

# Efficacy of Parenteral Granisetron in the Prevention of Post-Operative Nausea and Vomiting

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## Summary:

*Post-operative nausea and vomiting (PONV) is one of the most unpleasant complications following anaesthesia and surgery since long time. A non-randomized case control study of prevention of post operative nausea and vomiting with IV- Granisetron was done on 270 adult surgical patients who received general or spinal anaesthesia. All the patients were followed up to 48 hours after operation. A complete response was achieved in prophylaxis group*

## Introduction:

PONV is one of the most unpleasant complications following anaesthesia and surgery prior to 1960, when older inhalational agents such as ether and cyclo propane were widely used, the incidence of vomiting was reported to be as high as 60 %<sup>1,2</sup>. Better anaesthetic techniques along with a newer generation of antiemetics and shorter acting anaesthetic drugs reduced the incidence of PONV to about 25-30% in today's practice. Nevertheless, PONV still occurs, with an incidence as high as 60-70% in some high risk patients<sup>3,4</sup>. Incidence is lower in children less than 2 years of age<sup>5,6</sup>.

Some procedures like tonsillectomies, strabismus surgery, laparoscopic cholecystectomies are associated with high incidence of PONV<sup>7,8</sup>. High level of anxiety and post operative pain, specially pelvic or visceral origin may also be associated with higher incidence of PONV<sup>9-11</sup>.

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*as 92.6% and in control group as 90.4%(p-value=0.6637). In patient with PONV, gender incidence is equal in prophylaxis group. Female incidence is higher in control group. Majority of patients (90 to 100 %) had PONV within 24 hours after operation. As there is insignificant difference in the achievement between prophylaxis group and control group, anti emetic prophylaxis is recommended only for patient with one or more risk factors for PONV.*

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Apfed et al, developed a simplified risk score consisting of four predictors- female gender, history of motion sickness or PONV, non smoking status and use of opioids for post operative analgesia<sup>3</sup>.

Ambulatory patients appear to have lower incidence of PONV compared with in-patients<sup>12</sup>.

PONV may result in delayed hospital discharge, decreased patient satisfaction, increased use of resources including medical and nursing care and other supplies<sup>13</sup>.

Prevention of PONV is very important to patients and nation as well. Granisetron is an effective anti emetic belongs to serotonin antagonist having less adverse effects. We tried to evaluate the efficacy of Granisetron and justification of its use in prevention of PONV in general surgery unit.

## Methodology:

Type of study : Non randomized case control study.

Study period : 14 July 2005 to 14 December 2005.

Place of study : In a general surgery unit, Chittagong Medical College Hospital.

Study population: For case group/ prophylaxis, all the patients have undergone general surgical operations of different types, irrespective of general or spinal anaesthesia and sex, received IV Granisetron 1ml(1mg).

For control group: Those who did not receive IV Granisetron.

**Sample size:** The sample size was calculated by using software open Epi version 2007, by accepting the incidence of PONV after G.A/ spinal Anesthesia approximately 60% to ensure 95% confidence interval and power 80, 283 patients in each group.

**Selection criteria :** (For both control and prophylaxis group).

**Inclusion criteria -** All routine & emergency operations done in a surgical unit under GA or SA. Patients of both sexes are included .

**Exclusion criteria –** Patients who are unwilling to receive the study drug. Operations done under LA. Paediatric surgical cases - age below 15 years.

In every alternate patient Granisetron 1mg/1ml was introduced iv immediately after induction of anaesthesia. In other patients that is in control group no Granisetron was introduced and follow up were done up to 48 hours after operation for PONV & recorded in separate proforma for each patient. Statistical analysis were done.

Follow up were done by the author, registrar and assistant registrar of the unit.

Post operative period was standardized with proper analgesia , rehydration and other management.

### **Ethics**

Ethical clearance was obtained from the medical ethical clearance committee of Chittagong medical college. Proper written informed consents signed by the attendants were taken for each patient.

**Limitation of the study:** small sample size (135 patients in each group). Post study calculation showed the power 50.74%.

### **Results**

Out of 135 patients of prophylaxis group, PONV was recorded in 10 patients ( 7.4% ). 7 patients had laparotomy for different surgical conditions, gender incidence was equal and 90% patients had PONV within 24 hours of operation.

In 135 patients of control group, PONV was recorded in 13 patients (9.6%). 8 patients had laparotomy for different surgical pathologies, gender incidence was higher in female and 100% patients had PONV within 24 hours of operation.

A complete response, defined as no PONV and no need for another rescue anti-emetic, and was achieved as 92.6% and 90.4% in prophylaxis and control group respectively.

Almost all parameters used in this study are comparable between the control group and prophylaxis group.

**Table-I**

*Summary of Patients with PONV in Prophylaxis Group:*

Sl. No.	Operation	Anesthesia	Gender	Duration
1.	Gastro Jejunostomy	GA	F	< 24 hours
2.	Laparotomy & ileostomy	GA	M	< 24 hours
3.	Repair of Rec. Ing. Hernia	SA	M	< 24 hours
4.	Ovarian Cystectomy	GA	F	< 48 hours
5.	Cholecystectomy	GA	F	< 24 hours
6.	Laparotomy & Gut resection	GA	M	< 24 hours
7.	Partial Gastrectomy	GA	F	< 24 hours
8.	Cholecystectomy	GA	F	< 24 hours
9.	Piles Operation	SA	M	< 24 hours
10.	Repair of Hernia	SA	M	< 24 hours

**Table –II***Summary of Patients with PONV in Control Group:*

Sl. No.	Operation	Anesthesia	Gender	Duration
1.	Laparotomy & repair of DU perforation	GA	M	< 24 hours
2.	Emergency appendicectomy	GA	F	< 24 hours
3.	Repair of obstructed inguinal hernia	SA	M	< 24 hours
4.	Rt. hemicolectomy	GA	F	< 24 hours
5.	Repair of inguinal hernia	SA	F	< 24 hours
6.	Rt. nephrectomy	GA	F	< 24 hours
7.	Repair of inguinal hernia	SA	M	< 24 hours
8.	Laparotomy for intestinal obstruction	GA	F	< 24 hours
9.	Appendicular abscess drainage	GA	M	< 24 hours
10.	Repair of inguinal hernia	SA	M	< 24 hours
11.	Emergency appendicectomy	SA	F	<24 hours
12.	Interval appendicectomy	GA	F	<24 hours
13.	Emergency appendicectomy	SA	F	<24 hours

**Table-III***Incidence of PONV*

Total patients(n=270)	PONV	Complete response	P-value
Prophylaxis group (135)	10 (7.4%)	125 (92.6%)	P=0.6637(N.S) **
Control group (135)	13(9.6%)	122 (90.4%)	

\*\*=Fisher's exact test. N.S= Non significant

**Table –IV***Comparative analysis*

Patient	PONV	Gender		Anaesthesia		Period	
		Male	Female	General	Spinal	0-24 hrs.	25-48 hrs.
Prophylaxis Group	N = 10	5	5	7	3	9	1
Control Group	N = 13	5	8	7	6	13	0

**Table –V***Base line parameters*

Parameters	Prophylaxis group n=135	Control group n=135	P-value
Mean age in years	36.51±14.58	37.71±15.03	0.5063
Sex -male: female	93:42	82:53	0.1609
Mean BMI	29.83±5.2	31.05±6.16	0.245(N.S)
ASA Score –I	97	92	0.540 (N.S) §
–II	38	43	
WBC count	11.13±0.65	11.18±0.70	0.670(N.S)

± = Standard deviation; § = Chi square test; N.S= Non significant

**Discussion :**

The etiology of PONV is multifactorial. Factors such as age, obesity, a history of motion sickness and / or previous PONV, menstruation, surgical technique / duration, postoperative pain, dehydration, among others, are considered to affect the incidence of PONV. Consequences are also many like electrolytes imbalance, dehydration, Mallory weis tear, wound dehiscence and haematoma formation<sup>14-17</sup>, Hospital and increased nursing care time contribute to the economic related consequences of PONV.

There appears to be a direct relationship between the incidence of PONV and the operative site, with a higher incidence of PONV after eye, oral, plastic, ENT, head neck surgery, gynae and Obstretic, Laparoscopic and abdominal procedures than with other procedures<sup>16-22</sup>.

In our study incidence of PONV was higher in different laparotomy procedures of both prophylaxis and control group. As the study was done in general surgical unit so the other parts were considered less frequently.

Female patients have a 2 to 3 times greater incidence of PONV than males, due to increased gonadotrophin, oestrogen & plasma progesterone levels during menstrual cycle<sup>19,23,24</sup>.

In the present study the gender incidence is equal in the prophylaxis group but female preponderance in control group.

In adults, there is a correlation between increasing age and decreasing incidence of PONV<sup>19,25</sup>.

PONV are adverse effects of regional anaesthesia (spinal & epidural), with an incidence of approximately 10 to 20%<sup>14</sup>. The resulting incidence of PONV is due to decreased cerebral blood flow secondary to systemic hypotension, increased G.I. atony, vagal stimulation following intraabdominal G.I. manipulation<sup>26,27</sup>.

In our study group the incidence of PONV was observed more in patients having GA of both prophylaxis and control group. Probably because, majority of abdominal procedures were done in general surgical unit and mostly done under G.A.

The baseline parameters used in the study are- mean age of patients, sex male /female ratio, mean body

mass index, ASA score -1, 11 WBC count. With the exception of few all parameters are comparable between the control and prophylaxis group. The parameters which vary between the two groups of patients carry no importance in determining the outcome of the study.

Among numerous antiemetics, granisetron was found more effective. In one randomised double blind study on 120 patients, granisetron was found more effective than droperidol and metoclopramide in the treatment of PONV<sup>28</sup>.

Granisetron lacks the sedative, dysphoric, extrapyramidal symptoms associated with other non -5HT receptor antagonist such as droperidol and metoclopramide<sup>29</sup>.

The most common adverse event associated with the study drug is headache, was not judged to be clinically serious, no other significant adverse events occurred in any group.

The fact that granisetron is much more expensive than the traditional antiemetics may delay its wide spread use. This study did not include a cost - effectiveness analysis ( cost per unit success) but to justify its use in cases with one or more risk factors for PONV.

**Conclusion:**

While we have achieved significant advances in the management of PONV, it still occurs frequently in high risk patients. Not all the patients will benefit from anti emetic prophylaxis, thus identifications of patients who are at increased risk is imperative. The major risk factors for PONV are female gender, non smoking status, history of PONV or motion sickness, use of volatile anaesthetics, intra operative or post operative opioids, increased duration of surgery, type of surgery ( laparoscopic, ENT, neurosurgery, breast, strabismus and plastic surgery).

We recommend anti emetic prophylaxis in patients with one or more risk factors for PONV, preferably with serotonin antagonist.

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