

# Preoperative dexamethasone reduce postoperative pain and analgesic consumption in patient undergoing laparoscopic cholecystectomy

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## Abstract

**Background:** Pain after Laparoscopic cholecystectomy is multifactorial, and different treatments have been advocated to provide pain relief. Dexamethasone is best known for its anti inflammatory property that reduces tissue edema during surgical procedure. A single dose of Dexamethasone has been shown to reduce post operative pain scores as well as PONV. We evaluated the efficacy of analgesic effect of single dose (8 mg) of injection Dexamethasone 1 hour before induction of anaesthesia on reducing post operative pain and reduction in opioid usage in laparoscopic cholecystectomy.

**Materials and methods:** In this double blind prospective study 50 patients undergoing laparoscopic cholecystectomy received intravenous Dexamethasone (8 mg) or placebo (normal saline) one hour before induction of GA. Patients received standardised anesthetics, with similar surgical and multimodal analgesic treatment. Total dose of consumed analgesic and pain intensity during first 24 hours postoperative period were evaluated in both groups.

**Result:** Pain intensity in Dexamethasone group was significantly less than in control group in the first 12 hour post operative period ( $p < 0.05$ ). Opioid consumption in Dexamethasone group was significantly less than placebo group ( $p < 0.05$ ).

**Conclusion:** We concluded that 8 mg single dose of intravenous Dexamethasone given at least one hour prior to surgery is a safe, effective and inexpensive choice to control post operative pain and at the same time to reduce opioid consumption in comparison with placebo.

## Introduction

Laparoscopic cholecystectomy (LC) is a standard treatment for cholelithiasis, due to decreased post operative trauma and less side effects [1]. However, pain is still considered the most common complaint and the reason of prolonged hospitalisation, more morbidity and delayed functional recovery after LC [2,3]. There are many causes of laparoscopic induced pain [4], of which stretching of intra abdominal organs, peritoneal inflammation and phrenic nerve irritation by residual carbon di-oxide (CO<sub>2</sub>) in peritoneal cavity are important. Pain is more severe on the day of operation and the following day after LC [5]. Dexamethasone is a powerful anti-inflammatory drug with a long half life and its administration is considered safe for periods shorter than 2 weeks even in amount above the physiological doses [6].

Several clinical trials in many different surgical procedures evaluated the effects of a single dose of dexamethasone administered on post operative pain but have inconsistent findings [7,8]. Furthermore, there are very few articles on use of preoperative Dexamethasone for postoperative pain relief in the Indian Scenario. We therefore performed this study to observe the efficacy of use of preoperative Dexamethasone in reducing post operative pain as well as analgesic requirements in patients undergoing LC.

## Material and method

After taking institutional approval and informed consent 100

patients aged 18-60 yrs of both sexes ASA I and II scheduled for LC under general anaesthesia (GA) were selected for this study conducted at I Q City Medical College and Hospital, Durgapur. Patients with hepatic and renal insufficiency; history of corticosteroid hypersensitivity; previous gastric ulcer; diabetes mellitus; receiving any corticosteroid, immunosuppressive analgesics or opioid medications were excluded from the study. Visual Analogue Score (VAS) where 0 means no pain, 10 means worst possible pain were explained to all patients during their pre-operative visit. Patients were randomly allocated using a random number table and sealed envelope technique to receive intravenously one of two treatment regimes: Dexamethasone 8 mg (Group D) or normal saline as placebo (Group S). 50 patients in each group received either of the drugs.

Study medications (2 ml each) were prepared by personnel not involved in the study in identical 2 ml covered syringes to ensure blinding of the anesthetists and patients. These drugs were

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administered intervenously one hour before induction of GA. Patients and investigators who collected post operative data were blinded to the study drugs administered.

Patients received tablet alprazolam 0.5 mg orally on night before operation and were fasted for at least 6 hours before surgery. All subjects were hydrated with 10 mL.kg<sup>-1</sup> of Ringer's lactate (RL). Anaesthesia was induced with fentanyl 2 mcg.kg<sup>-1</sup>, followed by propofol 2 mg.kg<sup>-1</sup>. Intravenous atracurium (0.6 mg/kg) was given intravenously to facilitate oro-tracheal intubation. Anaesthesia was maintained with isoflurane (1% inspired concentration, along with nitrous oxide 66% in oxygen) with controlled ventilation adjusted to keep the end tidal CO<sub>2</sub> at around 35 to 45 mm Hg. Muscle relaxation for pneumoperitonium and surgical procedures was provided with additional doses of atracurium. Nasogastric (NG) tube was passed to empty the stomach content by suction. Before tracheal extubation NG tube was resuctioned and removed. During Laparoscopy the intra-abdominal pressure maintained at 8 to 12 mm Hg by a CO<sub>2</sub> insufflator and patient were placed in 15 to 20 degree head up position with slight left lateral tilt. After removal of the gall bladder injection ondansetron 8 mg was administered intravenously. Patients were monitored during GA by continuous ECG, NIBP, pulse oximetry and capnometry. At the completion of surgery residual neuromuscular blockade was antagonised with neostigmine (0.05 mg.kg<sup>-1</sup>) and glycopyrolate (0.01 mg.kg<sup>-1</sup>) administered intrvenously.

Trachea was extubated once the patient was awake. All patients received supplementation of oxygen (3 litres/min) by a face mask in the post operative period for 2 hours and were monitored continuously in the recovery room. After 2 hours the patients were sent to their respective wards. Pain intensity and capillary glucose concentration was measured at 0, 1, 2, 4, 6, 12 and 24 hours postoperatively. Pain was classified as mild - 0 to 3, moderate - 4 to 7 and severe - 8 to 10 based on the VAS score of the patients. If VAS score was  $\geq 3$ , pethidine 1 mg.kg<sup>-1</sup> was administered intravenously. Total consumed meperidine during the first 24 hours postoperative period was recorded. Details of adverse effects were recorded during study period by attending anaesthesiologist.

## Statistical analysis

Considering VAS scores from previous studies and power (1-beta)=75% and level of significance=5% sample size was calculated 35 for each arm. To increase the power of the study further we choose 50 patients in each group (Group D and S respectively). All of the statistical data was reported as mean  $\pm$  SD. One way ANOVA was used for comparisons of data which are commonly expected to be normally distributed, e.g. demographics, duration of analgesia, and intraoperative and postoperative analgesic use. Chi-square and Kruskal-Wallis tests were used for postoperative VAS scoring.

## Results

In this study 100 patients were divided into two groups receiving either 2 ml normal saline (group S) or Dexamethasone 8mg (group D) in identical 2 ml covered syringes, 1 hour before GA.

There were no difference between the two groups regarding demographic characteristics (in terms of age, sex height, weight and ASA grade) and duration of surgery ( $p>0.05$ ) (Table 1).

The meperidine consumption in the Dexamethasone group was significantly less (135.4  $\pm$  25.7 vs. 228.8  $\pm$  21.5 milligrams respectively; Table 2, Figure 1).

**Table 1.** Demographic Data.

	Group D (n = 50)	Group S (n = 50)
Age (years)	46.4 $\pm$ 10	44.8 $\pm$ 8
Height (cm)	143.7 $\pm$ 4	140.9 $\pm$ 5
Weight (kg)	54.2 $\pm$ 6	51.6 $\pm$ 8
BMI	26.2 $\pm$ 0.6	26.4 $\pm$ 0.4
ASA I/ASA II	42/8	43/7
Duration of surgery (min)	47.8 $\pm$ 26	50.1 $\pm$ 30

\* $p>0.05$

**Table 2.** Meperidine consumed per patient during study period (mean  $\pm$  std. deviation).

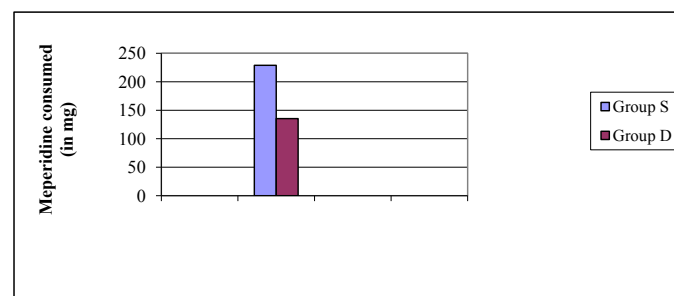
	Group S (n = 50)	Group D (n = 50)
Meperidine consumption (mg)	228.8 $\pm$ 21.5	135.4 $\pm$ 25.7 *

\* $p<0.05$

**Table 3.** Comparison of pain intensity amongst two study groups.

VAS	Group D	Group S
On arrival to PACU (0 hour)	5.4 $\pm$ 2.5	5.3 $\pm$ 2.7
After 1 hour	3.8 $\pm$ 1.2	5.4 $\pm$ 2.5*
After 2 hour	3.2 $\pm$ 1.4	5.5 $\pm$ 2.7*
After 4 hour	3.1 $\pm$ 1.5	5.20 $\pm$ 1.4*
After 6 hour	2.9 $\pm$ 1.7	4.8 $\pm$ 2.9*
After 12 hour	2.8 $\pm$ 1.3	4.2 $\pm$ 2.4*
After 24 hour	2.9 $\pm$ 1.4	2.8 $\pm$ 1.2

Data are presented as numbers or mean  $\pm$  SD, \*signifies a p value of significance ( $<0.05$ )



**Figure 1.** Average postoperative pethidine consumption in the two groups.

The mean post operative pain intensity based on VAS score for the first 12 hours in recovery room and ward in group D was significantly lower compared with group S ( $p<0.05$ ), Table 3. However, at 24 hours the VAS scores of the two groups were similar. There were no adverse events in any patient.

## Discussion

Our study result revealed that a single intravenous dose of preoperative dexamethasone 8mg reduced intensity of postoperative pain in first 12 hours in comparison with placebo and it also decreases total consumption of post operative analgesic.

The results are similar with studies conducted by Fukami *et al.* [8] and Lim *et al.* [9] The mechanism of pain relief by dexamethasone is mainly provided by peripheral suppression of phospholipase enzyme, thereby significantly decreasing the products of cyclooxygenase and lipoxygenase pathways in the inflammatory response [8,10]. Additionally dexamethasone reduced bradykinin which reinforces pain in the inflamed tissues and operated area, and also the decreased concentration of nerve proteins secreted from the peripheral nerve system are involved in the analgesic effect [11].

Postoperative pain after laparoscopic cholecystectomy is induced by multiple factors i.e. from skin incision, visceral pain, diaphragmatic irritation, different individual characteristics, nature of underlying diseases, surgical factors and type and volume of gas and also induced intra abdominal pressure. Hence the multimodal approaches are considered for post operative pain relief [12,13]. The timings of steroid administration is important to reducing postoperative pain, as initiation of its biological effect is one or two hour of its injection [14]. The dose of dexamethasone 8mg one hour before induction was based on previous reports showing a decrease in postoperative pain [9,15].

We measured the pain intensity of the patient at 12 hours followed by 24 hours after the operation. While pain relief was significantly more at 12 hours with Dexamethasone, it was similar at 24 hours compared with normal saline, a finding similar to the study of Mohtadi A *et al.* [15].

A limitation of this study was that we did not measure pain intensity at any time between 12 to 24 hours, so the exact duration of dexamethasone effect postoperatively could not be ascertained from our study. We also did not study of serum concentration of dexamethasone and stress hormones. We only studied perioperative glucose levels which was insignificant in our study.

With use of steroids complication such as delays recovery, postoperative infection, glucose intolerance and gastric mucosa ulcer can occur [9]. Sauerland *et al.* [16] reported in their meta analysis that there was no significant increase in complications when they used 15-30 mg.kg<sup>-1</sup> of methylprednisolone in one dose which is fifty times the amount of dexamethasone used in our study. In our study we did not find any complication related to use of a single dose of dexamethasone. To conclude, 8 mg dexamethasone pre operatively helps in better postoperative pain control as well as reduced opioid consumption.

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