COMPARATIVE STUDY BETWEEN GRANISETRON, ONDANSETRON AND PROPOFOL FOR THE PREVENTION OF EMESIS AFTER GYNAECOLOGICAL LAPROSCOPY

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ABSTRACT

Objective: *The aim of this work was to evaluate the efficiency and safety of granisetron versus ondansetron and Propofol for prevention of postoperative nausea and vomiting in patient undergoing day case gynaecological laproscopy under general anaesthesia.*

Material and Methods: This study was conducted in Alquwayiyah General Hospital and Riyadh Medical Complex. K.S.A, over and period of six months, from January 2004 to June 2004 (both Months inclusive). 120 adult non pregnant female patients (18-40 yrs of age) of ASA I-II scheduled for diagnostic gynaecological laproscopy were included in this study. Patients with severe systemic or endocrine disease who had predisposing factors for delayed gastric emptying, such as diabetes, cholecystitis or neuromuscular disorders were excluded.

Results: *This study was conducted in 120 patients classified into six groups (20 patients each). The first group received granisetron, the second group ondansetron, the third, fourth and fifth group received propofol in different does. The last group received normal saline as placebo (control group). Treatment with either granisetron (group-I) and ondansetron (group-II) resulted in significant lower incidence of nausea and vomiting over 12 hours observation postoperatively compared with other group. However granisetron resulted in significant in lower incidence than ondansteron.*

Conclusion: *It is concluded that preoperative prophylactic administration of intravenous granisetron 40 ug/kg is effective and superior to ondansetron and propofol in preventing nausea and vomiting after gynaecological laproscopic surgical procedures.*

Key works: *Granisetron, Ondansetron, Proprofol, Emesis, Laproscopy*

INTRODUCTION

Nausea, retching and vomiting are among the most common postoperative complaints and can occur after general, regional, or local anaesthesia. Nausea is defined as a subjective unpleasant, but not painful, sensation referred to the pharynx and upper abdomen, associated with a desire to vomit or the feeling that vomiting is imminent. It may be brief or prolonged, often occurring in waves and precedes retching and vomiting or occurs in isolation[1]. Many factors have over the years been associated with an increased incidence of PONV. Most modern studies have been conducted with small numbers of patients and have failed to take complete account of the multifactorial aetiology of Post Operative Nausea and Vomiting (PONV) in patient randomization. For example, some studies have failed to indicate the incidence of a previous history of PONV. Although factors have been identified, little attempt has been made to weight their importance either alone or in combination. Estimation of the significance of these factors is made more difficult when current PONV research is driven by the pharmaceutical industry whose interest is primarily focussed on new antiemetics

Orkin had found that, approximately three-quarters of the patients questioned rated freedom from nausea and vomiting as their most important postoperative requirement.[2] Patients were willing to accept dysphoria, loss of mental acuity and increased pain, in order to avoid nausea and vomiting. In a recent questionnaire analysis, nausea was second only to failure to wake up as a reason for fear of general anaesthesia. Although unpleasant and embarrassing, PONV may occasionally lead to significant morbidity from dehydration, electrolyte imbalance and aspiration of vomitus. Surgical complications such as abdominal wound dehiscence, bleeding beneath

skin flaps and loss of vitreous fluid following intraocular surgery may all follow severe PONV.

There are also economic implications of PONV particularly with the increasing tendency to day care surgery (60% of surgery in the USA and up to 30% of surgery in Europe). PONV resulting in an unanticipated admission leads to extra cost associated with nursing care, which may offset the cost savings of performing day care surgery Indeed PONV is cited as the most important factor in determining length of stay after ambulatory surgery and is one of the most frequent reasons for overnight admission [3].

MATERIAL AND METHODS

This study was conducted in Alquwayiyah General Hospital and Riyadh Medical Complex. K.S.A, over and period of six months, from January 2004 to June 2004 (both Months inclusive).

120 adult non-pregnant female patients (18-40 years of age) of ASA grade I-Il scheduled for diagnostic gynaecological laparoscopy were included in this study. Patients with severe systemic or endocrine disease whom had predisposing factors for delayed gastric emptying, such as diabetes, chronic cholecystitis or neuromuscular disorders were excluded. In addition patients who suffered from postoperative nausea and vomiting (PONV) or whom had received an antiemetic drug or narcotic medications within last 24 hrs were also excluded.

Patient groups:

These patients will be divided to six groups and will be randomly allocated to receive one of the following drugs:

Premedications:

All patients were premedicated with midazolam 0.1 mg/kg given I.V one hour before induction of anaesthesia.

Group I

Twenty (20) patients received Granisetron (40 ug/ kg^{-1} in 20 ml solution) 3 minutes before induction of anaesthesia. Induction of anaesthesia, with Thiopentone (3-5 ug/kg), is followed by maintenance with Isoflurane *(0.5* to 1.5%) N_20 (60%).

Group II

Twenty (20) patients received ondansetron (40-60 u.g/kg in 20 ml solution) 3 minutes before induction of anaesthesia. Induction of anaesthesia with thiopentone (3-5mg/kg) (3-5 maintenance with Isoflurane *(0.5* to *1.5%)* N_20 (60%).

Group III

Twenty (20) patients received propofol for induction (2-3 mg-kg), Isoflurane (0.5 to 1.5%) N_20 (66%) for maintenance.

Group IV

Twenty (20) patients received propofol (2 mg/kg) for induction, Isoflurane (0.5 to 1.5%) $N_20/0_2$ (66%) for maintenance. Fifteen minutes before closure, Isoflurane was discontinued and 50 to 150 ug /Kg^{-4} /min^{-4} of propofol was given to maintain anaesthesia.

Group V

Twenty (20) patients will receive propofol (2mg/kg) for induction, *(50-150* u.g-kg/min) N_20 (66%), O_2 all through the operation.

Group VI

Twenty (20) patients received 10ml of 0.9% normal saline (control group).

Anaesthesia Regimen

Formal consent was obtained from the patients. Routine preanaesthetic assessment and/laboratory tests (full blood count, chemistry, renal and liver function tests) were carried out.

Patient were brought to the operating room and monitored with an automatic blood pressure cuff, three-lead electrocardiogram pulse oximeter, as well as end tidal CO_2 monitor. All patients received Fentanyl (2-3ug/kg) before induction and Atracurium 0.5mg/kg for intubation. Ventilation was controlled mechanically and was adjusted to maintain $ETCO_2$ between 35-40mm Hg, using a Dragar Narkomed 2C ventilator in a closed circuit. A nasogastric tube was then inserted and prior to extubation of the trachea, the narogastric tube was suctioned and then removed. All patients received I.V. lactated ringer's solution (4ml kg/h). At the end of surgery, abdominal cavity was deflated from carbon dioxide insufflated by the surgeon. IM Diclofenac was given for postoperative analgesia. Vital signs including heart rate and blood pressure were noted upon arrival to the operating room. Vital signs measure were taken after induction of anaesthesia and at 5 minute intervals. Those measures were continued one hour after recovery, to be measured again after 12 hours.

Efficacy Assessment

1. The intensity of nausea was assessed hourly for 12 hours study period by retrospective verbal rating scale by (VRS).

   0 ---------- none

   1 ---------- mild

2 ---------- moderate

3 ---------- severe

Both vomiting and retching were considered as emetic event.

2. Sedation score: 0-->2 where zero points to the patient who is completely awake, 1 who is drowsy and 2 is the patient who is somnolent but responds to speech or physical stimulation fifteen minute after extubation

3 Haemodynamic data (arterial blood pressure and heart rate) were assessed preoperatively, 15 minutes after incision and every one hours. for 12 hours postoperatively.

4 Continuous monitoring of ETCO2, SPO2 were assessed intraoperative.

5. Side effects; Headache, seizures, dizziness abdominal pain, extra pyramidal manifestation (tremors and dystonia), the patients were questioned about any possible of these side effects (2-4-6 and 12 after operation).

RESULTS

This study was conducted on 120 patients classified into 6 groups (20 patients each). The first group (gp I) received granisetron, the second group (gp II) received ondansetron, the third (gp III), fourth (gp IV) and fifth (gp V) received propofol in different doses, the last group received normal saline as placebo treatment (control group). The demographic data of the different groups of patients included in this study are shown in table (1). There was no significant differences between the groups regarding age, weight, and duration of Anaesthesia.

Treatment with either granisetron (group I) and ondansetron (group II) resulted in significantly lower incidence of vomiting over 12 h observation postoperatively compared to other groups, however granisetron resulted in a lower incidence of vomiting than ondansetron. The number of patients who experienced vomiting were 3 patients *(15%)* and *5* patients *(25%)* in group I and group II respectively compared to 10 patients *(50%)* in group III, 8 patients (40%) in group IV, 7 patients (*35%)* in group V, and 11 patients *(55%)* in group VI respectively. The propofol groups and control group were not significantly different from each other.

Also, there was no statistically significant difference between group I and group II ($p > 0.05$).

As might be expected, the incidence of nausea was some what higher than that of vomiting because several patients experienced nausea without vomiting, whereas no patient experienced vomiting without nausea. Regarding the number of patients who experienced vomiting over the defined time bands, no patient in either group I or group II (who received granisetron or ondasetron) suffered from vomiting from 6-12 h postoperatively compared to 3 patients in group III, 2 patients in group IV, 2 patients in group IV, one patient in group V, and 4 patients in group IV. Table (2) , Fig. (1-3).

Intensity of Nausea

Nausea was scored according to the verbal rating scale (VRS). There was statistically significant difference between group I, II and the other groups regarding score 0, 1, 2, 3. A statistically signficiant decrease in the number of patients who had severe nausea (score 2) was observed in group I (granisetron) and group 2 (ondansetron) compared to the other groups. However, the number of patients who had severe nausea (score 3) were comparable with no significant difference in the 4 groups (III, IV, V, VI). Table (3), Fig (4).

Degree of sedation

It was found that about 18 patients were awake and 2 patients were drowsy in group I, 17 patients were awake and 3 patients were drowsy in group II, 17 patient were awake and 3 patients were drowsy in group III, 16 patients were awake and 4 patients were drowsy in group IV, 17

PATIENT DEMOGRAPHICS AND DURATION OF ANAESTHESIA

Characteristics	Gp I	Gp II	Gp III	Gp IV	Gp V	Gp VI
	Graisetron (n=20)	Ondasetron (n=20)	Propofol (n=20)	Propofol (n=20)	Propofol (n=20)	Control (n=20)
Age (year) (Mean ± SD)	25.4 ± 5	27.7±11.8	27.6±5.7	25.9±5.5	26.3±8.0	25.2±4.3
Weight in (kg) (means ± SD)	64±7	66±6	66.4±7	65.4±9.8	64±6	67.2±4
Duration of anaesthesia in min (means ±SD)	35±7	32±6	38±4	36±4	35±3	39±7

Table 1

FREQUENCY OF SYMPTOM FREE, NAUSEA, VOMITING IN THE FIRST 12 H DURING THE POSTOPERATIVE PERIOD IN DIFFERENT GROUPS.

Characteristics	Gp I	Gp II	Gp III	Gp IV	Gp V	Gp VI
	Graisetron (n=20)	Ondasetron (n=20)	Propofol (n=20)	Propofol (n=20)	Propofol (n=20)	Control (n=20)
Patient free of PONV n(%)	15(75%)	12 (60%)	8(40%)	9(45%)	10(50%)	7(35%)
Patient suffering of Postoperative nausea n(%)	5(25%)	8(40%)	12(60%)	11(55%)	10(50%)	13(65%)
Patient suffering of postoperative vomiting						
• Over all n (%)	3(15%)a	5(25%)b	10(50%)b	8% (40%)b	7(35%)b	11(55%)b
• 0-2h	0	1	3	2	2	4
• 2-4h	2	2	6	4	3	5
• 4-6h	1	2	2	1	2	3
• 6-8h	0	0	2	1	1	3
• 8-12h	0	0	1	1	0	1

Table 2

Value carrying letter (a) are significantly different from those carrying letter (b))p<0.05).

patients were awake and 3 patients were drowsy in group V, and 20 patients were awake in group VI. There was no statistically significant difference between the six groups regarding the degree of sedation (either awake, drowsy or asleep) table 4.

Drug-related adverse events

Headache was reported by 2 patients in group I (granisetron), 1 patient in group II and V.

Dizziness was reported by 2 patients in group I, one patient in both group II and V. Abdominal pain was reported by 2 patients in group VI.

No serious extrapyramidal side effects were seen in any of the subjects in the different 6 groups. Tablet (5)

DISCUSSION

In spite of many advances in anaesthesia and surgery over the last decades, it seems that postoperative nausea and vomiting is still a clinically important and frequent cause of discomfort during recovery[4].

This may be accentuated when care is provided on a day stay basis and may require unplanned admission to hospital[5].

Serious complications include Mallory-Weiss syndrome, rupture of the oaesophagus dehydration, alkalaemia and aspiration of vomitus[6].

Aetiology of PONV is multifactorial in origin, including patient-related factors, type of surgery as well as the anaesthetic agents and postoperative care[7].

The main patient related factors are, age, gender, history of migraine, motion sickness and experience of previous postoperative nausea and vomiting. Anaesthetic and operative factors include type and duration of surgery, type of the agents used in induction and during maintenance[8].

Cost effectiveness of the drugs used and bed turnover is an essential consideration nowadays.

Recent studies have reported that the incidence of PONV is in the range of 20-30% range, thereafter, it seems logical that routine prophylactic use may not be practical. However, in patients at a higher risk for PONV e.g. (patients undergoing laparoscopy, abdominal or strabismus surgery); prophylactic therapy even with a newer more costly drug may be appropriate[9].

There is a wide variety of antiemetic agents with different pharmacologic properties, although older and less expensive drugs, are used in every day practice. The most popular being antihistamines e.g. cyclizine, anti-cholinergic e.g. scopolamine, antidopaminergic (e.g. metaclopramide), butytyrohenonmies e.g. droperidol, and sympathomimetics (e.g. ephedrine). Although these antiemetics are generally effective they have undesirable side effects, including sedation, hypotension, extrapyramidal reactions, dry mouth, dysphoria and ha1lucination.

Given the current surgical climate with an ever-increasing number of procedures being performed on a day case basis, the absence of side

INTENSITY OF NAUSEA USING THE VERBAL RATING SCORE (VRS).

VRS	Gp I	Gp II	Gp III	Gp IV	Gp V	Gp VI
	Graisetron (n=20)	Ondasetron (n=20)	Propofol (n=20)	Propofol (n=20)	Propofol (n=20)	Control (n=20)
0	15	12	8	9	10	7
1	2	3	2	3	3	2
2	1	2	3	3	3	2
3	2	3	7	5	4	9

Table 3

- This table scores the intensity of nausea and vomiting all in each group.
- It is to be noted that:

VRS0: symptoms free

VRS1: nausea only

VRS2 or 3: nausea followed by vomiting

effects, especially that might be cause for hospital admission (e.g. sedation) is particularly a desirable characteristic of any drug being considered for routine prophylactice use.

Granisetron is a selective 5-hydroxytryptamine$_3$ *(5-HT$_3$)* receptor antagonist with little or no affinity for other serotonin receptors, including 5-HT$_1$, *5* HTIA, 5HTIB/c, 5HT$_2$, for alpha$_1$ alpha$_2$ or beta - adrenoreceptors, for dopamine - D$_2$, or for histamine-H$_1$, benzodiazepine, picrotoxin, or opioid receptors. Serotonin receptors of the 5-HT$_3$ type are located peripherally on vagal nerve terminal and centrally in the chemoreceptor trigger zone of the area postrema.

Ordansetron is a potent, highly selective 5-HT$_3$ receptor antagonist blocking the pathways associated with the vomiting reflex. Its antiemetic action was revealed initially by its ability to antagonize retching and vomiting induced by chemotherapy or radiotherpay in animals and human[10]. The mechanisms of action of ondansetron are both central and peripheral. It blocks the 5-MT$_3$ in the area postrema, nucleus tractus solitarius (NTS) and adjacent areas in the brain, which are related to nausea and vomiting. Also, it blocks 5-HT$_3$ receptors in the mucosal vagal afferents in the gastrointestinal tract.

Propofol is known to posses direct antiemetic effects. Its use for induction and maintenance of anaesthesia has been shown to be associated with a lower incidence of postoperative nausea and vomiting (PONV) when compared to any other anaesthetic drug or technique. However, its mechanism of action in this context is still not well-understood[11].

The present study was designed to evaluate the safety and efficacy of doses of I.V. granisetron (40 u.g/kg), I.V. ondansetrone (4 mg), different doses of propofol, for prevention of PONV in patients undergoing gynacological laparorscopic surgery.

Patient receiving general anaesthesia for laparoscopic procedures were chosen for this study as those patients represent a highly susceptible group for PONV with both anaesthetic and non-anaesthetic factors contributing to the problem and this type of surgery is performed nowadays on day-case basis.

Care was taken to ensure that the treatment groups were comparable in terms of type

DEGREE OF SEDATION ASSESSED IN THE DIFFERENT GROUPS FIFTEEN MINUTES AFTER EXTUBATION

VRS	Gp I	Gp II	Gp III	Gp IV	Gp V	Gp VI
	Graisetron (n=20)	Ondasetron (n=20)	Propofol (n=20)	Propofol (n=20)	Propofol (n=20)	Control (n=20)
Awake	18	17	17	16	17	20
Drowsy	2	3	3	4	3	0
Asleep	0	0	0	0	0	0

Table 4

- There was no statistically significant difference between the groups

of patients, demographic data and anaesthetic technique was standardized. In this study, non-steroidal anti-inflammatory analgesic (diclofenac) was used post-operatively for analgesia and this has led to the avoidance of the use of opioids postoperatively.

Also, nitrous oxide was not omitted as an anaesthetic adjuvant because many studies demonstrated that the use of nitrous oxide may confer some advantages for the production of smoother anaesthesia and thereby compensates for its tendency to increase postoperative emetic symptoms.[12]

Although the mechanism of PONV after laparoscopy is unclear, it is postulated that it is due to stimulation of the vagal afferents on the bowel and peritoneum when the peritoneal cavity is inflated with carbon dioxide during laparoscopy. Also, nitrous oxide used during Anaesthesia may contribute to the incidence of peritoneal and intestinal gas volumes which leads to the release of 5-HT_3 from enterochramaffic cells and this causes activation of the 5-HT_3 receptors located on the vagal afferents[13].

The present study showed that a greater percentage of patients in the granisetron group experienced no postoperative nausea or vomiting (75%) respectively compared to ondansetron (60%), propofol in different doses (40%, 45%, 50%), and control groups (3 5%) for the first 12h postoperatively.

The incidence of nausea was 65% in the control group, *(50%,55%,*60%) in propofol groups, 40% in the ondansetron group and *25%* in the granisetron.

In agreement with the present study, Fujii Y, Tanaka H and Kawasaki T. (2OOO)[14] evaluated the antiemetic efficacy of granisetron after randomized clinical trial of granisetron, droperidol and metaclopramide for the treatment of nausea and vomiting after laparoscopic cholecystectomy. After experiencing PONV during the first 3 h after recovery from anaesthesia, 120 patients (78 women) received, in a randomized double-blind manner, granisetron 40 ug/kg, droperidol 20 microg/kg or metoclopramide 0.2 mg/kg (n = 40 per group) intravenously. Patients were then observed for 24 h after administration of the study drug. They found that, complete control of established PONV, defined as no emetic symptoms and no need for another rescue antiemetic medication, was achieved in 88 percent of patients with granisetron, 60 per cent with droperidol and *55* per cent with metoclopramide ($p < 0.05$). No clinically adverse events were observed in any of the groups. Therefore, they reported that, a high dose of granisetron (40 microg/kg) was more effective than droperidol (20 microg/kg) or metoclopramide 0.2 mg/kg for the treatment of PONV after LC.

Also, Taylor and Rosen (1997)[15] have confirmed our findings in their study, which compare the effectiveness of granisetron with placebo in the treatment of established postoperative nausea and vomiting (PONV). This study was a randomized, placebo-controlled study, in 34 hospitals in Europe, Scandinavia and South Africa. A 519 ASA physical status I, II and III patients who developed PONV within 4 hours of the end of surgery performed with general anaesthesia. Patients received a single intravenous dose of granisetron 0.1 mg, 1mg, or 3 mg, or placebo when symptoms of nausea or vomiting were experienced. At all doses investigated, granisetron was significantly more effective ($p \leq 0.001$) than placebo in controlling vomiting 38%, 46%, and 49% of patients receiving granisetron 0.1 mg, 1.0 mg, and 3.0 mg, respectively, experienced no vomiting in the first 24 hours following drug administration, compared with 20% receiving placebo. There was a statistically significant linear relationship between vomiting control and granisetron dose ($p < 0.001$). Survival distributions of time to resolution of

DRUG RELATED ADVERSE EVENTS (POSTOPERATIVE 12HRS)

Characteristics	Gp I	Gp II	Gp III	Gp IV	Gp V	Gp VI
	Graisetron (n=20)	Ondasetron (n=20)	Propofol (n=20)	Propofol (n=20)	Propofol (n=20)	Control (n=20)
Headache	2	1	1	0	0	0
Dizziness	2	1	1	1	1	0
Abdominal pain	0	0	0	0	0	2
Extraphyramidal signs	0	0	0	0	0	0

Table 5

- There was no statistically significant between the groups

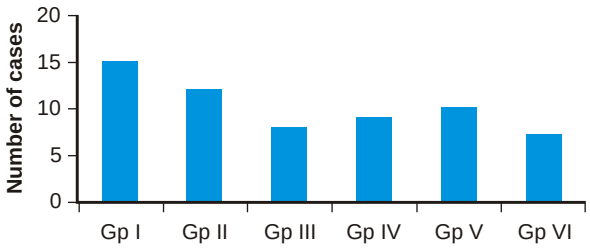

Fig 1. Frequency of symptom free cases in different groups.

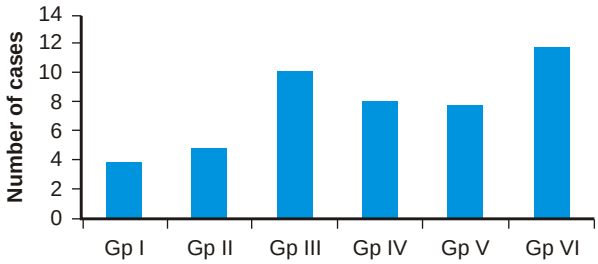

Fig 2. Frequency of nausea in symptom in different groups.

vomiting confirmed the statistically significant difference between patients receiving granisetron and those receiving placebo. Granisetron was well tolerated, the most common adverse experiences were pain, constipation, Anaemia, and headache, and the incidence of adverse experiences was not statistically significantly higher in any of the granisetron groups than in the placebo group. Taylor and Rosen concluded that, granisetron was signficiantly more effective than placebo in all groups.

In this study 60% of patients in ondansetron group (40 microg/kg) experienced no postoperative nausea or vomiting when compared to other groups (propofol, control) for the first 12 h postoperatively.

Paxton et al. (1995)[16] compared the efficacy of ondansetron, metoclopramide, droperidol and placebo in the prevention of postoperative nausea and vomiting in 118 day stay patients undergoing laparoscopc gynaecological procedures.

Patients received either ondansetron 4 mg I.V, metoclopramide 10 mg I.V, droperidol 1mg I.V or placebo prior to induction. All patient received a standardised general anaesthesia of fentanyl, propofol, nitrous oxide in oxygen and isoflurance. Nausea occurred in 8 of 32 (25%) of the patients who received ondansetron compared to 17 of 29 patients (59%) in metoclopramide group, 25 of 29 patients (86%) in the droperidol group 27 of 28 patients 96% in placebo group. Fewer patients vomited in the ondansetron group 6/32 (18%) compared to 12/29 (4 1%) in the metoclopramide group and 13/28 (48%) in placebo group. They have concluded that ondansetron 4mg was superior to metoclopramide 10 mg and droperidol 1mg for prophylaxis against PONV.

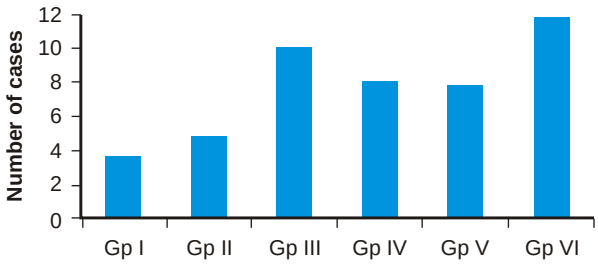

Fig3. Number of patients in the different groups who experienced vomiting in the 12 h postoperatively.

Propofol has been advocated for a day stay anaesthesia because of its good recovery characteristics and low incidence of PONV due to its antiemetic Property.

Propofol is known to possess direct antiemetic effects. It use for induction and maintenance of anaesthesia has been shown to be associated with a lower incidence of postoperative nausea and vomiting when compared to any other anaesthetic drug or technique. However, its mechanism of action in this context is still not well understood.

In agreement with this study, Chigusa S. et al. (1997)[17] have found that propofol reduce emesis. He evaluated the incidence of postoperative nausea and vomiting in gynecologic abdominal surgery patients after propofol anaesthesia and inhalational anaesthesia. Sixty patients were evaluated for the incidence of PONV. Thirty patients received oxygen-propofol epidural anaesthesia (propofol group) and the others was maintained with nitrous oxide-oxygen-isoflurane / servoflurane epidural anaesthesia (inhalational group). The incidence of PONV was 33.3% in propofol group and 60% in inhalational group ($p < 0.05$). For the gynecologic abdominal surgery patients, PONV was significantly less following intravenous anaesthesia with propofol than after isoflurane or sevoflurane inhalational anaesthesia. So this study indicated that propofol anaesthesia was useful in reducing PONV after gynecologic abdominal surgery. Also in the present study, no side effects especially extrapyramidal symptoms were observed with granisetron or ondansetron. This was in agreement with other studies.

Using three-point scale (awake, drowsy, asleep) in the present study, there was no difference in the postoperative sedation scores between the 6 groups. This was in agreement with other studies.

In conclusion, serotonin antagonists have

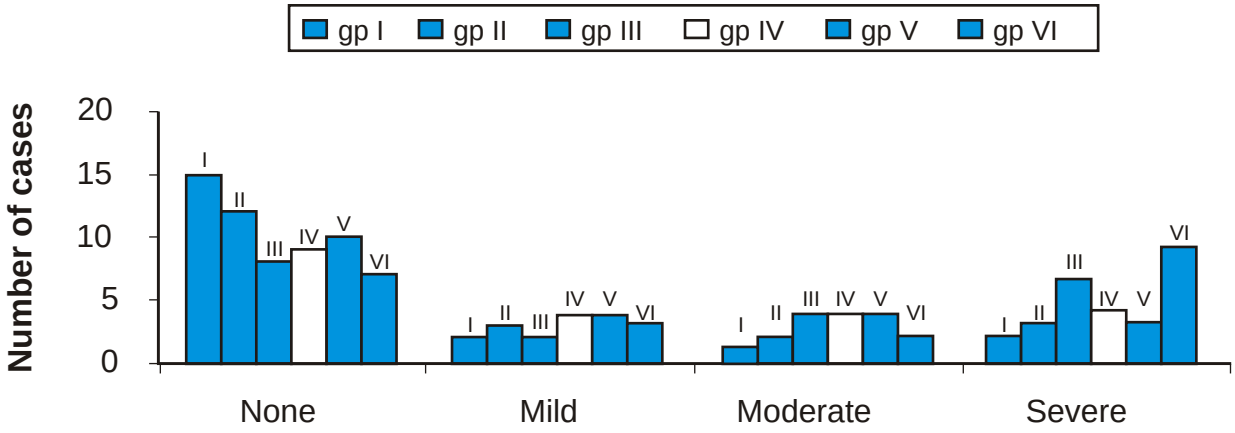

Fig 4. intensity of nausea (VRS) in different groups.

central a highly, selective and potent antagonism of $5HT_3$ receptors in the brain and this most probably is the main pathway of action of $5HT_3$ blocker in this group of patients.

A high density of $5HT_3$ receptors are found in the area postrema and the nucleus tractus solitarius, equating with the chemoreceptor trigger zone.'

The $5HT_3$ receptor antagonists are involved more in the peripheral mechanism in patients receiving cytotoxic drugs as the damage of gastrointestinal mucosa and the mobilization of 5-HT_3 from the mucosa of enterochromaffin cells increases the level of serotonin in the serum.

Therefore, the antiemetic action of granisetron and ondansetron are more specific and effective in patients receiving chemotherapy.

In addition the prophylactic adminstration of dimenhydrinate (Dramamine) is as effective as the use of ondansetron in prevention of PONV.[18]

Therefore in any out patient procedures any of the conventional drugs may be used effectively with no need for overnight hospitalization and the routine use of 5-HT_3 blockers should be re-evaluated, because economically granisetron was very costly for routine use in out-patients. However, 5-HT_3 blocker is very specific for the prevention of acute emesis especially in chemotherapy, and granisetron has only better safety profile than ondansetron.

CONCLUSIONS

As more and more surgery is being performed on a day case basis, the need for effective antiemetic with fewer side effects than currently in use, becoming more urgent. The development of the 5-hydroxytryptamine 3 receptor antagonists as a new class of antiemetics is a considerable advance in the management of this condition.

Granisetron is selective 5-hydroxytryptamine subtype 3 (5-HT_3) receptor antagonist, which lacks effects at cholinergic, adrenergic, dopaminergic and histaminergic receptors. It has been shown to be effective in preventing nausea and vomiting associated with cancer chemotherpay and radiotherapy

Ondansetron was better than propofol and control groups ~-regarding the incidence of nausea or vomiting. Sedation scores were not significantly different between the 6 groups.

It is concluded that preoperative prophylactic administration of intravenous granisetron 40 ìg/kg is effective and superior to ondansetron and propofol in preventing nausea and vomiting after Gynaecological laparascopic surgical procedures.

REFERENCES

1. Maston A, Palazoo M. Postoperative nausea and vomiting. Anaesth Analg 1995;19: 108.
2. Orkin F. What do patients want? Preferences for immediate postoperative recovery. Anaesth Analg 1992;74:225.
3. Green G, Jonsson L. The most important factor determining length of stay after ambulatory anaesthesia. A comparative study of isoflurance and or propofol techniques. Acta anaesthesiol Scand 1993; 37:742-6.
4. Quinn AC, Brown JH, Wallance PG, Ashury AJ. Studies in postoperative sequelae. Nausea and vomiting still a problem. Anaesthesia 1994; 49 62-5.
5. Gold BS, Kitz DS, Lecky, Neuhaus JM. Unanticipated admission to the hospital

following ambulatory surgery. J Am Med Assoc 1989:262: 3003-10.

6. Andrews PLR. Physiology of nausea and vomiting. Br J Anaesth 1992; 69 (Suppl 1): 2 S1-9.
7. Watcha ME, White PF. Postoperative nausea and vomiting: Its aetiology, Treatment, and prevention. Anaesthiology 1992 ; 77:162-184.
8. White PF, Shafer A. Nausea and vomiting: causes and prophylaxis. Semin Anesth 1988; 6:300-308.
9. White PF, Watcha ME. Are new drugs cost-effective for patients undergoing ambulatory surgery ? Anaesthesiology 1993; 78: 25.
10. Cunningham D, Hawthorn J, Pople A, et al. Prevention of emesis in patients receiving cytotoxic drugs by GR-3 8032 F, a selective 5-HT3 receptor antagonist. Lancet1987; 1:1461-3.
11. Borgeat A, Stirnemann HR. Antiemetic effect of propofol. Anaesthesist 1998; 47 (11): 918-24.
12. Sen gupta P, Plantevin OM Nitrous oxide and day-case laparoscopy: Effects on nausea, vomiting and return to normal activity.Br J Anaesth 1988; 60: 570-3.

13 Kenny GNC. Risk factors for postoperative nausea and vomiting. Anaesth 1994; 49 (supplement): 6-10.

14. Fujii 1, Tanaka H, Kawasaki 1. Randomized clinical trial of granisetron, droperidol and metoclopramide for the treatment of nausea and vomiting after laparoscopic cholecystectomy.Br J Surg 2000; 285-8.
15. Taylor AM, ROsen M, Diem unsch PA, Thorin D, Houweling PL. A double-blind, parallel group, placebo-controlled, dose ranging, multicenter study of intravenous granisetron in the treatment of PONV in patients undergoing surgery with general anaesthesia. J Clin Anesth 1997:65:8-63.

16 Paxton LD, Mckary Ac, Mirakur PK Prevention of nausea and vomiting after day case gynaecological, laparoscopy, A comparison of ondansetron, droperidol, metoclopramide and placebo. Anaesth 1995; 50:403-6.

17. Chigusa S, kaetsu H, Obara H. Postoperative nausea and vomiting after gynaecological abdominal surgery a comparison of propofol versus inhalatational technique. Anaesth 1997;7:10.
18. Kotharia SN, Boyd WC, Bottcher ML. Antientic efficacy of prophylactic dimenhydrinate (Dramamine vs ondansetron (zofran). Surg Enbdose, 2000; 14(10): 926-9.

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