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Research article

A COMPARATIVE STUDY BETWEEN ONDANSETRON AND GRANISETRON PREOPERATIVELY FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN ELECTIVE LSCS UNDER SPINAL ANAESTHESIA.

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ABSTRACT

Postoperative nausea and vomiting(PONV) is an unpleasant experience and most common reason for prolonged hospital stay [2, 1] in spite of various advances in drug remedies. So we conducted present study with 5-HT_3 receptor antagonists (ondansetron, granisetron)in patients undergoing LSCS ,who have high likelihood of experiencing PONV.In this prospective, randomized, single-blind study, total 100 patients posted for elective LSCS divided into two groups(each of 50 patients). Group O (Ondansetron)received 4mg iv and Group G (Granisetron) received 2mg iv before spinal anaesthesia Patients were observed for 24hrs post operatively for Nausea and vomiting and any side effects. Statistical analysis was done by applying Chi-square test, Z test to analyse the data, p value was determined. During first 6 hrs of postoperative period no significant difference was observed between the two groups. i.e. during early postoperative period(0-6hrs), ondansetron and granisetron were equally effective in prevention of PONV. In our study during 7-24hrs of postoperative period granisetron prevented nausea better than ondansetron and it was found statistically significant ($p<0.05$), though no patient in any group suffered from vomiting. In Group O, during 24hrs of postoperative period only 2(4%) had mild headache. In Group G, during 24hrs of postoperative period no patient experienced any side effects.Ondansetron is effectively reduces postoperative nausea and vomiting as granisetron in early post operative period but granisetron prevents PONV for longer period upto 24 hours postoperative without any significant side effects.

KEYWORDS: Granisetron, LSCS, Ondansetron, PONV, Spinal anaesthesia.

INTRODUCTION

Over last several decades as the risk of mortality due to surgery and anaesthesia has decreased, attention has been shifted to the factors that negatively influence patient morbidity and satisfaction such as postoperative nausea and vomiting[1].

The most important post operative concern listed by patients are pain, nausea and vomiting. Postoperative nausea and vomiting is an unpleasant experience and the most common reason for prolonged hospital stay [2, 1].

In spite of various advances, nausea and vomiting still occur with unacceptable frequency in association with surgery and anaesthesia. Incidence of post operative nausea and vomiting (PONV) after spinal anaesthesia for caesarean section as high as 75-80% [3].

The etiology and consequences of PONV are complex and multifactorial. These include trendelenburg position of the patient, intra-abdominal operations, rough handling of viscera and peritoneal stimulation, presence of bile in the stomach due to relaxation of sphincters, sudden fall

in blood pressure and hypoxia of vomiting centre. Crocker and Vandam (1959) believed that a sudden fall in blood pressure could trigger an emetic episode[4].

Commonly used older antiemetics for prevention and treatment of PONV include anticholinergics, phenothiazines, antihistamines, butyrophenones, benzamides and dopamine receptor antagonists. These antiemetics have adverse effects such as dry mouth, dysphoria, sedation, hypotension, tachycardia, extrapyramidal reactions, dystonic effects and restlessness [5].

The new class of antiemetics used for prevention and treatment of PONV are 5-HT_3 receptor antagonists (ondansetron, granisetron, tropisetron, dolasetron) do not have the adverse effects of the older antiemetics. Headache and dizziness are the only adverse effects of the serotonin receptor antagonists in the dosages used for PONV[6]. The commonly used drug ondansetron 4mg intravenously is the effective dose to prevent PONV [7]. Recently introduced another 5HT3 receptor antagonist, granisetron has more potent and longer duration of action than ondansetron against Cisplatin induced emesis[8].

We conducted a prospective randomized, single blind study to compare the efficacy of granisetron and ondansetron in prevention of postoperative nausea and vomiting in patients undergoing elective LSCS surgeries; a population that is supposed to have high likelihood of experiencing these complications[9].

AIMS/OBJECTIVES:

1. To compare the efficacy of prophylactic use of intravenous ondansetron (4mg) and granisetron (2mg) in preventing or reducing the incidence of postoperative nausea and vomiting (PONV) .
2. To compare the side effects of ondansetron (4mg) and granisetron (2mg).

MATERIAL AND METHODS:-

The present study was undertaken at Department of Anaesthesiology, Government Medical College and Hospital, over a period extending from October 2012 to September 2013.

It was a prospective, randomized, single-blind study carried out to evaluate the efficacy of ondansetron and granisetron in terms of prevention of postoperative nausea and vomiting and compare side effects.

Study Population:

Included total 100 patients belonging to ASA grade II with age between 18-40 years posted for elective LSCS. Patients were divided into two groups (each of 50 patients) i.e. Group O (Ondansetron) and Group G (Granisetron) depending upon the drug used.

Patient profile:

Inclusion criteria:

1) Patients consented for study. 2) Patients undergoing elective LSCS under subarachnoid block. 3) Age group 18-40 years. 4) ASA grade 2

Exclusion criteria:

1) Patient refusal. 2) Patients with renal, hepatic and endocrinal abnormalities. 3) Patients with history of PONV in previous surgery.4) Patients with history of motion sickness. 5) Patients with history of vomiting in last 24hrs. 6) Patients with Ryles tube in situ. 7)Documented hypersensitivity to any of the study drug. 8) Patient who has taken antiemetic drug within 24hr before surgery.

Anaesthesia technique: Spinal anaesthesia with Bupivacaine 0.5% H 2.0ml.

Drugs used for study: 1 . Inj.Ondansetron 4mg iv 2. Inj.Granisetron 2mg iv

Method:

The study was conducted after approval of our institutional ethical committee. Preoperative anaesthesia evaluation along with all routine investigations were carried out in detail. Patients were advised to remain nil orally after 10pm the day before surgery. When patient came to operation theatre her vitals and oxygen saturation were recorded. Preloading done with ringer lactate 1000ml. 50 patients received inj. ondansetron 4mg and 50 patients received inj. granisetron 2mg intravenously 3-5 minutes before spinal anaesthesia.

Under all aseptic precautionsspinal anaesthesia was given with Inj. Bupivacaine 0.5% heavy 2.0ml. Level of anaesthesia obtained upto T6.

Intra operative vitals and oxygen saturation were monitored every 5 minutes. The decrease in mean blood pressure more than 20% of baseline was treated with inj. Mephentermine 3mg iv and IV fluids after spinal anaesthesia.

Patients was observed for 24hrs post operatively .Nausea and vomiting recorded 0 hr, 1hr ,6hr, 12hr and 24hrs post operatively.

Method Of Collection Of Data:

At the end of each interval whether the patient experienced nausea, vomiting or any side effects were noted.

In this study we assessed postoperative nausea and vomiting by using PONV score[10] as :-
Number of episodes of vomiting were recorded.

No emesis (0) – complete control One episode (1) – Nearly complete control
Two episodes (2) – Partial control ≥3 episodes (3) - Failure/ No control

Several vomits occurring over a short time frame (5 min) is counted as one episode.
Nausea is graded as

(0)– Not at all (1) – Mild (sometimes)
(2) - Moderate (Often) (3) - Severe (Most of the time)

To calculate PONV scale score the numerical responses are added. A PONV scale score of ≥5 defines clinically important PONV. These patients were given rescue therapy with Inj. Metoclopramide 10mg i.v. and IV fluids.

Side effects like headache, constipation, dizziness, anxiety, allergic reactions and extrapyramidal symptoms were registered during recovery period and postoperative period.

Statistical Methods[11, 12]

Study Design:

A prospective comparative two group randomized clinical study with 100 patients with 50 patients in Group O (Ondansetron) and 50 patients in Group G (Granisetron) is undertaken to study PONV and side effects.

Statistical analysis was done by applying Chi-square test, Z test to analyse the data, p value was determined.

$P > 0.05$ is not significant $P < 0.05$ is significant $P < 0.001$ is highly significant.

RESULTS AND OBSERVATION:-

There was no significant difference in demographic data, duration of surgery, pulse rate and blood pressure in both groups.

Other result of study are as follows:

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Table No. 1:-Scoring of postoperative nausea and vomiting (PONV) of Group O

Score PONV	0-1 hr	2-6 hrs	7-12 hrs	13-24 hrs	Maximum score
0	38	38	36	45	32
I	2	2	9	3	5
II	4	4	4	2	6
III	2	2	1	0	3
IV	1	1	0	0	1
V	1	1	0	0	1
VI	2	2	0	0	2

Figure 1 showing maximum scoring of PONV of group O:-

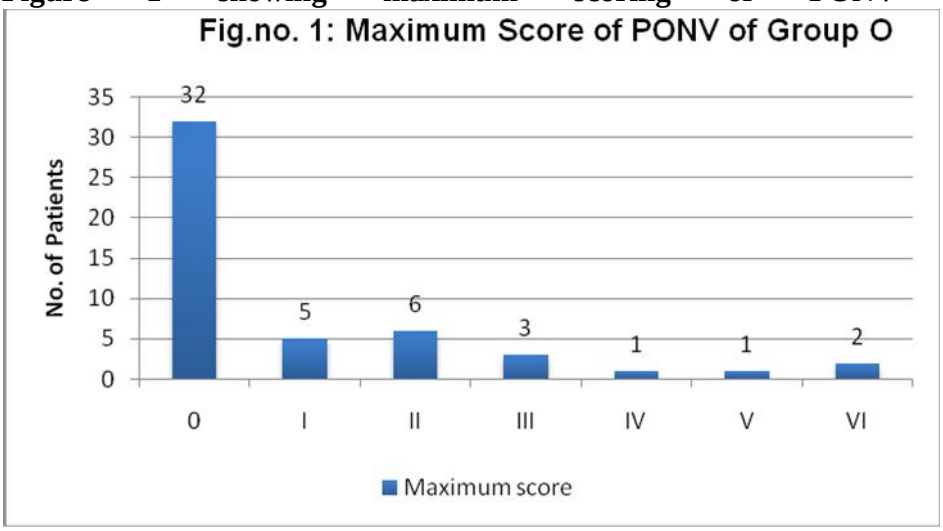

Table No. 2:-Scoring of postoperative nausea and vomiting(PONV) of Group G

Score PONV	0-1 hr	2-6 hrs	7-12 hrs	13-24 hrs	Maximum score
0	42	42	47	49	42
I	5	3	2	1	3
II	1	3	1	0	2
III	2	2	0	0	3
IV	0	0	0	0	0
V	0	0	0	0	0
VI	0	0	0	0	0

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Figure 2 showing Scoring of postoperative nausea and vomiting of Group G.

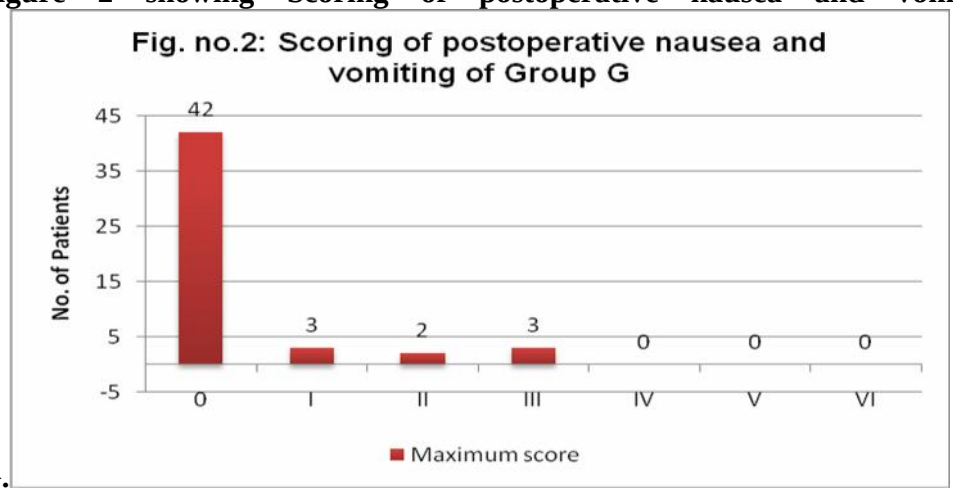


Table No. 3:-Comparison of maximum score between both Groups

Score PONV	Group O	Group G	X^2	p value	Association is
0	32	42	6.05	0.42	NS
I	5	3			
II	6	2			
III	3	3			
IV	1	0			
V	1	0			
VI	2	0			

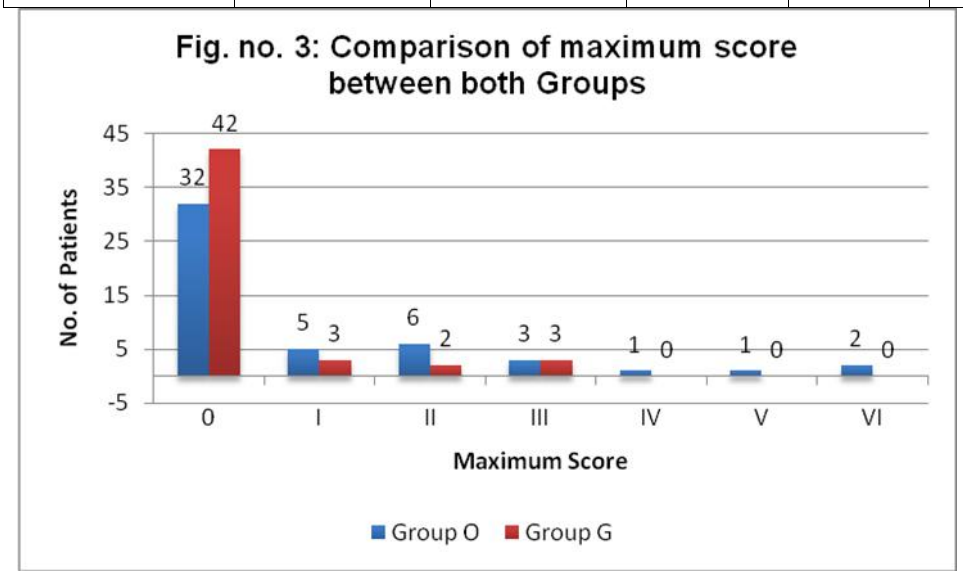
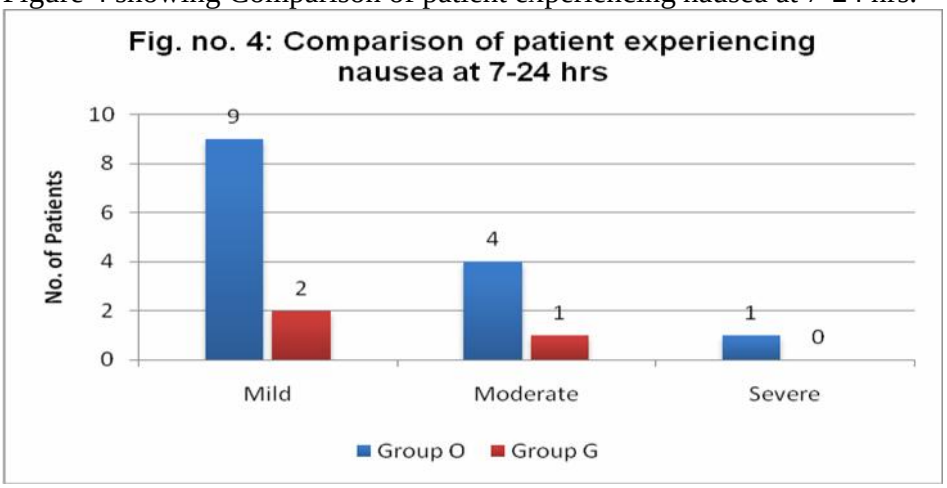


Table No. 4:- Comparison of patient experiencing nausea at 7-24 hrs

Nausea	Group O (n=50)	Group G (n=50)	X^2	p value	Association is
Mild	9	2	6.14	0.01	S
Moderate	4	1			
Severe	1	0			
Total	14	3			

Figure 4 showing Comparison of patient experiencing nausea at 7-24 hrs.

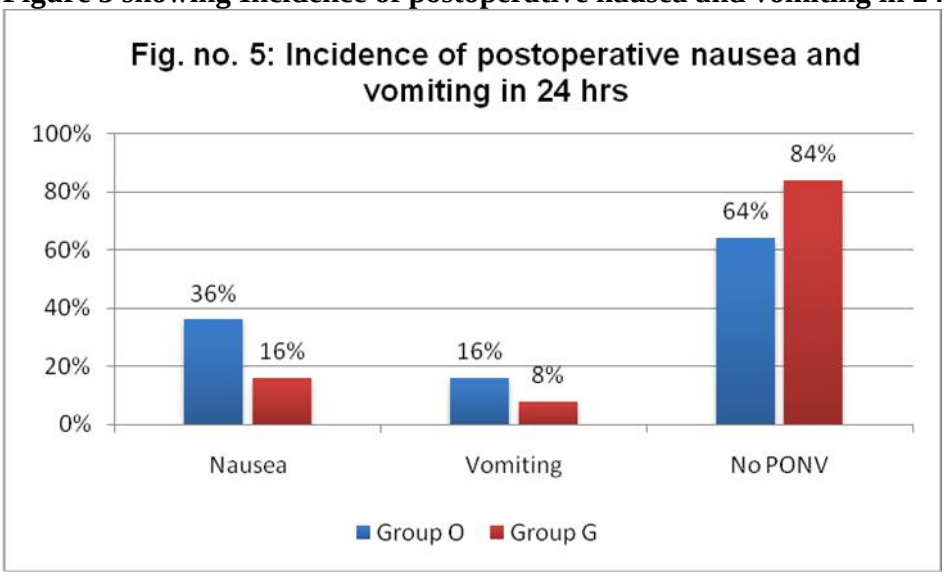


Difference in patient experiencing nausea and vomiting at 6 hrs in both groups was not significant and In period of 7-24 hrs no patient in any group experienced vomiting.

Table No. 5:- Incidence of postoperative nausea and vomiting in 24 hrs

	Group O		Group G		X^2	p value	Association is
	No.	%	No.	%			
Nausea	18	36%	8	16%	6.40	0.04	S
Vomiting	8	16%	4	8%			
No PONV	32	64%	42	84%			

Figure 5 showing Incidence of postoperative nausea and vomiting in 24 hrs.



Comparison of No. of patient with Rescue Treatment Required (RTR)

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In present study 3 patients in **Group O** needed rescue treatment. All the three patients needed rescue treatment within first 6 hrs. No patient in **Group G** needed rescue treatment. These results were compared using chi-square test and the association was found not significant (p=0.08).

In present study 2 patients in **Group O** experienced headache. Both the patients experienced headache in first 6 hrs. No patient in **Group G** experienced any side effects. The association between two groups is not significant (p=0.15).\

DISCUSSION:-

Ondansetron and Granisetron are selective $5HT_3$ receptor. The use of these $5HT_3$ receptor antagonists have been shown to improve patients' satisfaction, decrease recovery time, early discharge and reduce an unanticipated hospital admission.[13, 14] The main objective in our study was to compare antiemetic and adverse effects of prophylactic single-dose of 4mg ondansetron and 2mg granisetron administered intravenously for prevention of nausea and vomiting in early postoperative period (24hrs) in patients undergoing elective LSCS surgeries under spinal anaesthesia.

2 mg of granisetron was chosen in the study as it was found to be optimal dose for prevention of post operative nausea and vomiting. **Fujii et al[15]**, in 1994 administered granisetron in doses of 20, 40 or 60 ug/kg and assessed by means of a nausea and vomiting score .. **Fujii Y et al[16]** in 1998, showed that the incidence of nausea and vomiting was 64%, 52%, 14% and 12% after administration of placebo and granisetron in a dose of 20 micrograms/kg, 40 micrograms/kg and 80 micrograms/kg respectively ($P < 0.05$; overall Fisher's exact probability test). They concluded that prophylactic use of granisetron in a minimum dose of 40 micrograms/kg is effective for preventing nausea and vomiting.

4mg of ondansetron was chosen by **Claybon**[17] in 1994, by **Kavac et al**[18] in 1992, **L.D. Paxton** (1995) [19], **Tang et al** (1998)[20] and **Dipasri Bhattacharya**[21] in 2003 mentioned that 4mg ondansetron is effective dose.

Maximum PONV score in Group O:

Pan PH et al [22] **in** 1996, **Abouleish EI at el** [23] **in 1999** carried a study, patients received intravenously 8 mg of ondansetron or 0.625 mg of droperidol or saline depending on their treatment group. Sixty-nine(69%) percent of the ondansetron group, 75% of the droperidol group, and 31% of the placebo group were nausea free. This study showed a significantly lower incidence of nausea and vomiting and a tendency toward less severe emetic symptoms in the ondansetron and the droperidol groups than in the placebo.

In our study 32(64%) patients have a PONV score of 0. So 64% patients were free from PONV. Eighteen patients (36%) suffered from PONV. These results correlate with the above studies.

PONV score in Group G:

Fujji Y, Tanaka H et al[3] in 1998, **Dipasri Bhattacharya** [24] in 2003 carried a study for prevention of nausea and vomiting with granisetron, droperidol and metoclopramide during and after spinal anaesthesia for caesarean section. They found that PONV incidence in granisetron treated group was 14%. Eighty six (86%) patients were free form PONV. They also concluded that the severity of PONV in granisetron treated group was less compared to droperidol and metoclopramide.

In our study in Group G, 42 (84%) patients had a PONV sore of 0, so these patients were free from PONV. Eight (16%) patients suffered from I-III grade of nausea and vomiting. No patient suffered from severe grade (IV-VI) of PONV. So results correlate with the above studies.

Comparison of maximum score between both Groups:

Oksuz H, Zencirci B et al[25] in 2007, **Metaxari M, Papaioannou A**[26] et al Compared of the effectiveness of metoclopramide, ondansetron and granisetron on the prevention of nausea and vomiting after laparoscopic cholecystectomy**.** They concluded that Granisetron when given prophylactically resulted in a significantly lower incidence and severity of PONV than metoclopramide and ondansetron whereas metoclopramide was ineffective. Granisetron may be an effective treatment in the prophylaxis of PONV.

Comparison of patient experiencing nausea at 6 hrs:

Dasgupta M, Biswas B N et al [27] in 2012, **Dipasri Bhattacharya** [28] in 2003 found that a complete response (defined as no postoperative nausea and vomiting) during 0-4 h after administration of spinal anesthesia was achieved in 80 % of patients with granisetron and in 45 % of patients with placebo.

Comparison of patient experiencing nausea at 7-24 hrs:

Fujji Y, Tanaka H et al[3], **Fujii Y, Saitoh Y et al**[29], **Oksuz H, Zencirci B, et al**[25] , **Metaxari M, Papaioannou A et al**[26] in 2011 found that after administration of granisetron, droperidol, metoclopramide and placebo, respectively; the incidence during 3-24 h after surgery was 7%, 20%, 23% and 37% ($P < 0.05$; overall Fisher's exact probability test). They concluded that

Granisetron is highly effective for preventing nausea and vomiting during and after spinal anaesthesia for caesarean section.

Our results are comparable with the above results.

Comparison of patient experiencing vomiting at 7-24 hr:

During first 6 hrs of postoperative period no statistically significant difference was observed between the two groups. This showed that during early postoperative period (0-6hrs), ondansetron was as effective as granisetron in prevention of postoperative nausea and vomiting. In our study during 7-24hrs of postoperative period granisetron prevented nausea better than ondansetron and it was found statistically significant ($p<0.05$), though no patient in any group suffered from vomiting. During 7-24hrs of postoperative period granisetron was more effective than ondansetron in prevention of PONV.**Leeser J, Lip H** et al [15] in 1991, **Raphael and Norton**[30] in 1993, **Katsuya M et al** [31] in 1995, **Yoshitaka F et al** [32] in 1995, **Pan PH, Moore CH et al**[33] 1996.**Fujii Y, Saitoh Y et al**[34] in 1997 found that the incidence of PONV was 15% with granisetron, 41% with droperidol and 46% with placebo respectively.**Fujii Y, Saitoh Y**[29] **et al** in 1998 found that during the first 3 h after anaesthesia, PONV was seen in 36%, 44%, 92% and 92% of patients who received placebo, granisetron 20 micrograms/kg, 40 micrograms/kg and 100 micrograms/kg respectively; corresponding values during the next 21 h after anaesthesia were 40%, 44%, 88%, and 88%.**Fujii Y, Saitoh Y**[35] **et al** in 1998 found that the incidence of PONV during the first 24 hours after anaesthesia was 43, 40, 13 and 13% after administration of placebo and granisetron 20 micrograms/kg, 40 micrograms/ kg and 80 micrograms/kg respectively.

Our results were comparable with the above studies.

Comparison of No. of patients with Rescue antiemetic Treatment Required (RTR):

Katsuya M et al[31] in 1995 observed that the number of emesis free patients were significantly larger in granisetron group than in the control group (83%, 78% and 20% of patients receiving granisetron 20ug/kg and 40ug/kg and saline respectively). Our results were comparable with this study.

Comparison of adverse effects in both Groups:

Fujji Y, Tanaka H et al [3] in1998 obseved no clinically important adverse effects while using granisetron, droperidol and metoclopramide.

Due et al[36] in 2004 carried out a study to evaluate the comparative profile and efficacy of ondansetron and granisetron to prevent PONV after modified radical mastectomy and showed that incidence of adverse events was comparable among the groups.

Our results were comparable with above studies.

CONCLUSIONS:-

From the study we concluded that:-

1. During 7-24hrs of postoperative period nausea was observed in 14(28%) patients of Group O and 3(6%) of Group G. The incidence of nausea was more in Group O than Group G and it was statistically significant ($p<0.05$).
2. During first 7-24hrs of postoperative period vomiting was not observed in any Group.

3. During 24hrs of postoperative period postoperative nausea and vomiting (PONV) was observed in 18(36%) patients of Group O and 8(16%) of Group G. The incidence of PONV was more in Group O than Group G and it was statistically significant ($p<0.05$).
4. In Group O, during 24hrs of postoperative period only 2(4%) had mild headache and remaining patients were free of side effects. In Group G, during 24hrs of postoperative period no patient experienced any side effects.

REFERENCES

1. Myles PS, Williams DL, Hendrata M, Anderson H, Weeks AM, "Patient satisfaction after anaesthesia and surgery: results of a prospective survey of 10,811 patients" Br J Anaesth, 2000 Jan;84(1):6-10.
2. Gold BS, Kitz DS, Leeky JH, Nerchaus JM. Unaticipated admission to hospital following ambulatory surgery. JAMA 1989; 262: 3008-10.
3. Fujii Y, Tanaka H, Toyooka H. Prevetnion of nausea and vomiting with granisetron, droperidol and metoclopramide during and after spinal anaesthesia for caesarean section: A randomized, double-blind, placebo-controlled trial. Acta Anaesthesiol Scand. 1998;42(8):921-5.
4. Crocker JS, Vandam LD; Concerning nausea and vomiting during spinal anaesthesia; Anaesthesiology 1959; 20: 587-92.
5. Watcha MF, White PF; Postoperative nausea and vomiting: Its etiology, treatment and prevention; Anaesthesiology, 1993;78:403-6.
6. Watcha MF, While PF; Nausea and vomiting: its etiology, treatment and prevention; Anaesthesiology 1992; 77:162-184.
7. Mckenzie R, Tantisira B, Karambelkar DJ, Riley TJ, Abdelhady H; Comparision of ondansetron with ondansetron plus dexamethasone in the prevention of postoperative nausea and vomiting; Anesth Analg 1994; 79:961-4.
8. Andrews PRR, Bhadari, Davey PT, Binghar S; Are all 5 HT3 receptor antagonists the same?; Eur J Cancer 1992; 28:52-56.
9. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N; "A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers"; Eur J Anaesthesiol,1999 Sep;91(3):693-700.
10. Myles PS; Wengritzky R; Simplified postoperative nausea and vomiting impact scale for audit and post discharge review ; Br J of Anaesth, January 29, 2012;1-7
11. Robert H Riffenburg; Statistics in Medicine, second edition, 2005; Academic press. 85-125.
12. Sunder Rao P S S, Richard J: An Introduction to Biostatistics, A manual for students in health sciences, New Delhi: Prentice hall of India. 4th edition, 2006; 86- 160.
13. Rowbotham D J; Current management of postoperative nausea and vomiting; Br J Anaesth. 1992;69(S):46-59.
14. Lesser and Lip H; Prevention of postoperative nausea and vomiting using ondansetron- A new, selective, 5HT3 receptor antagonist; Anesth Analg 1991; 72:751-5.
15. Fuji Y, Tanaka H, Toyooka H; Optimal anti-emetic dose of granisetron for preventing postoperative nausea and vomiting; Can J Anaesth. 1994; 41(9):794-7.
16. Fujii Y, Tanaka H, Toyooka H; "Granisetron prevents nausea and vomiting during spinal anaesthesia for caesarean section"; Acta Anaesthesiol Scand. 1998 Mar;42(3):312-5
17. Claybon L; Single dose intravenous ondansetron for the 24 hr. treatment of postoperative nausea and vomiting; Anaesthesia 1994:49:24-9.
18. Kovac A, McKenie R et al; Prophylactic ondansetron in female outpatients undergoing gynaecological surgery: A multicentre dose comparison. Eur J Anaesthesiol. 1992; 6:37-47.
19. Paxton L D, Mckay A C and Mirakhur RK; Prevention of nausea and vomiting after day case gynaecological laparoscopy- A comparison of ondansetron, droperidol, metoclopra and placebo; Anaesthesia 1995;50(5);403-6.
20. Tang J, Wang B; Effect of timing of ondansetron administration on its efficacy, cost effectiveness and cost benefits as prophylactic, antiemetic in ambulatory settings; Anesth Analg 1998;86:274-82.
21. Bhattacharya D, Banerjee ; A Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy; IJA.2003;47(4):279-282.

22. Pan PH, Moore CH; "Intraoperative antiemetic efficacy of prophylactic ondansetron versus droperidol for cesarean section patients under epidural anesthesia"; Anesth Analg 1996 Nov;83(5):982-6.
23. Abouleish EI, Rashid S, Haque S, Giezentanner A, Joynton P, Chuang AZ; "Ondansetron versus placebo for the control of nausea and vomiting during Caesarean section under spinal anaesthesia", Anaesthesia. 1999 May;54(5):479-82)
24. Bhattacharya D, Banerjee ; A Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy; IJA.2003;47(4):279-282.
25. Oksuz H, Zencirci B, Ezberci M, "Comparison of the effectiveness of metoclopramide, ondansetron, and granisetron on the prevention of nausea and vomiting after laparoscopic cholecystectomy", J Laparoendosc Adv Surg Tech, 2007 Dec;17(6):803-8.
26. Metaxari M, Papaioannou A; Antiemetic prophylaxis in thyroid surgery: a randomized, double-blind comparison of three 5-HT_3 receptor antagonists; J Anesth, 2011 Jun; 25(3):356-62.
27. Dasgupta M, Biswas BN, Chatterjee S : Randomized, placebo-controlled trial of granisetron for control of nausea and vomiting during cesarean delivery under spinal anesthesia ; J Obstret Gynaecol India , 2012 Aug;62(4):419-23.
28. Bhattacharya D, Banerjee ; A Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy; IJA.2003;47(4):279-282.
29. Fujii Y, Saitoh Y, Tanaka H, Toyooka H; "Prophylactic antiemetic therapy with granisetron in women undergoing thyroidectomy", Br J Anaesth. 1998 Oct;81(4):526-8.
30. Raphael J H, Norton AC; Antiemetic efficacy of prophylactic ondansetron in laparoscopic surgery; Br J Anaesth. 1993;71:845-48.
31. Katsuya M, Yumiko T; The antiemetic efficacy of prophylactic granisetron in gynecologic surgery; Anesth Analg. 1995: 80:970-4.
32. Yoshitaka F, Hiroyoshi T; Prevention of postoperative nausea and vomiting with granisetron: A randomized, double blind comparison with droperidol; Can J Anaesth 1995; 42(10): 852-6.
33. Pan PH, Moore CH; "Intraoperative antiemetic efficacy of prophylactic ondansetron versus droperidol for cesarean section patients under epidural anesthesia"; Anesth Analg 1996 Nov;83(5):982-6.
34. Fujii Yoshitaka, Hiroyoshi Tannaka, Hidenori toyooka; Granisetron reduces the incidence and severity of nausea and vomiting after laparoscopic cholecystectomy; Can J Anaesth, 1997;44;4:396-400.
35. Fujii Y, Saitoh Y, Tanaka H, Toyooka H; Effective dose of granisetron for the prevention of post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy; Eur J Anaesthesiol. 1998 May;15(3):287-91.
36. Due N, Bhatnagar S, Mishra S, Singhal AK; Granisetron and ondansetron for prevention of nausea and vomiting in patients undergoing modified radical masterctomy; Anaesth Intensive Care 2004; 32 (6):761-4