Original Research Article

Comparison of ondansetron and combination of ondansetron and dexamethasone on preventing PONV on patients undergoing surgery under general anaesthesia

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Abstract

Background: Postoperative nausea and vomiting are frequent and well recognized unpleasant complications following anaesthesia and surgery. Ondansetron is effective in preventing nausea and vomiting but some cases refractory to ondansetron alone can be treated successfully with ondansetron plus dexamethasone in combination. **Aim:** To compare the efficacy of ondansetron alone with ondansetron and dexamethasone combination in preventing PONV. **Material and Methods:** A total of 172 patients were randomly allocated in Group A and Group B using lottery method. Group A was patients taking injection ondansetron 4mg alone and Group B was patients taking injection ondansetron 4mg plus injection dexamethasone 8mg I.V. in combination. PONV was assessed using VAS as mild, moderate and severe. **Results:** In Group A, 33 cases and in Group B, 12 cases experienced early nausea while in Group A, 27 cases and in Group B, 10 cases experienced delayed nausea. In Group A, 12 cases and in Group B, 2 case experienced early vomiting while in Group A, 17 cases and in Group B, 7 cases experienced delayed vomiting. **Conclusion:** The combination therapy of ondansetron and dexamethasone given intravenously just after induction is safe and more effective than injection ondansetron alone in reducing the incidence of early nausea and delayed nausea and vomiting. It is also effective in long term prevention of postoperative nausea and vomiting in patients undergoing elective surgeries under general anaesthesia.

Keywords: postoperative nausea and vomiting, general anaesthesia, ondansetron, dexamethasone

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INTRODUCTION

Postoperative nausea and vomiting (PONV) are frequent and well recognized unpleasant complications following anaesthesia and surgery. Antiemetic drugs play an important role in the therapy of PONV. Though many drugs have been tried in the prophylaxis and treatment of PONV, no drug has been proved significantly effective and a search for a better drug continues.[1] Ondansetron is effective in preventing nausea and vomiting but some cases refractory to ondansetron alone can be treated successfully with ondansetron plus dexamethasone in combination. Combination of ondansetron and dexamethasone was taken because though 5HT-3 antagonists are potent antiemetics no single drug has been successful in effectively controlling PONV. So, drugs acting by other mechanism have to be added to effectively control PONV.[2] Dexamethasone acts as an antiemetic by[3] reducing levels of 5-hydroxytryptophan in neural tissue by depleting its precursor tryptophan, anti-inflammatory properties prevent release of serotonin in the gut. Moreover, dexamethasone potentiates main effect of ondansetron as an antiemetic by sensitizing its receptors. Pain is important trigger factor of PONV, by its anti-inflammatory action dexamethasone reduces pain and

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hence PONV.[4,5] This study was conducted to compare the efficacy of ondansetron alone with ondansetron and dexamethasone combination in preventing PONV.

MATERIAL AND METHODS

The present prospective, randomized, double-blind study was conducted in 172 adult patients undergoing elective surgeries under general anaesthesia in our institution. After institutional committee approval and written informed consent, patients posted for various surgeries requiring general anaesthesia were selected.

Inclusion criteria: Patients undergoing surgeries under general anaesthesia. Patients of either sex: male/female. Patients aged between 18 to 50 years. Patients belonging to ASA-1 grade.

***Exclusion criteria*:** Patients' refusal for the study. Seriously /terminally ill patients. Pregnant or lactating women. Mentally challenged patients. Patients having cardiac arrhythmia or electrolyte imbalances. Patients taking medicine with known antiemetic activity.

Sample size

Sample size was calculated on the basis of previous study.[6] In their study, complete response was seen as 38% in group 1 taking injection ondansetron alone and 52% taking injection ondansetron plus injection dexamethasone. Population risk difference was assumed to be 0.1 with 80% C.I. 0.14% estimated risk differences and 20 % dropout, sample size comes to 86 per group. Sample size was calculated by master1.0 software. A total of 172 patients were selected from our hospital under general anaesthesia. Patients were randomly allocated by co-investigator in 2 groups, Group A and Group B using lottery method, that is by asking patients to pick one of two chits on which name of group was present. Group A was patients taking injection ondansetron 4mg alone and Group B was patients taking injection ondansetron 4mg plus injection dexamethasone 8mg I.V. in combination. Person not involved in study had prepared identical syringes containing the study drugs. This had been administered by one of the two investigators who were not aware of which treatment patient had receiving. In postoperative period one of the blinded investigator had assessed the patients.

Methodology

Preoperative evaluation

Preoperative visit was conducted on the day before surgery. Detailed history of patient's complaints was noted. General and systemic examination of cardiovascular and respiratory system was done. Basic investigations like haemoglobin, total count and differential count, ESR, blood sugar estimation, blood urea and serum creatinine and urine screening for albumin, sugar and microscopy were done. Other investigations included ECG, chest X-ray, HIV and HbsAg. Patients were advised to remain nil orally after midnight. On the morning of surgery, no premedication was given. Patients were explained in detail about the research and informed consents were taken from them. When patients were brought to operation theatre, their heart rate and blood pressure were recorded. An i.v. access with an appropriate size cannula was obtained. After pre-oxygenation for 3 minutes general anaesthesia was given by using injection midazolam 0.03mg/kg and injection fentanyl 2mcg/kg to provide analgesia and sedation. Injection propofol 2mg/kg was used as induction agent and injection vecuronium 0.1 mg/kg as muscle relaxant. Orotracheal /nasotracheal intubation with an appropriate sized cuffed portex tube was done. Anesthesia was maintained with nitrous oxide and oxygen in the ratio of 50:50, using controlled ventilation and injection vecuronium intermittently. Immediately after induction in Group A injection ondansetron 4mg and in Group B injection ondansetron 4mg plus injection dexamethasone 8mg i.v. were given. Continuous monitoring of pulse rate, blood pressure, ECG, SPO_2 urine output was done. After completion of surgery, thorough suctioning of mouth and throat was done. Injection neostigmine 0.05mg/kg with injection glycopyrrolate 8mcg/kg was used as neuromuscular reversal agent. After extubation patients were shifted to recovery room and after half hour when they were vitally stable shifted to ward. Patients were observed for 24 hours post-operatively. Nausea, vomiting and pain were recorded at 1, 2, 3, 6, 12 and 24 hours post-operatively. Any other complications were also noted.

Assessment

PONV was assessed using VAS from 0 to 10, mild (0 to 3), moderate (4 to 6) and severe (7 to 10). Each episode of vomiting producing at least 5ml was recorded; repeated vomiting within 1 to 2 minute period was recorded as single episode. Rescue antiemetic was given for VAS score of 5 or more both for nausea and vomiting. Injection metoclopromide 10 mg was used as rescue antiemetic. For pain injection paracetamol 1gm 6 hourly and injection diclofenac 1mg/kg 8 hourly were given.

Statistical analysis

Study results were analyzed by student's "t" test and categorical data was analyzed by chi-square test. A p-value of less than 0.05 was considered for statistical significance.

RESULTS

Mean age in group A was 31.36±7.96 and group B was 30.48±6.38 years. Group A and Group B contributes 86 cases in each group, out of 86 cases 45 i.e., 52.3% were males while 41 i.e., 47.7% were females in each group. Mean duration of anaesthesia in group A was 62.38±32.22 mins and group B was 71.95±38.67 mins. 19 i.e., 22.09% case in Group A compare to 8 i.e., 9.3% cases in group B needed Rescue antiemetic.

Table 1: Age and DOA in both group

Name of surgery	Group A	Group B
Umbilical Hernia Repair	5	4
Keloid excision	11	7
Stoma Closure	11	11
Lipoma excision	13	9
Hemithyroidectomy	9	5
Subtotal Thyroidectomy	3	3
Pancreaticojejonostomy	2	2
Thyroglossal cyst excision	5	5
Submandibular gland excision	4	4
Cystogastrostomy	1	3
Cardiomyotomy	3	2
Choledocal cyst removal	2	5
Superficial Parotidectomy	3	3
Near Total thyroidectomy	2	2
Open Cholecystectomy	1	1
Fibroadenoma excision	3	1
Choledocholithotomy	2	2
Total proctocolectomy with ileal pouch	1	4
Cystojejunostomy	1	4
Cystodudenostomy	1	2
Spleenectomy	1	4
Hyadit Cyst Removal	1	1
Truncal vagotomy with antrectomy	1	2

Table 1 shows that patients in both groups were subjected to nearly similar type of surgery and they were comparable in all aspects.

Table 2: Association of Early and Delayed Nausea in both Group

	Early Nausea (up to 6hrs)		Delayed Nausea (after 6 hrs)	
	Group A	Group B	Group A	Group B
No Evidence	53	74	59	76
Mild	27	09	27	09
Moderate	06	03	00	01
Total	**86(100%)**	**86(100%)**	**86(100%)**	**86(100%)**

Last two rows (mild and moderate nausea) were clubbed together. [Chi square: (df=1; p value=0.00, significant)]. In Group A, 33 cases and in Group B, 12 cases experienced early nausea while in Group A, 27 cases and in Group B, 10 cases experienced delayed nausea.

Table 3: Association of Early and Delayed Vomiting in both Group

	Early vomiting (up to 6 hrs)		Delayed vomiting (after 6 hrs)	
	Group A	Group B	Group A	Group B
No Evidence	74	84	69	79
Mild	08	02	12	07
Moderate	03	00	05	00
Severe	01	00	00	00
Total	86 (100%)	86 (100%)	86 (100%)	86 (100%)

Last three rows (mild, moderate and severe vomiting) were clubbed together [Chi square: (df=1; p value=0.009 and significant)]. In Group A, 12 cases and in Group B, 2 case experienced early vomiting while in Group A, 17 cases and in Group B, 7 cases experienced delayed vomiting.

DISCUSSION

Post-operative nausea and vomiting are the most common complaints after anaesthesia and surgery. PONV can contribute to the development of medical problems and patients with PONV consume more resources and require additional health care professional time compared with patients in whom these complications are avoided. The overall incidence of PONV during the first 24 hours after surgery is approximately 23% with comparable variability. This incidence may be larger depending on preoperative patient characteristics, factors related to operation and anaesthesia, the intensity of pain and its management in the postoperative period.[7] The mechanism of antiemetic action of corticosteroids is unknown, but may be related to inhibition of prostaglandin synthesis, decrease in 5 – HT3 level in the CNS and by an anti-inflammatory action at operative site.[8] Nucleus tractus solitarius in the medulla and Area Postrema are the main regions in which dexamethasone exerts its central antiemetic action. In our study, first 24hrs after surgery, patients were monitored for 1hr, 2hr, 3hr, 6hr, 12hr, and 24 hrs. In which 1hr to 6hr was early phase and onwards up to 24hrs was delayed phase. In our study of group A, 38.37% patients experienced early nausea while 31.39% patients experienced delayed nausea. In group B, 13.95% of patients had early while 11.62% patients experienced delayed nausea. Post-operative nausea was less in the combination group which is comparable to the study of Rajeeva *et al.*.[9] Fewer patients in combination group had late nausea similar to finding of Lopez *et al.*,[10] where only 12% of patients in combination group had delayed nausea as compared with 38% in the ondansetron group. Our study did not correlate with that of Rusch D *et al.*[11] whose study results found that the incidence of postoperative nausea did not differ much in the two high risk groups, 20% in the patients receiving ondansetron and 15% in patients receiving ondansetron and dexamethasone combination. Perhaps the difference in their study was due to inclusion of large number of subjects in their study and variability in surgeries conducted. Our study regarding incidence of early vomiting in ondansetron group was 13.95% and delayed vomiting was 19.76%. This is comparable to Rajeeva *et al.*[9] study who had 15% early emesis and 35% delayed emesis after ondansetron. In the combination group of our study, the incidence of early vomiting was found to be 2.32% and delayed vomiting 8.13%. This is also comparable to the study of Rajeeva *et al.*,[9] but does not agree with Lopez *et al.*,[10] where no patient vomited in early period but 4% patients had vomiting episodes by 24 hours. In their study patients were undergoing major gynaecological surgery of longer duration than in our study, which may explain their results. It also did not correlate with the study of Rusch *et al.*[11] in which the incidence of postoperative vomiting was similar in both groups 11% in the ondansetron group and 7% in ondansetron plus dexamethasone group. This may be because their study was done in only high risk groups and included a large number of patients. Sanchez –Ledesma *et al.*[12] in their study found out that a complete response defined as no nausea and no emetic episode occurred in 70% of patients who received ondansetron and dexamethasone which was comparable to our study where 94.76% of patients who received the combination showed a complete response. A wide dose range study[4] of dexamethasone (2-16 mg) has been used in the management of PONV and emesis related to chemotherapy and gynaecological surgeries.[13] Dexamethasone 8 mg was used most widely and found to be most cost effective and was the reason behind our selection for the present study. In our study, 22.09% of patients in group A required rescue antiemetic compared to 9.3% of patients in group B and was statistically significant. This was comparable to the study conducted by Rusch *et al.*[11] who showed that patients who were given combination of ondansetron and dexamethasone required less antiemetic. It also correlates with the study of Lopez-olaondo *et al.*[10] who showed that fewer patients in the combination group needed antiemetic rescue than patients treated with ondansetron alone. The adverse effects, related to the use of combination therapy versus ondansetron alone did not reveal significance in our study. This was in accordance with the study of Rusch D *et al.*[11] where it was found that the patients receiving ondansetron and dexamethasone combination had the same degree and number of adverse effects, as did those receiving only ondansetron. It also correlates with the study of Thomas R *et al.*[13] whose study reported that most frequent adverse events were fatigue, headache, dizziness, but there were no differences between groups. Furthermore, study by Gan TJ *et al.*[14] have found that adverse events have not been noted after a single bolus dose of dexamethasone. Different studies have been done to control PONV with various combination therapies. The potential advantages of combination therapy using drugs that act on different pathways in the emetic response include improved efficacy, extended duration of the antiemetic effect, the ability to combine drugs with greater antinausea versus greater antiemetic effects and the possibility of using smaller of individual drugs compared with monotherapy.[15]

CONCLUSION

From our study we conclude that the combination therapy of injection ondansetron 4 mg and injection dexamethasone 8 mg given intravenously just after induction is safe and more effective than injection ondansetron 4 mg i.v. alone in reducing the incidence of early nausea and delayed nausea and vomiting. It is also effective in long term prevention of postoperative nausea

and vomiting in patients undergoing elective surgeries under general anaesthesia. It can also be concluded that this combination therapy is safe with less adverse effects.

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