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Comparison of haloperidol with ondansetron in preventing post-operative nausea and vomiting after laparoscopic abdominal surgeries

Pradeep R[1,*], Amitha S[2], KV Srinivasan[3]

[1]Assistant Professor, [3]Professor & HOD, PESIMSR, Kuppam, [2]Assistant Professor, Dept. of Anaesthesiology, SSIMSR, Tumkur

***Corresponding Author:**
Email: paddu28384@gmail.com

Abstract

Background: Post-operative nausea and vomiting (PONV) is one of the commonest complications after general anesthesia despite advances in anesthesia techniques and newer anti-emetics.

PONV can result in other adverse events like aspiration pneumonitis, dehydration, disruption of surgical sutures.

Objectives: To compare the efficacy of haloperidol (2mg intravenous) with ondansetron 4mg intravenous in preventing PONV after laparoscopic abdominal surgeries(cholecystectomy, ovarian cystectomy, diagnostic laparoscopy).

Methods: A clinical, randomized, double blind study was conducted on ninety female patients who were admitted to Victoria and Bowring hospital, Bangalore, Karnataka. They were randomly grouped into three groups of thirty each by closed envelope technique. Group A received ondansetron 4mg intravenous, Group B received 2ml normal saline intravenous, Group C received Haloperidol 2mg intravenous, thirty minutes before the end of the surgery. Patients were followed up in the post-operative period for 24 hours and PONV, sedation, need for rescue anti-emetic and hemodynamic parameters were assessed. They were evaluated statistically using Chi-square, Fisher Exact and ANOVA tests.

Results: The patients in the Ondansetron 4mg group had lower incidence of vomiting than haloperidol 2mg group, but not statistically significant. Whereas, the incidence of nausea is similar in both ondansetron and haloperidol group with six (20%) patients each. And only two (6.6%) patients in haloperidol group had nausea in 0 to 2 hours in the post-operative period than compared to ondansetron group which had four (13.3%) patients in the same period. And also Ondansetron 4mg didn't show any added advantage with respect to side effects, nausea and usage of rescue anti-emetic when compared to Haloperidol 2mg group.

Conclusion: We conclude that Ondansetron 4mg is not having significant advantage over Haloperidol 2mg in preventing PONV after laparoscopic abdominal surgeries.

Keywords: Aspiration pneumonitis, dehydration, haloperidol, ondansetron, nausea, vomiting, laparoscopic abdominal surgeries, rescue anti-emetic.

Introduction

Post- operative nausea and vomiting(PONV) is one of the commonest complications after general anesthesia despite advances in anesthesia techniques and newer anti-emetics.

PONV can result in other adverse events like aspiration pneumonitis, dehydration, disruption of surgical sutures.

Risk factors for PONV includes

1. Age	< 50 years
2. Sex	females
3. Others	Infection, uremia, motion sickness, migraine, hypercalcaemia, anxiety etc.

Drugs and surgeries causing nausea and vomiting;

Drugs	Mechanism
Opioids and Chemotherapy	By stimulating Medullary Vomiting Center adjacent to Chemo Receptor Trigger Zone (CTZ)
Volatile anesthetics	By reducing serum levels of anandamide which would had suppressed vomiting and nausea.
Surgery	
Laparoscopic abdominal surgery	Peritoneal irritation
Tympanoplasy etc.	Vestibular stimulation

Single drug prophylaxis for PONV is usually suggested for patients with mild to moderate risk (1 to 2 risk factors). For patients with moderate to high risk (3 to 4 risk factors), a combination of two anti-emetics with different sites of action are commonly employed.

Haloperidol, a butyrophenone is a major tranquilizer with D2 (dopamine 2) receptor antagonistic effect. For more than 40 years it has been used as an anti-emetic in palliation of nausea and vomiting. A recent meta-analysis studies have shown that haloperidol is anti-emetic at doses 1mg to 4mg intravenous, which are much lower than those used to treat psychiatric disorders.(1) Also, haloperidol has rapid onset, safer at lower doses, and economical.(1)

The role of 5HT 3 antagonist like ondansetron as the effective anti-emetic is known and is the first line anti-emetic drug for prevention of PONV in many places. Ondansetron is thought to suppress nausea less effectively than vomiting, and there are reports showing

that PONV prophylaxis with 1mg Haloperidol is comparable with 4mg ondansetron.[3]

This study is designed to compare the efficacy and adverse effects of prophylactic administration of haloperidol 2mg intravenous with ondansetron 4mg intravenous in preventing PONV in patients undergoing laparoscopic abdominal surgeries(laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy).

Methodology

Source of data: Adult female patients ASA (American Society of Anesthesiologists) grade 1 and 2 undergoing elective laparoscopic abdominal surgeries(laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy) under general anesthesia at Victoria and bowring hospital, Bangalore, Karnataka.

Method of collection of data

Inclusion criteria: Adult female patients of ASA 1and 2 undergoing elective laparoscopic abdominal surgeries (laparoscopic cholecystectomy, diagnostic laparoscopy, laparoscopic ovarian cystectomy) under general anesthesia.

Exclusion criteria: Patients with difficult airway, obesity, pregnancy, psychiatric illness, major organ disease, history of anti-emetic medication, motion sickness, smoking.

Methods: The study was conducted on ninety adult female patients undergoing the above said laparoscopic abdominal surgeries after obtaining the informed consent and institutional ethical committee clearance**.**

The patients were divided into three groups of thirty patients each by double blind randomized technique, and each group was poised to receive the study drug thirty minutes before the end of surgery.

Group A: Ondansetron 4mg intravenous.
Group B: Normal saline (0.9%) 2ml intravenous.
Group C: Haloperidol 2mg intravenous.

General anesthesia was the standard anesthesia procedure planned. Patients were Premedicated with diazepam 5mg orally on the previous night, and on the day of surgery midazolam 1mg intravenous, glycopyrrolate 200mcg intravenous were given as premedication. Anaesthesia was induced with fentanyl 2mcg/kg intravenous, lidocaine 1mg/kg intravenous, and Thiopentone 4mg/kg intravenous. Patients were intubated endotracheally after paralyzing with succinyl choline 2mg/kg intravenous.

General Anesthesia was maintained with paralyzing agent vecuronium, inhalation agent halothane(0.4%), 70% nitrous oxide and 30% oxygen at the rate of 4litres/minute, and patients were ventilated with positive pressure controlled ventilation.

Patients were monitored for pulse rate, Non invasive blood pressure (NIBP), oxygen saturation, Electro cardiogram. Nasogastric suction was done prior to tracheal extubation and patients were extubated after giving reversal for residual neuro muscular blockade with neostigmine 0.06mg/kg intravenous and glycopyrrolate 0.01mg/kg intravenous.

Parameters evaluated

1. Incidence of nausea
2. Incidence of vomiting
3. Incidence of nausea and vomiting
4. Rescue anti-emetics used.
5. Nausea score.

Each group is observed for the above parameters over 24 hours in the postoperative room.

Nausea scoring done with verbal numeric scale from 0(no nausea) to 5(worst possible nausea)

Metaclopramide 25mg intravenous is the rescue drug given to score 4 and above.

Statistical Test used:

1. Chi-Square test
2. Fisher exact test
3. Analysis of variance.

Study Design: A clinical, controlled, double blind randomized anesthesia study with ninety patients randomized into three groups of thirty patients each, likewise thirty patients in Group A (ONDANSETRON), thirty patients in GROUP-B (Normal saline 0.9% 2ml) and thirty patients in GROUP-C(HALOPERIDOL-2MG), was undertaken to study the hemodynamic parameters, incidence of vomiting, nausea episodes, rescue anti-emetics used.

We determined that the sample size of 30 patients per group was adequate to meet the decrease in mean nausea intensity score from five to three and standard deviation of three assuming a 20% β-error and 5% α-error.

To reject the null hypothesis, the level of significance was established at 5% (p value < 0.05).

Results

Table 1: Patient's characteristics and variables related to PONV

Variables	Group A	Group B	Group C	P Value
Age(years)	32.87±8.19	31.93±7.17	35.07±7.92	0.282
Weight(kgs)	53+/-5.6	53.4+-4.3	53+/-4.9	0.9348
History Of Motion Sickness	8	10	12	0.548
Duration of	75+/- 15	80+/-10	78+/-12	0.286

Anesthesia (minutes)				
Laparoscopic Cholecystectomy(%)	9(30)	11(11)	8(26.6)	0.695
Diagnostic laparoscopy(%)	10(33.3)	10(33.3)	11(36.6)	0.951
Laparoscopic Ovarian cystectomy(%)	11(36.6)	9(30)	11(36.6)	0.821

Table 2: Comparison of Heart rate (beats per minute) in the three groups of patients studied

HR (bpm)	Group A	Group B	Group C	P value
1 hour	84.83±8.41	85.80±10.39	82.80±8.94	0.446
4 hours	75.27±5.39	76.83±8.42	74.80±4.97	0.444
8 hours	72.50±5.27	74.33±7.98	72.67±4.28	0.434
12 hours	73.20±5.45	73.20±7.17	73.60±6.36	0.961
24 hours	71.33±4.62	73.07±5.45	71.73±3.59	0.318

ANOVA Test
Bpm: Beats per minute.

Table 3: Comparison of Mean Arterial Pressure (mm Hg) in three groups of patients studied

MAP (mm Hg)	Group A	Group B	Group C	P value
1 hour	92.88±5.25	94.03±4.49	94.00±5.15	0.594
4 hours	89.23±5.17	90.71±2.74	89.82±4.97	0.433
8 hours	88.07±4.90	90.08±3.77	90.80±5.61	0.081
12 hours	88.12±4.61	89.93±3.82	90.70±5.02	0.081
24 hours	87.87±3.59	88.51±3.14	90.36±4.19	0.058

ANOVA Test
MAP (Mean Arterial Pressure)

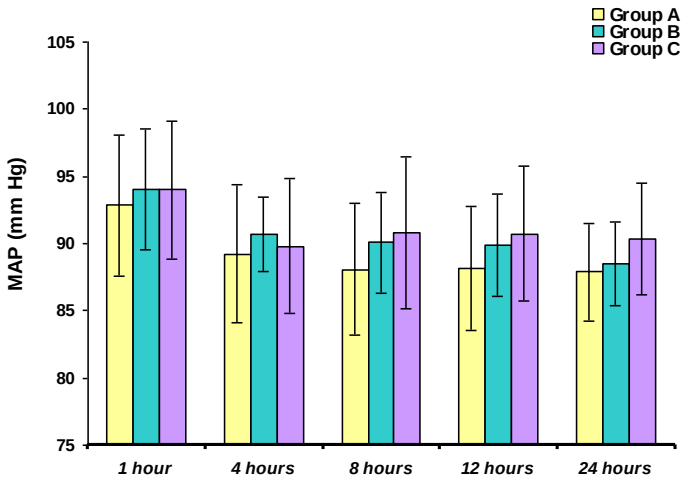

Fig. 1: Comparison of Mean Arterial Pressure (mm Hg) in three groups of patients studied

Table 4: Comparison of Incidence of Nausea in the three groups of patients studied over 24 hours

Nausea	Group A	Group B	Group C
Yes	6(20.0%)	10(33.3%)	6(20.0%)
No	24(80.0%)	20(66.6%)	24(80.0%)
Total	30(100.0%)	30(100.0%)	30(100.0%)
Inference	Incidence of nausea is statistically similar in all the three groups with p=0.381		

Table 5: Comparison of Time of Incidence of Nausea in three groups of patients studied

Time of incidence of Nausea	Group A (n=6)	Group B (n=10)	Group C (n=6)	P value
0-2 hrs	4(66.7%)	8(80%)[+]	2(33.3%)[+]	0.122
2-24 hrs	2(33.3%)	2(20%)	4(66.7%)	0.722
Total	6(100%)	10(100%)	6(100)	

[+] Suggestive significance P (0.079)

Table 6: Comparison of Incidence of Vomiting in the three groups of patients studied

Vomiting	Group A	Group B	Group C
Yes	1(3.3%)	4(13.3%)	3(10%)
No	29(96.7%)	26(86.7%)	27(90%)
Total	30(100.0%)	30(100.0%)	30(100.0%)
Inference	Incidence of vomiting is higher in Group B & C compared to group A with P=0.382		

Table 7: Comparison of Time of Incidence of Vomiting in the three groups of patients studied

Time of incidence of Vomiting	Group A (n=1)	Group B (n=4)	Group C (n=4)	P value
0-2 hrs	0	0	1(25.0%)	1.0
2-24 hrs	1(100.0%)	4(100.0%)	3(75.0%)	0.521
Total	30(100.0%)	30(100.0%)	30(100.0%)	

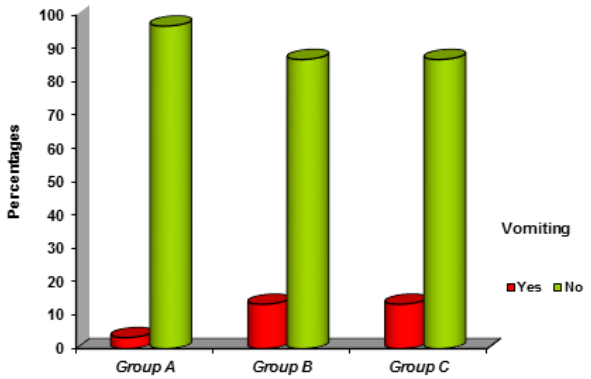

Fig. 2: Comparison of Incidence of Vomiting in the three groups of patients studied

Table 8: Comparison of rescue anti-emetics in the three groups of patients studied

Rescue anti-emetics	Group A	Group B	Group C
Yes	0	2(6.7%)	2(6.7%)
No	30(100.0%)	28(93.3%)	28(93.3%)
Total	30(100.0%)	30(100.0%)	30(100.0%)
Inference	Incidence of rescue antiemetic is statistically similar across three groups with p=0.540		

Fisher Exact Test

Table 9: Comparison of Sedation score in the three groups of patients studied

Sedation score	Group A	Group B	Group C
1.anxious, agitated or restless or both	0	0	0
2.co-operative, oriented and tranquill	28(93.3%)	27(90.0%)	25(83.3%)
3.responding to commands only	2(6.7%)	3(10.0%)	5(16.7%)
4.brisk response to	-	-	-

light glabellar tap			
5.sluggish response to light glabellar tap	-	-	-
6.no response to light glabellar tap	-	-	-
Total	30(100.0%)	30(100.0%)	30(100.0%)
Inference	Distribution of sedation score is statistically similar in three groups of patients with p=0.592		

Fisher Exact Test

Statistical Methods: Descriptive statistical analysis has been carried out in the present study. Results on continuous measurements are presented on Mean ± SD (Min-Max) and results on categorical measurements are presented in Number (%). Significance is assessed at 5% level of significance. The following assumptions on data is made, Assumptions: 1. Dependent variables should be normally distributed. 2. Samples drawn from the population should be random. 3. Cases of the samples should be independent. 4. Significant figures,
+ Suggestive significance (P value: $0.05<P<0.10$)
* Moderately significant (P value: $0.01<P \leq 0.05$)
** Strongly significant (P value: $P \leq 0.01$)
Statistical software: The Statistical software namely SAS 9.2, SPSS 15.0, Stata 10.1, MedCalc 9.0.1, Systat 12.0 and R environment ver.2.11.1 were used for the analysis of the data and Microsoft word and Excel have been used to generate graphs, tables etc**.**

Discussion

In this randomized double blind clinical study we found that patients who were given Ondansetron 4mg intravenous thirty minutes before the end of surgery had lower incidence of vomiting than the other two groups, but was statistically not significant. Ondansetron 4mg intravenous administered before the end of surgery has already given positive results in preventing PONV in other studies.[9]

In our study we found that haloperidol 2mg intravenous thirty minutes before the end of the surgery produced lower incidence of nausea and vomiting when compared to control group and further, out of six patients who complained of nausea only two patients were in 0 to 2 hours group. Whereas, out of ten patients who complained of nausea in the control group, 8 patients complained in the 0 to 2 hours' time period, (P value=0.079) when compared to haloperidol group.

Haloperidol has antiemetic properties at lower doses than that required for anti-psychotic purposes.[10] In a study by Aouad M.T et al showed that haloperidol 1mg is effective in preventing PONV in the early hours (0 to 2hours),[1] but in this study, study medications were given at the beginning of the anesthesia.

In our study we administered haloperidol thirty minutes before the end of the surgery because the peak plasma concentration of haloperidol is 10 to 15 minutes after intravenous administration, so that it will give sustained anti-emetic effect in the post-operative period.

Major side effects of Haloperidol include sedation, extra- pyramidal effects, QTc prolongation. But the dose we used, we didn't find significant sedation when compared to other two groups. In our study there were no extra pyramidal side effects and QTc prolongation.

In our study we found that the type of surgery, duration of anesthesia, and other risk factors were matching among the three groups and we believe that the result reflects the effect of the study medications.

Ondansetron when compared to Haloperidol is costlier, 4mg Ondansetron is nearly 10 times costlier than 2mg Haloperidol. In our study we didn't find any statistically significant advantage of 4mg Ondansetron intravenous over 2mg Haloperidol intravenous given thirty minutes before the end of the surgery in preventing PONV after laparoscopic abdominal surgeries.

In conclusion, ondansetron 4mg intravenous administered thirty minutes before the end of surgery produced lower incidence of vomiting than Haloperidol group, but it didn't find any statistically significant advantage over Haloperidol group.

Conclusion

We conclude that Ondansetron 4mg intravenous is not having significant advantage over Haloperidol 2mg intravenous in preventing PONV after laparoscopic abdominal surgeries.

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