ORIGINAL PROF-1594

POSTOPERATIVE NAUSEA AND VOMITING (PONV);

PREOPERATIVE DEXAMETHASONE IN LAPAROSCOPIC CHOLECYSTECTOMY PATIENTS

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Article Citation:
Ali Z, Ahmad I, Ahmad T, Rehan AG. Postoperative nausea and vomiting (PONV); Preoperative dexamethasone in laparoscopic cholecystectomy patients. Professional Med J Sep 2010; 17(3):394-399.

ABSTRACT... Objective: To evaluate the effect of preoperative single dose injection dexamethasone for prevention of PONV in patients undergoing laparoscopic cholecystectomy and comparing it with normal saline (placebo). **Design:** Experimental RCT study. **Place and duration of study:** The study was conducted at Madina Teaching hospital, University Medical & Dental College, Faisalabad from January, 2008 to October 2009. **Materials and Methods:** After approval from the hospital ethical committee, 200 patients with ASA I & II were included in the study. We divided the patients into two groups; group I received preoperative dexamethasone (8mg) and the group II received normal saline (placebo) 90 minutes before the surgery. Patients were observed for any episodes of nausea or vomiting, need for rescue antiemetics, and complete responses in the postoperative period. The complete response was defined as no nausea, no vomiting, and no ant emetic medication during a 24-h postoperative period. This was also the primary efficacy end point of the study. The data was analyzed using Pearson's Chi square test with $P < 0.05$ taken as significant. **Results:** Nineteen patients (19%) in the dexamethasone group reported nausea, compared with 43 (43%) in placebo group ($p<0.05$). Eight patients (8%) in the dexamethasone group reported vomiting and twenty two patients (22%) in the placebo group reported vomiting ($P <0.05$). In group I, thirteen patients (13%) asked for rescue anti-emetic where as in group II (placebo group) thirty six patients (36%) asked for rescue anti-emetic ($p<0.05$). Seventy three patients (73%) in the dexamethasone group showed a complete response, compared with 35 (35%) in placebo group ($p<0.05$). **Conclusion:** We concluded that preoperative dexamethasone (8mg) reduces the incidence of PONV as compared to placebo. As it is a cheap, freely available drug causing no complications, it should be used in otherwise fit selected patients undergoing laparoscopic cholecystctomy.

Key words: Laparoscopic Surgery, Preoperative Dexamethasone, Placebo, Postoperative Nausea and Vomiting (PONV).

INTRODUCTION

PONV is common (53%–72%) in patients undergoing laparoscopic cholecystectomy (LC) for cholelithiasis[1,2]. Nausea and vomiting are among the most unpleasant experiences associated with surgery and one of the most common reasons for poor patient satisfaction rating in the postoperative period[3]. The etiology of postoperative nausea and vomiting is multi factorial.

Patient, anesthesia, and surgery related risk factors have been identified. Pediatric age group, female gender, obesity, non smoking, preoperative anxiety, and a history of severe motion sickness are patient related factors. Laparoscopic surgery (50-90%) and strabismus surgery (60-90%) are important types of surgery associated with postoperative nausea and vomiting. Prolonged duration of surgery and anesthesia also leads to more frequent postoperative nausea and vomiting. Postoperative factors that may increase the incidence of PONV are

Article received on: 21/12/2009
Accepted for Publication: 02/03/2010
Received after proof reading: 05/08/2010
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pain, dizziness, ambulation, early oral intake, and aggressive use of postoperative opiate analgesics[4].

A number of agents have been tried to decrease the incidence of PONV including ondanseron, dolasetron, granisetron, transdermal scopolamine, prochlorperazine, promethazine, droperidol, dexamethasone and ephedrine. Dexamethasone was reported as an effective anti-emetic in patients receiving cancer chemotherapy in 1981[5]. Dexamethasone is a high-potency, long-acting glucocorticoid with little mineralocorticoid effect that has been extensively used in the perioperative setting. The exact mechanism by which glucocorticoids decrease the incidence of nausea and vomiting is not fully understood, but probably can be explained by centrally mediated anti-emetic action via inhibition of prostaglandin synthesis, or inhibition of release of endogenous opoids[6].

Several clinical trials have been conducted to determine the effects of glucocorticoids on surgical outcome. The incidence of postoperative nausea and vomiting has been significantly decreased by preoperative single dose steroid administration in several studies[2,7]. The aim of the present study was to investigate whether preoperative dexamethasone can reduce PONV in patients undergoing laparoscopic Surgery.

MATERIALS AND METHODS

This is a prospective randomized study of 200 patients undergoing laparoscopic cholecystectomy (LC) from January 2008 to October 2009. We obtained the approval from the hospital ethical committee and got the informed consent from the patients for the following study.

INCLUSION CRITERIA

Patients with ASA I & II were included in the study.

EXCLUSION CRITERIA

Patients with history of motion sickness, migraine, PONV during a previous surgery, pregnant and lactating females were excluded from study. Patients who received opioids or tranquilizers for more than one week prior to LC were not included. Patients with uncontrolled hypertension, diabetics, or on steroids were excluded from the study. Patients were excluded if the operation was converted from LC to open cholecystectomy.

In the ward, before shifting the patient to preoperative area, patients were randomly allocated into two groups of 100 patients each. Group I patients were given 8 mgs of dexamethasone and Group II patients received 4 ml 0.9 % saline. This was administered by a staff nurse about 90 minutes before the surgery.

The anesthetic sequence was standardized. The patients received single dose of injection (ceftriaxone 1gm) at the time of induction of anesthesia. All patients received injection Diclofenac 50mg i/m thrice daily for day1 and then as and when required. If patients developed nausea or vomiting, they were given injection Ondansetron 4 mg intravenously, irrespective the group. All the patients received similar type of standardized anesthetic regimen - induction with Propofol, maintenance with Isoflurane, relaxation with Atracuronium and reversal with Neostigmine.

During surgery, patients were positioned in the reverse Trendelenberg position with the right side of the table elevated. The abdomen was insufflated at supraumbilical port with CO_2. During laparoscopy, intrabdominal pressure (IAP) was maintained at 12 mm Hg and at the end of surgery; $C0_2$ was removed by suction and manual compression of abdomen. LC was preformed using standard 4 ports technique with two 10 mm and two 5 mm ports. Gall bladder was extracted through the epigastric port.

Intra operative monitoring included ECG, pulse oximetry, and non invasive blood pressure monitoring, which recorded systolic, diastolic and mean arterial blood pressure. Duration of surgery was also recorded in each patient.

Nausea and vomiting were evaluated by the following variables: the incidence of nausea and vomiting, episodes of vomiting, rescue antiemetics, and complete responses. For the purpose of data collection, retching (same as vomiting but without expulsion of gastric

content) was considered vomiting. A vomiting episode was defined as the events of vomiting that occurred in a rapid sequence (<1 min between events). If events of vomiting were separated by >1 min, they were considered separate episodes. Vomiting that occurred more than four times within 24 h was considered severe vomiting. Rescue antiemetics (intravenous Ondansetron) were given if vomiting occurred or at the patient's request.

The treatment was repeated if necessary. The complete response was defined as no nausea, no vomiting, and no antiemetic medication during a 24-h postoperative period, and this was also the primary efficacy end point of the study. The data of PONV were collected by direct questioning by a team or by spontaneous complaints of the patients. The patients and the investigators who collected the data were blinded to the patient's group. Patients were followed up in hospital from the day of surgery, to the day of discharge. Day of operation was defined as D 0; first day was defined as D1 and so on.

The data was analyzed using Pearson's Chi square test with $P < 0.05$ taken as significant.

RESULTS

We included 200 patients in the study; 100 patients were enrolled for both the groups. The data obtained from the patients undergoing LC were analyzed using Pearson's Chi square test with $P < 0.05$ taken as significant.

The characteristics of the patients and duration of surgery were similar between the two groups, as shown in Table-I.

Table-I. Patient demographics.

	Group I	Group I I
No. of patients	100	100
Female	88	83
Male	12	17
Mean age (yrs)	28-68 (40)	25-70 (38)
Duration of surgery	25-70 Minutes (40)	20-65 Minutes (35)

After surgery, patients were observed for any episodes of nausea or vomiting, or whether the patient required any anti-emetic drug in the postoperative period. (Table-II).

Table-II. Postoperative nausea and vomiting.

	Group I (dexamethasone)	Group II (placebo)	P-value
Nausea	19	43	<.001
Vomiting	08	22	0.006
Rescue antiemetics	13	36	<.001
Complete response	73	35	<.001

(The complete response was defined as no PONV and no antiemetic medication during a 24-h postoperative period).

Nineteen patients (19%) in the dexamethasone group reported nausea, compared with 43 (43%) in placebo group ($p<0.001$). Eight patients (8%) in the dexamethasone group reported vomiting and twenty two patients (22%) in the placebo group reported vomiting ($P <0.05$). In group I, thirteen patients (13%) asked for rescue anti-emetic where as in group II (placebo group) thirty six patients (36%) asked for rescue anti-emetic ($p<0.05$). Seventy three patients (73%) in the dexamethasone group showed a complete response, compared with 35 (35%) in placebo group ($p<0.05$).We did not have any postoperative complications in the form of wound infection, or delayed wound healing. There were no statistically significant differences as regards the postoperative vital signs.

DISCUSSION

PONV is common in patients (53%–72%) undergoing laparoscopic cholecystectomy (LC) for cholelithiasis[1,2]. The incidence and severity of PONV have been significantly decreased as shown in several studies[8]. This prophylaxis also seemed to reduce postoperative pain and early convalescence. BisGaard et al concluded that

preoperative dexamethasone reduced pain, fatigue, nausea, vomiting and duration of convalescence in patients undergoing LC, as compared to placebo and they recommend the routine use of dexamethasone[8]. Dexamethasone also prevents PONV in patients undergoing hysterectomy, tonsillectomy, and thyroidectomy[9,10,11]. Fukami Y et al in his study of preoperative dexamethasone in laparoscopic cholecystectomy patients, reported that preoperative 8 mg dexamethasone significantly reduces PONV, pain, and fatigue after LC[12]. P Gupta et al concluded that preoperative intravenous low dose dexamethasone reduces the incidence of PONV[13]. Coloma et al and Rüsch et al reported that ondansetron plus dexamethasone prevents PONV more effectively than ondansetron alone in patients at high risk for PONV[14,15].

Bisgaard et al noted that dexamethasone may offer additional benefits over traditional antiemetics in improving surgical outcomes. Dexamethasone phosphate[8] mg I.V. given 90 minutes before laparoscopic cholecystectomy has been demonstrated to significantly reduce postoperative fatigue, pain, total opioid requirements, and levels of C-reactive protein, in addition to reducing the frequency of PONV[8]. While Heffernan and Rowbotham said that dexamethasone has now emerged as potentially useful prophylaxis for PONV; its efficacy is comparable with other antiemetics but it may be more effective in the prevention of late PONV[16]. Multiple dose corticosteroid therapy (>1 week) may cause side effects such as increased risk of infection, glucose intolerance, delayed wound healing, superficial ulceration of gastric mucosa, avascular necrosis of femoral head, and adrenal suppression. However, these side effects are not found after a single dose of dexamethasone therapy[17,18]. A recent metanalysis concluded that, perioperative administration of high dose of methylprednisolone (30-35 mg/kg), a dose approximately 50 times that of the dose used in the study, was not associated with significant side effects[19]. Mohamed A. Dabbias in his study showed that single dose dexamethasone does not affect blood pressure, pulse rate or glucose level intraoperatively or postoperatively[20]. We did not have any postoperative complication which could be attributed to dexamethasone prophylaxis.

Many studies have used preoperative dexamethasone administration just before induction of anesthesia[17]. In the present study, we administered the IV dexamethasone, 90 min before skin incision was made. Glucocorticoids act on the intracellular receptor and the effects are mediated through altered prostaglandin synthesis, via gene transcription. Onset of biologic action of glucocorticoids is 1-2 hours. Since action of early mediators of metabolic response to surgery occurs immediately after surgical incision, it seems appropriate to administer Dexamethasone 1-2 hours preoperatively, to achieve full postoperative benefits of the treatment. The timing of steroid administration seems to be the key (1-2 hr preoperatively), if excess inflammatory and related postoperative morbidity is to be attenuated.

In our study, we found that incidence of PONV was significantly lower in dexamethasoe group as compared to control group. Incidence of nausea was 19% in dexamethasone group as compared to 43% in control group and incidence of vomiting was 8% as compared to 22% in control group, both of which are statistically significant. It also reduced the requirement for rescue antiemetics quite significantly (13% vs. 36%) in dexamethasone group. In dexamethasone group, complete response was seen in 73% of patients as compared to 35% of patients in control group.

CONCLUSION

Dexamethasone improved significantly postoperative nausea and vomiting and lowered the need for rescue antiemetics significantly in the postoperative period. Since the regimen used is safe and cheap, we suggest that preoperative dexamethasone should be used as routine in otherwise healthy patients undergoing elective laparoscopic cholecystectomy.

REFERENCES

1. Fujii Y, Saitoh Y, Tanaka H. **Ramosetron vs. granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy.** Can J Anaesth 1999;46:991–3.

2. Wang JJ, Ho ST, Liu HS, Ho CM. **Prophylactic antiemetic effects of dexamethasone in woman undergoing ambulatory laparoscopic surgery.** BJA 2000;84:459-62.

3. Klockgesthes R., Piorck V., Crozier TC, Kettler D. **Nausea and vomiting after laparoscopic surgery: a comparison of propofol and thiopentone/halothane anesthesia.** Eur J anaesthiol 1996;13:3-9.

4. Morgan D. **Management of Postoperative Nausea and Vomiting: The Role of Droperidol, Metoclopramide, and Ondansetron.** P&T News: 1994;14(7):245-51.

5. Italian Group for antiemetic research. **Dexamethasone, granisetron or both for prevention of nausea and vomiting during chemotherapy for cancer.** N Eng J Med 1995; 332:1-5.

6. Sapolsky RM, Romero LM, Munck AV. **How do glucocorticoids influence stress response? Integrative, permissive, suppressive stimulatory and preparatory action.** Endocr Rev 2000; 21:55-89.

7. Callery MP. **Preoperative steroids for laparoscopic surgery.** Ann Surg 2003;238:661-2.

8. Bisgaard T, Klarskov B, Kehlet H, Rosenberg J. **Preoperative dexamethasone improves surgical outcome after laparoscopic cholecystectomy-a randomized double blind placebo controlled trial.** Ann Surg 2003;238:651-60.

9. Henzi I, Walder B, Tramér M. **Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systemic review.** Anesth Analg 2000;90:186–94.

10. Wang JJ, Ho ST, Liu YH, et al. **Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy.** Br J Anaesth 1999;83:772–5.

11. Wang JJ, Ho ST, Lee SC, et al. **The use of dexamethasone for preventing postoperative nausea and vomiting in females undergoing thyroidectomy: a dose-ranging study.** Anesth Analg 2000;91:1404–7.

12. Fukami Y, Terasaki M, Okamoto Y, et al. **Efficacy of preoperative dexamethasone in patients with laparoscopic cholecystectomy: a prospective randomized double blind study.** J Hepatobilliary Pancreat Surg 2009;16(3):367-71.

13. P Gupta, J Khanna, A K Mitramustafi, V K Bhartia. **Role of pre-operative dexamethasone as prophylaxis for postoperative nausea and vomiting in laparoscopic surgery.** Journal of Minimal Access Surgery 2006;2(1):12-15.

14. Coloma M, White PF, Ogunnaike BO, Markowitz SD, Brown PM, Lee AQ, Berrisford SB, Wakefield CA, Issioui T, Jones SB, and Jones D: **Comparison of Acustimulation and Ondansetron for the treatment of established PONV.** Anesthesiology 2002;97:1387-92.

15. Rüsch D, Eberhart L, Biedler A, Dethling J, and Apfel CC. **Prospective application of a simplified risk score to prevent postoperative nausea and vomiting.** Can J Anesth 2005;52:478-84.

16. Heffernan AM, Rowbotham DJ. **Postoperative nausea and vomiting-time for balanced antiemesis?** Br J Anaesth, 2000,85,(5):675-77.

17. White PF. **Prevention of postoperative nausea and vomiting- a multimodal solution to a perspective problem.** N Eng J Med 2004; 350:2511-2.

18. Madan R, Bhatia A, Chakithandy S, Subramaniam R, Rammohan G, Desphande S, Singh M, and Kaul HL. **Prophylactic Dexamethasone for Postoperative Nausea and Vomiting in pediatric Strabismus surgery: A Dose ranging and safety evaluation study.** Anesth Analg 2005;100:1622-26.

19. Sauerland S, Nagelschmidt M, Mallman P. **Risk and benefits of preoperative high dose of methlyprednisolone in surgical patients- a systemic review.** Drug Safety 2000;23:443-61.19.

20. M. A. Daabiss: **Ephedrine- Dexamethasone Combination Reduces Postoperative Nausea and Vomiting in Patients Undergoing Laparoscopic Cholecystectomy.** The Internet Journal of Anesthesiology. 2008 Volume 18 Number1.

PREVIOUS RELATED STUDIES

Farzi F, Mehrafza M, Mirmansouri A, Oudi M, Tabar ZM, Hoseeini A. Propofol vs. Thiopental na on pregnancy outcome and postoperative nausea and vomiting (ponv) in art cycle. Professional Med J Sep 2009; 16(4): 542-549.