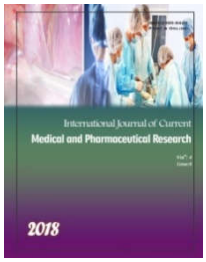
Research Article

INTERNATIONAL JOURNAL OF CURRENT MEDICAL AND PHARMACEUTICAL RESEARCH

ISSN: 2395-6429, Impact Factor: 4.656
Available Online at www.journalcmpr.com
Volume 4; Issue 6(A); June 2018; Page No. 3327-3330
DOI: http://dx.doi.org/10.24327/23956429.ijcmpr20180454



A PROSPECTIVE, RANDOMIZED SINGLE BLIND STUDY ON EVALUATION OF ANTI-EMETIC EFFECT OF DEXAMETHASONE VERSUS ONDANSETRON IN PATIENTS UNDERGOING LAPAROSCOPIC GYNAECOLOGICAL SURGERIES

Usha Vijayaraghavan[1] and Vijayaraghavan Srinivasan[2]

Department of Anaesthesiology, Annaii Medical College & Hospital, Pennalur, Sriperumbudur, Chennai-602117
Affiliated with TN Dr.M.G.R Medical University, Chennai, Tamilnadu, India

ARTICLE INFO

Article History:
Received 8th March, 2018
Received in revised form 10th April, 2018
Accepted 24th May, 2018
Published online 28th June, 2018

Key words:
Ondansetron, dexamethasone, postoperative nausea and vomiting, gynaecolgical surgeries

ABSTRACT

Context: Postoperative nausea and vomiting (PONV) remains a common problem after laparoscopic gynaecological surgeries and contributes to patient dissatisfaction. The type of surgery, choice of anesthetic technique and use of opioid analgesics can all influence the incidence of PONV. Additional factors influence the incidence of PONV which include previous history of motion sickness, gender, smoking status, pregnancy, phase of the menstrual cycle, preoperative hydration and perioperative hypotension.

Aim: To evaluate the antiemetic efficacy of dexamethasone and ondansetron in patients who had undergone laparoscopic gynaecological surgeries with respect to the use of rescue antiemetic agent.

Settings & Design: We conducted a prospective randomized double blind study in fifty female patients who underwent laparoscopic gynaecological surgeries. Patients were randomized to receive either dexamethasone 8mg (group A) or ondansetron 4mg (group B) 30 minutes preoperatively. Patients were observed for the incidence of PONV. The severity of nausea was assessed using visual analog scale.

Statistical Analysis used: The results were entered in excel sheet. Students t test and Chi square test were used for quantitative and qualitative data respectively.

Results: The mean value of worst possible nausea score using Visual Analog Scale was found to be 2.64±1.55 and 3.30±1.47 (p value of 0.0984) of group A and group B respectively. The time to rescue antiemetic usage was prolonged in dexamethasone group.

Conclusion: From our study we conclude that 8mg of dexamethasone is more effective than 4mg of ondansetron in preventing PONV after laparoscopic gynaecological surgeries. But the clinical profile of both drugs needs to be studied in detail by using large sample size.

INTRODUCTION

Postoperative nausea and vomiting (PONV) is an unpleasant experience commonly encountered in 20-30 % post-surgical patients[1]. PONV is the second most common problem in the postoperative period next to pain[2-8]. While the experience of PONV is generally self-limited, postoperative vomiting/retching (POV) can lead to rare but serious medical complications like aspiration of gastric contents, suture dehiscence, esophageal rupture etc. PONV may cause prolonged post anesthesia care unit stay and can be the leading cause of unexpected hospital admission after ambulatory anaesthesia[9]. The common risk factors associated with PONV based on Apfel study are female sex, non-smokers, prior history of motion sickness and history of opioid usage.

Many surgeries are associated with a high incidence of PONV. There is no question that patients undergoing laparoscopic gynaecologic surgeries have increased risk for PONV, with incidence of atleast 50%. The high incidence of PONV after gynecological surgery is likely to be observed because the surgery is conducted in women, who are more susceptible to PONV, and not because of the surgery itself. Prevention of PONV in high-risk patients significantly improves postoperative rating of well- being and satisfaction.

Ondansetron due to its superior efficacy for chemotherapy-induced nausea and vomiting, it is not surprising that ondansetron quickly established a reputation as the most effective antiemetic for prevention of PONV. Dexamethasone is well documented as an effective antiemetic and animal experiments suggest that it exerts its antiemetic effects through central inhibition of the nucleus tractus solitarii.[10,11] Earlier studies were conducted with 8-10mg of dexamethasone , but there is now convincing evidence from several dose-response trails that 2.5mg to 5mg can be considered the minimum

Corresponding author:* **Usha Vijayaraghavan
Department of Anaesthesiology , Annaii Medical College & Hospital, Pennalur, Sriperumbudur, Chennai-602117
Affiliated with TN Dr.M.G.R Medical University, Chennai, Tamilnadu, India

effective dose . Dexamethasone has a slow onset of action, which might be the reason why its application at the beginning of a case appears to be superior to later use. With this background we conducted a study for evaluating the prophylactic antiemetic effects of two drugs namely ondansetron and dexamethasone in patients undergoing laparoscopic gynecological surgeries. Both patient related (female sex) and surgery related (laparoscopic gynaecologic surgeries) risk factors are taken into consideration in our study due to higher incidence of PONV.

MATERIALS AND METHODS

We conducted a prospective, randomized, double blind study at our Institution after Ethical Committee approval. A single pre-induction intravenous dose of Dexamethasone (8mg fixed dose) or Ondansetron (4mg fixed dose) was administered to 50 female patients aged between 18-60 years undergoing laparoscopic gynaecological surgeries. A written informed consent was obtained from all study patients at the time of preoperative visit after clearly explaining about the study. Prior history of motion sickness or postoperative nausea and vomiting was clearly noted.

Exclusion criteria

- Pregnancy
- Distinct spells of nausea, vomiting or retching within 24 hours prior to surgery
- Use of other corticosterioids, psychoactive drugs or any other medications with known emetic or antiemetic effect within 24 hours prior to surgery
- Chronic kidney or liver disease

Randomization was done using computer generated random number list. The study drug was administered in a double blind manner, taking care to ensure that the patient and the principal investigator were not aware of the exact identity of the antiemetic drug that she received, either before or during the 48 hours observation period (study period) following surgery. A suitable peripheral vein was cannulated for administration of drugs and IV fluids at 6 am on the day of surgery in the ward. The study medication either dexamethasone (8mg) or ondansetron (4mg) was administered intravenously 30 minutes before induction of anesthesia, as per the randomization code. On arrival in the operation theatre, routine monitoring devices were connected, including non-invasive arterial pressure, ECG and pulse oximetry. The choice of anesthesia was based on the concerned anesthesia faculty posted in gynaecology theatre and patient related factors. In our Institution most of the laparoscopic gynaecological surgeries were performed under general anaesthesia/regional anaesthesia. If laparoscopy assisted procedure was planned or inadequate spinal blockade or failed spinal attempt, general anesthesia was administered to the patient with cuffed endotracheal intubation as per routine protocol.

For the purpose of the study, an episode of PONV denoted either a distinct spell of nausea, retching (an involuntary attempt to vomit but not actually productive of stomach contents) or vomiting (actual expulsion of stomach contents). The primary outcome measure was the total number of PONV episodes in the 24hrs period following surgical procedure

The secondary outcome variables were:

- Frequency of nausea, retching and vomiting episodes individually in the 24hrs period following the surgical procedure.
- Nausea severity score (as assessed using a 10 cm Visual Analogue Scale) at 2, 6, and 24hrs after completion of surgery.
- Use of rescue antiemetic medication (Metoclopramide 10 mg slow intravenous injection).
- Number of complete responders – no emetic episodes and no rescue medication.
- Overall satisfaction with the nausea-vomiting experience on a four-point Likert scale (Unsatisfied, neutral, satisfied, and highly satisfied) at 24hrs after surgery completion. Metoclopramide 10 mg slow intravenous injection was permitted as rescue medication, to be administered if nausea severity attained >4 cm or more on the VAS scale, or on demand. Hemodynamic variables such as heart rate, blood pressure and SpO2 were monitored at regular intervals and adverse effects related to the administered study drugs were also recorded. Postoperative pain was managed with opioids or paracetamol.

RESULTS

Sample size was calculated to the primary outcome (Patients with complete response). Statistical analysis was performed using SPSS version 16. Quantitative data were represented as mean and SD. Qualitative data were presented as number and percentage. Tests used were Student's t-test for analysis of age, weight, duration of surgery and nausea score and Chi square test for analysis of categorical variables. P-value less than 0.05 was considered statistically significant.

Table 1 Demographic Profile

Characteristics	Group A (Dexamethasone) (n=25)	Group B (Ondansetron) (n=25)	p Value
Age (in years)	44.00±10.20	39.60±.80	0.1264
ASA I/II	04/21	06/19	
Weight (in Kg)	58.28±9.29	54.88±8.82	0.1857
Previous H/o PONV/Motion Sickness	05/20	08/17	
Diabetes	03/22	07/18	
Systemic Hypertension	04/21	05/20	
Coronary Artery Disease	02/23	03/22	

Table 2 Perioperative details

Characteristics	Group A (Dexmethasone)	Group B (Ondansetron)	p Value
Opioid Usage (Postoperative period)			
Tramadol	11 (44%)	13 (52%)	
Pentazocine	06 (24%)	06 (24%)	
Pethidine	08 (32%)	06 (24%)	
Type of anesthesia			
General	21 (84%)	22 (88%)	
Regional	04 (6%)	03 (12%)	
Duration of surgery (in minutes)	66.44±20.50	65.68±21.64	0.8991(NS p>0.05)

The results are clearly depicted in figures and tabular columns. The demographic data such as age, physical status and weight were quiet comparable between two study groups. Five out of twenty five patients in dexamethasone group and 8 out of 25 patients in ondansetron group had a prior history of motion sickess. Almost all patients in our study received opioids in the postoperative period for pain relief namely injection tramadol, pethidine and pentazocine. More than 80% of study patients received general anaesthesia. The duration of surgery was quiet comparable between two groups and they were found to be statistically insignificant.

Table 3

Characteristics	Group A (Dexamethasone)	Group B (Ondansetron)	p Value
Nausea score (Worst possible VAS Score) during the 24 hrs postoperative period	2.64±1.55	3.36±1.47	0.0984
Vomiting Episodes			
1	02 (8%)	03 (12%)	
2	04 (16%)	06 (24%)	
3	01 (4%)	02 (8%)	
Time to Rescue Antiemetic (in hours)	5.02 ±1.35	4.16±1.55	0.0297
Complete response	19 (76%)	14 (56%)	

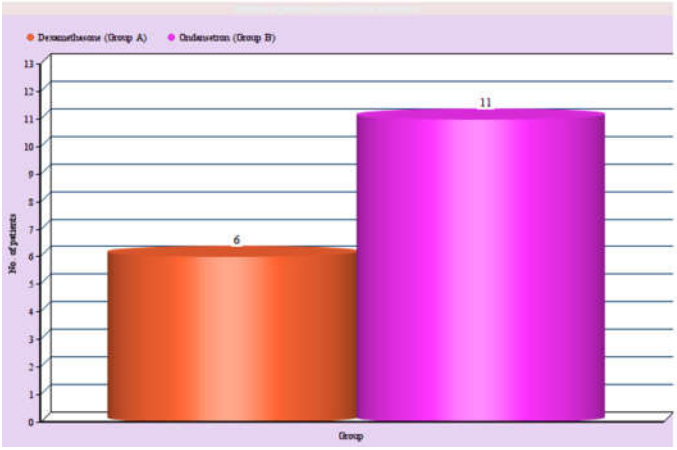


Figure 1 Number of patients needed rescue antiemetic

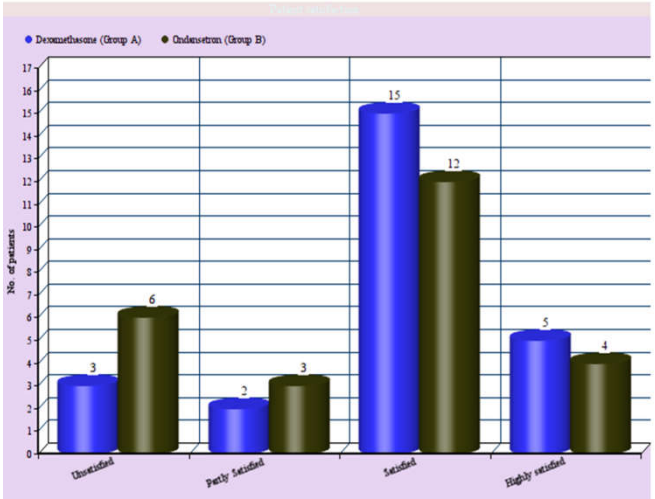


Figure 2 Patient satisfaction score

The worst possible nausea VAS score was found to be 2.64±1.55 and 3.30±1.47 (p value of 0.0984) of group A and group B respectively. The number of vomiting episodes between two study groups were quiet comparable (who had vomiting 1-3 times). The time to rescue antiemetic usage was comparatively prolonged in dexamethasone group. Almost 75% of patients in dexamethasone group had complete response (no episode of nausea and vomiting within 24 hours of postoperative period) and in ondansetron group only 56% of patients were symptom free (i.e no nausea or vomiting). Six out of twenty patients in dexamethasone group had rescue antiemetic during vomiting episodes which was quiet lesser than ondansetron group. In the postoperative period, all study participants were questioned about the satisfaction. These results were categorized into unsatisfied, partially satisfied, satisfied (neutral) and highly satisfied. The results of satisfaction survey are statistically comparable and clearly depicted in Figure 2.

DISCUSSION

Most prospective cohort studies using logistic regression analyses have identified female gender (in adults) as the strongest independent predictor for postoperative nausea, vomiting and use of rescue antiemetic treatment. Yet women have a lower threshold for motion sickness and hyperemesis gravidarum.[12] The reason for increased female susceptibility to nausea and vomiting is unclear but persists well after menopause and most of the rest of a woman's life.[13] There is no question that patients undergoing laparoscopic gynecologic surgeries have increased risk for PONV, with incidence of at least 50%.

We conducted a comparative study on PONV using two antiemetics namely dexamethasone and ondansetron as a single prophylactic drug pre operatively. Liu K *et.al* did a study on the effect of dose of dexamethasone for antiemesis after laparoscopic gynaecological surgery. To achieve the best antiemesis with fewer side effects, dexamethasone 10mg, 5 mg, 2.5mg and 1.25mg were compared with placebo surgical patients. They found 2.5mg to be the minimum effective dose of dexamethasone without discernible side effects. This was not quiet comparable with our study since we used dexamethasone 8mg for study participants.[14]

In another study done by Wang JJ *et.al* on the use of dexamethasone for preventing PONV in females undergoing thyroidectomy.[15] They recommended prophylactic dexamethasone 8–10 mg administered intravenously before induction of anesthesia as a safe and effective strategy for reducing the incidence of PONV. More high quality trials are warranted to define the benefits and risks of prophylactic dexamethasone in potential patients with a high risk for PONV. But we did not study about dexamethasone related side effects as well as ondansetron.

Peach, Michael J *et.al* conducted a study in female patients undergoing day care gynaecologic laparoscopy surgeries.[16] Patients at high risk of PONV often receive more than one prophylactic antiemetic drug, in that study, patients received four different dose combinations of dexamethasone and ondansetron. Average nausea scores were low in all four groups, but the incidence of nausea until 24 hours postoperative was significantly higher among groups received only 2mg of dexamethasone. This result was quiet comparable with our study since we used 8 mg of dexamethasone Souvik Maitra *et.al* did a meta analysis of comparative study between ondansetron and dexamethasone for prophylaxis of PONV in patients undergoing laparascopic surgeries.[17] Data of 592 patients from 7 randomized controlled trials have been

included in that meta-analysis. The incidence of postoperative nausea at 4-6 hours is significantly lower when dexamethasone was used instead of ondansetron. They concluded that dexamethasone is superior to ondansetron in preventing postoperative nausea after 4-6 hours of laparoscopic surgeries. However both the drugs are of equal efficacy in preventing PONV upto 24 hours after surgery. The results of this meta analysis were quiet comparable with our study.

In another study done by Xian-Xue Wang *et.al* on dexamethasone versus ondansetron in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery.[18] This was a meta-analysis of randomized controlled trials. Seven trials involving 608 patients were included in that meta-analysis, which found that dexamethasone had a comparable effectiveness in preventing PONV with that of ondansetron within 24 hours of laparascopic surgery. (Relative risk, 0.91;95% CI 0.73-1.13 p=0.39). There was no evidence of heterogeneity among the studies. In the early postoperative stage (0-6 hours), ondansetron was better at decreasing PONV than dexamethasone (RR,1.71;95% CI 1.05-2.77 p=0.03). This result was also comparable but not similar to the results of our study.

Limitation of our study

Our study included only smaller population of female patients. To measure the effectiveness of antiemetic, the number needed to treat (NNT) must be large enough. The effectiveness of a prophylactic intervention is probably measured by the absolute risk reduction (i.e to describe the actual benefit of an intervention when given to patients of a population with a high risk of PONV. Our study included surgery (gynaecological surgeries) and patient (female sex) related risk factors for high incidence of PONV. To determine the effectiveness and comparison between dexamethasone and ondanstron in antietemesis, our study has to be done in larger sample size.

CONCLUSION

From our study we concluded that 8mg of dexamethasone is highly effective in preventing postoperative nausea and vomiting in patients undergoing laparoscopic gynaecological surgeries. Its combination with other antiemetic needs to be evaluated in major gynaecological surgeries since female sex is prone to have high incidence of PON. Apfel risk score based prophylactic antiemetic selection must be done in order to have smooth and pleasant postoperative period.

Acknowledgement: None declared

Conflict of interest: Nil

References

1. Marcario A, Weigner M, Carney S, Kim A: Which clinical anesthesia outcomes are important to avoid? The perspective of patients. *Anesth Analg* 89:652-658,1999.
2. Palazzo M, Evans R: Logistic regression analysis of fixed patient factors for postoperative sickness: A model for risk assessment. *Br J Anaesth* 70:135-140,1993
3. Cohen MM, Duncan PG, DeBoer DP, Tweed WA: The postoperative interview: Assessing risk factors for nausea and vomiting. *Anesth Analg* 78:7-16,1994
4. Koivuranta M, Laara E, Snare L, Alahuta S: A survey of postoperative nausea and vomiting. *Anaesthesia* 52:443-449,1997
5. Apfel CC, Laara E, Koivuranta M, *et.al*: A simplified risk score for predicting postoperative nausea and vomiting: Conclusions from cross-validations between two centers. *Anesthesiology* 91:693-700,1999
6. Eberhart LHJ, Hogel J, Seeling W, *et.al*: Evaluation of three risk factors to predict postoperative nausea and vomiting. *Acta Anaesthesiol Scand* 44:480-488,2000
7. Stadler M, Bardiau F, Seidel L, *et.al*: Difference in risk factors for postoperative nausea and vomiting. *Anaesthesiology* 98:46-52,2003
8. Watcha MF, White PF: Postoperative nausea and vomiting: Its etiology, treatment and prevention. *Anesthesiology* 77:162-184.1992
9. Gold BS, Kitz DS, Kecky JH, Neuhaus JM: Unanticipated admission to the hospital following ambulatory surgery. *JAMA* 262:3008-3010,1989
10. Apfel CC, Korttila K, Abdalla M, *et.al*: A factorial trail of six interventions for the prevention of postoperative nausea and vomiting. *N Engl J Med* 350:2441-2451,2004
11. Carlisle J, Stevenson C: Drugs for preventing postoperative nausea and vomiting. *Cochrane Database Syst Revv* (3):CD004125,2006
12. Klosterhalfen S, Kellermann S, Pan F, *et.al*: Effects of ethnicity and gender on motion sickness susceptibility. *Aviat Space Environ Med* 76:1051-1057,2005.
13. Apfel CC, Greim CA, Goepfert C,*et.al*: Postoperative vomiting: A score for its prediction after inhalation anaesthesia. *Der Anaestheist* 47:732-740,1998.
14. Liu K, Hsu CC, Chia YY: The effect of dose of dexamethasone for antemesis after major gynaecological surgery. *Anesth Analg* 89:1316-1318,1999
15. 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* 91:1404-1407,2000
16. Paech, Michael J, Rucklidge Matthew W.M, Lain Jennifer *et.al*. Ondansetron and dexamethasone dose combinations for prophylaxis against postoperative nausea and vomiting. *Anesthesia and Analgesia*: April 2007;Vol.104.Issue 4.pp808-814
17. Souvik Maitra Anirban som, Dalim K, Baidya and Sulagra Bhattacharjee. Comparison of ondansetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing laparascopic surgeries. A meta-analysis of Randomized controlled trials. *Anesthesiolgy Research and Practice*, http;//dx.doi.org/10.1155/2016/7098454
18. Ian-Xue Wang, Quen Zhon, Dao-Bo Panet *et.al*. Dexamethason versus ondansetron in the prevention of postoperative nausea and vomiting in patients undergoing laparoscopic surgery. A meta-analysis of randomized controlled trials. *BMC Anaesthesiology* 2015 15:118/DOI:10.1186/612871-0105-010002

****