

# Comparison of Granisetron and Dexamethasone in management of post operative nausea and vomiting (PONV) in laparoscopic gynaecological surgery

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## Abstract:

**Background:** Postoperative nausea and vomiting (PONV) is a common problem. It is more common in laparoscopic surgery than in open surgery and following laparoscopic gynaecological surgery. PONV causes patient discomfort and can prolong the time of hospital discharge. It causes potential hospital burden and loss of unanticipated working time both for the patients and doctors. Management of this problem based on prevention rather than treatment. Various antiemetic drugs including steroids are effective in the prevention of PONV but which one is better still now a debateable one. On the basis of this fact there were numerous research, articles, analysis and publication work done all over the world.

**Objectives:** Comparison of granisetron and dexamethasone to detect which one is better in management of PONV after laparoscopic surgery.

**Method:** The patient were selected after ethical committee approval. After informed written consent we have selected 100 ASA- I & II patients undergoing general anaesthesia for laparoscopic gynaecological surgery in a prospective double blind randomized study. Patients who had received opioids, NSAIDs, steroids or antiemetic agent before previous 4 weeks or who has known hypersensitivity to granisetron or dexamethasone. Patients were divided as group-A (granisetron) and Group-B (dexamethasone). 50 patient were member of each group. Every patient got study drug during induction. Group-A got granisetron and group-B got dexamethasone for prevention of PONV. There were no differences in background factors or factors related to anaesthesia, analgesics consumption, pain or side effects between groups. The data collected in a fixed protocol form from the patient consented for the study. After collection of data were coded, edited, compiled and entered into computer system for analysis. The result will help to guide the anaesthesiologists practicing in the third world countries like Bangladesh in the management of PONV.

**Results:** The current study showed the intravenous injection of 8 mg dexamethasone, or 3 mg Granisetron have similar effects on PONV prophylaxis in laparoscopic gynaecological surgery. These results of the current study indicated that Dexamethasone is a suitable substitute for Granisetron.

**Conclusion:** Dexamethasone and Granisetron are comparable in management of PONV. These drugs injection before anesthesia induction have similar effects on nausea and vomiting prophylaxis after laparoscopic gynaecological surgery. Prophylactic use of dexamethasone should be routine to prevent PONV because dexamethasone is cost effective than granisetron.

**Keywords:** PONV, dexamethasone, granisetron, laparoscopy, nausea.

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## Introduction:

Postoperative nausea and/or vomiting (PONV) is an unpleasant experience that afflicts 20–30% of surgical patients after general anaesthesia.<sup>1</sup> It is

often unusually distressing to patients which give rise to worst memory of their hospital stay.<sup>2</sup> PONV decreases patient comfort and satisfaction and rarely, may cause dehydration and electrolyte

imbalances, aspiration of gastric contents, oesophageal rupture, suture dehiscence, and bleeding.<sup>3</sup> PONV and its resulting complications are costly for the healthcare sector worldwide, with several hundred million dollars spent annually in the USA alone---.<sup>4</sup> A number of patient-specific, anaesthesia-related, and surgery-related risk factors have been associated with higher incidences of PONV.<sup>5</sup> At present, the overall incidence of PONV after general anaesthesia has been estimated to range from 25% to 30%.<sup>6</sup> The incidence of intractable nausea and vomiting has been reported to be 0.18%.<sup>7</sup> Intractable PONV can increase medical costs by increasing nursing care time, and delaying discharge from the postanesthesia care unit or leading to unanticipated hospital admission. Among ambulatory surgery patients, PONV alone or combined with pain is the most common anaesthetic reason for delayed discharge and unanticipated hospital admission. Postoperative nausea was reported to continue on average for 1.7 days and vomiting for 0.7 days among outpatients suffering from the symptoms.<sup>8</sup>

The administration of antiemetic drugs reduces the incidence specially judicious use of multiple emetics.<sup>9</sup> Various anti emetic drugs, including anti histamins (e.g. hydroxyzine), butyrophenone (e.g. droperidol) and gastrokinetic agents (e.g. metoclopramide) have been used to reduce the incidence of PONV, but some of the older anti emetics are associated with undesirable side effects.<sup>10</sup>

Dexamethasone has been found to have a prophylactic effect on PONV in patients undergoing abdominal hysterectomy<sup>11</sup>. Granisetron, a selective 5-HT<sub>3</sub> receptor antagonist, has been successfully used for preventing PONV in middle ear surgery under general anaesthesia.<sup>12</sup> Granisetron antagonizes 5-HT<sub>3</sub> receptors in sites associated with antiemetic activity. Granisetron has many advantages, but is more expensive than dexamethasone.<sup>13</sup> If dexamethasone is as effective as granisetron, it may be a good cost-effective alternative. We have an intention to compare the prophylactic antiemetic efficacy of granisetron and dexamethasone for preventing PONV in women undergoing elective laparoscopic gynaecological surgery.

### Methods:

After ethical committee approval 100 patients aged 20-70 who were candidates for laparoscopic gynaecological surgery were included in the study.

Informed consent was obtained from patients before enrollment. The patients were in ASA-1 or ASA-II class in physical condition according to the American Society of Anesthesiology classification. Exclusion criteria included pregnancy, body mass index (BMI) higher than 30, existence of underlying diseases, and opium, or steroid consumption during the week before the operation. The patients were allocated, by computer-generated random numbers, into two groups. The random allocation sequence was concealed in sealed opaque envelopes until a group was assigned. Fifteen minutes before anesthesia induction, 3 mg Granisetron was injected intravenously to group A and 8 mg Dexamethasone to group B patients. All patients underwent general anesthesia with the same medications for induction, Thiopental sodium 5 mg/kg, Fentanyl 1.5 µg/kg and Atracurium 0.5 mg/kg for facilitation of tracheal intubation, during anesthesia patients were monitored by electrocardiography, pulse oximetry, non-invasive blood pressure. Anaesthesia maintenance in both groups was achieved by Isoflurane 1.2% and after 30 minutes from induction of anesthesia incremental doses of 10 µg fentanyl was administered every 15 minutes.

During laparoscopy, intra-abdominal pressure was maintained at 12 mmHg. At the end of operation CO<sub>2</sub> was carefully evacuated by manual compression of the abdomen with open trocars. Post-operative nausea and vomiting was assessed at three time intervals (0-6 hours, 6-12 hours, and 12-24 hours after consciousness).

10 mg of Metoclopramide was injected in case of PONV existence. SPSS software version 16 was employed to analyze data. In order to compare quantitative and qualitative data between the two groups Chi-square test and Fisher's exact test if required for frequencies less than Five. Was utilized for the qualitative variables and Student's t-test for quantitative variables. In cases of non adherence, and non-parametric, equivalent assessment was employed. The level of significance was  $P < 0.05$ .

### Results:

Maintaining the inclusion criteria 100 patients were enrolled into the study, out of which 50 patients were placed in Granisetron group (Group-A) and 50 patients in Dexamethasone group (Group-B). There was also no significant difference in operation characteristics between the two groups.

**i. Age incidence :****Table I.** Age incidence

Age in yrs	20-30	31-40	41-50	51-60	61-70	Mean age yrs
Granisetron group( n=50)	4	14	18	12	02	41.2
Dexamethasone group (n=50)	5	10	21	13	01	43.6

Mean age of granisetron group 41.2 years. Mean age of dexamethasone group 43.6 years. Data analysis indicated no significant difference in mean age between the two groups (p value 0.322).

**ii .Duration of anaesthesia during surgery:****Table II.** Duration of anaesthesia

Time in mins	<60	61-90	90-120	Mean time
Granisetron group (n=50)	4	20	26	95.23
Dexamethasone group (n=50)	2	25	23	93.22

Mean general anaesthesia time of granisetron group was 95.23 minutes .

Meangeneral anaesthesia time of dexamethasone group was 93.22 minutes.

There is no significant difference in between two groups(p value 0.439). Alon E et al.<sup>14</sup> study showed that mean anaesthesia time was 93 minutes which correlates with our study.

**iii. Duration of laparoscopic gynaecological surgery:****Table III.** Duration of surgery

Time in mins	<45	46-75	76-105	Mean time
Granisetron group (n=50)	3	21	26	72.11
Dexamethasone group(n=50)	1	27	22	70.21

Mean surgery time of granisetron group was 72.11 minutes. Mean surgery time of dexamethasone group 70.21 minutes. There is no significant difference ( p value 0.438) . In KK Karmaker et al<sup>15</sup> study showed that 71.50 minutes of mean surgery time which is correlates with our study.

**iv. Socioeconomic condition of the participant patients:****Table-IV.** Socioeconomic Condition

	A. Granisetron group (n=50)	B. Dexamethasone group (n=50)	P value
Upper Class	23	21	0.438
Middle Class	25	26	0.228
Lower Class	02	03	0.628

Here middle class patients are higher in both groups. In granisetron group 25 and dexamethasone group 26( p value 0.431). Upper class patient in granisetron group was 23 and dexamethasone group was 21( p value 0.228). Lower class patients are less in number in both groups was 02 & 03. It( p value 0.660) is Probably due to costly hospital policy.

There was no significant difference in between two groups.

**v. History of motion sickness and headache:****Table V.** Motion Sickness and headache

	Granisetron group(n=50)	Dexamethasone group (n=50)	P value
Motion sickness	13	10	0.447
Headache	06	04	0.543

Motion sickness of Granisetron group was 13 and Dexamethasone group 10(P value 0.447) where as headache was 06 and 10 (p value 0.543). There was no significant difference in between two groups.

**vi. According to types of surgery:**

**Table VI.** *Types of surgery*

	A. Granisetron group(n=50)	B. Dexamethasone group(n=50)	P value
Hysterectomy	10	09	0.234
Adnexectomy	15	18	0.362
Diagnostic laparoscopy	17	16	0.223
Myomectomy	08	07	0.248

Hysterectomy of group A 10 & group B 09 (p value 0.234).

Adnexectomy of group A 15 & group B 18 (p value 0.362).

Diagnostic laparoscopy group A 17 & group B 16 (p value 0.223).

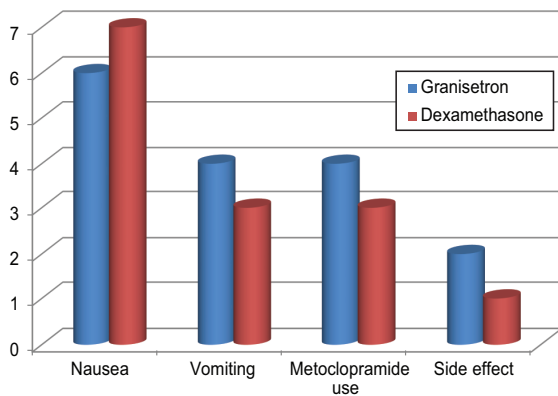
Myomectomy group A group 08 & group B 07 (p value 0.248)

There was no significant difference in between two groups.

**vii. Intervention outcome:**

**Table-VII.** *Intervention outcome*

	Granisetron group (n=50)	Dexamethasone group (n=50)	p-value
Nausea	6	7	0.587
Vomiting	4	3	0.750
Metoclopramide use	4	3	0.750
Side effects	2	1	0.614



**Figure-1** *Bar chart of intervention outcome measure*

In the first 24 hours after operation, 6 patients in Granisetron group and 7 patients in dexamethasone group experienced nausea (p value 0.587) and 4 patients had vomiting in granisetron group and on the other hand in Dexamethasone group 3 patients experienced vomiting (p value 0.750). Data analysis indicated there is no difference in nausea and vomiting prevalence in between two groups.

**viii. Anxiety experienced by patients :**

**Table-VIII.** *Grade of anxiety*

Anxiety grade	Granisetron (n=50)	Dexamethasone (n=50)	P value
0	13	16	0.342
1	17	14	0.324
2	11	12	0.224
3	09	08	0.240

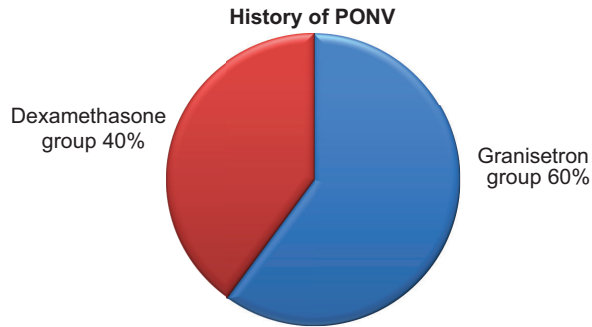
Anxiety level was graded as 0-3 . 0 stands for minimum and 3 stands for maximum experiences of anxiety. 13 patients of granisetron group and 16 of Dexamethasone group experiences no anxiety (p value 0.342). 17 of granisetron group and 14 of dexamethasone group experiences mild form of anxiety (p value 0.324). Moderate form experienced 11 of granisetron group and 12 of dexamethasone group (p value 0.224). 9 of granisetron group and 8 of dexamethasone group experienced severe form of anxiety (p value 0.240).

**ix. Previous history of PONV:**

**Table IX.** *Previous history of PONV*

Group –A. Granisetron(n=50)	Dexamethasone Group-B. (n=50)	P value
03	02	0.660

Experience of previous history of PONV was 03 patients in granisetron group and 02 patients in dexamethasone group (p value 0.660).



**Figure-2** Pie chart of previous PONV

#### x. Level of patient satisfaction :

**Table-X** Level of patient satisfaction:

Level	Granisetron group(n=50)	Dexamethasone group (n=50)	P value
0	5	4	0.410
1	7	8	0.468
2	24	25	0.338
3	14	13	0.308

Here minimum level of patient satisfaction graded as 0 and maximum level of satisfaction graded as 3. Minimum satisfaction expressed by 5 patients in granisetron group, 4 patients in dexamethasone group (p value 0.410), mild satisfied 7 patients in granisetron group, 8 patients in dexamethasone group (p value 0.468), moderately satisfied 24 patients in granisetron group and 25 patients in dexamethasone group (p value 0.338). Complete satisfied 14 patients in granisetron group and 13 on dexamethasone group (p value 0.308).

There is no significant difference in between two groups.

#### Discussion:

Nausea and vomiting are common and frequent complications following surgery and anaesthesia. Most of the incidence of nausea and vomiting occur during the first two hours of recovery from anaesthesia. The etiology of postoperative nausea and vomiting is multi-factorial. Many factor associated with anaesthesia and surgery may contribute to nausea and vomiting. In the present study concern factors are type of anaesthesia, female patient and gynecological surgery. Incidence of nausea and vomiting is two to three

times more in female due to changing endocrine environment which sensitize the brain stem emetic mechanism. During elective gynaecological surgery, general anaesthesia as well as some traction of vagal innervated gut may play role in triggering emesis. The reported overall incidence of nausea and vomiting after gynecological surgery is 75%.<sup>16</sup>

The anti emetics are now mainstay of therapy to prevent PONV. Now currently being widely used for treatment in our country are prochlorperazine, metoclopramide and promethazine and many study have done with these drugs. But these drugs have varying effectiveness and there use is limited because of delayed recovery, sedation and sometimes distressing side effect of extra pyramidal symptoms.

Granisetron is a newer drug and limited studies have done with this drug in our country. So we have chosen granisetron and dexamethasone for prevention of PONV in laparoscopic gynaecological surgery to compare these drugs about their efficacy and side effects during operations and 24 hours post operative period.

Maintaining the inclusion criteria 100 patients were enrolled into the study, out of which 50 patients were placed in Granisetron group (Group-A) and 50 patients in Dexamethasone group

(Group-B). There was also no significant difference in operation characteristics between the two groups.

Pain as well as commonly used analgesic pethidine may cause nausea and vomiting. For this reason postoperative control of pain we used ketorolac tromethamine and diclofenac as required instead of pethidine. The study confirmed the previous study regarding the safety of the patient as side effects were mild.

Our study showed that there is no significant difference in age, BMI, History of motion sickness, socioeconomic condition, type of surgery, mean anaesthesia time, mean surgery time among the study patients.

The current study showed the intravenous injection of 8 mg Dexamethasone, or 3 mg Granisetron have similar effects on PONV prophylaxis in laparoscopic gynaecological surgery

These results of the current study indicated that Dexamethasone is a suitable substitute for Granisetron.



Dr. Dipasri Bhattacharia and dr. Arnab Banarjee showed that granisetron effectively reduces PONV in day case laparoscopic gynaecological surgery.<sup>17</sup>

Fukami *et al.*<sup>18</sup> showed that Dexamethasone injection before laparoscopic cholecystectomy leads to significant reduction of nausea, vomiting and post-operative pain. Fukami's study was a clinical trial performed on 80 patients. In another clinical trial performed by Binachin *et al.* Dexamethasone had significant effect on PONV reduction after laparoscopic cholecystectomy but it had no effect on pain reduction and admission duration. In similar studies which were performed by Feo *et al* and Bisgard *et al.*<sup>19</sup> Dexamethasone effect on PONV reduction after laparoscopic cholecystectomy were confirmed. Karanicolas *et al* meta-analysis showed that dexamethasone leads to PONV reduction in comparison with placebo after laparoscopic cholecystectomy. They showed that injection of 8 mg Dexamethason is more effective than 3 mg Granisetron or 4 mg Ondansetron in PONV prophylaxis but the differences were not statistically significant. Erhan *et al.*<sup>20</sup> evaluated Dexamethasone, Granisetron and Ondansetron effects on PONV after laparoscopic cholecystectomy in comparison with placebo. They showed that injection of 8 mg Dexamethason is more effective than 3 mg Granisetron or 4 mg Ondansetron in PONV prophylaxis but the differences were not statistically significant. Dexamethason mechanisms in PONV prophylaxis are not known well. Elhakim *et al.*<sup>21</sup> expressed that Dexamethasone can act as a serotonin receptor inhibitor in gastrointestinal tract. Another study showed that Dexamethasone leads to reduction of parasympathetic impulses to the brain by decreasing tissue inflammation around surgery site.<sup>22</sup>

### Conclusion:

Dexamethasone and Granisetron are comparable in management of PONV. These drugs injection before anesthesia induction have similar effects on nausea and vomiting prophylaxis after laparoscopic gynaecological surgery. Prophylactic use of dexamethasone should be routine to prevent PONV bcause dexamethasone is cost effective than granisetron. Increased incidence of either postoperative nausea or vomiting distressed the

patients and was associated with decreased patient satisfaction. So dexamethasone should be use in management of PONV.

### Limitations of this study:

This study was not without a limitations and followings were the limitations of this study:

1. This study was conducted in two centre hospital only and may not reflect the actual situation of the country.
2. This study was done within a short period of time.
3. The sample size was small; This is the drawback of the study and a larger sample size can give a better conclusion.
4. There were several limitations to this study. First, because of ethical concerns, the placebo control group was kept out. Second, patients were observed for only 24 h postoperatively because most patients who underwent laparoscopic gynaecological surgery without complications were discharged a day after operation.
5. The patients with underlying diseases were excluded, so the results of the study should not be generalized to other patients with severe underlying diseases. Further studies should consider these limitations.

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