A Comparative Study Between On Dansetron and Granisetron for Post Operative Nausea Vomiting In Laparoscopichysterectomy

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ABSTRACT
Introduction
Postoperative nausea vomiting (PONV) is one of the commonest adverse event seen in anesthesia practice. Among all the incidence is high in gynecology patients, that to undergoing laparoscopic surgeries. In this randomized double blinded prospective study we compared the efficacy of ondansetron and granisetron for prevention of PONV in laparoscopic hysterectomies.

Objective
1. Compare the incidence of PONV between ondansetron and granisetron group
2. To assess the demand of rescue antiemetic (metoclopramide)
3. To compare the side effects of the two drugs

Methodology
A total of 160 patients undergoing laparoscopic hysterectomies were randomly allocated to one of the two groups of 80 patients each. Patient in group O were given 4mg of Ondansetron and patient in group G were given 2 mg of Granisetron. The standard general anesthesia technique was administered to all patients. Episodes of nausea, retching, vomiting were assessed during first 24 hours after anesthesia.

Results
There was statistical difference for demographic data among the two groups (p<0.05). Ondansetron, having shorter duration of action, requires further repeat doses which may extend twice to thrice a day, as compared to the long duration antiemetic action of a single dose of granisetron.

Conclusions
The incidence of PONV was significantly high in ondansetron than in granisetron given prophylactically in laparoscopic hysterectomies.

Keywords: PONV, Ondansetron, Granisetron, Laparoscopic surgery

GLOSSARY OF TERMS
PONV- Post operative nausea vomiting
IV- intravenous
MAC- Minimum alveolar concentration
Mg- milligrams
Kg- kilograms
ECG – electrocardiogram
Hrs- hours

I. INTRODUCTION
Over the last several decades, the risk of mortality due to surgery and anesthesia have decreased as the attention have been shifted to the factors that negatively influence patient's morbidity. Among all such factors, Postoperative Nausea vomiting (PONV) is the leading cause. Its incidence rate is 49% of all the patients. Postoperative nausea/vomiting can cause adverse consequences like patient's dissatisfaction, unexpected hospital stays, increase cost due to additional drug use, and delayed recovery and return to work.

It is the most common complication related to anesthesia. But nowadays the incidence have decreased to 75-80% since the ether era. Patient undergoing major gynaecological surgeries are esp. prone to PONV with reported incidence of 50-75%. Both PONV is multifactorial and in spite of advances in antiemetic therapy, incidence is high. It can be related to surgery, related to pre and post-operative factors, anaesthesia-related factors...
contributing to development of PONV.  

Preventing PONV is easier than treating it. Many drugs are used for preventing PONV like atropine, scopolamine, metoclopramide, midazolam, dexamethasone, promethazine and many more. But 5-HT3 receptors antagonists are most commonly used as they are highly specific and with minimal side effects. Ondansetron, granisetron, dolasetron, tropisetron, palonosetron belong to this group. Unlike ondansetron, granisetron is more selective and effective. Headache, diarrhoea, sedation are some of its side effects. Hence this study is being conducted in order to compare the two drugs Ondansetron and Granisetron in prevention of post operative nausea and vomiting in laparoscopic hysterectomies.

II. METHOD: 
Patients of ASA Grade I and II, between 18 - 55 years of age undergoing laparoscopic hysterectomies were included in the study. Pre-anesthetic assessment of all patients was done a day before the surgery. A detailed history and examination was done. All the basic investigations like haemoglobin, total leucocyte count, differential leucocyte count, electrocardiography were done. After informing the patient about the study and possible side effects of drug administration informed consent of the patient for participation in the study was taken. All the patients were advised to remain nil per oral after 10pm the day before surgery. And all the patients were premedicated with injection pantocid 40mg the day before surgery. On the day of surgery, after checking the patient’s identity, checking all the equipment, patient was taken for the surgery. All the vitals, that is blood pressure, heart rate, oxygen saturation were recorded before starting the procedure. The patients of Group O received injection Ondansetron 4mg (2ml) intravenously 2 minutes prior to induction of anesthesia and Group G were injected with injection Granisetron 2mg (2ml) intravenously 2 minutes before induction of anesthesia. No other antiemetic was given. Induction of anesthesia was with propofol (1-2.5 mg/kg) intravenously and fentanyl 2mcg/kg IV. After 3 mins of preoxygenation, tracheal intubation was done with the help of succinylcholine (1-2 mg/kg) IV following ryles tube insertion. To maintain the anesthetic state, Isoflurane (MAC 1) and 50% oxygen was given through inhalation. Atracurium with the loading dose 0.5mg/kg followed by the maintenance dose 0.1mg/kg was given every 15-20 minutes to maintain muscle relaxation. All the vitals that is blood pressure, heart rate, oxygen saturation, ECG was monitored intraoperatively. Intraoperative hypotension and hypertension were treated accordingly. Bradycardia (HR<40) was treated with IV atropine (0.01-0.02 mg/kg). Few minutes prior to completion of the surgery all the patients were administered with diclofenac (1.5mg/kg) intravenously. After completion of surgery, residual neuromuscular block was antagonised with IV neostigmine (0.04-0.08 mg/kg) and IV glycopyrrolate 0.2 mg for each 1 mg of neostigmine. Tracheal extubation was done on meeting the standard criteria for extubation. The patient was evaluated for postoperative nausea, vomiting, retching immediately after the surgery in the recovery
room and then episodes of nausea, vomiting or retching were recorded if patients complain about it till 24 hrs. Post operative analgesia were maintained with diclofenac. And metoclopramide IV (10 mg) was used as a rescue antiemetic if needed. The result was then be compiled and analysed statistically. Appropriate treatment was taken in case of side effects.

The data was taken as follows—Noemesis—complete control
1-2 episodes—nearly complete control 3-5 episodes—partial control

III. OBSERVATIONS AND RESULTS

The observations are presented as Mean ± Standard Deviation or as percentage as is applicable.

<table>
<thead>
<tr>
<th>Time</th>
<th>Granisetron (N=80)</th>
<th>Ondansetron (N=80)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Immediate</td>
<td>1</td>
<td>1.3</td>
<td>8</td>
</tr>
<tr>
<td>1 hour</td>
<td>1</td>
<td>1.3</td>
<td>3</td>
</tr>
<tr>
<td>2 hour</td>
<td>0</td>
<td>0</td>
<td>3</td>
</tr>
<tr>
<td>4 hour</td>
<td>1</td>
<td>1.3</td>
<td>0</td>
</tr>
<tr>
<td>6 hour</td>
<td>1</td>
<td>1.3</td>
<td>1</td>
</tr>
<tr>
<td>24 hour</td>
<td>1</td>
<td>1.3</td>
<td>9</td>
</tr>
</tbody>
</table>

Table 1: Frequency of Nausea among study subjects

Table 2: Frequency of Vomiting among study subjects

<table>
<thead>
<tr>
<th>Time</th>
<th>Granisetron (N=80)</th>
<th>Ondansetron (N=80)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Immediate</td>
<td>0</td>
<td>0</td>
<td>7</td>
</tr>
<tr>
<td>1 hour</td>
<td>1</td>
<td>1.3</td>
<td>1</td>
</tr>
<tr>
<td>2 hour</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>4 hour</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>6 hour</td>
<td>0</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>24 hour</td>
<td>1</td>
<td>1.3</td>
<td>10</td>
</tr>
</tbody>
</table>

Results reveal that there is a significant difference (p=0.020) in the mean number of episodes of vomiting immediate postoperatively, with no episodes of vomiting with granisetron as compared to ondansetron which had 7 episodes of vomiting. At 1 hr, 2 hr, 4 hr there was a non significant difference seen between the two groups as granisetron group there were 1, 0, 0 episode.
isodeofvomitingrespectively. Whilewithondansetron there were 1, 1.5 episodes of vomiting respectively. At 6 hrs, granisetron showed 0 episodes of vomiting while 9 episodes with ondansetron which was statistically significant (p=0.006). At 24 hrs only 1 episode of vomiting was seen with granisetron and 10 episodes with ondansetron which was statistically significant (p=0.012).

Table 3: Frequency of overall Nausea and Vomiting among study subjects

<table>
<thead>
<tr>
<th>Time</th>
<th>Granisetron (N=80)</th>
<th>Ondansetron (N=80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>%</td>
<td>N</td>
</tr>
<tr>
<td>Immediate</td>
<td>1</td>
<td>1.3</td>
<td>10</td>
</tr>
<tr>
<td>1 hour</td>
<td>2</td>
<td>2.5</td>
<td>4</td>
</tr>
<tr>
<td>2 hour</td>
<td>0</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>4 hour</td>
<td>1</td>
<td>1.3</td>
<td>4</td>
</tr>
<tr>
<td>6 hour</td>
<td>2</td>
<td>2.5</td>
<td>10</td>
</tr>
<tr>
<td>24 hour</td>
<td>1</td>
<td>1.3</td>
<td>11</td>
</tr>
</tbody>
</table>

Table 3 depicts the postoperative episodes of overall PONV when granisetron and ondansetron were given to the two groups of patients. Difference in mean number of PONV episodes observed immediately after surgery was 1 for granisetron and 10 for ondansetron respectively, which is significant (p=0.012). At 1 hr, 2 hr, 4 hr the mean number of episodes of PONV were 2, 0, 1 respectively in granisetron group as compared to ondansetron group which had 4, 5, 4 episodes of PONV at 1 hr, 2 hr, 4 hr respectively. At 6 hrs there were only 2 episodes of PONV in the granisetron group and 10 episodes of PONV in the ondansetron group, it was statistically significant (p=0.036). A significant difference was seen at 24 hours, only 1 episode of PONV was seen in granisetron as compared to ondansetron group which had 11 episodes of PONV (p=0.007).

Result reveal that the requirement of antiemetic in granisetron group was 0 immediately in the postoperative period at 1 hr, 2 hr, 4 hr. In the ondansetron group, requirement of antiemetic immediately at 1 hr, 2 hr, 4 hr is 3, 0, 1, 2 respectively. This difference was statistically non-significant. At 6 hr, a significant difference was seen where in granisetron group there was no requirement of antiemetic and in ondansetron group antiemetic was used 6 times. At 24 hrs, in granisetron group antiemetic was used only once while in the ondansetron group, antiemetic was used 8 times.
In our study, it shows that in the Group O
0 patients had constipation
while in the Group G had 7 patients who had constipation.
Granisetron group had 3 patients who complained of
headache and 12 patients complained of headache
in ondansetron group. And therest had no adverse effect.

IV. DISCUSSION

PONV is a very common and distressing
sequelae of GA, incidence being 20-30%. It is a
leading cause of delayed discharge, unanticipated
hospital admission after ambulatory surgical
procedures, pulmonary aspiration, wound
dehiscence and dehydration. Its multifactorial and despite advance
antiemetic therapy the incidence is high. Apfel et al65 stated that among patients receiving inhaled anaesthesia
a, females with a history of PONV from motion sickness, an
postoperative use of opioids were more important risk factors
so PONV and each additional risk factor increased
the PONV incidence rate to 21%, 39%, 61%, and 79%.

Many types of 5-HT3 receptors antagonist
are being used to prevent
PONV. Ondansetron, the first 5-HT3
receptor antagonist, is marketed and is most commonly used to control PONV. Granisetron
is a 2nd generation 5HT3 antagonist having unique
structural, pharmacological and clinical properties that distinguish it
from other 5-HT3 antagonist.

Naguib et al66 demonstrated that the
incidence of PONV after laparoscopic surgeries
in the placebo group was remarkably high at
72%. In our study the factor that would have contributed to
nausea and vomiting may be laparoscopic
surgery, female gender, menstrual cycle, etc. We
conducted study on 160 ASA I and II patients with
demographic data in terms of age, weight, duration
of anesthesia, duration of surgery which were
similar in two groups. Study done by
Paxton67 showed that PONV is
more common in younger and obese patients.

In our study there is no statistical
significant difference in the baseline values of
hemodynamic variables between the two groups,
before during or after giving the study drugs. In
PACU we recorded the SBP, DBP and HR at
regular interval, no hemodynamic alterations
between the results were observed.

Post-operative episodes of nausea our
results show significant difference between the
nausea episodes immediate after the surgery, where
ondansetron shows 8 episodes and granisetron only
1 episode (p<0.40) while for 1-2 hours
mean episodes were found to be only 1 episode with
grani seron, 3 episodes with ondansetron.

At 4.6 hours postoperatively shows both
ondansetron and granisetron almost shows similar
episode of vomiting, where at 24 hrs granisetron is
more effective than ondansetron as showing 1
episode with granisetron and 10 episodes
with ondansetron (pvalue<0.001). Similar to our study
in a study conducted by Upendranath et al,60
comparing efficacy of ondansetron and granisetron
laparoscopic surgeries, it was found that the 0-2
hours interval, out of 80, 9 (18%) patients ingroup
O had nausea while only 2 patients 4% in Group G
had nausea. This was statistically significant
(p<0.05). In the 3-6 hours only 1-3 patients of
Group O had nausea while 1-2 patients belonging to
Group G had nausea, respectively.

Our study reveals that there is a significant
difference (p<0.020) in the mean of episodes of
vomiting immediate after surgery where
ondansetron shows 7 episodes of vomiting among
80 patients while granisetron shows no episodes
of vomiting. However, 24 hours after

<table>
<thead>
<tr>
<th>Complications</th>
<th>Granisetron (N=80)</th>
<th>Ondansetron (N=80)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>7</td>
<td>0</td>
<td>0.020 (S)</td>
</tr>
<tr>
<td>Headache</td>
<td>3</td>
<td>12</td>
<td>&lt;0.001 (S)</td>
</tr>
<tr>
<td>Nocomplication</td>
<td>70</td>
<td>68</td>
<td>0.818</td>
</tr>
</tbody>
</table>
surgery, granisetron shows least no. of episodes of vomiting while ondansetron shows 10 episodes of vomiting among 80 patients. Thus, there is a significant difference (p=0.012) between the two groups. Similar to our study, Savant et al. compared the efficacy of intravenous ondansetron 4 mg and granisetron 2 mg during oral and maxillofacial surgical procedures; he found emetic episodes in ondansetron group in first 0-2 hrs postoperative period were 1 while that in granisetron was 0 (p<0.32). In 3-24 hrs period, incidence of vomiting was less with granisetron as compared to that of ondansetron.

Episodes of overall PONV
In our study, it was found that among the 80 patients whose received ondansetron 10 patients had the episodes of nausea and vomiting immediately after the surgery and randomly 1 episode of PONV in granisetron group. However, the incidence with granisetron was less as compared to ondansetron. Thus, concluding that granisetron is much more effective in immediate and up to 24-hour surgery. While incidence of PONV increased in ondansetron after 6 hrs. Similarly, in the study conducted by Gauchan et al., intravenous metoclopramide 10 mg IV was used as a rescue anti-emetic drug. Results reveal that the requirement of antiemetic immediately in the post-operative period was non-significant. While the incidence of use of antiemetic is significant at 24 hrs where the heuses was more in ondansetron group as compared to granisetron.

Use of rescue antiemetic
It has been recommended that in cases of PONV, repeat antiemetic should be of a different class than the one used for prophylaxis. This was why metoclopramide 10 mg IV was used as a rescue anti-emetic drug. Results reveal that the requirement of antiemetic immediately in the post-operative period was non-significant. While the incidence of use of antiemetic is significant at 24 hrs where the heuses was more in ondansetron group as compared to granisetron.

Adverse effects
The 5-HT3 antagonists granisetron and ondansetron have an enviable safety profile with most side effects being mild and transient. A small frequency of patients in both study groups experienced non-serious adverse effects like short duration headache, constipation. Apart from this, no side effects were observed in patients of both the groups in our study. As depicted by table we can observe that the incidence of headache was 3.8% in granisetron group while it was 15% in ondansetron group showing statistically significant difference (p<0.001). While the incidence of constipation was 8.7% in granisetron group and no such side effect was seen with ondansetron. No other serious adverse effects were noted.

Similar to our study, Om mitta et al. studied that the incidence of headache was 18% in ondansetron group while it was 11% in granisetron group showing statistically significant difference (p<0.05).

Completer response
Patient showing complete response (patients who had no nausea and vomiting and no need for rescue antiemetic during the 24-hour postoperative period) were significantly higher in group G (98.7%) while the percentage in group O was only 66.2%. As compared to Upendranath et al. in ondansetron group there were 10 (20%) patients received injection metoclopramide 10 mg, the rescue antiemetic in 24 hr postoperative period. And in granisetron group only 1 (2%) out of 50 patients needed rescue antiemetic. This was statistically significant (p<0.05).

Despite its low incidence, the issue of PONV remains a profound and often overwhelming postoperative complication. Both of the serotonin antagonists ondansetron and granisetron appear to work effectively for prevention and treatment of PONV. However, the effectiveness of both drugs when compared to each other, suggests an overall increased efficacy of granisetron along with the advantage of along duration of action. Even though, in this study, ondansetron exhibits favourable results during the initial 6 hours of post-operative period, but the statistical analysis clearly shows that a single IV dose of 2 mg granisetron led to effective control of overall PONV and hence lesser requirement addition of another, suggesting an overall increased efficacy of granisetron along with the advantage of along duration of action. Ondansetron, having shorter duration of action, requires further repeat doses which may extend from twice to thrice a day, which decreases its cost-effectiveness, as compared to the long duration anti-emetic action of a singledose of granisetron. Therefore, this study provides valuable reasoning for using granisetron for the
management of PONV.

**REFERENCES**


