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Study of the Effect of Pre-operative Single Dose Intravenous Dexamethasone on Peak Expiratory Flow Rate and Post Operative Analgesia after Laparoscopic Cholecystectomy

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Abstract

Background: Surgical trauma although less in laparoscopic cholecystectomy compared to open cholecystectomy, still provokes neuroendocrinal stress response causing significant post operative pain with visceral, parietal and shoulder components. **Methods:** 80 patients aged 20-50 years of ASA physical status I and II were randomly allocated into two groups of 40 each. The patients in group D received 2 ml (8 mg) intravenous (i.v) dexamethasone 90 minutes before skin incision. The patients in group C received 2 ml of normal saline i.v. over same period. Intensity of surgical site pain at rest, at deep inspiration and shoulder pain was assessed at 2, 6, 12 and 24 hours post surgery using Visual Analogue Scale (VAS). Analgesic consumption was also recorded. Peak expiratory flow rate was compared in both the groups at baseline, 6, 12 and 24 hours post surgery. **Results:** Dexamethasone significantly reduced dynamic component of incisional pain at 2 hours, visceral pain at 2 hours at rest ($p = 0.003$) and coughing ($p = 0.000$) and also at 6 hours on coughing ($p = 0.001$), reducing significantly the overall analgesic consumption (37.5 ± 37.98 mg in dexamethasone group and 101.25 ± 60.168 mg in the Control group. $p = 0.000$). Dexamethasone significantly improved post operative pulmonary function ($p < 0.05$). **Conclusion:** Single dose 8 mg dexamethasone given 90 minutes before skin incision in patients undergoing laparoscopic cholecystectomy is associated with lesser reductions in peak expiratory flow rate, requirement of rescue analgesics and lesser incidence of post operative nausea and vomiting.

Keywords: Cholecystectomy, Dexamethasone, Laparoscopic Postoperative Pain, Peak Expiratory Flow Rate

Introduction

Laparoscopic cholecystectomy is one of the most common elective surgical procedures and pain, though less than open technique, is still a dominant complaint and the primary reason for prolonged convalescence after laparoscopic cholecystectomy and may also predict development of chronic pain[1,2]. The overall pain is a conglomerate of three different and clinically separate components - incisional, visceral and shoulder pain, which is due to incision on the abdominal wall, trauma due to removal of gall bladder, diaphragmatic irritation due to carbonic acid formed by combination of CO_2 with peritoneal fluid. In addition, the release of inflammatory mediators is central to the eruption of pain[3]. All these factors can significantly affect the post operative respiratory function[4].

Various analgesic approaches have been studied which includes use of NSAIDS/COX-2 inhibitors, local anaesthetics (incisional, intraperitoneal instillation),

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opioids, steroids, epidural analgesia, gabapentin, clonidine and ketamine[2]. Glucocorticoids are important modifiers of post operative physiologic inflammatory, humoral and immunologic responses by regulation of trauma induced humoral mediators[5]. Preoperative single i.v. dose of dexamethasone, in addition to being simple, safe and inexpensive, obviates the need for multiple drugs and has been found to potentiate post operative analgesia and reduce the incidence of post operative nausea and vomiting[6]. However, there are few studies analyzing its impact on respiratory parameters in patients undergoing laparoscopic cholecystectomy. Hence, this study was conducted to determine the efficacy of preoperative single dose dexamethasone (8 mg i.v.), given 90 minutes before the incision, on post operative peak expiratory flow rate and post operative pain.

Materials and Methods

The study was a prospective randomized double blind clinical trial conducted in a tertiary hospital between May 2013 and November 2013, after approval from the Hospital Ethics Committee. The research method was explained to the patients to obtain their written consent. Sample size was estimated based on observations from a previous study[7]. Assuming an effect size of 25 lts/sec in PEFR at 24 hours between the two groups and a power of 80% and alpha error of 5%, the minimum sample size required was 37 in each group. A final sample of 40 patients in each group was taken to compensate for possible drop outs. 80 patients belonging to American Society of Anaesthesiologists (ASA) Class I and II aged 20-50 yrs scheduled for elective laparoscopic cholecystectomy were studied. Patients on steroids, analgesics, anti emetics, patients with respiratory disorders, sleep disorders, obesity (BMI > 35 kg/m^2), poorly controlled diabetes, endocrine disorders, motion sickness, contraindication for study drug and conversion to laparotomy during surgery were excluded from the study. The patients were randomly allocated into two groups: Saline group (Group C, n = 40) and dexamethasone group (Group D, n = 40).

Randomization was done based on a computer generated randomization sequence (www.random.org). The numbers generated were placed in sequentially numbered opaque sealed envelopes and opened just before intervention to ensure allocation concealment.

Pre anaesthetic check up was done one day prior to the surgery and necessary investigations were done. All patients were explained about study protocol and trained to use Visual Analogue Scale (VAS). Patients were kept fasting for 6 hours and administered tablet alprazolam 0.5 mg and tablet ranitidine 150 mg on the night before surgery.

Monitoring included Electrocardiography (ECG), oxygen saturation (SpO_2), Non-Invasive Blood Pressure (NIBP), End tidal Carbon Dioxide ($EtCO_2$) and respiratory rate. All patients received standard premedication with midazolam 0.03 mg/kg glycopyrrolate 0.005 mg/kg and fentanyl 2 mcg/kg intravenously. After preoxygenation with 100% oxygen, anaesthesia was induced with propofol 1.5–2 mg/kg and intubation facilitated with suxamethonium 1.5 mg/kg intravenously. A pneumoperitoneum was established. The intra abdominal pressure was maintained at 12-14 mm Hg throughout. Intraoperatively, depth of anaesthesia was maintained with isoflurane 1%-2%, air in oxygen 50% to ensure entropy values within 40–60 and intravenous vecuronium 0.02 mg/kg boluses for maintenance of muscle paralysis. Heart rate, systolic, diastolic and mean arterial pressures were recorded every 5 min till the end of surgery. Tachycardia and hypertension (more than 20% from baseline), inspite of adequate depth of anaesthesia was managed with intravenous fentanyl 1 mcg/kg bolus. Residual neuromuscular blockade was reversed with neostigmine 0.05 mg/kg and glycopyrrolate 0.005 mg/kg. Patients were extubated after adequate recovery of muscle power. Diclofenac 100 mg suppository was inserted to all patients at the end of surgery.

An anaesthesiologist unaware of group allocation recorded the peak expiratory flow rate using Wright's peak expiratory flow rate meter in litres/sec. at 6, 12 and 24 hours post surgery. At each session, three readings were taken and the best of three was considered. Pain was assessed at rest (static pain) and during deep inspiration and movement (dynamic pain) using visual analogue scale and VAS scores for static and dynamic pain was recorded at 2, 6, 12 and 24 hours after surgery. Diclofenac 75 mg was administered as intravenous infusion over 20 minutes for rescue analgesia when the VAS score was 3 or more. If pain persisted even after administration of diclofenac,

tramadol 50 mg was administered intravenously. The post operative rescue analgesic requirement for 24 hours was recorded. Ondansetron 4 mg was administered intravenously as rescue anti emetic. Also patients were also observed for nausea, vomiting, headache and dizziness.

All data collected and entered in Microsoft excel sheet. Quantitative data was analyzed for normal distribution and are mentioned as mean ± standard deviation or median with interquartile range as suitable. Categorical data is presented as numbers and frequencies.

Student t test (two tailed, independent) was applied for comparison of quantitative data between two groups. Repeated measures ANOVA were used for intragroup comparison. Chi-square/Fisher Exact test was used to find the significance of study parameters on categorical scale between two or more groups. p value <0.05 was considered significant. The statistical analysis was done using statistical software SPSS version 17.

Results

A total of 83 patients were enrolled for the study and all patients received intervention. 2 patients in group C and one patient in group D were excluded as there was conversion to open surgery due to adhesions, 40 patients were included for final analysis in each group. There were no significant differences in demographic parameters and duration of surgery between the groups (Table 1).

Table 1. Demographical data

	Group C (n = 40)	**Group D (n = 40)**	**P value**
Age (yr)	37.66 ± 10.72	35.16±12.29	
BMI (kg/m^2)	26.61 ± 2.65	27.36 ± 1.68	
Height (cm)	156.15 ± 3.43	155.73 ± 3.85	
Sex (M/F)	16/24	20/20	
ASA (I/II)	36/4	34/6	
Duration of surgery (min)	68 ± 16.86	64.25 ± 14.03	0.28

The preoperative peak expiratory flow rate was comparable between the groups. Post operatively, PEFR was comparable between the groups at 6th hour, but lower in group C compared to Group D at 12th and 24th hour. The PEFR values never reached baseline levels in both groups at 24 hours. There was greater median decrease in PEFR from baseline in group C compared to group D at all time points of measurement (Table 2). The maximum reduction in PEFR was noted at 6 hours after surgery with an average reduction of 28% in group C and 22% in group D from baseline.

The 24 hour median (IQR) rescue analgesic consumption (diclofenac) was 75 (75–150) mg in group C compared to 37.5 (0–75) mg in group D (p = 0.000) which was clinically and statistically highly significant. 8 patients in group C and 3 patients in group D required a single dose of intravenous tramadol in 24 hours in addition to diclofenac (p – 0.10).

Table 2. Comparison of peak expiratory flow rates

PEFR (lts/min) (mean ± SD)	Group C (n = 40)	Group D (n = 40)	P value
Basal	438.25 ± 38.29	421.5 ± 52.6	0.10
6 hrs	314.5 ± 35.51	327 ± 47.57	0.18
12 hrs	319.75 ± 35.70	345.75 ± 51.58	0.01
24 hrs	329 ± 40.18	368.75 ± 46.25	<0.001
PEFR reduction from baseline (lts/min) (median (IQR)			
At 6 hrs	120 (100-142.5)	100 (67.5–120)	<0.001*
At 12 hrs	110 (100–130)	80 (50 -100)	<0.001*
At 24 hrs	105 (80–130)	50 (30–62.5)	<0.001*

IQR – Interquartile range, *- Mann Whitney U test

The median static pain scores at 2 hours was significantly lower in the group D than group C (p = 0.003) (Figure 1). The dynamic component of pain at 2 hours and 6 hours postoperatively was significantly less in group

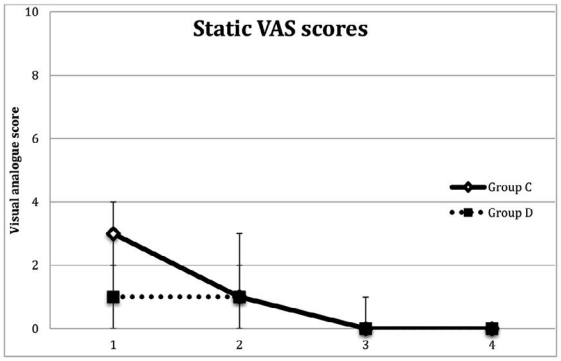

Figure 1. Comparison of static VAS scores between the groups.

D compared to group C (p value <0.001 at 2 hours and 0.001 at 6 hours respectively) (Figure 2). Shoulder pain was minimal in both the groups throughout the 24 hours post operative period. (Figure 3).

The average intraoperative consumption of fentanyl was 137.85 ± 20.84 mcg in group C and 136.25 ± 15.14 mcg in group D (p – 0.69). Intraoperatively, hypertension was noted in 5 and 7 patients in group C and group D respectively (p – 0.53) and tachycardia was noted in 6 and 7 patients in group C and group D respectively (p – 0.76). Incidence of post operative nausea and vomiting, need for rescue anti emetic was more in group C compared to group D (Table 3). None of the patients had any other side effects such as dizziness, headache or dysphoriain the post operative period.

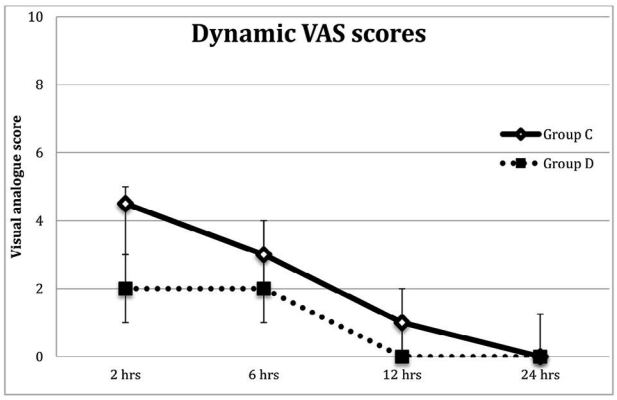

Figure 2. Comparison of dynamic VAS scores between the groups.

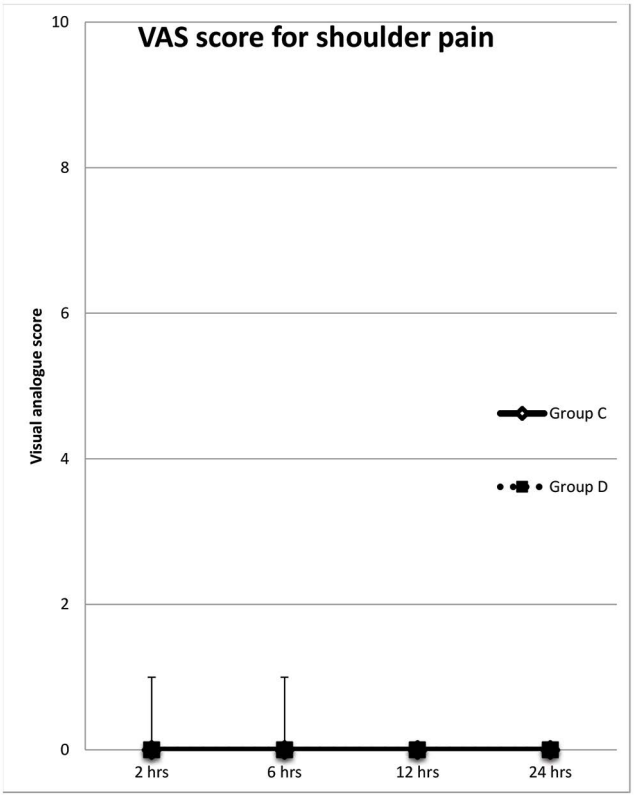

Figure 3. Comparison of VAS scores for shoulder pain between the groups.

Table 3. Comparison of Post Operative Nausea and Vomiting (PONV)

Parameter	Group C (n = 40)	Group D (n = 40)	P value
Incidence of PONV	31	7	<0.001
+Rescue anti emetic requirement			
0 doses	9	33	P < 0.001
1 dose	27	7	
2 doses	4	0	

Discussion

In the present study, it was noted that preoperative intravenous administration of dexamethasone 8 mg resulted in lesser reduction in PEFR and reduced requirement of post operative analgesics and anti emetics.

The analgesic effects of glucocorticoids (Dexamethas one) are provided through inhibition of the phospholipase enzyme and accordingly blockage of both the cyclooxygenase and the lipoxygenase pathway in the inflammatory chain reaction, as well as suppressing tissue levels of bradykin in and release of neuropeptides from nerve endings, both of which may enhance nociception in the inflamed tissue and the surgical wound[8,9]. The antiemetic effects of dexamethasone may be due to its inhibitory effects on serotonin, synthesis of prostaglandins and release of endogenous opioids[8,10].

In an earlier dose finding study, it was observed that a dose of 8 mg provided optimal anti emetic effect when used with ondansetron, where as the optimal dose for pain relief is not clear[11]. We selected a dose of 8 mg for our study.

Small dose of dexamethasone was found to improve quality of recovery scores including respiratory functions in patients undergoing cardiac surgery[12].

One study noted early recovery of pulmonary functions and significant improvement in PEFR with dexamethasone in patients undergoing laparoscopic cholecystectomy whereas; another author did not find any significant difference in pulmonary function in both the groups. There was significant improvement in PEFR after 12 hours in the present study[9,13].

The effect of dexamethasone on post operative pain scores and rescue analgesics are inconsistent. Few studies have reported reduction in pain scores and analgesic consumption with preoperative administration of intravenous dexamethasone, where as some have shown no significant benefit[9,10,13–15]. A metanalysis reported significant beneficial effects of dexamethasone on PONV where as no effect on post operative analgesic consumption in patients undergoing laparoscopic gynaecological surgeries[16].

Dexamethasone is consistently associated with reduction in PONV scores and requirement of rescue anti emetic medications and is concurrent with the observations of our study[17–21].

The present study has limitations. Respiratory parameters such as forced vital capacity, forced expiratory volume in one second were not studied, which would have given more insight into respiratory function. The duration of observation was also restricted to 24 hours and time taken for PEFR to reach baseline was not observed.

Conclusion

A single dose of 8 mg intravenous dexamethasone given intravenously 90 min before skin incision in patients undergoing laparoscopic cholecystectomy under general anaesthesia is associated with lesser reduction in post operative peak expiratory flow rate and reduction in rescue analgesic and anti emetic requirement.

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