



The effect of single dose of preoperative dexamethasone on postoperative nausea and vomiting after laparoscopic cholecystectomy: a randomized, double-blind, placebo-controlled study

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Abstract

Objective: To study the efficacy of single dose of preoperative dexamethasone in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

Materials and Methods: 110 patients were randomized in two equal groups. Each of the groups received either 2ml (8mg) intravenous dexamethasone (Group A) or 2ml intravenous normal saline as placebo (Group B).

Results: 6 patients (14.5%) in group A and 19 patients (34.5%) in group B had postoperative nausea and vomiting in first 6 hours whereas 2 patients (3.6%) in group A and 5 patients (9.0%) in group B had postoperative nausea and vomiting in 6-24 hours.

Conclusion: Preoperative dexamethasone improves the surgical outcome by reducing disabling symptoms of nausea and vomiting without apparent side-effects. So we suggest that single dose of preoperative dexamethasone should be used as a routine in patients undergoing elective laparoscopic cholecystectomy.

Keywords: Cholelithiasis, Dexamethasone, Laparoscopic cholecystectomy, Postoperative nausea and vomiting.

Introduction

Laparoscopic cholecystectomy has become the most frequently performed surgical procedure worldwide for symptomatic cholelithiasis. Despite the fact that it is a safe procedure, complications such as nausea, vomiting, and pain are frequent

during the postoperative period, and are among the main causes of patient complaints and dissatisfaction^[1] The origin of postoperative nausea and vomiting after laparoscopic cholecystectomy is not entirely clear. Female sex, prolonged carbon dioxide insufflation, length of

procedure, use of nitrous oxide, the utilization of slightly hypoxic mixtures during anaesthesia and postoperative opioid analgesic administration have been suggested as potential risk factors.^[2,3] Postoperative nausea and vomiting can lead to serious complications such as aspiration, dehydration, electrolyte disturbances and disruption of incision site. It can also increase the cost of treatment. Another impact of postoperative nausea and vomiting, is its unpleasant effect on patients. Some patients regard it as more disabling than the operation itself. Dexamethasone, a corticosteroid, has well-defined antiemetic, anti-inflammatory, immunomodulating and analgesic effects, in addition to having few side effects when administered in small doses. It is widely used for controlling nausea and vomiting after chemotherapy and surgical procedures including laparoscopic cholecystectomy.

The objective of this randomized, double-blind, placebo-controlled study was to assess the effectiveness of single dose of preoperative dexamethasone in the prophylaxis of postoperative nausea and vomiting after laparoscopic cholecystectomy.

Materials and Methods

After approval from the institutional ethical committee this prospective, randomized, double blind, placebo-controlled study was conducted in the department of surgery, Rohilkhand Medical College and Hospital, Bareilly, Uttar Pradesh, India. A total of 110 patients of either sex, with ASA grade I or II, aged 18 yrs - 50 years were enrolled for the study. The patients were randomly assigned using "computer generated random number table" to one of the following groups:

Group A (n=55): Were scheduled to receive dexamethasone 2 ml (8 mg) intravenously.

Group B (n=55): Were scheduled to receive normal saline 2 ml intravenously.

These drugs were prepared by the staff nurse on duty and given by the doctor on duty, two hours before the starting of the operation. Pre-anesthetic

checkup was done and patient was informed about the procedure. Tab. alprazolam 0.5 mg was given evening before surgery and at 5 Am in the morning with a sip of water. IV line was secured with 18 Gauze IV cannula and IV fluid was started. The patient was connected to all the standard monitors to record pulse rate, O₂ saturation, non invasive blood pressure, end tidal carbon dioxide and electrocardiogram. Premedication with inj. Midazolam 0.05 mg/kg body weight before the procedure was given.

After pre oxygenation for 3 minutes, with 100 % oxygen, anaesthesia was induced with injection propofol 2.0 mg /kg and 3 minutes after injection of vecuronium 0.1 mg/kg, direct laryngoscopy was performed and the patient was intubated with a well lubricated, appropriate sized poly vinyl chloride cuffed endotracheal tube. Bilateral air entry was checked and the tube was firmly secured and controlled ventilation was started. Anaesthesia was maintained with 30 % oxygen, 70 % nitrous oxide, 0.8% isoflurane and intermittent boluses of inj. vecuronium 0.02 mg/kg.

Pneumoperitoneum was created with open technique and laparoscopic cholecystectomy was performed using two ports of 10 mm and two of 5 mm, maintaining a 12 mm Hg intraabdominal pressure. At the end of procedure, the carbon dioxide was carefully evacuated from the abdomen. Monitoring of vital parameters such as heart rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and oxygen saturation were recorded at fixed intervals, i.e. preoperative, after intubation and then at 15, 30, 45, 60, 75 and 90 minutes following intubation.

At the end of surgery, all the anaesthetic agents were stopped, 100 % oxygen was given and oropharyngeal suction was done. After returning of respiratory efforts residual neuromuscular blockade was reversed by injection neostigmine 0.04 mg/ kg and Injection glycopyrrolate 0.02 mg/kg intravenously. Episodes of nausea, and vomiting were registered by the doctor on duty in first 24 hours after operation.

When respiration became normal and tidal volume was adequate, extubation was done. After extubation, patients were oxygenated with 100 % for 5 minutes and then shifted to postoperative ward. All the results were compiled, compared and analysed statistically by using the statistical package for the social science (SPSS 22.0, IBM, New York, USA). The data was compiled using Microsoft Excel Sheet (Windows 2010). For each variable the mean and standard deviation were calculated.

Numerical variables were compared between the groups by independent sample *t*-test if normally distributed and by Mann-Whitney U-test if skewed. Chi-square test and Fisher's exact test were used to compare the categorical variables between groups. All statistical analysis was two-tailed, and a *p*-value <0.05 was considered significant and <0.001 was considered highly significant.

Observations

Both the groups were comparable in the terms of Age, Gender, Body Mass Index, ASA Grade and

duration of surgery and no statistically significant difference was found (*p*-value >0.05) (Table-1).

6 patients (14.5%) in group A and 19 patients (34.5%) in group B had postoperative nausea and vomiting in first 6 hours whereas 2 patients (3.6%) in group A and 5 patients (9.0%) in group B had postoperative nausea and vomiting in 6-24 hours (Table-2).

Mean pulse rate was comparable in both the groups on starting of the procedure. Pulse rate changes during the entire intraoperative period were statistically not significant in both the groups (*p*-value > 0.05) (Figure-1).

Mean systolic blood pressure was comparable in both the groups on starting of the procedure. Systolic blood pressure changes during the entire intraoperative period were statistically not significant in both the groups (*p*-value >0.05) (Figure-2).

Mean Diastolic blood pressure was comparable in both the groups on starting of the procedure. Diastolic blood pressure changes during the entire intraoperative period were statistically not significant in both the groups (*p*-value >0.05) (Figure3).

Table 1 Comparison of Demographic Data

Parameters	Group A (n=55)	Group B (n=55)	<i>p</i> -value
Age (Years)	31.70±7.8	32.30±8.7	>0.05
Body Mass Index	23.59±2.9	22.82±3.2	>0.05
Gender (M/F)	32/23	34/21	>0.05
ASA (I/II)	44/11	46/09	>0.05
Duration of surgery (Minutes)	67.83±9.5	78.09±7.8	>0.05

Table 2: Post operative nausea and vomiting

Variables	Group A (n=55)	Group B (n=55)	<i>p</i> -value
0-6 HOURS AFTER SURGERY	8	19	<0.001
6-24 HOURS AFTER SURGERY	2	5	<0.001

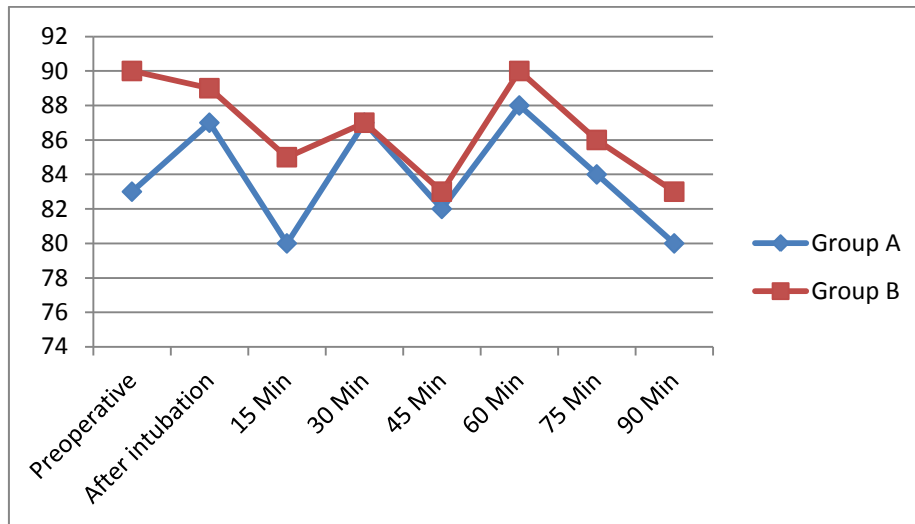


Figure – 1 Comparison of Mean Heart Rate (HR) in Group A and Group B

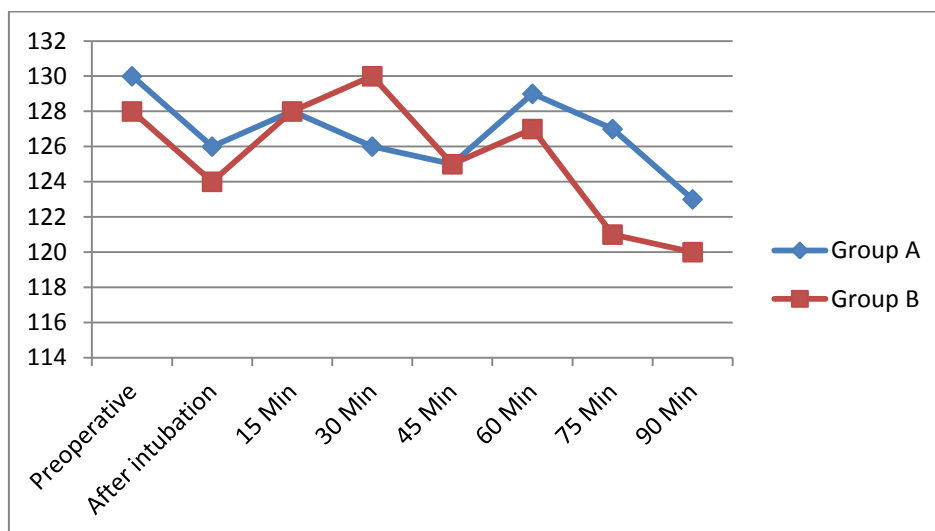


Figure – 2 Comparison of Mean Systolic Blood Pressure (SBP) in Group A and Group B

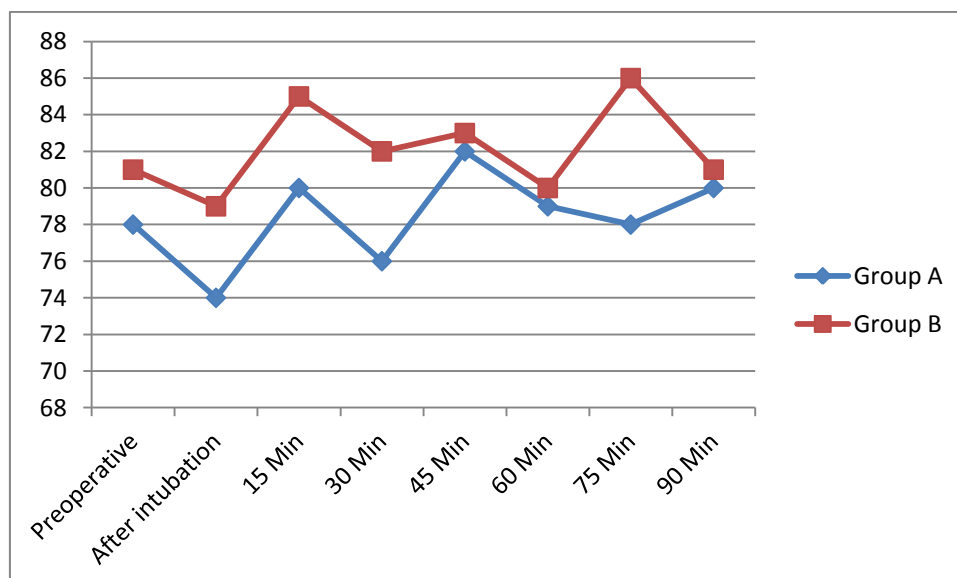


Figure – 3 Comparison of Mean Diastolic Blood Pressure (DBP) in Group A and Group B

Discussion

Now a day's laparoscopic cholecystectomy has almost replaced open cholecystectomy because laparoscopic surgeries have been claimed to reduce the metabolic, hormonal, inflammatory, and immune responses related to surgical trauma. It reduces duration of hospital stay and overall cost of surgery. Nonetheless, a high incidence of nausea and vomiting, the main reasons for extended hospital stays, is reported in the postoperative period.^[4] Nausea and vomiting after a laparoscopic cholecystectomy are caused by multiple factors, depending especially on intra-abdominal manipulation and formation of pneumoperitoneum, which stretches the peritoneum and irritates the diaphragm and viscera.^[5] Other causes of Postoperative nausea and vomiting after laparoscopic cholecystectomy includes pharyngeal stimulation due to tracheal stimulation, emetogenic anaesthetic agents used, pain, opioid analgesic agents used, hypoxia, hypotension, vestibular disturbances and psychological factors. There are certain factors which can predispose patients to postoperative nausea and vomiting, like age (more in children), gender (more in females), history of previous nausea and vomiting, history of motion sickness, long duration of operation and depth of anaesthesia, carbon dioxide retention, rough handling, lack of anaesthetist's skill, type of surgical procedure and number of visitors during recovery.^[6] Antiemetics currently prescribed for PONV, are serotonin subtype 3 antagonists (e.g., ondansetron and granisetron), anticholinergics, antihistamines and dopamine receptor antagonists. These may have side effects, such as sedation, dry mouth, restlessness, changes in arterial blood pressure, and extrapyramidal symptoms. Dexamethasone, a corticosteroid, is an inexpensive and effective antiemetic drug, with minimal side effects after a single-dose administration.^[7-9] The mechanism by which glucocorticoids alleviate these complications is not fully understood, but the effects are probably centrally mediated through inhibition of the

prostaglandin synthesis and inhibition of the release of endogenous opioids, serotonergic inhibition in the gastrointestinal tract, and decrease in inflammation of the surgical site, reducing parasympathetic impulses to the area postrema.^[10-12]

Dexamethasone was first used as an antiemetic in patients receiving cancer chemotherapy in 1981.^[13] Recently, dexamethasone has been reported to be effective in preventing PONV in patients undergoing tonsillectomy, thyroidectomy, abdominal hysterectomy and laparoscopic cholecystectomy. The commonly used dose is 8 to 10mg but the minimal effective dose, as suggested by Asad Ali Shah *et al* for postoperative nausea and vomiting in patients undergoing thyroidectomy was 5 mg.^[14]

Several randomized controlled trials have shown that single preoperative dose of dexamethasone is effective in reducing postoperative nausea and vomiting and antiemetic requirement after laparoscopic cholecystectomy.

Amer Riaz Bhutta *et al* in a study randomized 100 patients either in saline group receiving 2 ml intravenous normal saline or dexamethasone group receiving 2 ml intravenous dexamethasone and concluded that preoperative dexamethasone improves surgical outcome by reducing postoperative nausea and vomiting without apparent side effects.^[15]

J.J.Wang *et al* in a study on 90 patients found that a single dose of 8 mg preoperative intravenous dexamethasone reduces the incidence of postoperative nausea and vomiting after laparoscopic cholecystectomy.^[16]

Ahmadreza Mohtadi *et al* in a double blind prospective study on 122 patients aged 18-60 years undergoing laparoscopic cholecystectomy concluded that single dose of intravenous dexamethasone reduces incidence of postoperative nausea and vomiting.^[17]

Like our conclusion, Bis Gaard T *et al.* also concluded that, preoperative Dexamethasone reduces pain, fatigue, nausea, vomiting and duration of convalescence in patients undergoing

laparoscopic cholecystectomy, as compared to placebo and they recommend the routine use of single dose of preoperative dexamethasone in patients undergoing laparoscopic cholecystectomy [18]

In a study Feo CV *et al.* randomized 101 patients to receive either Dexamethasone 8mg (treatment group) or saline (control group), the frequency of postoperative nausea and vomiting in the treatment group was found significantly less as compared to placebo group ($p < 0.001$). [19]

In contrast to our study, Ionescu D *et al.* reported postoperative nausea and vomiting in 20% of patients who received preoperative dexamethasone as prophylaxis undergoing cholecystectomy and does not found any benefit in comparison to placebo. [20] Kashmiri Z A *et al.* used dexamethasone 8mg in patients undergoing laparoscopic cholecystectomy just before induction of anaesthesia. In their study, 27% of patient experienced postoperative nausea and vomiting during first 12 hours and 30% patients reported nausea and vomiting in next 12 hours. [21]

Wakasuqi M *et al.* in a large scale multicenter randomized double blind placebo controlled trial in Japan concluded that routine use of preoperative dexamethasone for postoperative nausea and vomiting after elective laparoscopic cholecystectomy was not shown to have any clinical advantage. [22]

The difference in their results could be due to use of different anaesthetic techniques, use of opioids and other analgesics in postoperative period, difference in patients population (male/female), duration of anaesthesia and duration of surgery.

Conclusion

Dexamethasone improve the surgical outcome by reducing disabling symptoms of nausea and vomiting without any side-effects. So single dose of preoperative dexamethasone may be used as a routine in patients undergoing elective laparoscopic cholecystectomy.

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