ISSN 2347-5579

Unique Journal of Medical and Dental Sciences

Available online: www.ujconline.net

Research Article

DEXAMETHASONE IN PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING AFTER LAPAROSCOPIC CHOLECYSTECTOMY: A PROSPECTIVE RANDOMIZED DOUBLE BLINDED STUDY

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Received: 30-09-2014; Revised: 27-10-2014; Accepted: 25-11-2014

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ABSTRACT

Background: Post operative nausea vomiting (PONV) is a distressing complain in patients undergoing laparoscopic cholecystectomy (LC). To determine whether intravenous Dexamethasone (8mg), during induction of anaesthesia, would decrease early postoperative nausea and vomiting PONV after LC.

Methods: In this double- blind, randomized controlled trial, 132 patients who underwent laparoscopic cholecystectomy were divided in two groups. In first group, 66 patients, who received Inj. Dexamethasone 8 mg (dexona group) were compared with placebo group of 66 patients who received Inj. Normal Saline (placebo group).

Results: Dexona group showed low frequency of nausea when compared to placebo group with p value of 0.02 at 12 hours post operatively. The incidence of nausea at 24 hours and vomiting was not significant.

Conclusion: Inj. Dexamethasone given during induction of anesthesia effectively controls postoperative nausea requiring medication.

Keywords: Dexamethasone, anaesthesia, Nausea, Vomiting, Cholecystectomy.

INTRODUCTION

Cholelithiasis is one of the commonest surgically treated disease all over world with a variable prevalence rate between 5-22% in general population[1,2]. Laparoscopic cholecystectomy (LC) is presently considered to be the gold standard for the treatment of symptomatic cholelithiasis and with advent of better intra-operative and post-operative care it is being performed even as day care surgery[3]. LC provides the advantage of smaller scars and reduced postoperative pain, a shorter hospital stay, prompt bowel activity, diminished neuroendocrine metabolic response and earlier return to normal activity[4]. The primary aim of LC is to provide convenience to the patients by abbreviating hospitalization, although patient's post operative convalescence remains the ultimate priority.

Postoperative nausea and vomiting (PONV) is an unpleasant, distressing, and exhausting experience for patients undergoing laparoscopic procedures[5,6]. PONV can thus defeat the very purpose of minimally invasive day care approach of LC by delaying oral intake, increasing nursing requirement and ultimately increasing post operative stay. The exact aetiology of PONV is not well understood but is thought to be the result of stress response of the body to surgical trauma as well as CO_2 pneumoperitoneumm which stimulates a series of hormonal, metabolic, CNS and inflammatory changes in the body. Among the commonly used antiemetics currently prescribed for PONV, serotonin subtype 3 antagonists (e.g., ondansetron and granisetron) are commonly used but are expensive and have significant cardiac and CNS side effects[5,7]. Other currently used, low-cost antiemetics (e.g., anticholinergics, antihistamines, and dopamine receptor antagonists) have side effects, such as sedation, dry mouth, restlessness, changes in arterial blood pressure, and extrapyramidal symptoms[5]. Dexamethasone, a corticosteroid, is an inexpensive and effective antiemetic drug, with minimal side effects after a single-dose administration[8,13]. It was first reported in 1981 as an effective single dose antiemetic in patients receiving cancer chemotherapy[9]. Since then, dexamethasone has been widely applied in the prevention of

nausea and vomiting after chemotherapy[7-11]. Dexamethasone can be a cheap and safe drug that can prevent PONV following LC but dose used in various studies is variable[7-12].
The aim of this double blind placebo controlled study was to evaluate the efficacy of single-dose dexamethasone (8 mg) on the prophylaxis of post operative nausea and vomiting after LC. Normal saline injection was used as control.

MATERIALS AND METHODS

The study was conducted at a University hospital between July 2012 to December 2012 among consecutive patients undergoing elective LC for symptomatic gallstones aged between 18-80 years with ASA I/II score. The exclusion criteria were pregnancy, comorbid conditions, patients taking opioids, tranquilizers or steroid, history of alcohol or drug abuse, conversion to open cholecystectomy, development of surgical complications requiring prolonged hospital stay and any suspicion of malignancy. After enrollment in the study the patients were randomly allocated to Dexamethasone group or placebo group by use of computer generated random number table. The study medication was prepared by a nurse in identical 2ml syringe to ensure blinding of surgeon, anaesthetist, patient and post operative evaluator. The drug was given by the anaesthetist immediately after induction of anaesthesia. The dexona group received Inj Dexamethasone 8 mg IV and placebo group received Inj normal saline 2 ml IV (Fig 1).
The anaesthesia techniques, anaesthetic drugs and surgical techniques were standardized. Anesthesia was induced with propofol 2–2.5 mg/kg IV, glycopyrrolate 0.2 mg IV, and fentanyl 2 µg/kg IV. Endotracheal intubation was facilitated with vecuronium 0.15 mg/kg IV. Anesthesia was maintained with 1.0%–2.5% (inspired concentration) isoflurane in oxygen. Ventilation was controlled mechanically and adjusted to keep an end-tidal CO_2 partial pressure of 30–40 mm Hg. Neuromuscular block was maintained with vecuronium IV. After tracheal intubation, a nasogastric tube was placed to promote baseline emptying of the stomach of air and gastric contents. All LCs were performed by VKS who is the senior most surgeon of the unit. During surgery, patients were positioned in the reverse Trendelenburg position (15^0), with the right side elevated. The abdomen was insufflated with CO_2, with an intraabdominal pressure of 12 mm Hg. LC was performed with the standard four ports of the abdomen. The IV fluid used during surgery was 0.9% saline. At the end of the surgery residual neuromuscular blockade was antagonized with neostigmine 0.05 mg/kg and glycopyrrolate 0.6 mg IV, and the trachea was extubated. No antiemetic drug was given intra operatively. Patient parameters, disease parameters, duration of surgery, volume of CO_2 insufflated and bile spillage were recorded.
After surgery patients were observed for minimum 24 hours before discharge. Immediately post operative observation was done in post operative ward where vital signs monitoring were done every 15 minutes and oxygen saturation was monitored continuously. Post operative fluid given was 5% Dextose and Inj Diclofenac 75 mg was given for postoperative analgesia. After observation for 1 hour and with stable vital signs patients were transferred to surgical ward. Postoperative pain was assessed with a 10-cm visual analog scale (0 = no pain to 10 = most severe pain) score. Analgesia was given with 75 mg of diclofenac every 12 h or when patients requested. Post operative nausea and vomiting was assessed by a nurse blinded to the randomization of the patient. Nausea was defined as subjective unpleasant sensation associated with an urge to vomit and vomiting as spontaneous forceful expulsion of gastric contents through the mouth. The events of nausea were recorded only when the patient demanded antiemetic and all events of vomiting were recorded. The rescue antiemetics used was metoclopramide 10 mg IV. The VAS data was collected at 12 and 24 hours and PONV data were collected every 4 hourly for first 24 hours and in uneventful cases patients were discharged at 24 hours.
Statistical analysis was carried out using SPSS version 15. Chi- square and Mann-Whitney U test were used for qualitative data. Independent sample t-test and one way Anova was used for quantitative data. P value < 0.05 was considered statistically significant.

RESULTS

Of 139 patients enrolled in the study 132 completed the study. One patient had conversion to open cholecystectomy, 4 had coexistent comobidities, 1 had co existent small bowel GIST and 1 had suspicion of malignancy. Of the 132 patients 66 patients were allotted to either of the two groups. The patients charecteristics, disease duration, operation time, stone parameters, bile leak and VAS score at 12 and 24 hours were comparable in both dexona group and placebo group (Table 1).
The dexona group showed significantly low events of nausea requiring antiemetics as compared to placebo group (8 vs 20, p value 0.02) at 12 hours while nausea at 24 hours and vomiting at 12 and 24 hours were similar in either of the two groups (Table 2).
On comparision of various variables in the dexona and the placebo group among patients with or without nausea the difference was found to be insignificant (Table 3 and 4).

DISCUSSION

Laparoscopic surgery has decreased the morbidity associated with cholecystectomy and has become a routine procedure for symptomatic cholelithiasis[13,14]. However, a frequent incidence of PONV ranging between 53%–72% has been reported[5,6.15-18].
A systematic review by Wu et al. reported post-discharge nausea in 17% and vomiting in 8% of patients after outpatient surgery[19]. LC is presently well accepted as a day care surgery and PONV can be a hindrance in convalescence and early discharge of these patients.
The cause of PONV after LC performed with the patient under general anesthesia is not fully understood. A variety of factors including age, female sex, history of motion sickness and previous PONV, menstruation, smoking, operative procedure, anesthetic technique, and postoperative pain are considered to affect the incidence of PONV[5,20]. The use of an opioid (e.g., fentanyl) during anesthesia is anathor factor contributing to an increased incidence of PONV[20]. Laparoscopic procedures

have been known to cause more significant PONV because of the creation of pneumoperitoneum involved in the procedure. This has its effects by two mechanisms, one of which is the stimulation of mechanoreceptors in the gut which are stimulated due to mechanical stretching of the structures in the creation of pneumoperitoneum. The second mechanism results from the absorption of CO_2, which is used in the creation of pneumoperitoneum. CO_2 is known to cause increased PONV by stimulation of nociceptors in the brain[19-22]. In this study, however, these factors were well balanced among the treatment groups (Table 1) along with the standardized anaesthetic drugs and the pneumoperitoneum pressure. Therefore, the difference in the rates of patients experiencing PONV among the groups can be attributed exclusively to the study drug.

Table 1: Comparison of variables between dexona and placebo groups

Parameters	Dexona group (n=66)	Placebo group (n=66)	p value
Age	42.09 ± 15.23 (24-75)	40.79 ± 14.61 (18-72)	0.72
Sex (M/F)	16 /50	22/44	0.42
Height (cms)	159.57 ± 10.69 (149-178)	160.14 ± 9.69 (149-180)	0.92
Weight (kg)	60.43 ± 14.09 (40-78)	55.29 ± 4.54 (50-63)	0.38
Disease duration (months)	1.15758 ± 1.13 (0.1-4.0)	1.0318 ±1.55 (0.1-8.0)	0.38
CO2 used (Litres)	58.91 ± 35.60 (22-190)	61.58 ± 37.87 (20-196)	0.74
Operating time (min)	20.36 ± 10.15 (10-45)	16.85 ± 6.48 (8-35)	0.19
Number of stones	1.97 ± 1.24 (1-5)	1.85 ± 1.48 (1-6)	0.38
Size of stones (mm)	6.42 ± 3.80 (2-18)	7.61 ± 4.03 (2-22)	0.14
Cholesterole stones	22 (33.3%)	30 (45.5%)	0.31
Mixed stones	44 (66.7%)	36 (54.51%)	0.31
Bile leak	30 (45.5%)	22 (33.3%)	0.3
Pain score 12 hours	1.42 ± 1.89 (0-5)	1.36 ± 1.18 (0-5)	0.92
Pain score 24 hours	1.85 ± 2.22 (0-7)	2.39 ± 2.22 (0-5)	0.29

Table 2: Post operative nausea and vomiting in dexona and placebo group

Assessment time	Parameter	Dexona group	Placebo group	p value
12 hours	Nausea present	8 (12.1%)	20 (30.3%)	0.02
	Vomiting present	4 (6.1%)	4 (6.1%)	NS
24 hours	Nausea present	2(3%)	4 (6.1%)	NS
	Vomiting present	0	0	NS

Table 3: Comparision of various parameters among patients without and with nausea in dexona group

Parameter	Without nausea (n=58)	With nausea (n=8)	p value
Disease time (months)	1.19 ± 1.11	0.93 ± 1.40	0.33
CO_2 used (Litres)	56.66 ± 32.06	75.25 ± 59.32	0.70
Surgery time (min)	20.28 ± 9.48	21.00 ± 16.15	0.58
Number of stone	1.97 ± 1.30	2.00 ± 0.82	0.61
Size of stone (mm)	6.62 ± 3.96	5.00 ± 2.16	0.46
Pain score at 12 hrs	1.41 ± 1.94	1.50 ± 1.73	0.85
Pain score at 24 hrs	1.72 ± 2.25	2.75 ± 2.06	0.33

Table 4: Comparision of various parameters among patients without and with nausea in placebo group

Parameter	Without nausea (n=58)	With nausea (n=8)	p value
Disease time (months)	0.94 ± 1.05	1.25 ± 2.40	0.80
CO_2 used (Litres)	63.87 ± 41.79	56.30 ± 28.02	0.71
Surgery time (min)	16.91 ± 6.72	16.70 ± 6.22	0.98
Number of stone	1.87 ± 1.39	1.80 ± 1.75	0.36
Size of stone (mm)	7.48 ± 4.36	7.92 ± 3.35	0.45
Pain score at 12 hrs	1.00 ± 1.60	2.20 ± 2.04	0.08
Pain score at 24 hrs	1.74 ± 2.14	3.90 ± 1.66	0.06

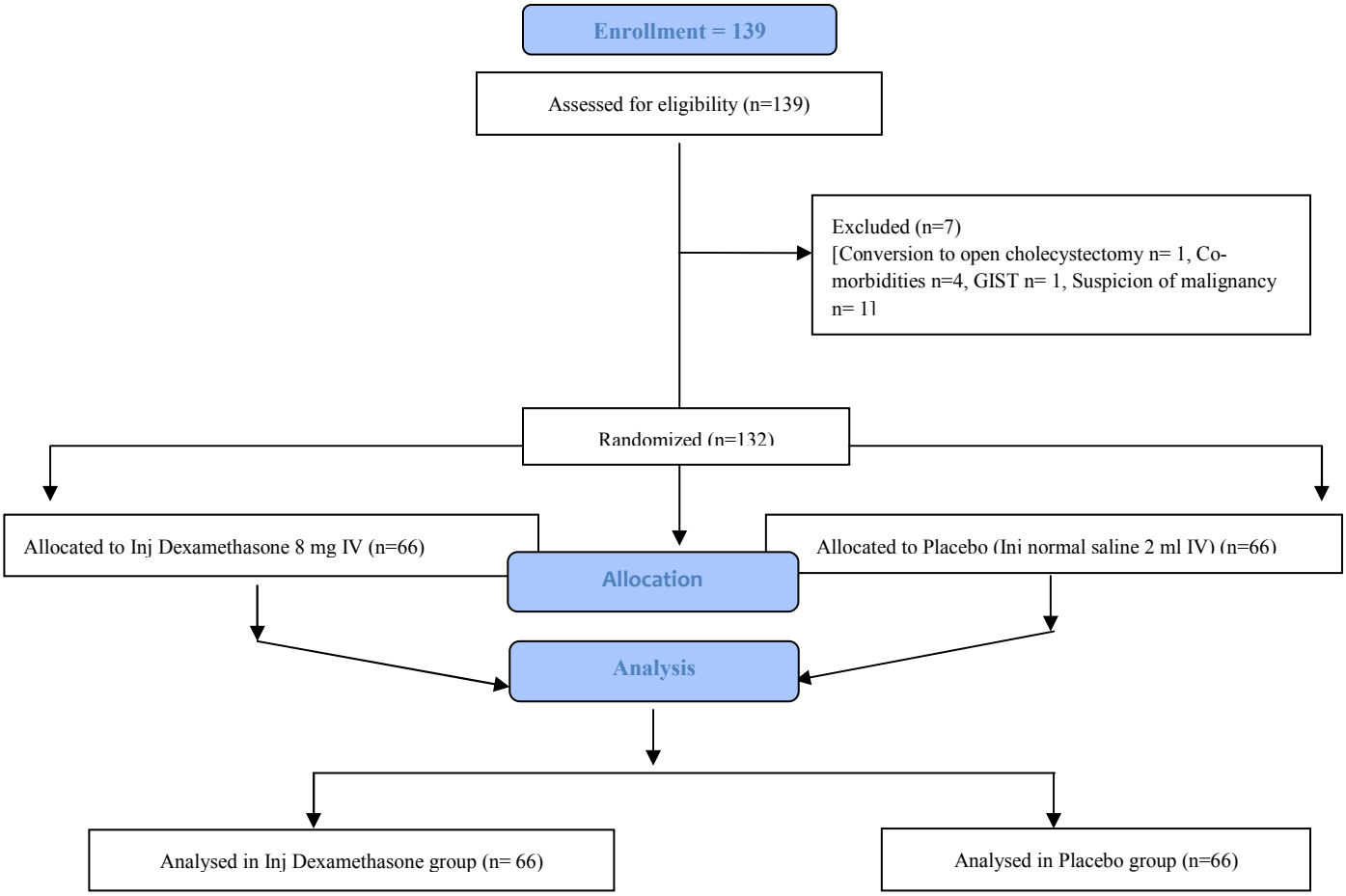

Figure 1: Consort Flow Diagram for study

The exact mechanism by which dexamethasone, a corticosteroid, exerts an antiemetic action is not fully understood. However, its antiemetic action is proposed both centrally by inhibition of the synthesis of prostaglandins[23], and changes in the permeability of the blood–brain barrier to serum proteins[24] as well as through some peripheral mechanism by inhibiting the production or secretion of serotonin[15,18]. Dexamethasone, a corticosteroid, has strong antiinflammatory actions and may significantly reduce tissue inflammation around the surgical sites and thus reduce the ascending parasympathetic impulses (like vagal stimulation) to the vomiting center and thus reduce PONV. In the present study we found that pre operative 8 mg dexamethasone reducd nausea after LC compared to placebo but the effect on vomiting was not significant. Various studies have been published favouring the use of preoperative dexamethasone in various dosages from 4-5mg to 8-10mg, combination and timing of administration in LC[7-12]. Seven randomized trials assessed the role of dexamethasone on PONV following LC[17,25-30]. The dose of dexamethasone in all these reports were 8mg as in the present study although the timings varied from 90 minutes preoperative to at the time of induction. In two trials dexamethasone was given with serotonin receptor antagonists and was found to further lower the rate of PONV from 20-35% to 3-5%[28,29].

We used single dose 8 mg dexamethasone just before induction without any other antiemetic and showed that it significantly reduced the incidence of nausea requiring medication. As compared to other studies we did not find any significant difference in the vomiting among the two groups. Apart from the above mentioned factors contributing to PONV following LC various other intra operative risk factors can contribute to PONV like volume of CO_2 used, duration of surgery, number, type and size of stones, bile spillage and VAS score at 12 and 24 hours. We analysed these factors among both the groups and found no significant difference. These factors were not analysed in previously published studies. Further these factors were again compared in patients having PONV and those not having PONV suggesting that the effect on nausea and vomiting can be attributed to the intervention and not to these risk factors (Table 3 and 4).

Dexamethasone lacks the sedative, dysphoric, and extrapyramidal signs associated with traditional antiemetics[5,20]. The single dose administration of dexamethasone lacks the corticosteroid associated adverse effects such as an increased risk for infection, glucose tolerance, delayed wound healing, superficial ulceration of the gastric mucosa, and adrenal suppression[31].

In previous reports also these adverse effects were not related to a single dose of dexamethasone administered[7-12, 17,25-30].

Thus this prophylactic antiemetic therapy with dexamethasone is considered to be relatively free of side effects.

CONCLUSION

In conclusion, prophylactic IV dexamethasone 8 mg given preoperatively at induction significantly reduces the incidence of PONV in patients undergoing LC.

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Source of support: Nil, Conflict of interest: None Declared