COMPARISON OF ONDANSETRON AND GRANISETRON FOR PREVENTION OF NAUSEA AND VOMITING FOLLOWING DAY CARE GYNAECOLOGICAL LAPAROSCOPY

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SUMMARY
The aim of the study was to compare the antiemetic effects of intravenous ondansetron 4mg (2 ml) and granisetron 2 mg(2 ml) in a double blind placebo controlled manner for prevention of nausea and vomiting in early postoperative period in patients undergoing daycare laparoscopic tubal ligation.

Ninety patients (ASA I and II) undergoing laparoscopic tubal ligation under general anaesthesia were randomly allocated into three equal groups. Group A (n=30) received 4 mg (2 ml) ondansetron intravenously, group B (n=30) received 2 mg (2 ml) granisetron intravenously and group C (n=30) received 2 ml of normal saline by the same route 2 minutes before induction of general anaesthesia. Anaesthetic procedure was common to all patients. Emetic episodes in early postoperative period (first six hours) were recorded and compared in different study groups. Results were analysed by chi square test. P < 0.05 was considered to be significant.

Emetic episodes were observed in 7% patients who had received intravenous granisetron (group B), in 20% who had received ondansetron (group A) and in 50% in patients who had received placebo (group C).

So to conclude, minimal emetic episodes were observed in early postoperative period in patients who had received intravenous granisetron in comparison to those who had received intravenous ondansetron and placebo.

Keywords : Gynaecological laparoscopy, Nausea, Vomiting, Granisetron, and Ondansetron.

The incidence of nausea and vomiting after outpatient gynaecological laparoscopic surgery is high (54–92%).1-5 The aetiology of post-operative nausea and vomiting (PONV) in patients undergoing laparoscopic tubal ligation is not fully understood.5,6 The risk factors such as a residual pneumoperitoneum, use of nitrous oxide, opioids, obese female, 20-40 years of age, one-week premenstrual phase all contribute to these episodes.5,6 Past history of postoperative nausea and vomiting (PONV) and motion sickness are additional risk factors.5 There are a number of drugs that are used to manage PONV. These drugs are generally antihistaminics, phenothiazine derivatives, anticholinergics and dopamine receptor antagonists with unwanted side effects like sedation, dysphoria, extrapyramidal symptoms, dry mouth, restlessness and tachycardia.5,7,8 Recently introduced 5HT₃ receptor antagonists are devoid of such side effects and highly effective in prevention and treatment of PONV. The commonly used drug is ondansetron; 4 mg intravenously is the effective dose to prevent PONV.9 Recently introduced another 5HT₃ receptor antagonist granisetron has more potent and longer acting activity against cisplatin induced emesis than ondansetron.10 Recent study demonstrated that granisetron reduces the incidence and severity of vomiting following strabismus repair and tonsillectomy.11 40 mgkg⁻¹ is the effective antiemetic dose for preventing PONV.11 The present study was done to compare the antiemetic effects of optimal dose of intravenous ondansetron (4 mg) and granisetron (2 mg) to prevent PONV following laparoscopic tubal ligation.

METHODS
After approval of the institutional ethical committee and informed written consent, 90 patients were allocated into three equal groups in a double blind randomized placebo controlled manner. Patients who were lactating, who had body weight more than 80 kg and patients on any medications were excluded from the study. All patients were ASA grade I and II and came in the postmenstrual phase (1st half of menstrual cycle) as advised. Patients were admitted for day case surgery following an overnight fast of 8-10 hours. At the pre anaesthetic interview the patients were familiarized with a postoperative questionnaire and a scale (0-10 cm) for recording visual analogue score (VAS). No premedication was administered. On arrival in the operating room, routine monitoring devices were placed, and baseline blood pressure, heart rate and pulse oximetry values were recorded.
Study medications (2 ml) were prepared by one of the investigators and were administered using double blind design. Group A (n=30) received 2 ml (4 mg) ondansetron, group B (n=30) received 2 ml (2 mg) granisetron and group C (n=30) received 2 ml of normal saline, 2 minutes before induction. The anaesthetic regimen and surgical procedure were standardized for all patients. Anaesthesia was induced with intravenous thiopentone 5 mg kg⁻¹. For intubation 0.5 mg atracurium was used. Anaesthesia was maintained with 66% nitrous oxide in oxygen, pethidine hydrochloride 1 mg kg⁻¹ and halothane 0.5%. Ventilation was controlled mechanically and adjusted so as to keep the end tidal carbon dioxide 35-40 mm of Hg. Laparoscopic tubal ligation was performed under video guidance. During surgery the patients were placed in trendelenberg position and the abdomen was insufflated with carbon dioxide with an intra abdominal pressure of 12-15 mm of Hg. At the cessation of surgery patients were made supine and residual neuro muscular block was reversed with glycopyrrolate 0.4 mg and neostigmin 2.5 mg and tracheal tube was removed. Intravenous Ringer’s lactate was used during intra-operative and immediate post-operative period. Blood pressure, heart rate, and respiratory rate were monitored every 15 minutes and oxygen saturation was monitored continuously. Pain intensity was assessed using a 10 cm visual analogue scale (0=no pain to 10=most severe pain). None of the patients complained of VAS score > 3. Because pain after laparoscopic tubal ligation is relatively minor¹² the patient did not receive further analgesic treatment during their 6 hrs stay in the hospital. They were advised to take diclofenac suppository (100 mg) when required after discharge. Patients were discharged from the hospital 6 hrs postoperatively with an escort, when they were fully conscious, could communicate, able to take oral fluids without any complaint. Emetic episodes were assessed immediately after operation and at 1hr interval for 6 hrs. Dexamethasone 8 mg intravenously was given as rescue antiemetic when required. Incidence of emetic episodes was compared in different study groups and the results were analysed by chi square test.

P < 0.05 was considered to be significant.

Results

All patients in the three groups were comparable according to age, body weight and height (table-1). Duration of anaesthesia and surgery were more or less same in the three study groups (table-2). Incidences of emetic episodes were 20% in ondansetron group (group-A), 7% in granisetron group (group-B) and 50% in placebo (group-C), (table-3). The result was both clinically and statistically significant (p<0.05). Graph-1 states the percentage of patients who were postoperative nausea and vomiting free. The percentage was 93% who received granisetron (group-B), 80% who received ondansetron (group B) and 50% who received placebo (group C).

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<th>Table - 1</th>
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<td>Group A n=30 (ondansetron)</td>
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<td>Age (yrs)</td>
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<td>Wt.(kg)</td>
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<td>Ht.(cms)</td>
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<tr>
<td>Group A (n=30) ondansetron</td>
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<tr>
<td>Duration of anaesthesia(mins)</td>
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<td>Duration of surgery(mins)</td>
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| Table - 3 | Incidence of emetic episodes observed. |
|-----------|
| Group A (n=30) ondansetron | Group B (n=30) granisetron | Group C (n=30) placebo |
| Emetic episodes | 6 * (20%) | 2 * (7%) | 15 (50%) |

*p < 0.05
Discussion

Postoperative nausea and vomiting (PONV) are common sequelae of general anaesthesia and a leading cause of delayed discharge and unanticipated hospital admission after ambulatory surgical procedures. This is very frequent in gynaecological ambulatory surgery leading to recommendation of routine prophylactic administration of antiemetics. The aetiology of nausea and vomiting after day case gynaecological laparoscopic surgery is multifactorial in origin. Age, menstrual cycle, type of surgery and anaesthetic procedure may influence PONV.

The complex act of vomiting involves coordination of the respiratory, gastrointestinal, and abdominal musculature and is controlled by the emetic center. The area situated in the lateral reticular formation close to the tractus solitarius in the brain stem is thought to be the emetic center. Stimuli from several areas within the central nervous system can affect the emetic center. These include afferents from the pharynx, gastrointestinal tract and mediastinum, as well as afferents from the higher cortical centers (including the visual center and the vestibular portion of the eighth cranial nerve) and the chemoreceptor trigger zone (CTZ) in the area prostræma. The area prostræma of the brain is rich in dopamine, opioid, and serotonin or 5-hydroxytryptamine (5HT3) receptors.

Four major neurotransmitter systems appear to play important roles in mediating the emetic response viz. dopaminergic, histaminic (H1), cholinergic, muscarinic and 5HT3. As there are four different types of receptors, there are at least four sites of action of the antiemetic drugs. Antiemetic agents may have actions at more than one receptor, but they tend to have a more prominent action at one or two receptors.

The introduction of 5HT3 receptor antagonist in 1990s was heralded as a major advance in the treatment of PONV because of the absence of adverse effects that were observed with commonly used traditional antiemetics. The 5HT3 receptor antagonists produced no sedation, extrapyramidal reactions, adverse effects on vital signs or laboratory tests or drug interactions with other anaesthetic medications. Current 5HT3 receptor antagonists include ondansetron, granisetron, dolasetron and tropisetron. Ondansetron and granisetron are now available in India. All the 5HT3 receptor antagonists have the same basic double nitrogen ring backbone for their chemical structure. This may be the chemical site of action of the 5HT3 receptor antagonists on serotonin (which is a six and five ring, nitrogen based structure). 5HT3 receptor antagonists are routinely used nowadays to prevent PONV following ambulatory gynaecological laparoscopy. The optimal dose of ondansetron to prevent PONV following ambulatory gynaecological surgery is 4mg. The optimal dose of granisetron to prevent PONV is 2mg. Comparison of single dose oral granisetron vs IV ondansetron in prevention of nausea and vomiting induced by moderately emetogenic chemotherapy has been done. A single oral dose of granisetron (2 mg) resulted in equivalent levels of antiemetic protection as IV ondansetron (32 mg). Giglio et al in their study to prevent nausea and vomiting following cancer chemotherapy concluded that both ondansetron and granisetron have similar antiemetic efficacy but dose of granisetron is much less than ondansetron. 2 mg of granisetron IV is equivalent to 8-16 mg of ondansetron IV. Moreover ondansetron has a shorter half-life of 3 hrs, whereas granisetron has a half life of 8-9 hrs, for which it is more effective in preventing nausea and vomiting. Granisetron is also a more selective 5HT3 receptor antagonist than ondansetron. 20 An IV dose as low as 0.04 mgkg is effective in preventing chemotherapy induced vomiting. A similar dose has been described as effective to prevent PONV. As the elimination half-life of granisetron is 9 hrs, which is 2.5 times longer than that of ondansetron it requires less frequent dosing. Granisetron is recently being used to prevent PONV after day care gynaecological procedures.

We have therefore studied the effects of granisetron 2 mg IV vs ondansetron 4 mg IV administered at induction of anaesthesia in patients who were to undergo laparoscopic tubal ligation under general anaesthesia.

Because many of the factors can interfere with the interpretation of the result of the study, we designed the study in such a way as to control all these factors. All patients underwent laparoscopic tubal ligation with a standardized anaesthetic regimen and surgical procedure. The duration of anaesthesia and surgery and the anaesthetic used were similar in all the three groups. All patients came in the similar phase of menstrual cycle. Therefore it is likely that the differences in the incidences of emetic episodes in the three groups were attributable to ondansetron, granisetron and placebo. In this study it was found that the incidence of PONV was 50% with placebo, 20% with ondansetron and 7% with granisetron within 6 hours post-operatively in patients undergoing daycare gynaecological laparoscopy.

So from the result of the study it can be concluded that granisetron is much more effective than ondansetron to prevent PONV following day care gynaecological laparoscopy.
References


ANNOUNCEMENTS

- The Indian Journal of Anaesthesiology has been indexed with INDEX MEDICUS FOR WHO SOUTH-EAST ASIA REGION (IMSEAR).
- For adequate publicity and dissemination of Indian Biomedical Research Indian Medlars Centre of National Informatics Centre (NIC) has indexed Indian Journal of Anaesthesiology in IndMED.
- Readers will be delighted to note that Indian Journal of Anaesthesia is being disseminated through Internet by NIC. This great leap forward heralds a new era for Indian Journal of Anaesthesia even before we welcome the millennium. Access to our journal of internet will be at the website.

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The official website of ISA, - www.isa-india.org is now ready with added features win attractive prizes by answering the questions in the monthly ‘Anaesthesia A Quiz.’ Update your knowledge by visiting our site! Give us your feed back on the site for our improvisation, to serve you better. The Indian Journal of Anaesthesia can also be accessed as a link through this website.

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