

	Journal Homepage: - www.journalijar.com INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR) Article DOI: 10.21474/IJAR01/16208 DOI URL: http://dx.doi.org/10.21474/IJAR01/16208	
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RESEARCH ARTICLE

COMPARISON OF EFFECT OF INJ DEXAMETHASONE WITH INJ ONDANSETRON AND INJ DEXAMETHASONE WITH INJ METOCLOPRAMIDE FOR PREVENTION OF POST-OPERATIVE NAUSEA AND VOMITING(PONV) AFTER GENERAL ANAESTHESIA AT TERTIARY CARE CENTER

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Manuscript Info

Manuscript History

Received: 30 November 2022

Final Accepted: 31 December 2022

Published: January 2023

Abstract

Introduction: Postoperative nausea & vomiting (PONV) are common distressing complications of anaesthesia. Pain ,nausea & vomiting are frequently listed by the patient as their most important postoperative concerns. PONV results in increased patient' s discomfort and dissatisfaction. Despite continuing advances in anaesthetic and surgical technique, both the incidence and severity of PONV remain relatively unchanged.

Material and Methods: A total of 200 patients belonging to ASA grade 1 and 2 posted for surgery under general anaesthesia were included after satisfying the eligibility criteria. They were divided into two groups.Group O received Dexamethasone 8 mg i.v. + Ondansetron 4 mg i.v.Group M received Dexamethasone 8 mg i.v. + Metoclopramide 10 mg i.v.In this study, the primary aim was to assess the incidence of post operative nausea and vomiting in the first 8 hrs after surgery in both the groups.

Results: In group M ,total 32 patients out of 100 had nausea as compared to group O where 14 patients had nausea.In group M, 19 patients had mild nausea as compared to 9 patients in group O. 13 patients had moderate nausea in group M as compared to 5 patients in group O. In group M 25 patients had episodes of vomiting out of 100 as compared to group O where 8 patients had vomiting episodes. In group M, 13 patients had mild vomiting episodes as compared to 4 patients in group O. 12 patients had moderate vomiting episodes in group M as compared to 4 patients in group O .The difference between two groups was statistically significant.

Conclusion: In this study ,nausea and vomiting score was significantly low in group O which is the combination of dexamethasone and ondansetron as compared to the M group which consists of dexamethasone and metoclopramide. Thus we can conclude that dexamethasone (8 mg) and ondansetron(4 mg) combination has better antiemetic effect than the combination of dexamethasone (8 mg) and metoclopramide 10 mg) to prevent PONV after general anaesthesia.

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Introduction:-

Postoperative nausea and vomiting (PONV) is one of the most unpleasant and distressing symptoms which follows anaesthesia and surgery and leads to serious postoperative complications¹. Postoperative nausea and vomiting, commonly abbreviated as PONV, is defined as nausea and or vomiting that occurs within 24 hours after surgery and can occur following general, regional or local anaesthesia². PONV has been a potential complication following surgery and anaesthesia since the “ether era, with an occurrence of 75% to 80% at that time³. The overall incidence of PONV has been reported to be between 20% and 30%, but can increase up to 80% in high risk patients^{1,4}.

Postoperative nausea and vomiting is often referred to as the “big, little problem” within the anaesthesia world and has been a common complication for both in-patients and out-patients undergoing virtually all types of surgical procedures^{5,6}.

PONV occurs frequently in gynecological, obstetric, ocular, breast and middle ear surgeries⁷. Patients undergoing major gynaecological surgeries are especially prone to PONV, with reported incidence of 50-75%^{7,8}.

A number of factors influence the occurrence of PONV. Patient factors like age, female gender, nonsmoker, obesity, anxiety, history of motion sickness or previous PONV and gastro paresis, operative procedures, anaesthetic techniques like drugs for general anaesthesia, regional anaesthesia and monitored anaesthesia care, and post-operative factors like pain, ambulation, oral in-take and opioids, determine the incidence of PONV^{7,8}.

PONV frequently results in prolonged postoperative stay, unanticipated admission and increased health care costs⁹. It is apparently a major concern of many patients scheduled to undergo elective surgical procedures. Patients often perceive PONV as one of the most bothersome complication of anaesthesia – related adverse effects and may consider it as distressing as the pain associated with the surgical procedure. Until recently, PONV was considered a relatively unimportant postoperative complication, but the growing emphasis on day-care surgery has focused attention on complications, which might delay discharge. Development of an effective antiemetic therapy has been hampered by the multifactorial nature of PONV, involving anaesthetic, surgical, and individual risk factors⁹.

The consequences of PONV are surgical, physical and anaesthetic complications for patients and financial implications for the hospitals or institutions. The anaesthetic consequences are increased aspiration pneumonitis and discomfort in recovery. For institutions there is increased financial burden because of increased nursing care, delayed discharge and unexpected admissions. In ambulatory surgery too, PONV delays the hospital discharge. This necessitates the use of prophylactic antiemetics¹⁰.

None of the available antiemetics are entirely effective for preventing PONV, especially in high-risk patients¹¹. The management of PONV has improved greatly in recent years, with the introduction of 5-Hydroxytryptamine (5-HT₃) receptor antagonists and are widely regarded as the most efficacious antiemetics available today and are currently recommended as the agents of first choice to control PONV in most instances¹¹.

Since at least four major receptor systems are involved in the etiology of PONV, a better prophylaxis might be achieved by using a combination of agents acting at different receptor sites¹¹. For example, if the serotonin receptors have already been blocked, consider adding an anticholinergic, antidopaminergic or antihistaminic. The concept of combination antiemetic therapy was first introduced in chemotherapy induced vomiting. Its success prompted similar research in the field of PONV¹¹. There is increasing evidence that the multimodal approach may improve the outcome. Double and triple antiemetic combinations are recommended for patients with high risk for PONV^{10,11}. Several studies are being conducted with different drug combinations and different dosages. Combination of 5HT₃ receptor antagonists and Dexamethasone has been recommended for prophylaxis in high risk group¹². The most common prophylactic antiemetic combination used to prevent PONV in our institution is a combination of Intravenous ondansetron, a 5HT₃ receptor antagonist with Dexamethasone.

Hence the present study was designed to assess the efficacy and safety of dexamethasone and ondansetron versus dexamethasone and metoclopramide in preventing and reducing the incidence of PONV for surgeries performed under general anaesthesia.

Methods:-

The present study was conducted in the department of anaesthesiology of a medical college and tertiary health care centre. A total of 200 patients undergoing surgery under general anaesthesia were included after satisfying the eligibility criteria. Written informed consent was taken from all the patients. Detailed clinical history and investigational findings (complete blood count, bleeding time, clotting time, blood sugar levels, renal function tests, chest x-ray, ECG, serology status) were recorded in a structured proforma (Annexure I).

All patients were premedicated with inj. glycopyrrolate 0.004 mg/kg body weight i.v. inj. Midazolam 0.04 mg/kg body weight i.v. and inj. Ranitidine 50 mg i.v. and preoxygenated with 100 % oxygen for 3 minutes. Before induction of anaesthesia randomly selected 100 patients were administered dexamethasone (8 mg) with ondansetron (4 mg) and another 100 patients were administered dexamethasone (8 mg) with metoclopramide (10 mg). Induction of anaesthesia was done with propofol 2 mg/kg body weight i.v. slowly followed by inj. succinylcholine 2 mg/kg body weight i.v. Patients were ventilated with 100 % oxygen with IPPV till the onset of action of succinylcholine and after proper relaxation tracheal intubation was done with proper size endotracheal tube. Anaesthesia was maintained with 50 % oxygen and 50 % nitrous oxide and isoflurane. Neuromuscular blockade was achieved with injection vecuronium 0.05 mg/kg body weight i.v. At the end of the surgery reversal of neuromuscular blockade was done with inj. neostigmine 0.05 mg/kg body weight i.v. and inj. glycopyrrolate 0.01 mg/kg body weight. After extubation, patients were observed in the recovery room until they were haemodynamically stable, fully conscious and comfortable.

In this study, the primary aim was to assess the incidence of post operative nausea and vomiting in the first 8 hrs after surgery. The incidence of nausea and vomiting in each group was noted separately. The data was reported as mean $\pm$ SD (standard deviation) and difference between two groups was determined using repeated measures of analysis. A p value of < 0.05 is considered statistically insignificant.

The Nausea score was evaluated using an 11- point numerical scale, where 0 = [no nausea] and 10 = [nausea as bad as can be]

Mild : < 5 episodes .

Moderate : = 5 episodes.

Severe : > 5 episodes.

The severity of emetic episodes in terms of no. of episodes per patient in each group was tabulated .The number of episodes per patient will be classified as

Mild : < 2 episodes.

Moderate : = 2 episodes.

Severe : > 2 episodes.

Results:-

A total of 200 patients belonging to ASA grade 1 and 2 posted for surgery under general anaesthesia were included after satisfying the eligibility criteria. They were divided into two groups.

Group O received Dexamethasone 8 mg i.v. + Ondansetron 4 mg i.v.

Group M received Dexamethasone 8 mg i.v. + Metoclopramide 10 mg i.v

The mean age in group O was 30.3 ± 6.3 years against 30.1 ± 5.9 years in group M.

The mean duration of surgery in group O was 62.8 ± 18.8 minutes as compared to group M where it was 63 ± 16.1 minutes. There was no statistically significant difference between the two groups with regards to age and duration of surgery (p value > 0.05). Refer to table 1.

In group M, 53 patients were female and 47 patients were male among 100 patients against 52 patients were female and 48 patients were male in group O. The differences was found to be statistically insignificant (p value > 0.05). Refer to table 2. In group M, 75 patients were operated under ASA grade 1 and 25 patients in ASA grade 2 out of 100 patients whereas in group O out of 100 patients, 86 patients were operated in ASA grade 1 and 14 patients in

ASA grade 2. There was no statistically significant difference between the two groups with regards to the ASA grading (p value > 0.05). Refer to table 3.

Patients in both the group M and O were subjected to similar type of surgeries and They were comparable in all aspects.

In group M, total 32 patients out of 100 had nausea as compared to group O where 14 patients had nausea. In group M, 19 patients had mild nausea as compared to 9 patients in group O. 13 patients had moderate nausea in group M as compared to 5 patients in group O. None of the patients in both the groups had severe nausea. The difference between two groups was statistically significant (p value < 0.05). Refer to table 4.

In group M 25 patients had episodes of vomiting out of 100 as compared to group O where 8 patients had vomiting episodes. In group M, 13 patients had mild vomiting episodes as compared to 4 patients in group O. 12 patients had moderate vomiting episodes in group M as compared to 4 patients in group O. None of the patients in both the groups had severe vomiting. The difference between two groups was statistically significant (p value < 0.05). Refer to table 5.

In group M, 6 patients out of 100 had side effects and in group O, 6 patients had side effects. There was no statistically significant difference between the two groups with regard to the side effects (p value > 0.05). In group M, 3 patients had complaints of dizziness as compared to 1 patient in group O. 3 patients had complaints of headache in group M as compared to group O where 5 patients had complaints of headache. The difference was statistically insignificant (p value > 0.05). Refer to table 6.

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 professionals.

The overall incidence of PONV during the first 24 hours after surgery is approximately 30% 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 period⁴. The pathophysiology of vomiting reveals that vomiting can occur by different neurotransmitters acting on various receptors at various sites. The combination of dexamethasone and ondansetron provides blockade of these receptor actions at different sites.

Ondansetron is a selective 5HT₃ receptors antagonist, has been shown to be effective in the treatment and prevention of PONV¹³. Since none of the available antiemetics, including ondansetron is entirely effective in all the patients, the concept of combination therapy was introduced. The mechanism of action of corticosteroids is unknown but may be related to inhibition of prostaglandin synthesis, decrease in 5HT₃ level in CNS and by an anti inflammatory action at operative site¹⁴.

In our study of group M, 32% patients experienced nausea while in group O, 14% of the patients had nausea. Post-operative nausea was less in the group O which is comparable to the study of L. Lopez et al¹⁵ and Rusch D et al¹⁶ both of which had incidence of nausea 16 % and 15 % respectively. In group M the incidence of nausea was 32 % which was comparable to the study of MM Maddali et al¹⁷.

In our study, incidence of vomiting was 25 % in group M which is comparable to study by Fujii et al¹⁸ having an incidence of 24 % and that of Usha et al¹⁹ having an incidence of 27 %. Post operative vomiting incidence in group O was 8 % which was comparable to the study by Usha et al¹⁹, Thomas R et al²⁰, Panda et al²¹ which had incidence of vomiting 10 %, 7 % and 6 % respectively.

All the patients in both the groups underwent the same preoperative fasting and premedication, the same standardized balanced anaesthesia and the same post-operative care. None of the patients in any group required any rescue anti-emetics in the recovery room.

Sanchez- Ledesma et al²² found in their study that a complete response defined as no nausea and no emetic episode occurred in 70 % of the patients in group O who received dexamethasone and ondansetron which was comparable to our study where 68 % of the patients showed a complete response

The adverse effects, related to the use of dexamethasone and ondansetron versus dexamethasone and metoclopramide did not reveal significance in our study. This was similar to the study of Rusch D et al¹⁶ where it was found that the patients had the same degree and number of adverse effects in both the combinations. It also correlates with the study of Thomas R et al²⁰ and Fujji et al¹⁸ whose study reported that most frequent adverse events were headache, dizziness etc. but there was no difference between groups. Furthermore, the study by Gan TJ et al²³ have found that adverse events have not been seen after a single bolus dose of dexamethasone.

Tables:-

Table 1:- Age and duration of surgery wise distribution of patients.

Variable	Group	N	Mean	SD	p-value*
Age	O	100	30.3	6.3	0.78
	M	100	30.1	5.9	
Duration (min.)	O	100	62.8	18.8	0.95
	M	100	63.0	16.1	

* Student's t test

Table 2:- Sex distribution of the patients.

Sex	Group		Total	p-value*
	M	O		
Female	53	52	105	0.89
	50.5%	49.5%	100%	
Male	47	48	95	
	49.5%	50.5%	100%	
Total	100	100	200	
	100.0%	100%	100%	

* Student's t test

Table 3:- ASA grade distribution of the patients.

ASA Grade	Group		Total	p value*
	M	O		
I	75	86	161	0.74
	46.6%	53.4%	100%	
II	25	14	39	
	64.1%	35.9%	100%	
Total	100	100	200	
	100.0%	100.0%	100%	

* Student's t test

Table 4:- Nausea scores of the patients.

Nausea	Group		Total	p value*
	M	O		
No	68	86	154	< 0.01
	44.2%	55.8%	100%	
Yes	32	14	46	
	69.6%	30.4%	100%	
Total	100	100	200	
	100.0%	100.0%	100%	

* Chi square test

Table 5:- Vomiting scores of the patients.

Vomiting	Group		Total	p value*
	M	0		
No	75	92	167	<0.01
	44.9%	55.1%	100%	
Yes	25	8	33	
	75.8%	24.2%	100%	
Total	100	100	200	
	100.0%	100.0%	100%	

* Chi square test

Table 6:- Type of side effect distribution in patients.

Side Effects	Group		Total	p value*
	M	0		
None	94	94	188	0.47
	50.0%	50.0%	100%	
Dizziness	3	1	4	
	75.0%	25.0%	100%	
Headache	3	5	8	
	37.5%	62.5%	100%	
Total	100	100	200	
	100.0%	100.0%	100%	

*Chi square test.

Conclusion:-

No single antiemetic drug has proved to be a universal solution to postoperative nausea and vomiting. It is not feasible to give very high doses of a single drug because of saturation effects and safety, so combinations of antiemetic drugs are a possibility and they are deemed to be more useful for balanced anti-emesis.

In this study, reduction of nausea and vomiting score and its frequency was better achieved by the combination of dexamethasone and ondansetron as compared to dexamethasone and metoclopramide. Thus we can conclude that dexamethasone (8mg) and ondansetron(4mg) combination has better antiemetic effect than the combination of dexamethasone (8 mg) and metoclopramide (10 mg) to prevent PONV (Post Operative Nausea and Vomiting) after general anaesthesia.

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