

# Role of Dexamethasone in Postoperative Nausea and Vomiting in Laparoscopic Cholecystectomy

ASAD ALI SHAH, ATIF PERVEZ, AZHAR BASHIR

## ABSTRACT

**Objective:** was to investigate the outcome in terms of Postoperative nausea and vomiting within 24 hours in patients undergoing Laparoscopic Cholecystectomy receiving preoperative dexamethasone and those not receiving .

**Study design:** Randomized, Placebo-controlled, Double blind study.

**Materials and methods:** 100 patients were randomized in two equal groups i.e., either Saline (S group) or Dexa (D group). Each of the group received either saline (2ml) intravenous (Group S) as placebo or dexamethasone (8mg) intravenous (Group D).

**Results:** Six patients (12%) in the treatment group and 15 (30%) in the control group had postoperative nausea. 6 patients (12%) treated with dexamethasone had vomiting as opposed to 15 (30%) receiving placebo. Nausea and vomiting were significantly reduced during the entire observation period compared with placebo: in particular, eleven patients (22%) in the treatment group had postoperative nausea and vomiting versus 26(52%) in the placebo.

**Conclusion:** Dexamethasone improves the surgical outcome by reducing disabling symptoms of nausea and vomiting without apparent side-effects. So preoperative dexamethasone may be used as a routine in patients undergoing elective laparoscopic cholecystectomy.

**Key words:** Laparoscopic Cholecystectomy, Postoperative nausea and vomiting, Dexamethasone .

---

## INTRODUCTION

Laparoscopic cholecystectomy (LC) is one of the most common , popular and accepted procedure for the patients with symptomatic cholelithiasis due to many advantages like small wound size, better cosmetic results, short postoperative hospital stay, decreased morbidity, cost effective and early return to job. Although serious adverse events are uncommon after Laparoscopic Cholecystectomy, 50% to 75% of patients experience postoperative nausea or vomiting (PONV).

The origin of postoperative nausea and vomiting after laparoscopic cholecystectomy is not entirely clear. Female sex, prolonged carbon dioxide insufflation, length of procedure, use of nitrous oxide, the utilization of slightly hypoxic mixtures during anaesthesia and postoperative opioid administration have been suggested as potential risk factors. PONV can lead to serious complications such as aspiration, dehydration, electrolyte disturbances and disruption of incision site. It can also lead to increase cost of treatment. Another impact of PONV, is the effect on patient, some regard it as more disabling than the operation itself. Dexamethasone has been reported to reduce the incidence of vomiting in patients undergoing chemotherapy and surgical procedures

including laparoscopic cholecystectomy. Few randomized clinical trials have addressed the effect of the administration of a perioperative single dose of a glucocorticoid on surgical outcome. The aim of this randomized, double-blind, placebo-controlled trial was to investigate whether a single dose of dexamethasone before surgery would improve nausea, vomiting and pain in patient undergoing laparoscopic cholecystectomy.

## MATERIALS AND METHODS

This study was conducted at Department of Surgery, Ibn-e-Siena Hospital affiliated with Multan Medical and Dental College from 1<sup>st</sup> March to 31<sup>st</sup> September 2010. Sample Size was 100 patients; 50 in each group. All those patient between 18-60 years of age being operated for laparoscopic cholecystectomy, American Society of Anesthesiology class I & II were included in the study.

One hundred patients were randomized in two equal groups i.e either Saline (S group) or Dexa (D group). Each of the group received either saline (2 ml) intravenous (Group S) as placebo or dexamethasone (8 mg) intravenous (Group D). These drugs were prepared by the staff nurse on duty and given by the doctor on duty, two hours before the start of the operation. Episodes of nausea, and vomiting were registered by the doctor on duty in first 24 hours after operation.

---

*Department of Surgery, Ibn-e-Siena Hospital, Multan Medical & Dental College .*

*Correspondence to Dr. Asad Ali Shah , Senior Registrar ,  
Email : drasadalishah@hotmail.com*

Pneumoperitoneum was created with open technique and laparoscopic cholecystectomy was performed using two ports of 10 mm and two of 5 mm, maintaining a 12 mm Hg intraabdominal pressure. At the end of procedure, the carbon dioxide was carefully evacuated from the abdomen.

**RESULTS**

six patients (12%) in the treatment group and 15(30%) in the control group had postoperative nausea (Table 3). Six patients (12%) treated with dexamethasone had vomiting as opposed to 15(30%) receiving placebo (Table 3). Nausea and vomiting were significantly reduced during the entire observation period compared with placebo in particular, eleven patients (22%) in the treatment group had postoperative nausea and vomiting versus 26(52%) in the placebo group (Table 3). Fifteen patients (30%) receiving dexamethasone and seven (14%) receiving placebo required postoperative deep I/M Inj. Diclofenac Sodium during hospital stay.

Table-1 Gender distribution

Gender	D Group , n=50		S Group , n=50	
	Frequency	%age	Frequency	%age
Male	7	14	5	10
Female	43	86	45	90

Table-2 Demographic data

Group	D Group	S Group
Age (years)	42.3(13) {mean (s.d.)}	42.6 (14) {mean (s.d.)}
Gender (male/female)	7 / 43	5/45
ASA (I-II)	49-4	50-6
Duration of Surgery (Mins)	69 ( 35–95 )	66 (38–110)
Duration of Anaesthesia (Minutes)	77(50-165)	78 (60-170)

Table-3: Effect of 8mg dexamethasone given 2 hours before surgery in patients undergoing laparoscopic cholecystectomy

	D Group n = 50	S Group n=50
Nausea	06(12%)	15(30%)
Vomiting	06(12%)	15(30%)
Postoperative nausea and vomiting	11(22%)	26(52%)
Diclofenace Sodium required	15(30%)	07(14%)

Table 4 : Postoperative Nausea and Vomiting , n = 100

Parameters	Yes	No	Total
PONV (D Group)	6 (12%)	44(88%)	n=50
PONV (S Group)	15 (30%)	35 (70%)	n=50
	21(21%)	79(79%)	n=100

**DISCUSSION**

Dexamethasone was first reported as an antiemetic in patients receiving cancer chemotherapy in 1981<sup>1</sup>. Recently, dexamethasone has been reported to be effective in preventing PONV in patients receiving tonsillectomy, thyroidectomy, abdominal hysterectomy and laparoscopic cholecystectomy<sup>2,3</sup>. A wide range of doses of dexamethasone (8-32mg) has been used in the management of PONV and emesis associated with chemotherapy.

The first clinical trial that suggested that dexamethasone may prevent postoperative nausea and vomiting (PONV) was published in 1993<sup>4</sup>. Several randomized controlled trials have shown that single preoperative dose of dexamethasone is effective in reducing postoperative nausea and vomiting and antiemetic requirement after laparoscopic cholecystectomy. In a study of 101 patients who were randomized to receive either Dexamethasone 8mg (treatment group, n=49) or saline (control group, n=52), the frequency of postoperative nausea and vomiting (PONV) in the treatment group n=7 (14%) is found significantly less as compared to placebo group n=24(46%), (P=0.001)<sup>5</sup>.

The causes of PONV are multiple, including pharyngeal stimulation, gastrointestinal distention, abdominal distention, abdominal surgery, anaesthetic agent, pain, opioids, hypoxia, hypotension, vestibular disturbances and psychological factors. There are certain factors which can predispose patient to postoperative nausea and vomiting, like age (more in children), gender (female), history of previous nausea and vomiting , history of motion sickness, long duration of operation and depth of anaesthesia, carbon dioxide retention, rough handling, lack of anaesthetist's skill, type of surgical procedure and number of visitors during recovery<sup>6</sup>.

Among the antiemetics currently prescribed for PONV, serotonin subtype 3 antagonists (e.g., ondansetron and granisetron) are expensive<sup>7,8,9,10</sup>. Other currently used, lower 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. Dexamethasone, a corticosteroid, is an inexpensive and effective antiemetic drug, with minimal side effects after a single-dose administration<sup>11,12,13</sup>. It was first reported in 1981 as an effective antiemetic in patients receiving cancer chemotherapy<sup>14</sup>. Since then, dexamethasone has been widely applied in the prevention of nausea and vomiting after chemotherapy<sup>15,16</sup>. The commonly used dose is 8 to 10mg but the minimal effective dose is suggested to

be 5 mg for PONV in patients undergoing thyroidectomy.

Henzi et al stated that glucocorticoids have been shown to have various effects on the central nervous system; they regulate transmitter levels, receptor densities, signal transduction, and neuronal configuration. In the nucleus of the solitary tract, the nucleus of raphe, and the area postrema, numerous glucocorticoid receptors are found. These nuclei are well known to have considerable neuronal activities on the regulation of nausea and vomiting responses. Other theories include: prostaglandin antagonism, release of endorphins resulting in mood elevation, a sense of well-being, reduced levels of serotonin in neural tissue, and prevention of release of serotonin in the gut. Following the successful use of dexamethasone in the prevention and treatment of chemotherapy induced emesis, this agent has been evaluated and found to be effective for the management of PONV<sup>17,18</sup>. First, corticosteroids may reduce levels of 5-hydroxytryptophan in neural tissue by depleting its precursor tryptophan<sup>19</sup>. Second, the anti-inflammatory properties of corticosteroids may prevent the release of serotonin in the gut. Third, dexamethasone may potentiate the main effect of other antiemetics by sensitizing the pharmacological receptor<sup>20</sup>. 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<sup>21</sup>.

Generally, the biological action of glucocorticoids begins 1–2 h after administration<sup>22</sup>. So in this trial dexamethasone was administered 120 min before skin incision. The etiology and mechanism by which dexamethasone reduces both nausea and vomiting are not fully understood. Probably, the effects are centrally mediated through the inhibition of both prostaglandin synthesis and endogenous opioid release<sup>23</sup>. The origin of postoperative nausea and vomiting after laparoscopic cholecystectomy is not entirely clear; prolonged carbon dioxide insufflation<sup>24</sup>, use of nitrous oxide<sup>25,26</sup>, the utilization of slightly hypoxic mixtures during anaesthesia<sup>27,28</sup>, and postoperative opioid administration have been suggested as potential risk factors. Anaesthetic factors, such as use of volatile agents and intraoperative opioids, can increase the risk of postoperative nausea and vomiting<sup>29</sup>. The risk related to opioid administration for general anaesthesia is well established, and it is less than its beneficial effect on postoperative pain control<sup>30</sup>. No impaired wound healing, postoperative infection or other complications were associated with the use of dexamethasone in this trial. These results are similar to others reported in the literature<sup>31</sup>. In addition, a

recent meta analysis on postoperative nausea and vomiting has shown no increase in infectious or other complications using a single dose of dexamethasone<sup>32</sup>. In the current study, a single dose of 8mg dexamethasone did not cause wound infection or delay wound healing. In addition, no other side effects were found after the usage of a single dose of dexamethasone.

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<sup>33</sup>.

Ionescu and colleagues reported PONV in 20% of patients who received dexamethasone as prophylaxis undergoing cholecystectomy<sup>34</sup>. Kashmiri et al. used dexamethasone 8mg in patients undergoing laparoscopic cholecystectomy just before induction of anaesthesia. In their study, 27% of patient experienced PONV during first 12 hours and 30% patients reported nausea and vomiting in next 12 hours<sup>35</sup>. The difference in these results could be due to use of different anaesthetic technique, different surgical approach, different type of surgery, use of opioids and postoperative analgesics, difference in patients population (male/female), duration of anaesthesia and surgery.

## CONCLUSION

Dexamethasone improve the surgical outcome by reducing disabling symptoms of nausea and vomiting with out apparent side-effects. So preoperative dexamethasone may be used as a routine in patients undergoing elective laparoscopic cholecystectomy.

## REFERENCES

1. Aapro MS, Alberts DS. Dexamethasone as an antiemetic in patients treated with cisplatin. *N Engl J Med* 1981; 305: 520.
2. Wang JJ, Ho ST, Lee SC, Liu YC, Liu YH, Liao YC. The prophylactic effect of dexamethasone on postoperative nausea and vomiting in women undergoing thyroidectomy: a comparison of droperidol with saline. *Anesth Analg* 1999; 89:200-3.
3. Splinter WM, Rhine EJ. Low-dose ondansetron with dexamethasone more effectively decreases vomiting after strabismus surgery in children than high dose ondansetron. *Anesthesiology* 1998; 88:72-5.
4. Baxendale BR, Vater M, Lavery KM. Dexamethasone reduces pain and swelling following extraction of third molar teeth. *Anaesthesia* 1993;48:961–4.
5. Feo C, Sortini D, Ragazzi R, De Palma M, L iboni A. Randomized clinical trial of the effect of preoperative dexamethasone on nausea and vomiting after laparoscopic cholecystectomy. *Br J Surg* 2006; 93: 295–99.

6. Ashfaq M. Prevention of postoperative nausea and vomiting: a review of causative factors and management. *Med Channel* 1998; 4:43-52.
7. Watcha MF, White PF. Postoperative nausea and vomiting: its etiology, treatment, and prevention. *Anesthesiology* 1992;77:162-84.
8. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. *Drugs* 2000;59:213-43.
9. Alon E, Buchser E, Herrera E et al. Tropisetron for treating established postoperative nausea and vomiting: a randomized, double-blind, placebo-controlled study. *Anesth Analg* 1998; 86:617-23.
10. Purhonen S, Kauko M, Koski E, et al. Comparison of tropisetron, droperidol, and saline in the prevention of postoperative nausea and vomiting after gynecologic surgery. *Anesth Analg* 1997; 84:662-7.
11. Wang JJ, Ho ST, Liu YH, et al. Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. *Br J Anaesth* 1999;83:772-5.
12. 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.
13. Sehine I, Nishiwaki Y, Kakinuma R, et al. Phase II study of high-dose dexamethasone-based association in acute and delayed high-dose cisplatin-induced emesis: study 9413. *Br J Cancer* 1997; 76:90-2.
14. Aapro MS, Alberts DS. Dexamethasone as an antiemetic in patients treated with cisplatin. *N Engl J Med* 1981;305:520.
15. Dexamethasone, granisetron, or both for the prevention of nausea and vomiting during chemotherapy for cancer: the Italian Group for Antiemetic Research. *N Engl J Med* 1995;332:1-5.
16. Ondansetron versus metoclopramide, both combined with dexamethasone, in the prevention of cisplatin-induced delayed emesis: the Italian Group for Antiemetic Research. *J Clin Oncol* 1997;15:124-30.
17. Henzi I, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg* 2000; 90: 186-94 .
18. Bolton CM, Myles PS, Nolan T, Sterne JA. Prophylaxis of postoperative vomiting in children undergoing tonsillectomy: a systematic review and meta-analysis. *Br J Anaesth* 2006; 97(5): 593-604.
19. Young S. Mechanism of decline in rat brain 5-hydroxytryptamine after induction of liver tryptophan pyrrolase by hydrocortisone :roles of tryptophane catabolism and kynurenine synthesis. *Br J Pharmacol* 1981;74:695.
20. Sagar S. The current role of anti-emetic drugs in oncology: a recent revolution in patient symptom control. *Cancer Treat Rev* 1991;18:95-135.
21. Heffernan AM ,Rowbotham DJ. Postoperative nausea and vomiting-time for balanced antiemesis? *Br J Anaesth*, 2000, 85,(5): 675-77.
22. Sapolsky RM, Romero LM, Munck AU. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. *Endocr Rev* 2000; 21: 55-89.
23. Holte K, Kehlet H. Perioperative single-dose glucocorticoid administration: pathophysiologic effects and clinical implications. *J Am Coll Surg* 2000; 195: 694-712.
24. Fredman B, Jedeikin R, Olsfanger D, Flor P, Gruzman A. Residual pneumoperitoneum: a cause of postoperative pain after laparoscopic cholecystectomy. *Anesth Analg* 1994; 79:152-154.
25. Cohen MM, Duncan PG, DeBoer DP, Tweed WA. The postoperative interview: assessing risk factors for nausea and vomiting. *Anesth Analg* 1994; 78: 7-16.
26. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. *Anesthesiology* 1992;77: 162-184.
27. Apfel CC, Korttila K, Abdalla M, Kerger H, Turan A, Vedder I et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med* 2004; 350: 2441-2451.
28. Apfel CC, Korttila K, Abdalla M, Biedler A, Kranke P, Pocock SJ et al. An international multicenter protocol to assess the single and combined benefits of antiemetic interventions in a controlled clinical trial of a 2x2x2x2x2 factorial design (IMPACT). *Control Clin Trials* 2003; 24: 736-751.
29. Gan TJ, Meyer T, Apfel CC, Chung F, Davis PJ, Eubanks S et al. Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 2003; 97: 62-71.
30. Apfel CC, Laara E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology* 1999; 91: 693-700.
31. Sauerland S, Nagelschmidt M, Mallmann P, Neugebauer EA. Risks and benefits of preoperative high dose methylprednisolone in surgical patients: a systematic review. *Drug Safety* 2000; 23: 449-461.
32. Henzil, Walder B, Tramer MR. Dexamethasone for the prevention of postoperative nausea and vomiting: a quantitative systematic review. *Anesth Analg* 2000; 90:186-194.
33. 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.
34. Ionescu D, Mitre C, Leuke L, Bertianu C, Paskarenko G, Puia C, et al. Procedures for preventing postoperative nausea and vomiting after laparoscopic cholecystectomy: dexamethasone and ondansetron. *Anesteziol Reanimatol* 2007; 2: 50-2.
35. Kashmiri ZA, Sheikh Z, Haider S. Injection dexamethasone in preventing postoperative nausea and vomiting: a comparison with placebo in the patients undergoing laparoscopic cholecystectomy. *J Coll Physicians Surg Pak* 2006; 16: 689-92.