

COMPARATIVE STUDY OF GRANISETRON VERSUS COMBINATION OF GRANISETRON WITH DEXAMETHASONE IN THE PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN THE PATIENTS UNDERGOING ELECTIVE PLASTIC SURGICAL PROCEDURES IN HEAD AND NECK REGION

¹FIRDOSE SHAFI SHIEKH, MBBS, MD (ANESTHESIOLOGY)

²SHABEER AHMAD WANI, MBBS, M.S (SURGERY), MCH (PLASTIC SURGERY), M.R.C.S (GLASGOW)

⁴MOHAMMAD AKBAR SHAH, MBBS, MD (ANESTHESIOLOGY)

⁴GAZI PARVEZ CHIKEN, MBBS, MD (ANESTHESIOLOGY),

ABSTRACT

Postoperative nausea and vomiting is a major challenge with an incidence of 70% to 80%. This study evaluated the efficacy of Granisetron with or without Dexamethasone in reducing postoperative nausea and vomiting in patients undergoing elective plastic surgery procedures in Head and Neck region.

A prospective, randomized, double blinded study of 90 patients undergoing plastic surgery procedures in Head and Neck region under general anesthesia with prophylactic Granisetron alone or combination of granisetron and dexamethasone or placebo was done. The main outcome measures were the occurrence of vomiting and severity of nausea up to 24 hours postoperatively.

There was statistically significant difference in occurrence of postoperative nausea and vomiting when prophylaxis of granisetron alone or in combination with dexamethasone was given versus no prophylaxis. Although addition of dexamethasone further decreased the incidence of nausea and vomiting but the difference was not statistically significant

It was concluded that in patients undergoing plastic surgery procedures in Head and Neck region, the addition of dexamethasone to granisetron decreased the incidence of postoperative nausea and vomiting up to 24 hours.

Key Words: Granisetron, combination with dexamethasone, post-operative nausea prevention.

INTRODUCTION

Postoperative nausea and vomiting is a common complication after general anesthesia¹ with an overall incidence up to 30% in all surgeries^{2,3}. Patients at increased risk have high incidence of postoperative nausea and vomiting ranging from 70% to 80%.

Various high risk factors for postoperative nausea and vomiting are females, previous history of com-

plications, history of motion sickness, nonsmoking status, use of opioids and long duration of surgery. They form the basis of predictive scores for postoperative nausea and vomiting^{1,4,5,6}. Patients who are undergoing plastic surgery procedures experience a very high risk for postoperative nausea and vomiting⁶. There is not a single antiemetic that is totally effective in the prevention of postoperative nausea and vomiting⁷. However with combination of antiemetics the incidence is reduced by 25%².

Address for correspondence: ¹Assistant Consultant, Department of Anesthesiology. King Fahad Medical City, Riyadh 11525, Mobile 00966554340491 E-mail: shiekhfirdose@gmail.com

² Associate Consultant, Division of Plastic surgery

³ Assistant Consultant. Department of Critical Care

⁴ Assistant Consultant, Department of Anesthesiology

(All from King Fahad Medical City)

In previous studies comparing the effect of various antiemetic's especially Ondansetron, Granisetron with or without Dexamethasone in open abdominal and breast surgeries, it was observed that addition of Dexamethasone was more effective in prevention of postoperative nausea and vomiting.^{8,9}

Granisetron is a serotonin 5 HT₃ receptor antagonist used as an antiemetic to treat nausea and vomiting following chemotherapy. Its main effect is to reduce the activity of the vagus nerve, which activates vomiting centre in medulla oblongata. It does not have much effect on vomiting due to motion sickness. It was developed by chemists working with British drug company Beecham in 1988. The drug was approved by FDA in 1994.

Granisetron breaks down slowly, staying in the body for a long time. One dose usually lasts 4 to 9 hours and is usually administered once or twice daily. This drug is removed from the body by the liver and kidneys.

The purpose of this study was to determine whether dexamethasone in combination of Granisetron decreased the incidence of postoperative nausea and vomiting up to 24 hours in patients undergoing plastic surgery procedures in Head and Neck region when compared to granisetron alone.

METHODOLOGY

This study was conducted on adult patients between age range of 25 to 65 years with American Society of Anesthesiologists (ASA) status of 1 to 3 who were considered high risk for postoperative nausea and vomiting⁴ and who were undergoing elective plastic surgery procedures in Head and Neck region under general anesthesia. This was a prospective, randomized, double blinded study. Subjects were recruited on the day of surgery during the preoperative evaluation by the principal senior author of this article who was the anesthesiologist involved with the patients.

The inclusion categories were;

Previous history of postoperative nausea and vomiting, non smoking status and postoperative use of opioids.

Exclusion criteria were; patients refusing to participate in study, history of allergy to these drugs and history of chronic opioid use.

The study was done after taking approval from the hospital ethical committee and written informed consent was taken from each patient who participated in the study. Patients were randomly assigned to one of the three groups. Group (G) received 1mg of granisetron, group (D) received 8mg of Dexamethasone and 1mg of Granisetron and group (P) received normal saline. These drugs were prepared in 3 ml of syringe and were administered immediately after induction of anesthesia. The syringes were prepared by the technician in the operating room and given according to the table of randomized numbers. The anesthesiologist, surgeon and the nurses were blinded to the study of drugs.

All the patients received a standardized general anesthesia with premedication. After application of monitors all the patients received intravenous induction with 2-3mg /kg of propofol, 0.6-0.8mg/kg of rocuronium to facilitate intubation.

Maintenance of anesthesia was done with sevoflurane, oxygen, fentanyl as analgesia and muscle relaxant. And the surgical procedure was performed. On completion of surgery the residual effect of muscle relaxant was reversed in a standard fashion and the patients were extubated and shifted to the postoperative care unit. The incidence of postoperative nausea and vomiting was observed for 24 hours. The data were collected by on duty anesthesiologist blinded to the study groups. The patients rated their postoperative nausea and vomiting (PONV) experience on a scale comparable to a numeric rating scale where 0 is no PONV and 10 is the worst possible PONV event. Patients who rated their experience more than 1 were considered to have PONV. The antiemetic therapy of the patients who got PONV was left to the discretion of the primary surgical team who were allowed to use every reasonable and available antiemetic to help the patients. Results of the study were analyzed statistically.

RESULTS

A total of 90 patients underwent randomization to receive an anti emetic prophylaxis of Granisetron (Group G), combination of Granisetron and Dexamethasone (Group D) and no prophylaxis (Group P). Age and weight distribution of the three groups are shown in Table 1 and Table 2. As seen in tables the three groups were comparable in age and weight.

There was highly significant difference in incidence of nausea and significant difference in incidence of vomiting between the three groups (Table 3 and Table 4).

There was statistically significant difference in the occurrence of PONV between the groups who received prophylaxis of granisetron alone or combination with dexamethasone and group which received no prophylaxis as is obvious in Table 5 and 6.

With the addition of dexamethasone to granisetron the incidence of PONV decreased further but this difference was statistically not significant as seen in observations in Table 7.

DISCUSSION

This study is different from other studies as we compared the efficacy of granisetron versus combination of granisetron and dexamethasone in high-risk patients undergoing plastic surgery procedures in the Head and Neck region. This prospective, randomized, controlled therapeutic trial showed that the addition of dexamethasone to granisetron decreased postoperative vomiting rate and severity of nausea but this difference was not statistically significant.

In the present study the incidence of postoperative vomiting was reduced when dexamethasone was added to granisetron. A lot of factors are considered to affect the incidence of PONV but these factors are compa-

rable in all the three groups. Use of opioids in anesthesia is associated with an increased incidence of PONV but in this study these factors were well balanced amongst the treatment groups.

Dexamethasone is effective in control of emesis in patients receiving chemotherapy for various tumours.¹⁰ It has been seen that dexamethasone reduces the incidence of PONV in patients undergoing gynecological, breast surgery and tonsillectomies.^{11,12,13} The exact mechanism of dexamethasone in preventing PONV is not known but several suggestions, such as central inhibition of production of serotonin¹⁴, central inhibition of synthesis of prostaglandins¹⁵ and change in the permeability of blood brain barrier to several proteins.¹⁶ The long term use of dexamethasone may cause adverse effects such as increased risk of infections, glucose intolerance and delayed wound healing. However these effects are not related to a single dose of dexamethasone¹⁷.

Granisetron has been reported to be effective in reducing the incidence of PONV. No precise mechanism of action is known, but it has been suggested that it may act on the sites containing 5HT₃ receptors.

The patient satisfaction is closely tied to PONV and if patient satisfaction is considered a major outcome, eliminating vomiting to a degree that was found in this study is noteworthy although the difference was not statistically significant.

TABLE 1: AGE DISTRIBUTION

Groups	No. of cases	Age in years			F value	P value	Remarks
		range	average	variance			
P	30	25-65	44.133	140.878	0.8943	0.4125	Not Significant (NS)
G	30	22-65	40.733	165.305			
D	30	22-65	40.366	127.895			

TABLE 2: WEIGHT DISTRIBUTION

Groups	No. of cases	Weight (Kgs)			F value	P value	Remarks
		range	average	variance			
P	30	42-70	59.66	55.633	0.00609	0.9939	(NS)
G	30	42-70	59.733	74.616			
D	30	45-68	59.533	39.429			

TABLE 3: COMPARISON OF NAUSEA AND VOMITING IN THE STUDY PERIOD OF 24 HOURS OF THREE GROUPS

PONV episode	Group P	Group G	Group D	X ²	P value	Remarks
Nausea	22 (73.33%)	9 (31%)	5 (16.67%)	21.94	0.00001	HS
Vomiting	12 (40%)	4 (13.33%)	2 (6.67%)	11.67	0.002	S

HS-Highly significant S-Significant

TABLE 4: COMPARISON OF COMPLETE RESPONSE BETWEEN THREE GROUPS IN THE STUDY PERIOD

Groups	Complete response in 24 hrs no. (%)	X ²	P value	Remarks
P	8 (26.67%)	28.17	0.000001	HS
G	21 (70%)			
D	24 (80%)			

TABLE 5: COMPARISON OF PONV BETWEEN GROUP P AND GROUP G

Time interval (hrs)	Group P	Group G	X	P value	Remarks
0-24	22 (73.33%)	9 (30%)	11.28	0.0007	HS

TABLE 6: COMPARISON OF PONV BETWEEN GROUP P AND GROUP D

Time interval (hrs)	Group P	Group D	X ²	P value	Remarks
0-24	22 (73.33%)	6 (20%)	17.14	0.00003	HS

TABLE 7: COMPARISON OF PONV BETWEEN GROUP G AND GROUP D

Time interval (hrs)	Group G	Group D	X ²	P value	Remarks
0-24	9 (30%)	6 (20%)	0.81	0.37	NS

Addition of dexamethasone increases the cost to granisetron in present study but it is well offset by the cost reduction from decreased complications of PONV.

This study has the limitations that granisetron has been shown to be more effective when administered towards the end of surgery rather than at induction.¹⁷ In the present study however granisetron was given before induction of anesthesia because of variation in surgical duration. Another limitation of this study is that our groups were not comparable in terms of nature of the surgical procedures, as some procedures in the Head and Neck region are known to cause higher incidence of PONV.

CONCLUSION

Addition of dexamethasone decreases PONV severity when combined with granisetron in patients undergoing plastic surgical procedures in Head and Neck region in whom vomiting may be deleterious for outcome.

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