



Original Article

Palonosetron – A better antiemetic for management of PONV.

Swati Adivarekar, Sandhya Gujar, Gajanan More, Harshraj Bhendale

Assistant professor, Professor and Head, Junior resident, Junior resident, Department of Anaesthesiology, ESI-PGIMS, Andheri.

ARTICLE INFO

Keywords:

Pneumonia
traditional child rearing practices
under 5 mortality

ABSTRACT

ABSTRACT: AIM AND OBJECTIVE: To compare and assess the clinical features and outcome of pneumonia occurring in infants with traditional child rearing practices and in infants without traditional child rearing practices. To assess the influence of individual traditional child rearing practices with the outcome of pneumonia occurring in infants. **MATERIALS AND METHODS:** : For this study detailed clinical history was taken. Infants with clinical and radiological evidence of pneumonia were selected as per the selection criteria. The study. After eliciting necessary history some children were excluded using exclusion criteria. Detailed questionnaires were asked to mother / care taker which included details regarding various traditional child rearing practices. **RESULTS:** On comparing and analyzing the clinical parameters and outcome of pneumonia in infants between traditional child rearing practices and without traditional child rearing practice. it is found that increased morbidity pattern of pneumonia in infants associated with traditional child rearing practices is high while comparing non traditional child rearing infants. **CONCLUSION:** In my study increased morbidity in the infants is attributed to traditional child rearing practice, mortality was very less probably due to increased vaccination status and also due to increasing literacy rate in mothers.

© Copyright 2018 BioMedSciDirect Publications IJBMR - ISSN: 0976:6685. All rights reserved.

Introduction

Postoperative nausea/vomiting (PONV) is defined as any nausea, and or vomiting occurring within the first 24 hours of surgery. It is so distressing to the patient that is rated equal to pain by the patient. It is also one of the most common causes of unanticipated hospital admission after Day Care Surgery, which effectively increases the cost of surgery.

PONV actually refers to two distinct entities i.e. nausea and emesis. It is further divided into early (within 6 hours) and late PONV (6 to 24 hrs after surgery)¹

Patho-physiology-Nausea is feeling of the need to vomit but patient is not able to bring the stomach content out which is a feeling, very unpleasant and distressing one. Vomiting OR Emesis is expulsion of stomach content and is associated with antiperistaltic contraction of ileum and jejunum, closure of glottis, contraction of diaphragm along with abdominal muscle contraction. The whole process is controlled by the vomiting centre in the medulla oblongata. Above the vomiting centre lies chemoreceptor trigger zone (CTZ) which detects noxious stimuli in blood.

There are multiple neurotransmitters modulating activity of vomiting centre.

Anatomic areas which activate vomiting centre mostly are vestibular area, related to middle ear, thalamus, cerebral cortex and G.I.tract itself. After getting activated vomiting centre sends efferent signals via the Cranial Nerves V, VII, IX, X, XII through vagal parasympathetic and sympathetic chain, hence vestibular area and nerves supplying middle ear are mostly responsible for stimulating vomiting centre and development of PONV. Middle ear surgeries are associated with greater incidence of PONV because of above mentioned sequence of events.

It is necessary to calculate risk factors associated with PONV as routine treatment with antiemetic is not recommended by American Society of Anaesthesiologist as it is not without side effects and it also increases cost of treatment,

Risk factors for PONV are mainly patient, surgical and anaesthesia dependent. Patient factors – Women because of effects of progesterone and estrogen on CRTZ. Surgical factors – Middle ear surgeries, laparoscopic surgeries, ophthalmic, ENT, and G.I.tract surgery

* Corresponding Author : **Dr. Swati Adivarekar**

There are various unpleasant complications of PONV viz. physical complications like tachycardia, sweating, dehydration, electrolyte imbalance, increased chances of oesophageal tear and rupture in severe cases. Surgical complications include surgical site bleed, wound dehiscence, rupture of vascular anastomosis, increased intracranial pressure etc. And anaesthetic complications related to aspiration pneumonia resulting into delayed recovery and higher cost of treatment due to prolonged hospital stay.

Various prophylactic drugs like antihistaminic, anticholinergics and dopamine receptor antagonists have been used to prevent PONV. But 5-HT₃ receptor antagonists are now preferred due to their effectiveness, more safety due to lack of sedative and extra pyramidal side effects of the drug and it acts directly on causative factors i.e. neurotransmitters from vomiting centre.

Ondansetron was the first 5-HT₃ receptor antagonist with relatively less antiemetic efficacy and short half life of 3 to 5 hours.² Palonosetron is the most recent 5-HT₃ receptor antagonist having strong receptor binding affinity and a long plasma elimination half life (40 hrs) making it more efficacious and thus more cost effective as compared to ondansetron.³

Hence, we conducted a study to compare the advantages and disadvantages of Palonosetron over Ondansetron in terms of efficacy for prevention of PONV when used as the only prophylactic antiemetic agent and the need of rescue medication. Side effects like headache, diarrhoea, constipation etc. were also observed. Patients were also observed for Serotonin syndrome including altered mental status, autonomic instability, and neuromuscular symptoms with concomitant use of 5 HT₃ receptor antagonist and serotonergic drugs like SSRI and SNRI.

Aim of study- To study effect of prophylactic single intravenous dose of 0.075 palonosetron and 8 mg of Ondansetron given just before induction of anaesthesia in decreasing and /or preventing incidence of PONV in middle ear surgery

Objectives-

- 1) To calculate risk of PONV in middle ear surgery patient
- 2) To assess PONV score in post operative period
- 3) To study side effects associated with both antiemetic drugs
- 4) Patient comfort and satisfaction

Material and Methods-

60 patient were divided into two groups of 30 each

- 1) Group X – received Inj. Ondansetron 8mg IV
- 2) Group Y – received Inj. Palonosetron 0.075 mg IV

All patients requiring general anaesthesia for middle ear surgery were included in the study.

Exclusion criteria were patient having additional risk factors for PONV like hepatic dysfunction. Acid peptic disease, previous history of vomiting and nausea and patient having concomitant serotonergic drug administration

A thorough pre-anaesthetic evaluation was done. All patients will be explained about the anesthesia technique and written informed consent was taken. Multipara monitor was attached to the patients in the operation theatre. All the patients were administered general anaesthesia by standard technique. Pre-medication Inj. glycopyrrolate 0.2 mg, Inj. pentazocine 0.6 mg/kg, Inj. midazolam 0.01mg/kg IV were given.

Single intravenous dose of Inj. Palonosetron 0.075 mg and Inj. ondansetron 8 mg were given slowly according to group during which time the patient were preoxygenated for 3 minutes with 100% oxygen. Anesthesia was induced with Propofol 2mg/kg and tracheal intubation done with help of Succinylcholine injection. Anaesthesia was maintained with oxygen, nitrous oxide and inhalational agent Isoflurane with controlled ventilation. Inj. vecuronium 0.1 mg/kg iv was given for maintenance. And subsequent anaesthetic management was according to surgical requirements. After the surgical procedure patients of both the groups were reversed with Inj. neostigmine 2.5 mg + Inj. glycopyrrolate 0.5 mg IV. And patients were extubated after complete recovery. Duration of anaesthesia and duration of the surgery were noted.

All the patients were observed in the postoperative recovery room for next 2 hours and then were shifted to the SICU for further monitoring upto 24 hours for hemodynamic monitoring along with any episode of nausea and /or vomiting.

Monitoring of PONV was done for first 24 hours, postoperatively, at intervals of 30 minutes each till first 4 hours, then at 2 hr. interval till next 8 hrs. And then each 6 hrs. Interval till 24 hrs. Two groups were observed for PONV score. PONV Score: 0 = No nausea and vomiting, 1= Nausea only, 2= Vomiting once, 3= Vomiting more than once. Patients with PONV Score 2 or greater were given Inj. metoclopramide 10 mg IV as a rescue medication. Frequencies and time of rescue medication were noted.

Complete response was considered as absence of nausea and vomiting and no need of rescue medication during first postoperative 24 hrs. Side effects like headache, constipation, diarrhoea etc. were recorded. Patients with palonosetron group were observed for serotonergic reactions.

Statistical Tests:

Data was entered in MS Excel. Analysis was done using SPSS21, chi square test, student-t test. The clinical accuracy was evaluated. Tables and charts were used wherever necessary. All quantitative data was expressed as mean ± standard deviation (SD). A p value less than 0.05 was considered statistically significant.

Kaplan-Meier Survival plot was used to present the time-to-event graphically.

Results:

Table 1: Baseline characteristics of the study participants in the two groups [Mean (Standard Deviation)]

Baseline characteristics	Group X	Group Y	p value
Age (yrs)	34.8 (10.3)	38.2 (11.9)	0.243
Weight (Kg)	48.50 (6.85)	49.37 (7.04)	0.62
Duration of Anaesthesia(min)	191.5 (16.9)	194.5 (13.7)	0.453
Duration of Surgery (min)	160.0 (17.2)	166.5 (15.6)	0.130
Sex [Frequency (Percentage)]			
Male	17 (56.7)	17 (56.7)	1.000®
Female	13 (43.3)	13 (43.3)	

* Significance level < 0.05, Unpaired t test used. ® Chi-square Test used

Table 2: The distribution of PONV Scores among participants in the two groups

PONV Score	Group X	Group Y	p value
0	2 (6.7%)	24 (80%)	<0.0005*
1	6 (20%)	6 (20%)	
2	9 (30%)	0 (0%)	
3	13 (43.3%)	0 (0%)	

*Significant at 0.05 level of significance using Chi-square test.

Table 3-incidence of nausea in the two groups

Groups	Number of Patients having Nausea PONV - 1	Total Participants	p-value	Exp(B) or Hazard ratio	95.0% CI for Exp(B)
Group X	6	30	0.855*	1.112	0.358 - 3.449
Group Y	6	30			

*Not significant at 0.05 level of significance

Table 4: incidence of vomiting in the two groups

Groups	Number of Patients having Vomiting	Total Participants	p-value	Exp(B) or Hazard ratio	95.0% CI for Exp(B)
Group X	22	30	0.010*	101.174	2.988 - 3425.670
Group Y	0	30			

* Significant at 0.05 level of significance

Figure 1: Kaplan-Meier Plot for Survival function (No Nausea) during 24 hrs postoperative period for the two study groups.

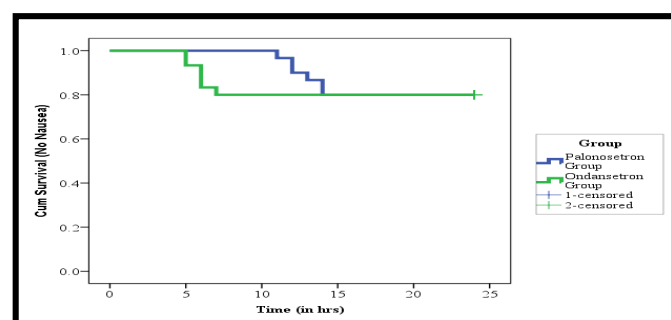


Figure 2: Kaplan-Meier Plot for Survival function (No Vomiting) during 24 hrs postoperative period for the two study groups.

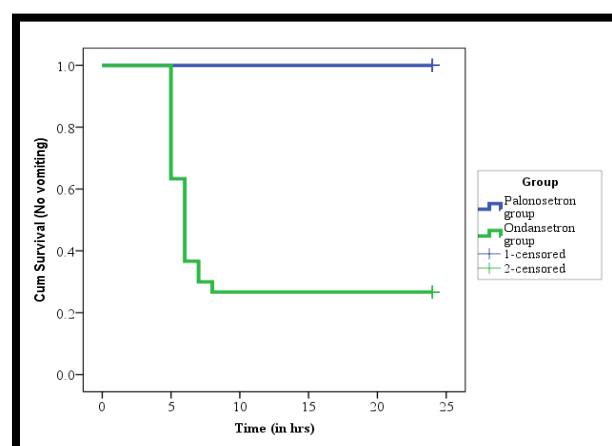


Table 5: Requirement of rescue medication postoperatively in the two groups [Frequency (Percentage)]

Number of times rescue medication was required	Group X	Group B	p value
0	8 (26.7)	30 (100)	<0.0005*
1	9 (30)	0 (0)	
2	9 (30)	0 (0)	
3	4 (13.3)	0 (0)	

*Significant at 0.05 level of significance using Fisher Exact test

The mean number of times, rescue medication was administered to the participant in Group X-Ondansetron (mean of 1.3 and standard deviation of 1) as compared to group Y (no participant required rescue medications) was significantly different. ($p < 0.0005$).

Table 6: Incidence of side effects in the two groups in the 24 hr post-operative period

Complication	Group A	Group B	p value
Headache	3 (10)	0 (0)	0.237#
No complaint	27 (90)	30 (100)	

#not significant at Significance level < 0.05 , Fisher Exact test used.

Total 60 patients were divided into two groups of 30 each GROUP X- Inj. ondansetron 8 mg IV and Group Y- Palonosetron 0.075 mg IV as single intravenous dose at the time of induction of anaesthesia. Both the groups were compared in terms of duration of prophylaxis and efficacy for prevention of PONV when used as sole antiemetic agent. The need of rescue medication and the drug related side effects were also studied.

Patients were comparable in their characteristics like age, sex, weight, duration of anaesthesia (Table 1)

The hemodynamic data were noted both during the intraoperative and postoperative periods at regular intervals. On consideration of PONV scores in 24 hours, it was observed that, out of 30 patients only 2 patients (6.7%) showed complete antiemetic response (PONV score = 0) in group X, whereas in group Y, 24 patients (80%) showed complete response. The PONV score is significantly higher in group X as compared to the group Y. (Table 2)

Six patients ie 20% had developed **nausea** with ponv score of 1 in both groups but time at which they developed nausea was much earlier in group X as compared to group Y. (Table 3 & Figure 1)

It was observed that 22 patients (73.33%) in group X out of 30 patients suffered with vomiting, whereas not a single patient from group Y had the similar complaint and the results are statistically significant. (Table 4 & Figure 2)

Rescue medication was required in almost all patients in group X whereas none of patient from group Y required it. (Table 5)

Side effects were statistically insignificant in both the groups. (Table 6)

Discussion

Postoperative nausea and vomiting (PONV) is very distressing and frequent complication after middle ear surgeries under general anaesthesia.¹ It may lead to dehydration, electrolyte imbalance, pulmonary aspiration, wound dehiscence resulting into delayed recovery and higher cost of treatment due to prolonged hospital stay.

5-HT₃ receptor antagonists are now preferred as a prophylaxis of PONV due to their effectiveness, easy availability and more safety due to lack of sedative and extrapyramidal side effects of the drug.

Palonosetron is a second generation 5-HT₃ receptor antagonist which creates a conformational change in the serotonin receptor so that serotonin binding is indirectly inhibited. Palonosetron has higher affinity with 5-HT₃ receptors, resulting into greater potency and longer duration of action.

The efficacy of 0.075 mg palonosetron and 8 mg ondansetron, was studied for prevention and /or decreasing incidence of PONV in patients when administered just prior to the induction of anaesthesia.

In a study conducted by Kovac AL et al⁶ in 2008, Inj. palonosetron was studied in various doses of 0.025mg, 0.050 mg and 0.075 mg intravenously along with the placebo. Complete response rate was statistically higher for 0.075 mg dose than for 0.025 and 0.050 mg for the first 24 hours and also thereafter till 72 hours. Similar results were obtained in a study conducted by Candiotti KA et al⁷. Hence, we decided to use palonosetron 0.075 mg intravenously for our study.

Study conducted by Paventi et al⁵ concluded that single dose of 8 mg of iv Inj. ondansetron is superior to 4 mg Inj. ondansetron in the prevention of PONV. In our study also we gave Inj. ondansetron 8 mg intravenously.

In our study, on consideration of PONV scores in 24 hours, it was observed that, out of 30 patients only 2 patients (6.7%) showed complete antiemetic response (PONV score = 0) in group X, whereas in group Y, 24 patients (80%) showed complete response. The significantly high PONV score in patients receiving ondansetron as compared to those who received palonosetron proves that palonosetron is more efficacious in preventing and /or decreasing

incidence of PONV when used alone prior to the induction of general anaesthesia. Similarly, though the same number of patients suffered with nausea (PONV score = 1) in both the groups, patients receiving ondansetron suffered much earlier at 5 to 6 hours postoperatively, compared to those who received palonosetron, who had the incidence of nausea after 12 to 14 hours postoperatively. This proves the prolonged duration of anti-nauseatic action of palonosetron than that of ondansetron.

In our study, very high number of patients, premedicated with ondansetron, suffered with vomiting whereas none of the patients premedicated with palonosetron had the similar complaint. Similar results were also found in studies done by Park SK⁸, Baisakhi Laha⁹, Bajwa SS¹⁰, Moon YE¹¹.

As we compared two drugs of the same group, the rescue antiemetic, i.e. Inj. metoclopramide was selected, which belongs to different group^{14,15}. Large number of ondansetron premedicated patients needed rescue medications whereas none of the palonosetron premedicated patients required the same.

The drug related side effects are negligible and statistically insignificant..

Conclusion:

Preventing PONV is easier than treating it. As middle ear surgeries are associated with high risk of developing postoperative nausea and vomiting it is concluded that prophylactic treatment with a single intravenous dose of palonosetron is effective in treating postoperative nausea / vomiting as the overall incidence of PONV is less with more number of patients showing complete response and none of the patients requiring the rescue medication in palonosetron group as compared to the ondansetron group.

REFERENCES

1. Michael M., David G., Antiemetics, Stoelting's Pharmacology and physiology in anaesthetic practice. Fifth edition, Page no. 692.
2. Michael M., David G., Antiemetics, Stoelting's Pharmacology and physiology in anaesthetic practice. Fifth edition, Page no. 696.
3. Palonosetron, <https://en.wikipedia.org/wiki/Palonosetron>.
3. Stadler M, Bardiau F, Seidel L, Albert A, Boogaerts JG. Difference in risk factors for postoperative nausea and vomiting. *Anesthesiology: The Journal of the American Society of Anesthesiologists*. 2003 Jan 1;98(1):46-52.
4. Apfel CC, Kranke P, Katz MH, Goepfert C, Papenfuss T, Rauch S, Heineck R, Greim CA, Roewer N. Volatile anaesthetics may be the main cause of early but not delayed postoperative vomiting: a randomized controlled trial of factorial design. *British Journal of Anaesthesia*. 2002 May 1;88(5):659-68.
5. Rojas C, Stathis M, Thomas AG, Massuda EB, Alt J, Zhang J, Rubenstein E, Sebastiani S, Cantoreggi S, Snyder SH, Slusher B. Palonosetron exhibits unique molecular interactions with the 5-HT₃ receptor. *Anesthesia & Analgesia*. 2008 Aug 1;107(2):469-78.
6. Yang LP, Scott LJ. Palonosetron: in the prevention of nausea and vomiting. *Drugs* 2009; Nov 12;69(16):2257-78.
7. Paventi S, Santevecchi A, Ranieri R. Efficacy of a single-dose ondansetron for preventing post-operative nausea and vomiting after laparoscopic cholecystectomy with sevoflurane and remifentanyl infusion anaesthesia. *European review for medical and pharmacological sciences*. 2001 Mar;5:59-64.
8. Kovac AL, Eberhart L, Kotarski J, Clerici G, Apfel C, Palonosetron 04-07 Study Group. A randomized, double-blind study to evaluate the efficacy and safety of three different doses of palonosetron versus placebo in preventing postoperative nausea and vomiting over a 72-hour period. *Anesthesia & Analgesia*. 2008 Aug 1;107(2):439-44.
9. Park SK, Cho EJ. A randomized, double-blind trial of palonosetron compared with ondansetron in preventing postoperative nausea and vomiting after gynaecological laparoscopic surgery. *Journal of International Medical Research*. 2011 Apr;39(2):399-407.
10. Laha B, Hazra A, Mallick S. Evaluation of antiemetic effect of intravenous palonosetron versus intravenous ondansetron in laparoscopic cholecystectomy: a randomized controlled trial. *Indian journal of pharmacology*. 2013 Jan;45(1):24.
11. Bajwa SS, Bajwa SK, Kaur J, Sharma V, Singh A, Singh A, Goraya SP, Parmar SS, Singh K. Palonosetron: A novel approach to control postoperative nausea and vomiting in day care surgery. *Saudi journal of anaesthesia*. 2011 Jan;5(1):19.
12. Moon YE, Joo J, Kim JE, Lee Y. Anti-emetic effect of ondansetron and palonosetron in thyroidectomy: a prospective, randomized, double-blind study. *British journal of anaesthesia*. 2012 Jan 25;108(3):417-22.
13. Wallenborn J, Eberhart LH, Kranke P. Postoperative nausea and vomiting--what's new in anti-emetic pharmacotherapy?. *Anesthesiologie, Intensivmedizin, Notfallmedizin, Schmerztherapie: AINS*. 2009 Apr;44(4):296-304.
14. Basu A, Saha D, Hembrom BP, Roy A, Naaz A. Comparison of palonosetron, granisetron and ondansetron as anti-emetics for prevention of postoperative nausea and vomiting in patients undergoing middle ear surgery. *Journal of the Indian Medical Association*. 2011 May;109(5):327-9.
15. Chakravarty NU, Raghuvanshi SK. Comparison between efficacy of palonosetron and ondansetron in postoperative nausea and vomiting in middle ear surgery: a randomized double blind study. *Int J Pharma Bio Sci*. 2013;4:B67-74.
16. White PF, Watcha MF. Postoperative nausea and vomiting prophylaxis versus treatment. *Anesth Analg* 1999; 89: 1337-9.
17. Shadangi BK, Agrawal J, Pandey R, Kumar A, Jain S, Mittal R and Chorasias. A prospective, randomized, double-blind, comparative study of the efficacy of intravenous ondansetron and palonosetron for prevention of postoperative nausea and vomiting. *Anaesth Pain & Intensive Care* 2013; 17(1):55-58.