Original Article

Indian Journal of Anaesthesia and Analgesia
Volume 4 Number 2, April - June 2017 (Part–1)
DOI: http://dx.doi.org/10.21088/ijaa.2349.8471.4217.6

Utilization of Ondansetron and Dexamethasone for Post-Operative Nausea and Vomiting (PONV) after Laparoscopic Cholecystectomy at Bhuj, Kutch, Gujarat: A Randomised Control Trial

Mandakinee Thacker*, Naitik Patel*

Abstract

Background and Aim: Post-operative nausea and vomiting still occur with unacceptable frequency and the description of it as the 'Big Little Problem' encapsulates much of the general perception. The incidence is quite high even after laparoscopic surgeries including gall bladder surgeries. Present study was conducted to assess the level of PONV following laparoscopic cholecystectomy and the effect of dexamethasone and ondansetron, individually on PONV following laparoscopic cholecystectomy.

Materials & Methods: The study was conducted at Department of Anesthesia Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat. 60 patients presenting for elective laparoscopic cholecystectomy were randomised to 3 groups. Group 1 as control, group 2 received dexamethasone and group 3 received ondansetron for PONV prophylaxis. All three groups were evaluated for incidence of post-operative nausea and vomiting. Comparison of the observation among different groups was done and statistically analyzed using Fisher's exact test and Mann-whitney-U test. *Results:* The incidence of PONV was 50% in the control group, compared to 12% in the dexamethasone group and 22% in the ondansetron group during the first 24 hours. At 1 hour the total incidence of PONV was 85% in control group, 30% in dexamethasone group and 25% in ondansetron group. At 4 hours the total incidence of PONV was 60% in control group, 5% in dexamethasone group and 15% in ondansetron group. The incidence of PONV at 8 hours was 55% in control group, 10% in dexamethasone group and 40% in ondansetron group. *Conclusion:* The incidence of PONV following laparoscopic cholecystectomy is high and both dexamethasone and ondansetron effectively reduce the incidence of PONV in these patients.

Keywords: Cholecystectomy; Dexamethasone; Nausea; Vomiting.

Introduction

Within 18 months of introduction of general anesthesia in Great Britain, John Snow in 1848 first described the phenomenon of postoperative nausea and vomiting (PONV) [1]. Over the next 150 years there has been a general trend towards a decrease in the incidence and intensity of this problem because of the identification of the predictive factors, improved anesthetic and operative techniques, and the use of less emetic anesthetic drugs etc. However in spite of these advances, postoperative nausea and vomiting still occur with unacceptable frequency and the description of it as the 'Big Little Problem' encapsulates much of the general perception [2]. The incidence is quite high even after laparoscopic surgeries including gall bladder surgeries [3,4]. PONV can increase pain, prolong the post anesthesia care unit (PACU) stay and can cause unplanned hospital admission [5]. As more and more patients undergo surgery under day case, the humanitarian and economic implications of postoperative nausea and vomiting are becoming increasingly important [6].

A number of pharmacological and nonpharmacological methods to reduce PONV have been tried in the past with variable success. These include

Author's Affiliation:
*Associate Professor, Department of anesthesia , Gujarat Adani Institute of Medical Science, Bhuj, Gujarat.

Corresponding Author:
Mandakinee Thacker, Associate Professor, Department of Anesthesia, Gujarat Adani Institute of Medical Science, Bhuj, Gujarat 370001.
E-mail:
mturologyhospital@gmail.com,
researchguide86@gmail.com

Received on 09.02.2017

Accepted on 15.02.2017

acupuncture, acupressure, and drugs like droperidol, metoclopramide, atropine, hyoscine, cyclizine, and perphenazine 2014 recommendation Ondansetron is a highly selective 5HT3 antagonist [7]. It has been used successfully in chemotherapy-induced emesis, is also shown to be effective in preventing and treating PONV [8]. Although it lacks the sedative, dysphoretic and extrapyramidal side effects of other commonly used antiemetics, its cost is substantial [9]. The antiemetic effect of dexamethasone is reported to be equal to or better than 5HT3 antagonists, also adverse effects of single dose of dexamethasone are extremely rare [10,11,12]. Although various studies have proved the antiemetic efficacy of dexamethasone, not much work has been done to assess the effect of dexamethasone on PONV after laparoscopic cholecystectomy. Also the studies carried out so far on PONV after laparoscopic cholecystectomy have used various drugs either alone or in combination but the comparison of ondansetron and dexamethasone on the same surgical population has not been reported. present study is aimed to assess the magnitude of PONV after laparoscopic cholecystectomy and to evaluate and compare the effects of ondansetron and dexamethasone on the same in patients reported at Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Giujarat.

Materials and Methods

The study was conducted at Department of Anesthesia Gujarat Adani Institute of Medical Science, Bhuj, Kutch, Gujarat. Ethical approval was taken from institutional review board and ethical committee of the college and written informed consent was obtained from all participants. Sixty adult recruited ASA Grade l or ll patients of age groups 18 to 60 admitted hospital, who underwent elective laparoscopic cholecystectomy under general anesthesia. Patients with history of motion sickness, pregnant and lactating patients, those with hypersensitivity to ondansetron or dexamethasone were not included in the study. Patients who were on steroid therapy or had received antiemetics or drugs known to produce emesis within 48 hours before surgery were also excluded. All patients were shown the Visual Analogue Scale and were appraised about the same during a pre-operative visit one day prior to surgery. The patients were asked to restrict oral intake overnight or at least six hours before surgery. The patients were randomly divided into three groups of twenty patients each. Group l: patients in this group served as control and received 10ml of normal saline. Group 2: patients in this group received dexamethasone 0.15mg/kg diluted to 10 ml with normal saline. Group 3; patients in this group received ondansetron 0.1mg/kg diluted to 10 ml with normal saline. Pre anesthetic medication consisting of oral diazepam 10 mg was given to all patients on the night before surgery.

On arrival to the operating room, the monitoring gadgets comprising of ECG (lead ll), noninvasive automatic blood pressure monitor and pulse oximeter were applied to all the patients. Baseline heart rate, blood pressure and spO_2 were recorded. A suitable peripheral vein was secured in all the patients 10 minutes prior to induction of anesthesia.

In all patients drug under study was administered as a slow intravenous injection in a double blind fashion 10 minutes before induction. Induction was accomplished by thiopentone sodium (2.5%) 3-5mg/kg and fentanyl 2 microgm/kg followed by vecuronium 0.1 m/kg to facilitate tracheal intubation. Ventilation was controlled to maintain $EtCO_2$ of 35-40 mmHg. Anesthesia was maintained with isoflurane (0.5%) with 66%N_2O in O2. muscle relaxation was maintained with additional doses of vecuronium. Intra operative analgesia was supplemented with additional doses of fentanyl 1-2 microgm/ kg, if blood pressure and heart rate rose by 30% from the base line, after excluding other causes of tachycardia and hypertension. A nasogastric tube was inserted after induction of anesthesia for baseline emptying of the stomach and the same was removed soon after. Standard monitoring comprising of pulse rate, blood pressure, ECG, SpO_2 and $EtCO_2$ were carried out throughout the surgical procedure. Before closure, each laparoscopy port was infiltrated with 5 ml of 0.25% bupivacaine, for postoperative analgesia. Residual neuromuscular blockade was reversed with glycopyrrolate and neostigmine. Postoperatively pulse rate, blood pressure, respiratory rate, incidence of PONV and visual analogue scale score were recorded at 1,2,4,8 and 24 hours in all the patients. No distinction was made between vomiting and retching. Nausea and Vomiting were evaluated on a 3-point scale (0- none, 1-nausea, 2-vomiting). Rescue antiemetic in the form of metoclopramide 0.15-mg/kg i.v was given if the patient vomited more than once or demanded treatment.

Postoperative analgesia was supplemented with intramuscular diclofenac sodium, whenever VAS score was more than 3 or on demand. The total

amount of metoclopramide and diclofenac consumed were recorded. Side effects if any were observed and recorded.

Statistical Analysis

Data are presented as median or mean ± standard deviation (SD) as appropriate. Data were analyzed using the Mann–Whitney U test, the chi-square test and the Wilcoxon signed-rank test using SPSS version 15.0). Statistically significance was set at 5% p value.

Results

The three groups were comparable with respect to their age, weight and duration of surgery and did not differ statistically. The sex ratio of the patients, in all the three groups was also comparable. PONV was assessed using a 3-point scale i.e. (0-none,1-nausea, 2-vomiting) at 1hour, 2 hours, 4 hours, 8 hours and 24 hours after surgery. At 1 hour, the percentage of patients who had nausea was 25% in-group 1 compared to 10% in-group 2 and 10% ingroup 3. The percentage of patients who had vomiting was 60% in group 1, compared to 20 % in-group 2 and 15% in-group 3. The difference in the occurrence of PONV at 1hour was statistically very significant between group 1 and 2 ($p<0.001$) and between group 1 and 3 ($p<0.001$). The difference was not statistically significant between groups 2 and 3 ($p=0.5$).

At 2 hours, the percentage of patients who had nausea was 20% in-group 1 compared to 5% in both group 2 and 3. The percentage of patients who had vomiting was 35% in-group l compared to 5% in both group 2 and 3. The difference in incidence of PONV score was statistically very significant between group 1 and 2 ($p=0.002$) and between group 1 and 3 ($p=0.002$). The difference was statistically not significant between group 2 and 3 ($p=0.7$).

At 4 hours, the percentage of patients who had nausea was 30% in group 1 compared to 0% in group 2 and 5% in group 3. The percentage of patients who had vomiting was 30% in group 1, compared to 5 % in group 2 and 10% in group 3. The difference in the occurrence of PONV at 4hours was statistically very significant between group 1 and 2 ($p<0.001$) and between group 1 and 3 ($p=0.003$).

The difference was not statistically significant between 2 and 3 ($p=0.3$). At 8 hours, the percentage of patients who had nausea was 25% in-group 1 compared to 5% in group 2 and 15% in group 3. The percentage of patients who had vomiting was 30% in group 1, compared to 5 % in group 2 and 25% in group 3.

The difference in the occurrence of PONV at 8 hours was highly significant between group 1 and 2 ($p=0.002$) but not between group 1 and 3 ($p=0.26$). The difference was also statistically significant between groups 2 and 3 ($p=0.03$). At 24 hours, the percentage of patients who had nausea was 0% in group 1 compared to 0% in group 2 and 5% in group 3. The percentage of patients who had vomiting was 15% in group 1, compared to 5 % in group 2 and 15% in group 3.

The difference in the occurrence of PONV at 24 hours was not of statistical significance between the groups, even though the percentage of patients who had vomiting was less in group 2. Metoclopramide 0.15 mg/kg intravenously was used as the rescue antiemetic if the patients vomited more than once or when patient demanded. The mean amount of total meoclopramide consumed by each patient in milligrams was 7.357±4.404 in group 1, 0.987±3.040 in group 2 and 1.375± 3.391 in group 3. The difference in the total metoclopramide consumption was statistically very significant between group 1 and 2 ($p<0.001$) between group 1 and 3 ($p<0.001$).

The difference was statistically not significant between group 2 and 3 ($p=0.63$). In the 24hours after operation, patients in all groups made a comparable number of the demands and consumed similar amounts of diclofenac intramuscularly. The proportion of patients who had nausea and vomiting were more in patients who received repeat dose of fentanyl. Of the six patients who received repeat fentanyl, five had postoperative nausea and vomiting. PONV was more in patients with past history of PONV. But the number of patients with past history of PONV (8 out of 60) was too small to reach a conclusion. There was no constant relationship observed between the phases of menstrual cycle and PONV.

Table 1: Total dose of metoclopramide consumed in patients undergoing Anesthesia

Variable	Group 1	Group 2	Group 3
Mean	7.35	0.99	1.36
SD	4.4	3.04	3.40

SD: Standard Deviation

Discussion

Postoperative nausea and vomiting is area of concern as nearly 53-72% of patients require antiemetic therapy after laparoscopic cholecystectomy. Post-operatively incidence of nausea and vomiting was recorded on a 3-point scale (0=none, 1= nausea, 2= vomiting) at 1 hour, 2 hours, 4 hours, 8 hours and 24 hours. Rescue antiemetic in the form of metoclopramide 0.15 mg/kg iv was given if the patient vomited more than once or demanded treatment. Lopez-Olando et al [13] concluded that prophylactic administration of a combination of dexamethasone. Gynaecological surgery with fewer patients requiring rescue antiemetic compared to other regimens of placebo, ondansetron or dexamethasone [14].

Biswas et al [15] also found that combination of dexamethasone and ondansetron provided adequate control of PONV in patients undergoing laparoscopic tubal ligation with overall complete response in 78% of patients. Postoperative analgesia was supplemented with intramuscular diclofenac sodium, whenever VAS score was more than 3 or on demand. Total amount of metoclopramide and diclofenac consumed was recorded. In recent years interest has been focused on combination therapy because no single agent is effective against PONV. This may be because it is multifactorial in origin and there is no single stimulus for PONV. The idea of combination therapy for prevention and treatment of postoperative nausea vomiting came from various studies where Ondansetron plus dexamethasone have been used successfully to treat emesis refractory to Ondansetron alone [15].

It was found that there was a high incidence of postoperative nausea and vomiting after laparoscopic cholecystectomy. Both intravenous dexamethasone and ondansetron were effective in reducing the postoperative nausea and vomiting. Dexamethasone in a dose of 0.15-mg/kg i.v and ondansetron in a dose of 0.1-mg/kg i.v were highly effective in reducing the incidence of PONV for 8 hours and 4 hours respectively after surgery. Both the drugs significantly reduced the requirement of rescue antiemetics during the 24-hour postoperative period. We did not observe any untoward effects with the use of either of the drugs. Postoperative pain scoring and consumption of rescue analgesic were similar in all the three groups.

Dexamethasone was reported as an effective ant-emetic in patients receiving cancer chemotherapy in 1981 [16]. Glucocorticoids have been recognised as an important modifier of postoperative physiology, inflammatory, humoral and immunological response, by regulation of trauma induced humoral factors. 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 ant-emetic action via inhibition of prostaglandin synthesis, or inhibition of release of endogenous opoids [8]. A metanalysis on perioperative administration of high dose of methylprednisolone (30-35 mg/kg), was not associated with significant side effects [17].

The major concern regarding the use of dexamethasone is infection, delayed wound healing and other side effects. But various studies in the literature have shown that a single-dose dexamethasone does not increase complications [18].

The introduction of serotonin (5HT3) receptor antagonists in 1991 has heralded a major advance in treatment of PONV because of absence of adverse effects that were observed with commonly used antiemetic drugs. Ondensetron produces no sedation, no extra pyramidal symptoms and adverse effects on vital signs. Serotonin (5HT3) receptor antagonists affect the chemoreceptor trigger zone and act at vagal afferents in the gastrointestinal tract. Ondansetron has been shown to be effective in the prevention and treatment of PONV in many studies. No single drug has proved to be universal solution to PONV. It is not feasible to give very high doses of such drugs because of saturation effects and safety, so combination of antiemetic and corticosteroid drugs are a possibility. The real benefit to patients will be realised if effective prophylactic combination of drugs make postoperative nausea and vomiting a rare occurrence.

Conclusion

The results of our study indicate that, the incidence of postoperative nausea and vomiting after laparoscopic cholecystectomy is very high. Prophylactic dexamethasone in a dose of 0.15mg/kg i.v is highly effective in reducing the incidence of postoperative nausea and vomiting for 8 hours after surgery and it significantly reduced the requirement of rescue antiemetics during the 24-hour postoperative period. Ondansetron in a dose of 0.1mg/kg i.v is highly effective in reducing the incidence of postoperative nausea and vomiting for 4

hours after surgery and it also significantly reduced the consumption of rescue antiemetics during the 24-hour postoperative period. Both intravenous dexamethasone and ondansetron are safe and effective method for attenuating the postoperative nausea and vomiting after laparoscopic cholecystectomy, but duration of antiemetic action of dexamethasone is more.

References

1. Andrews.P.L.R. Physiology of nausea and vomiting. Br. J. Anesth. 1992; 69 (suppl 1):2-19.
2. Fisher. M. D. The "Big Little Problem" of postoperative nausea and vomiting. Anesthesiology 1997; 87:1271-1273.
3. Koivuranta M. K, Laara. E, Ryhanen P.T. Antiemetic efficacy of prophylactic ondansetron in laparoscopic cholecystectomy Anesthesia1996; 51:52-55.
4. L. Shamseer, D. Moher, M. Clarke et al., "Preferred reporting items for systematic review and meta-analysis protocols (prisma-p): Elaboration and explanation," British Medical Journal, 2015; 349: 647.
5. Ahmed.A.B, Hobbs.G.J, Curran.J.P. Randomized, placebo controlled trial of combination antiemetic prophylaxis for daycase gynecologic laparoscopic surgery. Br J Anesth 2000; 85:678-682.
6. N. D'souza, M. Swami et al. Comparative study of dexamethasone and ondansetron for prophylaxis of postoperative nausea and vomiting in laparoscopic gynecologic surgery. International Journal of Gynecology and Obstetrics. 2011; 2:124–127.
7. Rowbotham. D.J. Current management of post-operative nausea and vomiting. Br J Anesth. 1992; 69 (suppl.1): 46-59.
8. Joslyn.A.F ondansetron, clinical development for postoperative nausea and vomiting: current studies and future directions. Anesthesia, 1994; 49(suppl): 34-37.
9. Russell.D, Kenny. G.N.C, 5 HT3 antagonists in postoperative nausea and vomiting. Br J Anesth. 1992; 69(suppl 1):63-68.
10. Italian group of antiemetic research. Dexamethasone, granisetron or both for the prevention of nausea and vomiting during chemotherapy for cancer. N Engl J Med, 1995; 332:1-5.
11. Italian group for antiemetic research. Ondansetron vs metoclopramide, both combined with dexamethasone in the prevention of cisplatin induced delayed emesis. J Clin Oncol 1997; 15:124-130.
12. Wang.J.J, Ho.S.T, Liu.Y.H. dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. Br J Anesth. 1999; 83:772-775.
13. Lopez-Olaondo L, Carrascosa F, Pueyo FJ, Monedero P, Busto N and Saez A. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. Br J Anaesth 1996; 76:835-840.
14. Biswas BN, Rudra A and Mandal SK. Comparison of ondansetron, dexamethasone, ondansetron plus dexamethasone and placebo in the prevention of nausea and vomiting after laparoscopic tubal ligation. J Indian Med Assoc 2003; 101:638,640,642.
15. Smith DB, Newland ES, Spruyt OW, Begent RHJ, Rustin GJ, Mellor B and Bagshawe KD. Ondansetron (GR38032F) plus dexamethasone: effective anti-emetic prophylaxis for patients receiving cytotoxic chemotherapy. Br. J Cancer 1990; 61:323-324.
16. Italian Group for antiemetic research. Ondansetron versus metoclopromide, both combined with dexamethasone in the prevention of Cisplatin induced delayed emesis. J Clin Oncol. 1997; 15:124-130.
17. Sauerland S, Nagelschmidt M and Mallman P. Risk and benefits of preoperative high dose of methylprednisolone in surgical patients- a systemic review. Drug Safety 2000; 23:443-461.
18. Wang JJ, Ho ST, Wong CS, Tzeng JI, Liu HS and Ger LP. Dexamethasone prophylaxis of nausea and vomiting after epidural morphine for post caesarean analgesia. Can J Anaesth.2001; 48:185-190.