seen with injection levosulpiride 25 mg is a risk reduction of about 30%-points in absolute terms, which is promising.

The efficacy shown by levosulpiride appeared not to be at the expense of any toxicity. Of note, no extrapyramidal side effects were seen. Risk of cardiotoxicity too appears to be much lower. Levosulpiride has several attractive features for use in patients undergoing laparoscopic cholecystectomy. As it has a low propensity for drug interactions (Spina, 2007), it can be safely used in elder patients and in patients with renal failure.

This study demonstrates a significant benefit of pre-operative administration of injection levosulpiride 25 mg in the prevention of PONV. All efficacy measures the incidence of PONV, requirement of rescue anti-emetic and duration of hospital stay, were reduced by a significant magnitude.

It is therefore concluded that the usage of injection levosulpiride 25 mg in patients undergoing laparoscopic cholecystectomy prevents PONV which thus improves quality of life postoperatively.

CONCLUSIONS

The pre-operative administration of injection levosulpiride 25 mg in patients undergoing elective laparoscopic cholecystectomy surgeries under general anesthesia significantly reduces the incidence of PONV. It was hence seen to improve the quality of life in early stage of post-operative rehabilitation and also decreases the duration of hospital stay.

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