Section: Anesthesia

Research

A COMPARATIVE STUDY ON EFFICACY OF ONDANSETRON AND GRANISETRON IN PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC SURGERIES UNDER GENERAL ANESTHESIA

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Abstract

Background: The current study, conducted at Department of Anesthesia, Rajiv Gandhi Institute of Medical Sciences, (RIMS), Adilabad, Telangana, India compared the efficacy of intravenous Ondansetron and granisetron in preventing postoperative nausea and vomiting in patients undergoing laparocscopic surgeries under general anaesthesia between September 2021 to August 2022. **Materials and Methods:** 100 ASA grade I and II patients undergoing laparoscopic surgery under general anaesthesia were allocated into two groups of 50 each. Before induction, group O took 4mg Ondansetron and group G received 1mg granisetron. CHI square test and student's unpaired t-test were used to analyse observations. **Result:** Both groups had similar demographics (age, age-gender distribution, weight, weight-gender distribution, and mean surgery length). Heart rate, systolic, diastolic, and mean arterial pressure were similar between groups. 36% reported nausea. **Conclusion:** In Group O and Group Gwhich was low. Group O had 22% retching and Group G 2%. Group O (16%) had more vomiting than Group G (2%) PONV was less common in group G (12%) than group O(36%). Group O (20%) required more antiemetics than group G (2%). Both groups had no side effects. In Group O, 12% of patients had headaches, while in Group G, 4% did. One patient in Group O had dizziness, although these were not serious adverse effects.

INTRODUCTION

Since many years ago, the use of general anaesthetics during surgical procedures has been linked to nausea and vomiting. The "huge little problem of PONV" has drawn more attention as the focus has shifted from inpatient to outpatient, hospital and office-based medical/surgical treatment. Within 18 months of the introduction of anaesthesia to Britain, John Snow completed one of the first in-depth descriptions of the phenomena, which was published in 1848. He noticed that if the patient had recently eaten, vomiting was more likely to happen.[1,2]

However, despite these improvements, nausea and vomiting still happen too frequently in connection with surgery and anaesthesia, and the phrase "the huge little issue" best captures the prevalent opinion.[3]

The following are some of PONV's many negative effects:

Physical: Vomiting and retching can be quite violent motions that put a lot of strain on particular structures, which can result in esophageal tears, bleeding (Mallory-Weiss syndrome), esophageal rupture (Boerhaave syndrome), rib fractures, stomach herniations, muscular strain, and exhaustion. After plastic surgery, vomiting can result in wound dehiscence, ophthalmic haemorrhage, and upper body skin flap bleeding. Aspiration of vomitus, respiratory obstruction, and aspiration pneumonia are the three main issues related to vomiting in the postoperative period.[4,5]

Metabolic: Alkalemia, dehydration, and anorexia are some of the metabolic consequences. Psychologically, nausea is an extremely unpleasant sensation that, if it is brought on by a surgical procedure, may result in a lifelong aversion to surgery. Numerous strategies have been employed over time to manage PONV. It has been claimed that a number of methods, including olive oil and insulin-glucose infusions, are efficient. In 1912, Robert Ferguson discussed the usage of olive oil. He

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proposed that whatever ether that may have been present in the stomach was "absorbed" by oil.[6] When he noted that "in the very great majority of cases, the addition of a specific amount of atropine to morphine eliminates the nausea and vomiting occurring with morphine alone" in 1883, Brown-Sequard demonstrated his understanding of the impact of atropine. 3 In the late 19th century, phenothiazines were first created using synthetic means. Promethazine was discovered to have antiemetic properties in the late 1930s. In 1949, Charpentier created chlorpromazine, but its main side effects were drowsiness and hypotension.

Serotonin (5-HT3) receptor antagonists such ondansetron, granisetron, tropisetron, and dolasetron are the most recent family of antiemetics utilised for both prevention and treatment of PONV. Unlike more ancient, conventional antiemetics, these medications have no negative side effects.[7]

Some sources claim that the annual cost of PONV in the United States is close to $1 billion. 5-HT3 antagonists, one class of available antiemetics, are effective at very low doses. 5 As a result, prophylaxis can reduce expenditures and prevent pharmacological side effects, hence lessening the financial burden brought on by problems and higher medical care brought on by PONV. In the current trial, the effectiveness of intravenous ondansetron and granisetron in preventing postoperative nausea and vomiting is being examined.[8,9]

MATERIALS AND METHODS

The present clinical study was conducted at Department of Anesthesia, Rajiv Gandhi Institute of Medical Sciences, (RIMS), Adilabad, Telangana, India during the period September 2021 to August 2022. After obtaining approval from institutional ethics committee, the present study was undertaken to evaluate the efficacy of intravenous ondansetron vs graninsetron on post operative nausea and vomiting following laparoscopic surgeries done under general anesthesia. It was a prospective study done on 100 patients undergoing elective laparoscopic surgeries under GA.[10]

Inclusion criteria

- ASA grade I and II patients.
- Age between 20 – 60 years of either gender.
- Elective laparoscopic surgeries posted under GA.

Exclusion criteria

- Patients belonging to ASA Grade III and above.
- Pregnancy, hyperemesis gravidarum.
- Patients with motion sickness.
- Allergic to study drugs.
- Patients who have received antiemetics 48hrs before surgery.
- Patients with BMI >30

Methods

All patients underwent extensive clinical evaluations and pertinent laboratory tests prior to giving their informed, valid, written consent to participate in the trial and receive GA. All patients were kept off food and liquids for eight hours prior to surgery, and the day of the procedure, at bedtime, an oral dose of alprazolam (0.01 mg/kg body weight) was given to each patient. On the morning of the procedure, at 6am, a 150mg ranitidine tablet was given orally.

Anesthesia was induced by an injection of thiopentone sodium (5 mg/kg), and succinylcholine (2 mg/kg) was administered as a muscle relaxant before an appropriate-sized endotracheal tube was utilised for intubation. Depending on the kind and length of the procedure, inj. fentanyl 1 g/kg IV was given for analgesia and inj. vecuronium 0.08 mg/kg IV was used to provide muscular relaxation throughout surgery.[11,12]

Halothane was used with regulated ventilation along with nitrous oxide (66%) and oxygen (33%), maintaining anaesthesia. During the intraoperative period and up until the conclusion of operation, hemodynamic parameters (HR, SBP, DBP, MAP) and EtCO2 were measured at 0mins, 3mins, 5mins, 10mins, and for every 15mins. Following surgery, injections of neostigmine (0.05 mg/kg i.v.) and glycopyrrolate (0.1 mg/kg i.v.) were used to reverse any residual paralysis. After ensuring an appropriate degree of consciousness and intact reflexes, patients were taken to the recovery room, and then to the ward, where postoperative paracetamol infusions were administered every six hours to relieve pain.

Within the first 24 hours following surgery, instances of PONV were noted at intervals of 0-2 hours, 3 hours, 6 hours, 12 hours, and 24 hours. The patients' own complaints or direct questions were used to detect PONV episodes. HR, SBP, DBP, and MAP were measured at 0, 1, 2, 3, 4, 6, and 12 hours following surgery.[13,14]

Statistics

Mean: The mean of a collection of numbers is their arithmetic average, computed by adding them up and dividing by their number.[15]

Standard deviation (SD): It is a statistical measure of spread or variability. The standard deviation is the root mean square (RMS) deviation of the values from their arithmetic mean.[16]

In the present study, student's unpaired t-test (HR, SBP, DBP, MAP and EtCO2) and Chi-square test (nausea, vomiting, retching and rescue antiemetic) was usedfor measuring the stastical significance between both the groups. These were used because two sets of population were compared which were independent and identically distributed.[17]

'p'value: It indicates the probability of error and a value less than 0.05 is considered statistically significant.[18]

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RESULTS

Following were the observations and results of present study

Table 1: Comparison of Age Wise Distribution In Both The Groups. (N=100)

Age in years	Group O (n=50)	Group G (n=50)
20-30	16 (32%)	15(30%)
31-40	20(40%)	24(48%)
41-50	8 (16%)	6(12%)
51-60	6(12%)	5(10%)

Table 2: Comparison of age (mean±sd in years) in both the groups (N=100)

	Group O (n=50)	Group G (n=50)	p-value
Mean Age± SD	34.46±10.3	35.42± 10.6	p > 0.05

p-value <0.05 was taken as significant.
Mean age was comparable between both the groups.

Table 3: comparison of weight wise distribution in both the groups (n=100)

Weight in Kilograms	Group O (n=50)	Group G (n=50)
40-50	17(34%)	24(48%)
51-60	19(38%)	12(24%)
61-70	14(28%)	14(28%)

Weight wise distribution was similar in both the groups

Table 4: Comparison of Weight (MEAN±SD IN Kgs) in both the groups (N=100)

	Group O (n=50)	Group G (n=50)	p-value
Mean Weight in Kilograms	57.46±9.86	56.83±9.3	p>0.05

p-value <0.05 was taken as significant.
Mean weight was comparable between both the groups

Table 5: comparison of gender in both the groups (N=100)

Gender	Group O (n=50)	Group G (n=50)	P value
Male	12(24%)	12(24%)	>0.05
Female	38(76%)	38(76%)	>0.05

p-value <0.05 was taken as significant.
In the present study females predominated males in Ondansetron group and Granisetron group.

Table 6: Comparision of ASA grade in both the groups (N=100)

ASA Grade	Group O (n=50)	Group G (n=50)	P value
Grade I	39(78%)	40(80%)	(>0.05)
Grade II	11(22%)	10(20%)	(>0.05)

p-value <0.05 was taken as significant.
Both groups had no significant difference in ASA I and ASA II category

Table 7: Groupwise distribution of patients based on procedures (N=100)

Type of surgery	Group O (n=50)	Group G (n=50)
Laparoscopic cholecystectmy	36(72%)	33(66%)
Laparoscopic Appendicectomy	8(16%)	7(14%)
Laparoscopic mesh repair	3(6%)	2(4%)
Diagnostic laparoscopy	1(2%)	1(2%)
Total Laparoscopic hysterectomy	2(4%)	4(8%)
Laparoscopic ovarian cystectomy	0	2(4%)
Laparoscopic adhesolysis	0	1(2%)

In present study laparoscopic cholecystectomy predominated as shown in the table

Table 8: Comparsion of mean duration of surgery (MEAN ± SD in mins) in both the groups (N=100)

	Group O (n=50)	Group G (n=50)	p-value
Mean Duration of surgery(mins)	106.68±23.17	104.6±21.5	p>0.05

P value is >0.05 hence it is insignificant

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Table 9: distribution of cases according to the occurrence of nausea in the postoperative period in groups O and G (N=100).
Nausea: it's a sensation of unease or discomfort in the upper stomach with an involuntary urge to vomit.

Duration	Group O (Ondansetron)	Group G (Granisetron)	P VALUE
	No of cases (Percent)	No of cases (Percent)	
0-2 hours	9(18%)	2(4%)	0.04
3hrs	1(2%)	1(2%)	>0.9
6hrs	1(2%)	2(4%)	0.56
12hrs	3(6%)	1(2%)	0.32
24hrs	4(8%)	0(0%)	0.041
Total	18(36%)	6(12%)	0.0027

p-value <0.05 was taken as significant

[Table 9] shows the occurrence of nausea during the first 24-hour postoperative period. During the 0-2 hour's interval, out of 50 patients, 9(18%) patients in Group O had nausea while only 2 patients (4%) in group G had nausea. This was found to be statistically significant (P<0.05). In the 3 hour, 6 hour and 12 hour intervals, 1 (2%), 1 (2%) and 3 (6%) patients of Group O had nausea while 1 (2%), 2 (4%) and 1 (2%) patients belonging to Group G had nausea, respectively. These results were found to be statistically non-significant. However, in the 24-hour interval, 4 out of 50 (8%) Group O patients complained of nausea while no Group G patients had similar complaints. This was found to be statistically significant (P < 0.041).

Overall, 18(36%) patients out of 50 in Group O had nausea while only 6(12%) out of 50 in Group G had nausea. Group O patients were found to have significantly higher occurrence of nausea compared to patients in Group G (P < 0.005)

Table 10: Distribution of Cases According to the Occurrence of Retching in the Postoperative Period in Groups O and G (N=100)
Retching: it is the reverse movement of stomach and esophagus without vomiting.

Duration	Group O (n=50)	Group G (n=50)	P Value
	No of cases (Percent)	No of cases (Percent)	
0-2 hours	5(10%)	0(0%)	0.028
3hrs	1(2%)	0(0%)	0.31
6hrs	1(2%)	1(2%)	>0.9
12hrs	2(4%)	0(0%)	0.16
24hrs	2(4%)	0(0%)	0.16
Total	11(22%)	1(2%)	0.006

p-value <0.05 was taken as significant

Table shows the occurrence of retching during the first 24-hour postoperative period. During the 0-2 hour interval, 5 (10%) patients out of 50 in Group O had retching, while none in Group G had retching. This analysis was found to be statistically significant (P < 0.028).

In the 3-hour, 6 hour, 12 hour and 24 hour intervals, 1 (2%), 1 (2%), 2 (4%) and 2 (4%) Group O patients had retching, respectively.

However, out of the 50 patients in Group G, only 1(2%) patient had retching and this occurred in the 6-hour interval. This analysis was found to be statistically non-significant.(p>0.9)

Overall, 11(22%) patients in group O had retching, while only 1(2%) patient ingroup G had retching. A significantly higher occurrence of retching was observed in group O compared to group G (P value 0.006).

Table 11: comparison of ETCO2 (Mean±SD in mmHg) in Both the Groups(N=100).

Time in minutes	Group O (n=50)	Group G (n=50)	p value
0	32.68±1.6	33±1.49	p>0.05
3	32.96±1.45	32.8±1.52	p>0.05
5	32.54±1.6	32.65±1.59	p>0.05
10	32.50±1.62	32.70±1.56	p>0.05
15	32.40±1.64	32.81±1.51	p>0.05
30	32.72±1.60	33.00±1.34	p>0.05
45	32.62±1.50	32.87±1.62	p>0.05
60	32.64±1.54	32.78±1.70	p>0.05
75	33.00±1.55	32.80±1.60	p>0.05
90	33.18±1.56	32.50±1.62	p>0.05
105	32.90±1.51	32.48±1.64	p>0.05
120	32.78±1.43	32.72±1.60	p>0.05

p-value <0.05 was taken as significant.

Mean of end tidalCO2 was comparable between both the groups.

DISCUSSION

According to Tramer M et. al, the related benefits of lower morbidity and a shorter hospital stay, laparoscopic operations have become the preferred treatment for numerous treatments. PONV has a high occurrence in patients undergoing laparoscopic

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procedures under general anaesthesia, and its pathogenesis is complicated.[19]

Varun reddy et al said the current study examined the incidence of PONV in patients who had different preoperative antiemetic regimens, such as ondansetron and granisetron, and observed the incidence of PONV in patients undergoing laparoscopic surgery. It was deemed unethical to use a placebo group because PONV is a known side effect of laparoscopic surgeries. As a result, the placebo group was excluded from the current study.[20]

Cholwill J. M et al concluded Ondansetron and granisetron are two 5HT3 (serotonin) receptor antagonists that are very specific and selective for nausea and vomiting. The serotonin 5HT3 receptor is located in the chemoreceptor trigger zone (CTZ) and at vagal afferents in the gastrointestinal tracts, where members of this group bind to produce their effects. Granisetron is 1000:1 more likely than ondansetron to bind the 5HT3 receptors when compared to other receptors, including the 5HT1A, 5HT1B, 5HT1C, 5HT1, and 5HT2 or 1 and 2 adrenergic, dopamine D2, histamine H1, benzodiazepine, adrenergic, and opioid receptors.[21]

Apfel C. C et al, said the bulk of the variables in the current investigation (age, gender, weight, duration, and procedure type), which are linked to an increased incidence of PONV, were not statistically significant between the two groups. All patients had general anaesthesia with regulated ventilation as per the same anaesthetic protocol. In order to provide postoperative analgesia, intravenous paracetamol was administered every six hours because opoid analgesics are linked to an increased risk of PONV. In light of this, the research medicines themselves can be held solely responsible for the occurrence of PONV in both groups.[22]

Morris R. W. Concluded the dosage of ondansetron (4 mg) in the current study was chosen in accordance with earlier research by Yuksek MS et al. in 2003, Rajeeva V et al. in 1999, Argiriadou H et al. in 2002, and Naguib M et al. in 1996. Based on research done in 1996 by Wilson J. et al., the dosage of granisetron (1 mg) was chosen. They carried out a dosage-ranging research and came to the conclusion that 1 mg was the ideal amount for prophylactic therapy for PONV.

Koivuranta et al, on the basis of earlier studies conducted by Honkavaara P in 1996, Biswas BN et al. in 2003, and Bhattacharya D and Banerjee A in 2003, it was decided to deliver the study medicines two minutes prior to the induction of anaesthesia.[23]

Rajeeva et al. defined early onset nausea and vomiting as happening within two hours, while delayed vomiting was defined as occurring over the course of two to twenty-four hours. By assessing the incidence at regular intervals, Biswas BN et al. (2003) and Yuksek M et al. (2003) examined the overall incidence of PONV in the first 24 hours. They did not distinguish between early-onset and delayed-onset nausea and vomiting specifically. Similar to the previous study, this one has taken into account the overall incidence of PONV and examined episodes of PONV at intervals of 0–2 hours, 3–6 hours, 12–24 hours.[24]

The mean ages of the ondansetron and graninsetron groups in the current study were 34.46 10.3 and 35.42 10.6 years, respectively. The groups' average ages were comparable. The present study's ondansetron and graninsetron patient mean ages (36.9 and 35.8 years, respectively) and OmmidM etal's (2013) (32.1 and 29.10 years, respectively) were comparable.[25]

The mean weights for Group O and Group G in the current study were 57.469.86 kg and 56.839.3 kg, respectively. The mean weight of the patients in Groups O and G of the current study (65.8 and 11 and 64.1 and 12.2, respectively) was comparable to that of Saha.S. and Chatterjee S. (2014). In the study done by Ommid M et al. (2013), the mean weight of the patients in Group O and Group G was 55.28.4 and 54.69.4, respectively.[26]

In the current study, there were a total of 12 male patients in Group O and 12 female patients in Group G, whereas there were 38 and 38 female patients in Group O and Group G, respectively. The gender split of Group O and Group G in the current study is consistent with Saha S. and Chatterjee S.'s research (2014). Because more female patients than male patients underwent laparoscopic procedures, a greater number of females were included in the current study.

In the current study, every patient had their postoperative nausea, retching, and vomiting episodes monitored for 24 hours.[27]

The study collected data on the patients who had nausea, retching, and vomiting at various postoperative time points: 0–2 hours, 3–6 hours, 12–24 hours, and so on. Any undesirable side effects were also recorded. In the current investigation, the difference between the incidence of nausea at various time points between the granisetron and ondansetron groups is statistically significant (p 0.05). The prevalence of nausea in the first 24 hours following surgery in this study is consistent with the prevalence of nausea in Saha S. and Chatterjee S. (2014) and Bendre R. et al (2015). However, compared to the current study, the incidence of nausea is higher in the odansetron group over time, which cannot be attributable to any specific cause.[28]

Granisetron's group in the current study experienced a lower incidence of retching at various intervals than the ondansetron group, which was statistically significant (p 0.05). The current study's incidence of retching in the first 24 hours following surgery was consistent with Bendre et alincidence. .'s (2015). The use of a higher dose of granisetron in the study by Gauchan et al. (2014), i.e. 40g/kg compared to 1mg in the present study, and the administration of drugs at the end of surgery, as opposed to the administration of study drugs 2 mins prior to

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induction, can be blamed for the lower incidence of retching.[29]

In the current investigation, there is no discernible difference between the occurrence of negative effects for the two groups. The results of this study are consistent with those of Saha S and Chatterjee (2014) and Bendre R et al (2015).[30]

Only three patients out of thirty (10%) in the group receiving granisetron experienced nausea in Bendre et al(2015) .'s prospective randomised double-blind study, compared to eight (26.7%) patients in the group receiving ondansetron. P 0.10 was used to determine its statistical significance. Vomiting was seen in 16% of Group O participants and 3% of Group G participants, both of which were statistically significant. According to this study, granisetron causes less postoperative nausea and vomiting overall than ondansetron does.[31]

In 2003, Bhattacharya D and Banerjee A conducted a double-blind, placebo-controlled study on 90 patients (ASA I & II) undergoing daycare laparoscopic tubal ligation under general anaesthesia to compare the antiemetic effects of intravenous ondansetron 4 mg (2 ml) and granisetron 2 mg (2 ml) for prevention of nausea and vomiting in the early postoperative period. The patients were divided into three equal groups. Two minutes before to the onset of general anaesthesia, group C (n = 30) received 2 ml of sterile water by the same route, whereas group A (n = 30) received 4 mg (2 ml) of ondansetron, 2 mg (2 ml) of granisetron, and group B (n = 30) received 2 mg (2 ml) of granisetron intravenously. Emotional episodes were seen in 7% of patients in group B (granisetron), 20% of patients in group A (ondansetron), and 50% of patients in group C following the anaesthetic procedure that was given to all patients (placebo). They therefore came to the conclusion that Granisetron is significantly more efficacious than Ondansetron at preventing PONV after daycare gynaecological laparoscopy.[32]

Because laparascopic tubal ligation is a quick procedure and fewer cases were included in Battacharya's study, the incidence of PONV there was lower than it is in the current study.[33]

CONCLUSION

The results of the current study indicate that both medications are hemodynamically stable, and IV administration of Granisetron at a preoperative dosage of 1 mg for laparoscopic procedures performed under general anaesthesia provides the following advantages to ondensetron. According to the current study, individuals at high risk for PONV who are prophylactically treated with granisetron had a lower overall need for rescue antiemetics than those who are treated with ondansetron. As a result, granistron outperforms ondansetron as a preventative measure against PONV after laparoscopic surgeries.

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