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A Comparative Study Between On Dansetron and Granisetron for Post Operative Nausea Vomiting In Laparoscopichysterectomy

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ABSTRACT

Introduction

Postoperative nausea vomiting(PONV) is one of the commonest adverse event seen in anesthesia practice. Among all the incidence is high in gynecology patients,that to undergoing laparoscopic surgeries. In this randomized double blinded prospective study we compared the efficacy of ondansetron and granisetron for prevention of PONV in laparoscopic hysterectomies.

Objective

1.Compare the incidence of PONV between ondansetron and granisetron group
2. To assess the demand of rescue antiemetic(metoclopramide)
3. To Compare the side effects of the two drugs

Methodology

A total of 160 patients undergoing laparoscopic hysterectomies were randomly allocated to one of the two groups of 80 patients each. Patient in group O were given 4mg of Ondansetron and patient in group G were given 2 mg of Granisetron. The standard general anesthesia technique was administered to all patients. Episodes of nausea,retching,vomiting were assessed during first 24 hours after anesthesia.

Results

There was statistical difference for demographic data among the two groups ($p<0.05$). Ondansetron, having shorter duration of action, requires further repeat doses which may extend twice to thrice a day,as compared to the long duration antiemetic action of a single dose of granisetron.

Conclusions

The incidence of PONV was significantly high in ondansetron than in granisetron given prophylactically in laparoscopic hysterectomies.

Keywords: PONV,Ondansetron,Granisetron, Laparoscopic surgery

GLOSSARY OF TERMS

PONV- Post operative nausea vomiting
IV- intravenous
MAC- Minimum alveolar concentration
Mg- milligrams
Kg- kilograms
ECG – electrocardiogram
Hrs- hours

I. INTRODUCTION

Overthelastseveraldecadestheriskofmortality duetosurgeryandanesthesia have decreased as the attention have been shifted to the factors thatnegatively influencepatient'smorbidity.AmongallsuchfactorsPostOperativeNausea vomiting (PONV) is the leading cause. Its incidence rate is 49% of all thepatients.[1]Postoperativenauseavomitingcancausead verseconsequenceslikepatient's dissatisfaction, unexpected hospital stays, increase cost due to additionaldruguseand delayed recoveryand return to work.

It is the most common complication related to anesthesia. But nowadays theincidence have decreased to 75-80% since the ether era. Patient undergoing major gynaecological surgeries are esp. prone toPONVwith reported incidenceof 50-75%.[2,3]PONVismultifactorialandinspiteofadvancesinantiemetictherapyincidence is high. It can be patient related, surgery related, pre and post-operativefactors,anesthesiarelated factors

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contributingtodevelopment of PONV.[18]

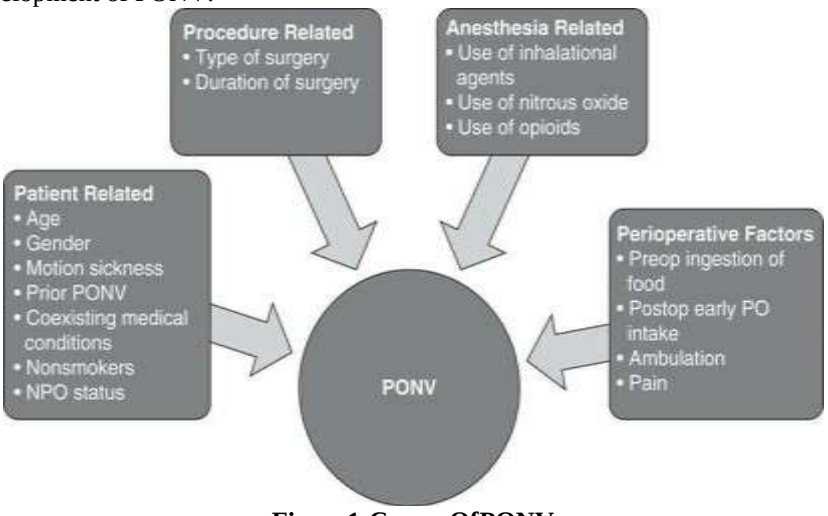

Figure1:CausesOfPONV

Preventing PONV is easier than treating it. Many drugs are used for preventingPONVlikeatropine,scopolamine,metoclopramide,midazolam,dexamethasone,promethazine and many more. But 5-HT3 receptors antagonists are most commonly used as they are highly specific and with minimalsideeffects.Ondansetron,granisetron,dolesetron,tropisetron,palanosetron belong to this group. Unlike ondansetron, granisetron is moreselective and effective.Headache,diarrhoea, sedation aresome ofits sideeffects.[28]Hence this study is being conducted in order to compare the two drugs Ondansetron and Granisetron in prevention of post operative nausea and vomiting in laparoscopic hysterectomies.

II. METHOD:

Patients of ASA Grade I and II, between 18 - 55 years of age undergoinglaparoscopic hysterectomies were included in the study. Pre-anesthetic assessmentof all patients was done a day before the surgery. A detail history and examinationwas done. And all the basic investigations like haemoglobin, total leucocyte count,differential leucocyte count, electrocardiography were done. After informing thepatient about the study and possible side effects of drug administration informedconsent of the patient for participation in the study was taken. All the patients wereadvised toremain nil per oral after 10pm the day before surgery. And all thepatientswere premedicated withinjectionpantocid40 mg the day before surgeryandontheday ofsurgery.Ontheday ofsurgery,aftercheckingthepatient'sidentity preoperatively, confirming the NBM status, checking all the equipment,patient was taken for the surgery. All the vitals, that is blood pressure, heart rate,oxygen saturation was recorded before starting the procedure. The patients of GroupOreceivedinjectionOndansetron4mg(2ml)intravenously 2minutespriortoinduction of anesthesia and Group G were injected with injection Granisetron 2mg(2ml) intravenously 2 minutes before induction of anesthesia. No other anti-emeticwas given. Induction of anesthesia was with propofol (1-2.5 mg/kg) intravenouslyand fentanyl 2mcg/kg IV. After 3 mins of preoxygenation, tracheal intubation wasdone with the help of succinylcholine (1-2 mg/kg) IV following ryles tube insertion.To maintain the anesthetic state Isoflurane (MAC 1) and 50% oxygen was giventhrough inhalation. Atracurium with the loading dose 0.5mg/kg followed by themaintenancedose0.1mg/kgwasgiveninevery15-20minutestomaintainthemuscle relaxation. All the vitals that is blood pressure, heart rate, oxygen saturation,ECG was monitored intraoperatively. Intraoperative hypotension and hypertensionweretreatedaccordingly.Bradycardia(HR<40)wastreatedwithIVatropine(0.01-0.02 mg/kg). Few minutes prior to completion of the surgery all the patients wereadministeredwithdiclofenac(1.5mg/kg)intravenously.Aftercompletionofsurgery,residualneuromuscularblockwereantagonisedwithIVneostigmine(0.04-0.08 mg/kg) and IV glycopyrolate 0.2 mg for each 1 mg of neostigmine. Trachealextubation was done on meeting the standard criteria for extubation. The patient wasevaluatedforpostoperativenausea,vomiting,retchingimmediatelyafterthe surgery in the recovery

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room and then episodes of nausea, vomiting or retching wererecorded if patients complain about it till 24 hrs. Post operative analgesia weremaintained with diclofenac. And metoclopramide IV (10 mg) was used as a rescueantiemetic if needed. The result was then be compiled and analysed statistically.Appropriatetreatment wastaken in caseof sideeffects.

The data was taken as follows---Noemesis-completecontrol
1-2 episodes- nearly complete control3-5 episodes-partial control
>5episodes- Failure

Nauseawillbeinterpretedas
Grade0=NoNausea,Grade1=MildNausea,Grade2= Moderate Nauseaand
Grade3=SevereNausea.

OUTCOMEMEASURES:

1. Incidenceofpost-operativevomiting/nausea/retchingepisodes.
2. Timingandamount ofrescueantiemetic(metoclopramide)required.

III. OBSERVATIONSANDRESULTS

TheObservationsarepresentedasMean±StandardDeviationoraspercentageas is applicable.

Table1:FrequencyofNauseaamongstudysubjects

Time	Granisetron(N=80)		Ondansetron(N=80)		Pvalue
	N	%	N	%	
Immediate	1	1.3	8	10	0.040(S)
1hour	1	1.3	3	3.8	0.613
2hour	0	0	3	3.8	0.244
4hour	1	1.3	0	0	1.000
6hour	1	1.3	1	1.3	0.477
24hour	1	1.3	9	11.25	0.022(S)

Table 1 depicts the postoperative episodes of Nausea when granisetron andondansetron were given separately to two randomized groups of patients. It showsthat immediate postoperatively only 1 episode of nausea while with ondansetron 8episodes of nausea which was statistically significant ($p<0.040$). At 1 hr,1 episodeofnauseawithgranisetronascomparedtoondansetronshowing3episodesofnausea. With granisetron these were 0,1,1 episodes of nausea at 2 hr, 4 hr, 6 hrrespectively as compared with ondansetron having 3, 0, 1 episode ofnausea. And at24 hr granisetron shows only 1 episode ascompared to ondansetron showing 9episodes,which is statisticallysignificant ($p=0.022$).

Table2:FrequencyofVomitingamongstudysubjects

Time	Granisetron(N=80)		Ondansetron(N=80)		Pvalue
	N	%	N	%	
Immediate	0	0	7	8.8	0.020(S)
1hour	1	1.3	1	1.3	0.477
2hour	0	0	1	1.3	1.000
4hour	0	0	5	6.3	0.069
6hour	0	0	9	11.3	0.006(S)
24hour	1	1.3	10	12.5	0.012(S)

Results reveal that there is a significant difference ($p=0.020$) in the meannumber of episodes of vomiting immediate postoperatively, with no episodes ofvomiting with granisetron as compared to ondansetron which had 7 episodes ofvomiting. At 1 hr, 2 hr, 4 hr there was a non significant difference seen between thetwogroupsasingranisetrongrouptherewere1,0,0ep

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isodeofvomitingrespectively.Whilewithondansetron therewere1,1,5episodesofvomitingrespectively. At 6 hrs, granisetron showed 0 episodes of vomiting while 9 episodeswith ondansetron which was statistically significant (p=0.006). At 24 hrs only 1episodevomitingwasseenwithgranisetronand10epi sodesofvomitingwithondansetronwhich was statisticallysignificant (p=0.012).

Table3:FrequencyofoverallNauseaandVomitingamongstudysubjects

Time	Granisetron(N=80)		Ondansetron(N=80)		Pvalue
	N	%	N	%	
Immediate	1	1.3	10	12.5	0.012(S)
1hour	2	2.5	4	5	0.677
2hour	0	0	5	6.3	0.069
4hour	1	1.3	4	5	0.363
6hour	2	2.5	10	12.5	0.036(S)
24hour	1	1.3	11	13.75	0.007(S)

Table3 depictsthepostoperativeepisodesofoverallPONVwh engranisetron and ondansetron were given to the two groups of patients. Difference inmean number of PONV episodes observed immediately after surgery was 1 forgranisetron and 10 for ondansetron respectively, which is significant (p=0.012).
At1hr,2hr,4hrthemeanno.ofepisodesofPONVwere2, 0,1respectively ingranisetron group as compared to ondansetron group which had 4,5,4 episodes ofPONV at 1 hr, 2 hr, 4 hr respectively. At 6 hours there were only 2 episodes ofPONVinthegranisetrongroupand10episodesofPO NVwithondansetrongroup,it was statistically significant (p=0.036). A significant difference was seen at 24hours, only 1 episode of PONVwas seen granisetron as compared to ondansetrongroup which had 11episodes of PONV(p=0.007).

Table4:Frequencyof antiemeticuseamongstudysubjects

Time	Granisetron(N=80)		Ondansetron(N=80)		Pvalue
	N	%	N	%	
Immediate	0	0	3	3.8	0.244
1hour	0	0	0	0	-
2hour	0	0	1	1.3	1.000
4hour	0	0	2	2.5	0.477
6hour	0	0	6	7.5	0.037(S)
24hour	1	1.3	8	10	0.022(S)

Result reveal that the requirement of antiemetic in granisetron group was 0immediately inpostoperativeperiodat1hr,2hr,4hr.Inondansetrongr oup,requirement of antiemetic immediately, at 1 hr, 2 hr, 4 hr is 3, 0, 1, 2 respectively.Thisdifferencewasstatisticallynon-significant.At6hr,asignificantdifferencewas seen where in granisetron group there was no requirement of antiemetic and inondansetron groupanti-emetic was used 6 times.
At 24 hrs, in granisetron group antiemetic was used only once while in theondansetron group,antiemetic was used 8 times.

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Table5:Frequencyofcomplicationsamongstudysubjects

Complications	Granisetron(N=80)		Ondansetron(N=80)		Pvalue
	N	%	N	%	
Constipation	7	8.7	0	0	0.020(S)
Headache	3	3.8	12	15	<0.001(S)
Nocomplication	70	87.5	68	85	0.818

In our study, it shows that in the Group O 0 patients had constipation whileintheGroupGhad7patientswhohadconstipation .Granisetrongrouphas3patients who complained of headache and 12 patients complained of headache inondansetron group. And therest had no adverseeffect.

IV. DISCUSSION

PONV is a very common and distressing sequelae of GA, incidence being20-30%. It is a leading cause of delayed discharge, unanticipated hospital admissionafter ambulatory surgical procedures, pulmonary aspiration, wound dehiscence anddehydration.Itismultifactorialanddespiteadvance sinantiemetictherapytheincidenceishigh.Apfeletal[65] statedthatamongpatientsreceivinginhaledanaesthesi a,femaleswithahistoryofPONVormotionsickness,an dpost-operativeuseofopioidsweremoreimportantriskfactor sofPONVandeachadditional risk factor increased the PONV incidence rate to 21%, 39%, 61%, and79%.

Many types of 5-HT3 receptors antagonist are being used to prevent PONV.Ondansetronwasthefirst5-HT3 receptorantagonistto be marketed and ismostcommonlyusedto controlPONV. Granisetron is a 2nd generation 5HT3antagonisthaving unique structural,pharmacological and clinicalpropertiesthatdistinguishit fromother5-HT3 antagonist.

Naguib et al[66] demonstrated that the incidence of PONV after laparoscopicsurgeries in the placebo group was remarkably high 72%.In our study the factorsthat would have contributed to nausea and vomiting may be laparoscopic surgery,female gender, menstrual cycle, etc. We conducted study on 160 ASA I and IIpatients with demographic data in terms of age, weight, duration of anesthesia,duration of surgery which were similar in two groups.Study done by Paxton[67]showedthat PONVis morecommoninyoungage and obesepatients.

In our study there is no statistical significant difference in the baseline valuesof hemodynamic variables between the two groups, before during or after giving thestudy drugs. In PACU we recorded the SBP, DBP and HR at regular interval, nohemodynamicalterations between the results wereobserved.

Post-operative episodes ofnausea our results show significant differencebetween the nausea episodes immediate after the surgery, where ondansetron shows8episodesandgranisetron only 1episodes(p<0.40) while for 1-2hours meanepisodeswerefoundtobeonly1episodewithgrani setron,3episodeswithondansetron.

At 4,6 hour postoperatively shows both ondansetron and granisetron almostshows similar episode of vomiting, where at 24hrs granisetron is more effectivethan ondansetron as showing 1 episode withgranisetronand 10 episodes withondansetron(pvalue<0.001).Similartoourstudyi nastudyconductedbyUpendranath et al,[60] comparing efficacy of ondansetron and granisetron laparoscopicsurgeries, it was found that the 0-2 hours interval, out of 80, 9 (18%) patients ingroup O had nausea while only 2 patients 4 % in Group G had nausea. This wasstatistically significant (p<0.05). In the 3-6 hours only 1-3 patients of Group O hadnauseawhile 1-2patientsbelongingtogroup Ghad nausea, respectively.

Our study reveals that there is a significant difference (p<0.020) in the meanno. of episodes of vomiting immediate after surgery where ondansetron shows 7episodes of vomiting among 80 patients while granisetron shows no episodes ofvomiting. However, 24 hours after

surgery,granisetron showsleast no.of episodesofvomitingwhile ondansetronshows 10 episodesofvomitingamong80 patients.

Thus, there is a significant difference (p=0.012) between the two groups.Similartoourstudy,Savantetal[68]comparedthe efficacyofintravenousondansetron4mgandgranisetr on2mgduringoralandmaxillofacialsurgicalprocedur e, he found emetic episodes in ondansetrongroup in first 0-2hrs postoperative period were 1 while that in granisetron was 0 (p<0.32). In 3-24 hrs periodof time incidence of vomiting was less with granisetron as compared to that ofondansetron.

Episodesofoverallponv

Inourstudyitwasfoundthatamongthe80patie ntswhoreceivedondansetron 10 patients had the episodes of nausea and vomiting immediately afterthesurgeryandonly1episodeofPONVingranisetr ongroup.Howevertheincidence with granisetron was less as compared to ondansetron. Thus, concludingthatgranisetronismuchmoreeffectiveimm ediately andupto24-hoursurgery.WhileincidenceofPONV increaseinondansetronafter 6 hrs.

Similarly,inthestudyconductedbyGauchanSetal[69]inl aparoscopiccholecystectomy it was evaluated and found that in first 3 hours period each of thedrughadasimilarantiemeticeffect(p>0.05).Andbe tween4-12hrsalsotheepisodes of nausea, retching as well as vomiting were statistically insignificant inbothgroups.Inlast12hoursepisodeofnausea,retchin gandvomitingweresignificantlyhigher in ondansetron group. While in granisetron group the incidencewas low in first 24 hrs.The difference in both the studies found can be due to thefactthatheusedthedrugattheendofthesurgeryandin ourstudy,weusedthedrugat theinduction time.

Useof rescueantiemetic

IthasbeenrecommendedthatincasesofPON V,repeatantiemeticshouldbeofadifferentclassthanth eoneusedforprophylaxis.Thiswaswhymetocloprami de 10 mg IV was used as a rescue anti-emetic drug.Results reveal thatthe requirement of antiemetic immediately in the post operative period was non-significant. While the incidence of use of antiemetic is significant at 24 hours wheretheusewas morein ondansetron group as compared togranisetron.

Adverseeffects

The 5-HT3antagonists granisetron and ondansetron have an enviable safetyprofile with most side effects being mild and transient. A small frequency of patientsin both study groups experienced non serious adverse effects like short durationheadache, constipation. Apart from this no side effects were observed in patients ofboth the groups in our study. As depicted by table we can observe that the incidenceof headache was 3.8% in granisetron group while it was 15% in ondansetron groupshowingastatisticallysignificantdifference(p< 0.001).Whiletheincidenceofconstipation was 8.7% in granisetron group and no such side effect was seen withondansetron.No anyother serious adverse effectwas noted.

Similartoourstudy Ommidetal[52]study showedthattheincidenceofheadache was 18% in ondansetron group while it was 11% in granisetron groupshowingastatisticallysignificant difference(p<0.05).

Completeresponse

Patientsshowingcompleteresponse(patientswhohad nonauseaandvomitingandnoneedforrescueantiemeti cduringthe24hourspostoperative

period) were significantly higher in group G (98.7%) while the percentage in groupO was only 66.2%. As compared to Upendranath et. al[60] in ondansetron group therewere10(20%)patientsreceivedinjectionmetoclo pramide10mg,therescueantiemetic in 24 hr postoperative period. And ingranisetron group only 1 (2%) outof50patients neededrescueantiemetic. This wasstatisticallysignificant(p<0.05).

Despite its low incidence, the issue of PONV remains a profound and oftenoverwhelmingpostoperativecomplication.Both oftheserotoninantagonists,ondansetron and granisetron appear to work effectively for prevention and treatmentof PONV. However, the effectiveness of both drugs when compared to one another,suggests an overall increased efficacy of granisetron along with the advantage of along duration of action. Even though, in this study, ondansetron exhibits favourableresults during the initial 6 hours of post-operative period, but the statistical analysisclearly shows that a single IV dose of 2 mg granisetron led to effective control ofoverallPONVandhencelesserrequirementaddition alanti-emeticsforaslongas24 hours post operatively. Ondansetron, having shorter duration of action, requiresfurther repeat doses which may extend from twice to thrice a day, whichdecreasesits cost-effectiveness, as compared to the long duration anti-emetic action of a singledoseofgranisetron.Therefore,thisstudyprovide savalidreasonforusinggranisetron for the

management of PONV.

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