ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 05 | May - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

COMPARISON OF ONDANSETRON AND ONDANSETRON PLUS DEXAMETHASONE FOR PREVENTING POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

Anaesthesiology

Dr. Komal Bende* Junior Resident Department of Anaesthesiology, Government Medical College and Hospital, Aurangabad, Maharashtra, India *Corresponding Author

Dr. Mukund Parchandekar Associate Professor Department of Anaesthesiology, Government Medical College and Hospital, Aurangabad, Maharashtra, India

ABSTRACT

Background and Aims: Postoperative nausea and vomiting (PONV), the most common and distressing symptoms experienced by patients after laparoscopic cholecystectomy often need prophylactic antiemetic therapy. Multimodal prophylactic antiemetic therapy is found to be more effective than any single antiemetic drug. The primary objective of the study was to compare efficacy of ondansetron and ondansetron plus dexamethasone for preventing PONV in patients undergoing laparoscopic cholecystectomy. **Material and Methods:** A prospective, randomized, comparative, double blinded study was carried out on 60 ASA Grade I and II patients of either sex aging 26-60 years undergoing laparoscopic cholecystectomy under general anaesthesia. Patients were divided into 2 groups of 30 each by systemic randomization method. Group O: received Ondansetron 4 mg IV, and Group OD: received Ondansetron 4 mg plus Dexamethasone 8mg IV, 10 min before induction of anaesthesia. PONV was assessed immediately after surgery and at 30-min intervals for 2 hours in the recovery room and then in the ward at 6, 12 and 24 hours post-surgery. The occurrence of nausea and vomiting was evaluated on a 3-point ordinal scale. 0 = no nausea or vomiting, 1 = nausea only, 2 = retching and / or vomiting. The primary end point was a "complete response", defined as no episode of PONV during the first 24 hrs after recovery from anaesthesia. Failure of prophylaxis was considered as a need for rescue antiemetic. **Results:** 13 (43.33%) and 22 (73.33%) patients from Group O and Group OD respectively had complete response ($p=0.018$). 17 (56.66%) patients in Group O and 8 (26.66%) patients in Group OD, who had episode of PONV, 12 and 5 patients respectively needed rescue antiemetic ($p>0.05$). The duration of hospital stay was longer in Group O than Group OD ($p<0.05$). **Conclusion:** In patients undergoing laparoscopic cholecystectomy, prevention of postoperative nausea and vomiting is better with combination of ondansetron plus dexamethasone than ondansetron alone.

KEYWORDS

PONV, laparoscopic cholecystectomy, ondansetron, dexamethasone

INTRODUCTION:

In patients undergoing laparoscopic cholecystectomy, incidence of the most common and distressing symptoms, postoperative nausea and vomiting (PONV) ranges between 46 to 72%. [1-3] In laparoscopic surgery, the risk of PONV is due to pneumo-peritoneum causing stimulation of mechanoreceptors in the gut. The high incidence of PONV has persisted in part because of the tremendous growth in this ambulatory surgery. [4,5] Younger age, female gender, history of motion sickness, non-smoking status of patient and previuos PONV are attributed to higher incidence of PONV. Preanesthetic medication, gastric distension, anaesthetic agents like nitrous oxide, volatile anaesthetics, ketamine and postoperative pain also contribute to emetic symptoms in postoperative period.[6]

Prophylactic antiemetic therapy is needed for all these patients with moderate to high risk of PONV as this may result in dehydration, electrolyte imbalance, wound dehiscence, pulmonary aspiration and delayed hospital discharge. Pharmacological management of PONV tailored to patient's risk level to minimize the potential for adverse side effects in postoperative period. [5,7] Since any single antiemetic drug has been shown to have limited efficacy against PONV, multimodal therapy has been proposed because a combination of antiemetic with different sites of activity would be more effective than one drug alone. [8,9] As dexamethasone has interaction with neurotransmitter serotonin, its combined use with ondansetron improves antiemetic efficacy in patients at high risk for PONV. [9, 10] And combination found to be effective in preventing early and late PONV for patients undergoing laparoscopic cholecystectomy. [8] Efficay achieved by comination is not different than achieved by single agent, but combination of ondansetron and dexamethasone is effective in male and younger patients than ondansetron alone in preventing PONV. [11] So, the present study was carried out with aim to compare the efficacy of ondansetron and ondansetron plus dexamethasone for preventing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy.

MATERIAL AND METHODS:

After obtaining Institutional Ethics Committee approval, this prospective, randomized, comparative, double blinded study was conducted in tertiary care hospital, over a period of 2 years. After acquiring written informed consent, 60 patients, Aged 26 - 60 years, of either sex, ASA Grade I and II, Height 150 to 180 cm, Weight 40 to 70 kg, planned for elective laparoscopic cholecystectomy under general anaesthesia were included in the study. Patients having nausea and / or vomiting, previous PONV, who have taken antiemetic medication within 48 hrs before surgery, history of allergy to study drug, pregnancy and menstruation, history of motion sickness, patients having gastrointestinal disorders, diabetes mellitus, major systemic illness, refusal to participate in the study were excluded from the study.

On the day before surgery in the evening, thorough pre-anaesthesia evaluation was carried out. The purpose of study, entire procedure and effect of drugs being used were explained in detail to participants. Patients were kept fasting for 6 hours before the proposed study time based upon the NPO guidelines.

Patients enrolled were divided into two groups of 30 each by systemic randomization method. Each odd number patient was to receive Ondansetron and even number patient was to receive a combination of Ondansetron plus Dexamethasone.

- Group O – Ondansetron 4 mg I.V.
- Group OD – Ondansetron 4 mg I.V. plus Dexamethasone 8mg I.V.

In operation theatre, Baseline pre-operative pulse rate, systolic and diastolic blood pressure, mean arterial pressure, SPO2, respiratory rate, ECG were noted. Venous access secured. Each treatment regimen was diluted with normal saline to make a volume of 10 ml. 10 min before induction of anaesthesia, drug preparations were administered intravenously slowly over 5 min.

Patients were preoxygenated with 100% oxygen for 5 minutes. Premedication given with Inj. Glycopyrrolate 0.2 mg, Inj. Midazolam 0.02 mg/kg and Inj. Fentanyl 2 µg/kg intravenously. Anaesthesia was induced with 2mg/kg propofol intravenously and tracheal intubation with appropriate size cuffed endotracheal tube was facilitated with succinylcholine 2 mg/kg IV. Anaesthesia was maintained with N_2O, O_2 in the ratio of 50:50 and inspired 1.0 to 2.5% concentration of Isoflurane and muscle relaxation was achieved with Inj. Atracurium 0.5 mg/kg bolus and 0.1 mg/kg incremental doses. Ventilation was mechanically controlled and was adjusted to $ETCO_2$ concentration at 30 to 35 mmHg. Fluids were administered by calculating fluid deficit and fluid and blood loss. An orogastric tube was inserted to empty the stomach of air and other contents, the orogastric tube was removed at the completion of surgery before tracheal extubation. Abdominal insufflation for laparoscopic was achieved with CO2 and intrabdominal pressure was maintained between 14 to 18 cmH2O. At the end of the surgical procedure residual neuromuscular blockage was

antagonized by injection glycopyrrolate 10µg/kg and neostigmine 0.05 mg/kg and the patient was extubated once the patient became awake. No other sedative, analgesic or antiemetic drug was administered.

The variables recorded during intraoperative period included: total amounts of Fentanyl and fluids administered, durations of carbon dioxide insufflation, surgery and anaesthesia and occurrence of any hemodynamic instability.

After surgery, patients were observed for 24 hours. Nausea and vomiting were assessed immediately after surgery and at 30-min intervals in the post anaesthesia care unit for 2 hours and then in the ward (at 6, 12 and 24 hours post-surgery).

The occurrence of nausea and vomiting was evaluated on a 3-point ordinal scale. [8]

- 0 = no nausea or vomiting
- 1 = nausea only
- 2 = retching and / or vomiting.

If two PONV score-points was reached or if patients specifically demand antiemetic treatment in the presence of nausea, rescue antiemesis was provided with 10 mg metoclopramide intravenously. These patients were then injected the same drug at an interval of eight hrs. The "complete response", defined as no episode of PONV during the first 24 hrs after recovery from anaesthesia. Failure of prophylaxis, considered as a need for rescue antiemetic, was recorded at 2, 6, 12 and 24 hrs.

The PONV events occurring within six hrs and after six hrs was considered as early and late PONV respectively. Drug related complications, duration of hospital stay, pain intensity scores in postoperative period were recorded at 2, 6, 12, and 24 hours using a 10 cm visual analogue scale by an independent observer.

Post operative pain relief was provided with injection diclofenac sodium 75 mg (IM) when patient demanded analgesia (pain score ≥ 4 VAS) and then followed by every eight hours regimen. Further analgesia was provided with Inj. Fentanyl 25 µg intravenously if the patient demanded analgesia.

Data collected was analysed by appropriate statistical method with statistical software SPSS Version 20 (Statistical package for the social sciences). The results were expressed as mean ± standard deviation for continuous variables while frequency and percentage for discrete data. Continuous variables were analysed using unpaired two-tailed Student's 't' test. Discrete data was analysed using Chi-square test.

RESULTS:

Patients in Group O and Group OD were comparable with regards to demographics (Table:1) and baseline parameters (Table:2). Duration of CO_2 insufflation, duration of surgery, duration of anaesthesia and intraoperative IV fluids administered during intraoperative period were comparable between the groups. (Table:3). During intraoperative and postoperative period, haemodynamic parameters were comparable between the groups.

Table 1: Demographic parameters

Parameters	Mean				p-value
	Group O		Group OD		
Age (years)	44.86 ± 8.28		45.13 ± 7.60		0.89
Sex composition	male	Female	Male	female	0.14
	10 (33.33%)	20(66.67%)	5(16.66%)	25(83.33%)	
Height (cm)	156.3 ± 4.37		155.96 ± 3.43		0.74
Weight (kg)	58.17 ± 6.25		58.4 ± 5.30		0.88

Table 2: Baseline parameters

Parameters	Baseline		p-value
	Group O	Group OD	
Pulse rate / min	82.63 ± 11.08	82.63 ± 5.99	p>0.05
SBP (mmHg)	125.67± 6.62	127.26 ± 4.91	
DBP (mmHg)	80 ± 4.92	80.73 ± 5.07	
MAP (mmHg)	94.5 ± 5.80	96 ± 4.35	
SPO2 %	97.43±0.86	97.77±0.67	
Respiratory Rate/min	17.47±1.96	16.8±1.79	

Table 3: Other observed values

Parameters	Mean		p-value
	Group O	Group O	
Duration of CO2 insufflation(min)	99.13 ± 32.35	111.2 ± 24.56	0.11
Duration of surgery(min)	108.17± 32.79	120.57 ± 25.73	0.11
Duration of anaesthesia(min)	118.83 ±34.33	130.37 ± 26.55	0.15
Total intraoperative IV fluid(ml)	1243.33±197.72	1230± 160.06	0.78

Postoperative nausea and vomiting:

Overall, 17 patients (56.66%) of Group O and 8 patients (26.66%) of Group OD had nausea and/ or vomiting in 24hours (Chi-square-5.55, p value-0.018). 5 patients (16.67%) of Group O and 3 patients (10%) of Group OD had PONV in early postoperative period (Chi-square-0.58, p value-0.45) There was no PONV in first 60 min of postoperative period in both the groups. 12 patient (40%) of Group O and 5 patients (16.67%) of Group OD had PONV in late postoperative period (Chi-square-4.02, p value-0.045).

Incidence of vomiting was more in Group O. 8 (26.67%) patients of Group O and 3 (10%) patients of Group OD had vomiting in 24 hrs postoperative period (Chi Square value 2.78, p value 0.095). 2 patients of group O and 1 patient of Group OD had vomiting in early postoperative period while 6 patients of Group O and 2 patients of Group OD had vomiting in late postoperative period. (Table:4)

Table 4: Number of patients having PONV

Period	No. of Patients								
	Group O			Group OD			Total		
	N	V	PONV	N	V	PONV	N	V	PONV
Early Postoperative Period (0 – 6 hours)	3	2	5	2	1	3	5	3	8
Late Postoperative Period (6-24 hours)	6	6	12	3	2	5	9	8	17
Total (in 24 hours)	9	8	17	5	3	8	14	11	25

Need of Rescue Antiemetic:

Table 5: Need of Rescue Antiemetic

Period	No. of Patients					
	Group O		Group OD		Total	
	PONV	Rescue Antiemetic	PONV	Rescue Antiemetic	PONV	Rescue Antiemetic
Early Postoperative Period (0 – 6 hours)	5	3	3	2	8	5
Late Postoperative Period (6-24 hours)	12	9	5	3	17	12
Total (in 24 hours)	17	12	8	5	25	17

17 (56.66%) patients in Group O and 8 (26.66%) patients in Group OD had episode of PONV. Of these 17 and 8 patients of Group O and Group OD, 12 and 5 patients needed rescue antiemetic respectively (Chi Square Value 0.163, p value 0.685).

Time For Rescue Antiemetic: Mean time duration of need for rescue antiemetic in postoperative period was 934.17 ± 438.87 (min) and 635 ± 495.98 (min) in in Group O and Group OD respectively (p>0.05).

Postoperative Pain: 8 out of 17 PONV patients in Group O and 5 out 8 PONV patient had VAS ≥ 4 at the time of PONV. (Chi Square Value 3.69, p value 0.055)

Perioperative Adverse Events: 2 patients in Group O and 1 patient in Group OD had intraoperative bradycardia. 2 patients in Group O and 1 patient in Group OD had shivering in early postoperative period, none of the other adverse events observed. (Chi Square value 0.74, p value 0.39)

Duration of Hospital Stay: Mean duration of hospital stay in Group O and Group OD was 80.77 ± 6.56 and 76.43 ± 5.06 hours respectively. Difference in duration of hospital stay was significantly longer in Group O than Group OD (p<0.05).

DISCUSSION:

PONV is a major cause of patient's fear and dissatisfaction[12] and most undesirable postoperative complication from patient's perspective. [5] Laparoscopic cholecystectomy has a relatively high incidence of PONV due to effects of intraperitoneal CO_2 insufflation on residual stretching and irritation of peritoneum.[2,6]

As causes of PONV are multifactorial and there are multiple emetic neuroreceptors, it suggests that combination antiemetic approach using antiemetics that block different neuroreceptors may be necessary to treat PONV. [13] Combination antiemetic therapy was a disadvantage with traditional antiemetics (i.e., antihistamines, phenothiazines, butyrophenones, etc.) because of possibility of additive toxic CNS effects (i.e., hypotension, sedation, dry mouth, EPS, etc.). Recent studies have evaluated and supported the effectiveness of the 5-HT3 receptor antagonists when used in combination with other antiemetics. [14]

Ondansetron was the first 5-HT_3 receptor antagonist approved for PONV by both oral and intravenous administration in adults and children. [15-18] Dexamethasone was first reported to be effective antiemetic agent in patients receiving cancer chemotherapy in 1981. [19] Dexamethasone has also been shown to provide greater protection from delayed chemotherapy-induced nausea and vomiting compared with Ondansetron. [20] Dexamethasone and ondansetron are the two most commonly used drugs in clinical practice for PONV prophylaxis. [21] McKenzie et al [22] found that the prevention of PONV was significantly greater in the combined ondansetron plus dexamethasone group than in patients receiving ondansetron alone.

Pain is inseparably combined with nausea and vomiting and the need to administer narcotic based pain killer often can intensify the frequency of PONV, [23] for this reason we administered nonsteroidal anti-inflammatory drugs postoperatively. In our study, need of rescue antiemetic (p value 0.28), time for rescue analgesic (p value 0.11), VAS pain scores (p value 0.055) were similar between groups

Overall, 17 patients (56.66%) of Group O and 8 patients (26.66%) of Group OD had nausea and/ or vomiting in 24hours (p value0.018). 5 patients (16.67%) of Group O and 3 patients (10%) of Group OD had PONV in early postoperative period (p value0.45) and 12 patient (40%) of Group O and 5 patients (16.67%) of Group OD had PONV in late postoperative period (p value0.045).

In our study, during the first six hrs Ondansetron and Ondansetron-Dexamethasone combination were equally effective in preventing early PONV (16.67% vs 10%). (p value0.45) Gautam B et al [11] found incidence of early PONV was significantly higher in Group D (21.3%) compared to 6.3% and 2.1% of patients in Group O and OD respectively.

In our study in late postoperative period number of patients having PONV are significantly more (40%) in Group O compared to (16.67%) in Group OD (p value-0.045). Thongrong C et al [24] compared the effects of dexamethasone plus ondansetron with placebo in patients who underwent microvascular decompression surgery. At 24 hr post-surgery Group D had a lower incidence (66.7%) and lower severity of PONV than placebo Group (81.5%). Wang JJ et al [4] observed that 10 % patients in dexamethasone group compared with 34% in saline group had vomiting, total incidence of nausea and vomiting was 23% in dexamethasone group compared with 63% in saline group.

Overall PONV observed for 24 hours postoperatively in our study was significantly more in Group O (56.66%) than in Group OD (26.66%) (p value0.018). Complete response was observed in 43.33% and 73.33% patients in Group O and Group OD respectively. Gautam B et al [11] observed complete response i.e., no PONV in 24 hours in 66.7%, 66%, and 89.4% patients in Groups O, D and OD respectively. Lopez-olaondo L et al [25] studied combination of ondansetron and dexamethasone in patients undergoing general anesthesia for major gynecological surgery. Complete response (no PONV) occurred in 84% of patients in ondansetron plus dexamethasone group, 60% of patients in dexamethasone group, 52 % of patients in ondansetron group and 20 % of patients in placebo group.

During 24 hrs after recovery from anaesthesia, the need for rescue antiemetic in patients who received a combination of Ondansetron and Dexamethasone was less than those in patients who received Ondansetron alone. But the difference between the groups was statistically insignicant. (PONV 17 vs 8, and Need for Rescue antiemetic 12 vs 5 in Group O and Group OD respectively) (p value 0.685). Gautam B et al [11] found that in the late postoperative period (6-24 hr) patients in the Ondansetron Group required more frequent antiemetic rescue compared to patients in the combination Group. Rajeeva V et al [26] observed that pain scores, need for rescue analgesic and antiemetic did not differ among Groups.

Baseline, intraoperative and postoperative hemodynamic parameters were comparable in both study groups.

In our study, 2 patients in Group O and 1 patient in Group OD had intraoperative bradycardia and 2 patients in Group O and 1 patient in Group OD had shivering in early postoperative period. No any other adverse event observed in both the groups. The lack of difference in side effects among groups in our study suggests that a single dose of these study drugs is safe. Further larger scale studies and a longer follow-up are indicated. Joss RA et al [27] observed that 20% patients in ondansetron plus placebo and 25% in ondansetron plus dexamethasone group experienced at least one, usually mild adverse event (headache, epigastric pain, constipation, diarrhea, facial flushing). Koivuranta MK et al [28] found that headache was most frequently reported adverse event (9 in ondansetron group and 6 in placebo group) in patients undergoing laparoscopic cholecystectomy

Most commonly reported side effect of ondansetron is headache, a weak antagonistic effect at 5-HT1 receptors may precipitate headache in susceptible individuals. Abnormal bowel function (constipation more often than diarrhoea), seizure activity and excessive fatigue and weakness have also been associated with ondansetron.[29] By rapid intravenous administration, ondansetron can produce significant hypotension with tachycardia that can lead to syncopal episodes in awake patients. In rare situations, ondansetron can induce angina.[30] The side effect profile of ondansetron should be considered along with its efficacy in preventing unwanted nausea and vomiting.[31] Dexamethasone is known to cause side effects such as increased incidence and severity of infection, adrenal suppression and delayed healing in surgical patients. [32]

PONV resulting into dehydration, electrolyte imbalance, wound dehiscence, pulmonary aspiration may lead to delayed hospital discharge. [5,7] Combination of antiemetic therapy is more effective than one drug alone in preventing PONV after laparoscopic cholecystectomy with no difference in time to discharge.[9] In our study, duration of hospital stay was longer in Group O than Group OD (mean 80.77±6.56 versus 76.43±5.06 hours, $p<0.05$). Mean duration of hospital stay observed by Gautam B et al [12] was 53.6 ± 2.1, 57.5 ± 2.2, and 58.3 ± 2.6 hours in group O, group D, and group OD respectively and the difference was comparable. In our study, we didn't assess patients after 24 hours and whether more incidence of PONV has prolonged hospital stay in group O or any other cause beyond 24 hours of our observation period led to this delay is difficult for us to interpret.

Limitations Of Study:

1. We didn't assess frequency and duration of PONV.
2. Patient's satisfaction with regards to prevention of PONV was not assessed.
3. In our study, PONV and other postoperative adverse effects beyond 24 hours were not assessed.

Further Scope Of The Study:

1. Sample size of our study was smaller and to generalize the results further study with larger sample size can be carried out including assessment of frequency and duration of PONV, patients' satisfaction and incidence of postoperative adverse effects till discharge.
2. Further study with different timing of administration of ondansetron and dexamethasone can be carried out to assess prevention of early PONV. Timing of administration of dexamethasone can be 4–6 hours prior to induction of anaesthesia and ondansetron at induction.

CONCLUSION:

Combination of ondansetron plus dexamethasone is more effective than ondansetron alone for preventing postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy. Comparable incidence of PONV in early postoperative period and better prevention of PONV in late postoperative period by addition of dexamethasone to ondansetron can be attributed to late onset and prolonged duration of action of dexamethasone.

REFERENCES:

1. Cunningham AJ. Anesthetic implications of laparoscopic surgery. The Yale journal of biology and medicine. 1998 Nov;71(6):551.
2. Stanton JM. Anaesthesia for laparoscopic cholecystectomy. Anaesthesia. 1991 Apr;46(4):317-.
3. Wang JJ, Ho ST, Liu YH, Lee SC, Liu YC, Liao YC, Ho CM. Dexamethasone reduces nausea and vomiting after laparoscopic cholecystectomy. British journal of anaesthesia.

1999 Nov 1;83(5):772-5.
4. Kapur PA. The big "little problem". Anesthesia & Analgesia. 1991 Sep 1;73(3):243-5.
5. Cao X, White PF, Ma H. An update on the management of postoperative nausea and vomiting. Journal of anesthesia. 2017 Aug;31:617-26.
6. Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology. 1992 Jul 1;77(1):162-84.
7. Gupta V, Wakhloo R, Lahori V, Mahajan MK, Gupta SD. Prophylactic antiemetic therapy with ondansetron, granisetron and metoclopramide in patients undergoing laparoscopic cholecystectomy under general anaesthesia. JK Science April-June 2008;10(2):74-77
8. Gautam B, Shrestha BR, Lama P, Rai S. Antiemetic prophylaxis against postoperative nausea and vomiting with ondansetron-dexamethasone combination compared to ondansetron or dexamethasone alone for patients undergoing laparoscopic cholecystectomy. Kathmandu University Medical Journal. 2008;6(3):319-28.
9. Fujii Y. The utility of antiemetics in the prevention and treatment of postoperative nausea and vomiting in patients scheduled for laparoscopic cholecystectomy. Current pharmaceutical design. 2005 Sep 1;11(24):3173-83.
10. Chu CC, Hsing CH, Shieh JP, Chien CC, Ho CM, Wang JJ. The cellular mechanisms of the antiemetic action of dexamethasone and related glucocorticoids against vomiting. European journal of pharmacology. 2014 Jan 5;722:48-54.
11. Alia I, Gillani M, Hanif A. Comparison of ondansetron and combination of ondansetron and dexamethasone for prevention of post-operative nausea and vomiting in patients undergoing elective laparoscopic cholecystectomy. Age (years). 2015 Oct 1;40(67):40-9.
12. Thune A, Appelgren L, Haglind E. Prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. A prospective randomized study of metoclopramide and transdermal hyoscine. The European journal of surgery= Acta chirurgica. 1995 Apr 1;161(4):265-8.
13. Kovac AL. Prevention and treatment of postoperative nausea and vomiting. Drugs. 2000 Feb;59:213-43.
14. Markman M, Sheidler V, Ettinger DS, Quaskey SA, Mellits ED. Antiemetic efficacy of dexamethasone: randomized, double-blind, crossover study with prochlorperazine in patients receiving cancer chemotherapy. New England Journal of Medicine. 1984 Aug 30;311(9):549-52.
15. Leeser J, Lip H. Prevention of postoperative nausea and vomiting using ondansetron, a new, selective, 5-HT3 receptor antagonist. Anesthesia & Analgesia. 1991 Jun 1;72(6):751-5.
16. Kenny GN, Oates JD, Leeser J, Rowbotham DJ, Lip H, Rust M, Saur P, Onsrud M, Haigh CG. Efficacy of orally administered ondansetron in the prevention of postoperative nausea and vomiting: a dose ranging study. British Journal of Anaesthesia. 1992 May 1;68(5):466-70.
17. McKenzie R, Kovac A, O'Connor T, Duncalf D, Angel J, Gratz I, Tolpin E, McLeskey C, Joslyn A. Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in women undergoing ambulatory gynecologic surgery. Anesthesiology. 1993 Jan 1;78(1):21-8.
18. Kovac AL, Pearman MH, Khalil SN, Scuderi PE, Joslyn AF, Prillaman BA, Cox F. Ondansetron prevents postoperative emesis in male outpatients. Journal of clinical anesthesia. 1996 Dec 1;8(8):644-51.
19. Aapro MS. Dexamethasone as an antiemetic in patients treated with cisplatin. N Engl J Med. 1981;305:520.
20. Jones AL, Hill AS, Cunningham D, Soukop M, Hutcheon AW, Cassidy J, Kaye SB, Sikora K, Carney DN. Comparison of dexamethasone and ondansetron in the prophylaxis of emesis induced by moderately emetogenic chemotherapy. The Lancet. 1991 Aug 24;338(8765):483-7.
21. Maitra S, Som A, Baidya DK, Bhattacharjee S. Comparison of ondansetron and dexamethasone for prophylaxis of postoperative nausea and vomiting in patients undergoing laparoscopic surgeries: a meta-analysis of randomized controlled trials. Anesthesiology research and practice. 2016 Oct;2016.
22. McKenzie R, Tantisira B, Karambelkar DJ, Riley TJ, Abdelhady H. Comparison of ondansetron with ondansetron plus dexamethasone in the prevention of postoperative nausea and vomiting. Anesthesia & Analgesia. 1994 Nov 1;79(5):961-4.
23. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. The Journal of the American Society of Anesthesiologists. 1999 Sep 1;91(3):693-.
24. Thongrong C, Chullabodhi P, Kasemsiri P, Kitkhuandee A, Plailaharn N, Sabangban L, Jimarsa T. Effects of intraoperative dexamethasone and ondansetron on postoperative nausea and vomiting in microvascular decompression surgery: a randomized controlled study. Anesthesiology Research and Practice. 2018 Oct;2018.
25. Lopez-Olaondo L, Carrascosa F, Pueyo FJ, Monedero P, Busto N, Saez A. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. British Journal of Anaesthesia. 1996 Jun 1;76(6):835-40.
26. Rajeeva V, Bhardwaj N, Batra YK, Dhaliwal LK. Comparison of ondansetron with ondansetron and dexamethasone in prevention of PONV in diagnostic laparoscopy. Canadian Journal of Anesthesia. 1999 Jan;46:40-4.
27. Joss RA, Bacchi M, Buser K, Kirchner V, Neuenschwander H, Orth B, Aapro MS, Thürlimann B, Swiss Group for Clinical Cancer Research (SAKK. Ondansetron plus dexamethasone is superior to ondansetron alone in the prevention of emesis in chemotherapy-naive and previously treated patients. Annals of oncology. 1994 Mar 1;5(3):253-8.
28. Koivuranta MK, And EL, Ryhänen PT. Antiemetic efficacy of prophylactic ondansetron in laparoscopic cholecystectomy: A randomised, double blind, placebo controlled trial. Anaesthesia. 1996 Jan;51(1):52-5.
29. Russell D, Kenny GN. 5-HT3 antagonists in postoperative nausea and vomiting. British Journal of Anaesthesia. 1992 Jan 1;69(Supplement_1):63S-8S.
30. Bosek V, Hu P, Robinson LA. Acute myocardial ischemia after administration of ondansetron hydrochloride. The Journal of the American Society of Anesthesiologists. 2000 Mar 1;92(3):885-.
31. Ye JH, Ponnudurai R, Schaefer R. Ondansetron: a selective 5 HT3 receptor antagonist and its applications in CNS related disorders. CNS drug reviews. 2001 Jun;7(2):199-213.
32. Baxendale BR, Vater M, Lavery KM. Dexamethasone reduces pain and swelling following extraction of third molar teeth. Anaesthesia. 1993 Nov;48(11):961-4.