

Pre-Emptive Dexamethasone for Managing Post Operative Pain in Patients Undergoing Laparoscopic Cholecystectomy Under General Anaesthesia: A Prospective Randomized Study

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Abstract

Background: Pain after laparoscopic cholecystectomy arise from multiple sources and so require multimodal approaches to manage it. Dexamethasone is a corticosteroid drug with excellent anti-inflammatory properties. Present study was designed to study the effect of administering an intermediate dose of dexamethasone (8 mg), one hour before the induction of anaesthesia, on post-operative analgesia, time to first analgesia and total number of analgesics used in twenty four hours. **Material and Methods:** A total of 80 patients were randomly allocated into two study groups by computer generated randomization. Group 1 received 8 mg/2 ml of Inj. Dexamethasone intravenously 1 hour prior to induction of General Anaesthesia slowly over a period of 5 minutes. Group 2 received 2 ml of Normal Saline (NS) intravenously 1 hour prior to induction of General Anaesthesia slowly over a period of 5 minutes. **Results:** The mean Visual analogue score of group 1 was lower than that of group 2 and the difference was statistically significant at 0, 2, 6 and 12 hours postoperatively ($p < 0.05$). The mean time taken by the patients in group 1 for the first rescue analgesic was (11.65 ± 4.59) hours, which was statistically significant as compared to group 2 (4.01 ± 2.03) hours ($p = 0.0001$). Mean total number of analgesic used in Group I was significantly less as compared to Group 2 ($p = 0.0001$). **Conclusion:** Use of dexamethasone 8 mg intravenously one hour before induction of general anaesthesia for post-operative analgesia causes a significant decrease in overall VAS score at 0, 2, 6 and 12 hours post-operatively, increases the duration between the surgery and the need for first rescue analgesia and decreases the total number of analgesics used with minimal adverse effects after laparoscopic cholecystectomy.

Keywords

Dexamethasone, Post-operative Pain, Laparoscopic Cholecystectomy, General Anaesthesia

Introduction

High-quality post-operative analgesia is crucial in promoting early recovery in surgical patients. Even though there is a decreased incidence of pain with laparoscopic surgery than with open surgery, it still needs to be

adequately managed.^[1] There are multiple causes of Pain after Laparoscopic Cholecystectomy (LC) which includes incisional, local visceral, peritoneal and referred pain.

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Various multimodal approaches have been used to achieve effective post-operative analgesia because of multiple sources of pain in LC. This include use of opioids, non opioid analgesics like NSAID, Lignocaine, Gabapantine, Dexamethasone etc and peripheral nerve blocks.^[2] Perioperative use of opioids can be associated with a variety of side effects like respiratory depression, pruritus, urinary retention, nausea, vomiting, ileus or constipation that can lead to increased morbidity in patients.. Glucocorticoids are known for their analgesic, anti-inflammatory, antiemetic and immune-modulatory effects. Dexamethasone is among the most potent corticosteroids available, with a biologic half-life of 36–72 hours. Dexamethasone has been used in various studies in different doses ranging from 1.25 mg to 20mg both preoperatively as well as intraoperatively for post operative analgesia.^[3,4,5] The present study was designed to study the effect of intermediate dose of dexamethasone (8 mg) given one hour before induction of anaesthesia. The primary outcome of the study was to evaluate the post-operative pain relief as assessed by visual analogue score. The secondary outcome of the study was to evaluate time to first rescue analgesia, number of doses of the rescue analgesia used in 24 hours and to study the adverse effects of the drug.

Material and Methods

Study Design: This was a prospective, randomized, double blind study conducted in a tertiary care hospital. Study population

After obtaining clearance from the institutional ethical committee (ASCOMS/IEC/RP&T/2020/406) this study was conducted on 80 patients, American Society of Anaesthesiology physical status Class I and II, age between 18 and 75 years, both male and female and BMI between 18 and 30 kg/m², scheduled for elective laparoscopic cholecystectomy over a period of one year (Nov 2020- Oct 2021). A written informed consent was obtained from these study participants. Exclusion criteria was patients refusal, age <18 and > 75 years, ASA physical status grades III and IV, patients with hepatic and renal insufficiency, previous gastric ulcers, diabetes mellitus, pregnant and nursing mothers, history of corticosteroid hypersensitivity, patients already on corticosteroid, immunosuppressive, analgesic or opioid medications, emergency surgery, inability to understand and use the VAS, chronic pain syndrome where pain evaluation will be unreliable due to neurological disease.

Patients were made familiar with 10 point visual analogue scale preoperatively and were instructed to point the intensity of pain on a 10 cm scale. Zero end of scale was taken as no pain and 10 cm as maximal possible pain.

Patients were randomly assigned into two study groups, each group having 40 patients, according to a computer-generated table of randomization. Randomization was performed by an anaesthesiologist who was not involved in the trial. Participants, the surgeon, anaesthesiologists and the investigator following the participant postoperatively were blinded to study group allocation.

Group 1 – Patient in this group received 8 mg/2 ml of Inj. Dexamethasone intravenously one hour prior to induction of General Anaesthesia (GA) slowly over a period of 5 minutes.

Group 2 – Patient in this group received 2 ml of Normal Saline (NS) intravenously one hour prior to induction of GA slowly over a period of 5 minutes.

After receiving the patient in the operation theatre, monitoring was established with baseline recording of heart rate, NIBP, ECG, pulse oximetry (SpO₂). Standard anaesthetic technique for GA was followed in all the patients. Induction was done with Inj. propofol 2 mg/kg and Inj. fentanyl 2 µg/kg, followed by Inj. atracurium 0.5mg/kg intravenously and airway was secured by endotracheal tube. Maintenance of anaesthesia in both groups was with 50% N₂O in O₂, isoflurane, and intermittent atracurium as required. Fifteen minutes prior to the end of surgery, all patients received intravenous paracetamol 1gm infusion and ondansetron 4 mg. CO₂ was carefully evacuated at the end of surgery by manual compression of abdomen with open trocars. and 2 ml of 0.25% bupivacaine was infiltrated in each port site. Neuromuscular blockade was reversed with IV neostigmine and glycopyrrolate and the patients were extubated after regaining consciousness and were transferred to the post anaesthesia care unit (PACU). The time of arrival in post-operative unit was defined as 0 hour postoperatively.

Following parameters were recorded

- (1) Post-operative pain was assessed by visual analogue scale at 0, 2, 6, 12 and 24 hours interval. Patient with score e” ≥4 received Inj. Diclofenac 75 mg as a rescue analgesia and was not repeated before 8 hours (maximum 3 doses can be given in 24 hours). In case of breakthrough pain PCM infusion 1 gm I/ V was given.
- (2) Time to first rescue analgesic i.e. the time that elapsed between extubation and first analgesic dose) was noted.
- (3) Number of total doses of the rescue analgesia used in 24 hours was calculated
- (4) Adverse effects like nausea, vomiting, perianal pruritis were noted. Patients were given inj

Ondansetron 4mg/kg IV in case of nausea or vomiting.

Statistical Analysis

At the end of study all the data was compiled and analyzed statistically. Continuous variables were summarized in the form of means and standard deviations and categorical variables were expressed as frequencies and percentages. Graphically the data was presented by bar diagrams. Comparison of mean value among the two groups was done using students t-test and percentage comparison was done using the Chi Square test, Fisher's exact test whichever appropriate. The P value of less than 0.05 was considered statistically significant. The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 21.0 (SPSS Inc., Chicago, Illinois, USA).

Results

The distribution of the demographic parameters were comparable between two groups as shown in *Table 1*. Figure 1 shows the consort flow chart of the study.

The mean VAS score of Group 1 was lower than that of Group 2 and the difference was statistically significant at 0 hr (p=0.0003), 2 hr (p=0.0001), 6 hr (0.0001) and 12 hr (p=0.0011) post-operatively. The difference between the VAS scores at 24 hours postoperatively was statistically non-significant (0.3878) (*Table 2*).

The mean time taken by the patients in group 1 for the first rescue analgesic was 11.65±4.59 hours which was significantly higher than that of group 2 which was 4.01±2.03 hours respectively. The difference in mean

time to first rescue analgesia was statistically significant (p-value=0.0001). (*Table 3*)

Table 3: Comparison of mean time to receive first analgesic (hours) among Group 1 and Group 2.

| Groups | Mean time Mean ± SD | p-value |
|--------|------------------------|-------------|
| 1 | 11.65 ± 4.59 | 0.0001 (S*) |
| 2 | 4.01 ± 2.03 | |

P – value < 0.05 Significant

The mean total doses of analgesic used in groups 1 and 2 were 1.18 ± 0.38 and 2.25 ± 0.44 respectively. There was a statistically significant decrease in the amount of analgesia used in group 1 as compared to group 2 (p-value = 0.0001). (*Fig 2*)

Out of 40 patients 1 (2.5%) patient developed nausea in Group 1 as compared to 6 (15%) in Group 2. Postoperatively 1 (2.5%) patient in group 1 and 4 (10%) patients in group 2 had vomiting. The incidence of nausea and vomiting in group 2 was higher than in group 1 and the difference was statistically significant (p=0.0001)

Discussion

Efficient perioperative pain control is required in laparoscopic surgeries for improved quality of recovery, early ambulation and discharge from the hospital. To achieve this various multimodal analgesia approaches have been suggested to manage post-operative pain. One of these is administration of perioperative dexamethasone. This drug has been used in different doses perioperatively

Table 1: Demographic Data of the patients.

| Variable | Group 1(n=40) | Group 2(n=40) | p value |
|---------------------------|---------------|---------------|---------|
| Age (years) | 43 +14.14 | 42.88+13.67 | 0.87 |
| ASA (class) | 18/22 | 20/20 | 0.77 |
| Gender (M/F) | 22/18 | 20/20 | 0.57 |
| BMI kg/m ² | 24.60 3.15 | 25.58 3.15 | 0.98 |
| Duration of surgery (mts) | 60.35 15.20 | 58.00 14.58 | 0.06 |

Table 2: Comparison of mean VAS score (cm) among Group 1 and Group 2.

| Time Interval | Group 1 | | Group 2 | | P-Value |
|---------------|---------|------|---------|------|--------------|
| | Mean | SD | Mean | SD | |
| 0 hr | 2.08 | 0.86 | 2.66 | 0.47 | 0.0003(S*) |
| 2 hr | 2.43 | 0.60 | 3.48 | 0.81 | 0.0001(S*) |
| 6 hr | 2.76 | 0.89 | 3.8 | 0.79 | 0.0001(S*) |
| 12 hr | 3.35 | 1.01 | 4.02 | 0.73 | 0.0011(S*) |
| 24 hr | 2.68 | 0.83 | 2.83 | 0.71 | 0.3878 (N.S) |

P – value < 0.05 Significant

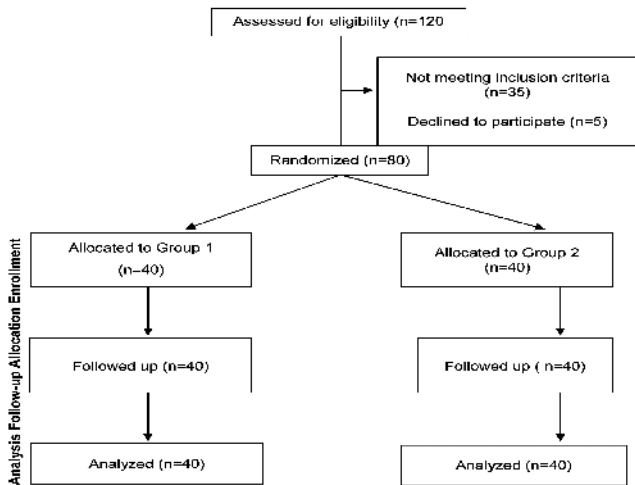


Fig 1: Consort Flow Chart

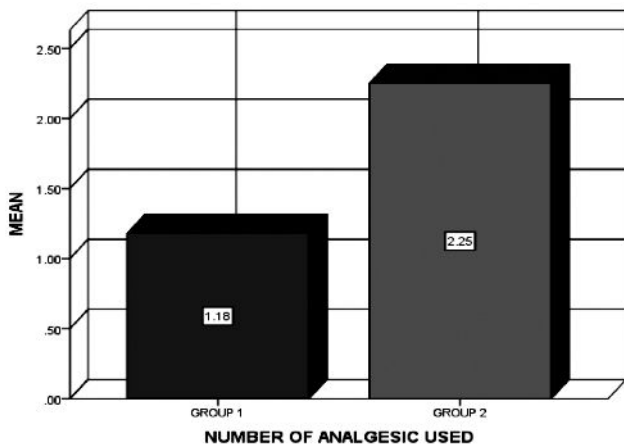


Fig 2 : Mean number of analgesics used in Group 1 and

for providing analgesia and control of post-operative nausea and vomiting. We evaluated the role of intermediate dose of dexamethasone as a component of multimodal analgesia for managing post-operative pain. Glucocorticoids are well known for their analgesic, anti-inflammatory, immune modulating and anti-emetic effects. Dexamethasone, a most potent corticosteroid with biological half-life of 36-72 hours, is long-acting glucocorticoid with little mineralocorticoid effect that has been used in the perioperative setting.^[6] In the present study, the mean VAS score of the dexamethasone group was lower than that of the normal saline group and the difference was statistically significant at 0, 2, 6 and 12 hours' post-operatively. The reason cited for the analgesic effect of dexamethasone is that it causes peripheral inhibition of phospholipase, thereby decreasing

the products of cyclooxygenase and lipoxygenase pathways in the inflammatory response. At the molecular level, unbound glucocorticoids readily cross cell membranes and bind with high affinity to specific cytoplasmic receptors.^[7,8] This binding ultimately affects protein synthesis, which may inhibit leukocyte infiltration at the site of inflammation, interfere with the function of mediators of the inflammatory response and suppress humoral immune responses. The net effect includes a reduction in edema or scar tissue and a general suppression of the immune response. The inflammatory mediators that are inhibited include interleukin, C-reactive protein, tumor necrosis factor X and leukocyte receptors. The results of our study were consistent with the study of Jamil *et al.*^[9] who showed a significant decrease in post-operative pain (VASscore) just after surgery and at 2, 6, 12, and 24 hours after surgery in patients undergoing laparoscopic cholecystectomy. Another study by Asad *et al.*^[10] and Ahmad *et al.*^[11] found a significant decrease in post-operative mean pain score as assessed by VAS in patients receiving dexamethasone.

In our study, the meantime taken for the first rescue analgesic by the patients in the group 1 was significantly higher than that of the group 2. The timing of dexamethasone injection is important in reducing post-operative pain since the initiation of its biological effect occurs 1-2 hours after injection. Our results are consistent with the studies of Joung *et al.*^[12] Shirazi *et al.*^[13] and Sharma *et al.*^[5] who found that the time to requirement of the first dose of rescue analgesia was prolonged in the dexamethasone group as compared to the control group. In the present study, the mean total amount of rescue analgesic used in 24 hours in the Group 1 and Group 2 was 1.18 ± 0.38 and 2.25 ± 0.44 respectively. There was a statistically significant decrease in the amount of analgesia used in the dexamethasone group as compared to the normal saline group. Mitchell *et al.*^[3] did a systematic review and metaanalysis on impact of dexamethasone on post operative pain in adults undergoing general anaesthesia for elective abdominal surgeries and concluded that a single perioperative dose of dexamethasone leads to better analgesia, decrease opioid requirement and increase the time to first analgesia. They further emphasized that the administration of intermediate dose as used in our study has the greatest impact on outcomes. Similar results of a decrease in the total amount of rescue analgesia used in the dexamethasone group have been found by Gomez-Hernandez *et al.*^[14] and Koh *et al.*^[15]

On comparing the adverse effects in the two groups, the incidence of nausea and vomiting was significantly lower

in the dexamethasone group as compared to the normal saline group. The antiemetic mechanism of dexamethasone is caused by central inhibition of prostaglandin synthesis, inhibition of endogenous opioid release and changes in the permeability of blood brain barrier to serum proteins.^[16,17,18] There was no incidence of perianal pruritus reported in our study.

Conclusion

Pre-emptive use of dexamethasone 8 mg intravenously in patients undergoing laparoscopic cholecystectomy under general anaesthesia resulted in a significant decrease in overall VAS score post-operatively, increases the duration for first rescue analgesia and decreases the total number of analgesics used with minimal adverse effects. It can be used as a component of multimodal analgesia.

Limitations

The main limitation of our study is that we have used a single dose of dexamethasone (8 mg). However, researchers have used it in dose of 1.25-20 mg. Secondly, duration of action of dexamethasone is persists for 72 hours but we have monitored the patients only for 24 hours as most of the patients of laparoscopic cholecystectomy are discharged after 24 hours.

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Nil.

Conflicts of Interest

There are no conflicts of interest.

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