COMPARISON OF METOCLOPRAMIDE, PROCHLORPERAZINE AND PLACEBO IN PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING (PONV) FOLLOWING TONSILLECTOMY IN YOUNG ADULTS

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Background: Postoperative nausea and vomiting following anaesthesia and surgery are common and can create considerable problems regarding management of patients and outcome of the surgical procedure. **Methods:** This study evaluates and compares the efficacy and safety of the metochlopramide to that of prochlorperazine in the prevention of postoperative nausea and vomiting after tonsillectomy in young adult patients. 150 patients, of either sex, undergoing tonsillectomy under the same anaesthetic technique were studied in a randomized, double blind, placebo controlled manner. Either metoclopramide 0.1-0.2 mg kg^{-1}, prochlorperazine 0.1-0.2 mg kg^{-1} or 5% Dextose and normal saline (5% D/N.S) (2ml) as placebo was injected intravenously 10 minutes before induction of general anaesthesia. Episodes of nausea, retching/ vomiting, adverse events, vital signs, the need for rescue antiemetic drug (metoclopramide 0.1-0.2 mg kg^{-1} IV) were recorded until four hours from the end of the surgical procedure. **Results:** The overall frequency of PONV was 18%, 16%, and 24% in group A (metoclopramide), B (prochlorperazine) and C (placebo) respectively. The need for rescue antiemetic was 2%, 8% and 12% in Prochloperazine group, metoclopramide group and control group respectively. These differences did not reach statistical significance (P>0.05). During the study period 82%, 84% and 76% of patients in group A, B and C respectively were found free from postoperative nausea and vomiting, and no adverse events related to either of the test medication were noted in any patient. **Conclusion:** It is concluded that the differences in the results of occurrence of PONV in the experimental group and control group are not statistically significant. However either Prochloperazine 0.1 – 0.2 mg kg^{-1} or metoclopramide 0.1 – 0.2 mg kg^{-1} can be safely administered as Prophylactic antiemetic till the availability of more efficacious and safe antiemetic drugs.

Keywords: Postoperative nausea and vomiting (PONV), metoclopramide, prochlorperazine, tonsillectomy.

INTRODUCTION

Nausea and vomiting being among the most common postoperative complaints can occur after general, regional or local anaesthesia.[1] The aetiology of postoperative nausea and vomiting (PONV) is multifactorial and includes factors like patients characteristic, type of surgery, anaesthetic techniques and postoperative care.[2-4]

Although considered a minor postoperative complication PONV can be the most distressing, resulting in bleeding, dehydration, electrolyte[5] and acid base imbalance. Persistent, retching and vomiting can impair the results of various surgical procedures and increase the risk of pulmonary aspiration of vomitus. It may prolong the stay in the post anaesthesia care unit, delay discharge[1] and increase hospital admission rate.

Severe vomiting has been mentioned to result in dehiscence of abdominal wounds, rupture of esophagus, surgical emphysema and bilateral pneumothraces.[6]

The frequency of postoperative nausea and vomiting can be reduced by refined anaesthesia technique and by avoiding the factors predisposing to it. Although routine antiemetic prophylaxis in elective operations is not indicated but it may be justified in patients, who are at the greater risk of PONV.[7]

Non pharmacological measures like acupressure and acupuncture for prevention of PNOV have been found ineffective.[8] Prophylaxis and treatment has been attempted with various drugs like benzodiazepines[9], 5-hydroxytryptamine ($5HT_3$, serotonin) antagonists[10], benzamides,[11,12] butypro-phenones,[13] Phenothiazines,[14] antihistamines,[15] ginger root[16] and antichloinergics.[17] High dose metoclopramide is also considered to be $5HT_3$ antagonist but extrapyramidal side effects are possible problems.

This study has been conducted to test prevention of PONV with either metoclopramide or Prochlorprazine, both administered intravenously ten minutes before induction of anaesthesia in a double blind, placebo controlled fashion.

The objective was to evaluate efficacy of each drug in the prevention of PONV and to compare the frequency of PONV in the experimental groups to that in the control group.

MATERIAL AND METHODS

This study was conducted in the operation theatre and wards of ENT department of Post Graduate Medical Institute, Govt. Lady Reading Hospital Peshawar. A total of 150 patients from the ENT wards were included in the study. All of them were admitted in the ENT wards a day before surgery through the out patient department. They were suffering from chronic tonsillitis and underwent tonsillectomy.

Three independent samples each of size 50 randomly selected from normally distributed population of young adults of either sex with the same variance were named as group A, B and C according to prophylactic antiemetic they received.

All patients included were adults (16–30 years), American Society of Anesthesiologists (ASA) Physical status class I of both sexes being selected randomly. Patients suffering from preoperative emesis, taking anxiolytic or Sedatives, having history of drug allergy, clotting disorders, vertigo or ear disease, airway difficulty or pregnancy were excluded from the study. These patients were kept nothing per oral for 6 hours preoperatively. An Intravenous line was secured with an 18-gauge cannula on the dorsum of the hand in all patients. The patients randomly received in a double blind fashion either metoclopramide 0.1 – 0.2 mg kg^{-1} (2ml), prochlorperazine 0.1 – 0.2 mg kg^{-1} (2ml) or 5% Dextose in Normal Saline (2ml) intravenously in the preparation room, 10 minutes before induction of anaesthesia. The same anaesthetic technique was used for all patients. On entry into the operation theatre, replacement of the fluid deficit was started with Ringer lactate & Dextose 5% (Ringolact D). Morphine 0.05 mg kg^{-1} and atropine 0.01 mg kg^{-1} were administered intravenously to each patient just before induction of general anaesthesia.

The patients were preoxygenated with 100% oxygen via facemask for three to five minutes. Thiopentone sodium 4 – 5 mg kg^{-1} IV was given followed by suxamethonium 1 – 1.5 mg kg^{-1} IV to facilitate nasotracheal intubation.

Anaesthesia was maintained with halothane 0.5% - 2% and nitrous oxide 60% in oxygen (40%), via a Bain circuit. The patients were provided assisted ventilation manually till resumption of spontaneous respiration. Ringolact D was infused intravenously for replacement of deficit and maintenance fluids. The patient's radial pulse was monitored by regular palpation for rate, rhythm and volume. The arterial blood pressure (systolic and diastolic) was monitored every ten minutes. Standard lead 11 was used for continuous ECG display. The respiration of the patient was monitored clinically by observation of the respiratory rate, chest expansion and auscultation of the chest for breath sounds. Arterial haemoglobin oxygen (Sao_2) saturation and pulse rate were also continuously displayed by the pulse oximetry using a finger probe.

At the completion of surgery the anesthetics were turned off and the patient extubated. They were put on the lateral side with slight head down tilt to avoid aspiration of secretion, blood, regurgitated or vomited materials into the lungs during the early postoperative period. Their airways were kept cleared of clots or secretions. Oxygen was provided via facemask 4 – 6 L/min till full recovery of the patients in the recovery room. Radial pulse for the rate, rhythm and volume, systolic and diastolic blood pressure, respiratory rate and temperature were watched half hourly.

Ringolact D solution was infused as maintenance fluid till the patients were allowed orally for fluid intake. A trained nurse unaware of the nature of the study drugs observed and nursed the patients in the recovery room and wards. She assessed the patients for the frequency of the nausea, retching, vomiting or any side effects of drugs for 4 hours in the postoperative period. A rescue antiemetic (metoclopramide 0.1 – 0.2 mg kg^{-1} IV) was administered either on the demand of the patient or at the discretion of the observing nurse. A Performa designed for the recording of the demographic data, the type of the prophylactic antiemetic drug given, the rescue antiemetic used if indicated and the record of postoperative emetic sequelae, was attached with the chart of the patient.

The patients were assessed for PONV and categorized as following:-

Category 1: Patients experienced no nausea, retching or vomiting.

Category 2: Patients felt only nausea.

Category 3: Patients suffered from retching / vomiting.

At the completion of study the patients were divided into three groups according to the prophylactic antiemetic they received.

Group A: Patients received metoclopramide, 0.1 – 0.2 mg kg^{-1} IV.

Group B: Patients received Prochlorperazine, 0.1 – 0.2 mg kg^{-1} IV.

Group C: Patients received placebo 5% Dextose with normal saline (5%D/N.S) 2ml IV.

A fixed effect model was used for analysis of variance (ANOVA) in order to test for the equality of means. Chi square test was used for analysis of the frequency of postoperative nausea, vomiting, overall frequency of PONV and the need for rescue antiemetic drug. The exact value for probability was obtained when our null hypothesis was true a value of the test statistic as extreme or more extreme in the

appropriate direction than the one actually computed was quoted as p-value where ever appropriate. P<0.05 was considered as significant. The results were shown in the form of tables.

RESULTS

Patients in all the three groups were similar with no statistically significant difference regarding age (P=0.192), weight (P=0.4803). There was also similarity amongst the groups with respect to ASA physical status, the history of previous anaesthetic exposure, history of motion sickness, type and duration of surgical procedure. (Table-1)

Table-1: Demographic data of the patients.

Groups	A	B	C
Age (years) Mean±SEM	19.6 ± 0.627	18.14 ± 0.479	18.88 ± 0.539
Weight (kg) Mean±SEM	56.26 ± 1.295	55.46 ± 1.074	54.34 ± 0.977
ASA Physical Status I	50	50	50
Sex Male	21	18	15
Female	29	32	35
History of motion sickness	12	10	15
Previous anaesthetic history	2	3	2
Duration of operation (minutes) Mean±SEM	39.54 ± 0.325	39.75± 0.591	45.18± 1.19

Nausea was experienced by 4% of patients in group A, 12% in group B and 14% in group C during the study period. The frequency of nausea was less in group A when compared with group C and B, but the difference did not reach statistical significance (P>0.05) (Table-2).

Table-2:Number of Patients experiencing nausea

Groups	Number of patients	%
A (n=50)	2	(4%)
B (n=50)	6	(12%)
C (n=50)	7	(14%)

P=0.211189

The frequency of vomiting was 14%, 4% and 10% in groups A, B and C respectively. It was considerably less in group B than in group A and C. (Table-3)

Table-3:Number of Patients experiencing vomiting

Groups	Number of patients	%
A (n=50)	7	(14%)
B (n=50)	2	(4%)
C (n=50)	5	(10%)

P=0.224249

Overall frequency of PONV was 18%, 16% and 24% in group A, B and C respectively.

Thus the overall frequency of PONV was comparable in group A and B and higher in group C as compared to the other two groups (Table-4).

Table-4: Overall frequency of PONV

Groups	Number of patients	%
A (n=50)	9	(18%)
B (n=50)	8	(16%)
C (n=50)	12	(24%)

P=0.574072

In group A 8% of patients received metoclopramide as a rescue antiemetic to control PONV. In group C, 12% received metoclopramide while in group B, 2% of patients needed it to alleviate PONV during the 4 hours follow up period (Table-5).

Table-5: The need for rescue antiemetic (metoclopramide 0.1-0.2 mg kg $^{-1}$ I.V)

Groups	Number of patients	%
A (n=50)	4	(8%)
B (n=50)	1	(2%)
C (n=50)	6	(12%)

P=0.155673

These differences were not statistically significant (P>0.05).

DISCUSSION

Nausea and vomiting are unpleasant sequelae of anaesthesia and surgery. It is distressing to the patient and potentially detrimental to the postoperative recovery.

It may arise after regional anaesthesia, particularly if hypotension occurs but are more common after general anaesthesia. The overall incidence of emesis was a high as 75 – 80% when ether and cyclopropane were in routine use. This fell to 20% - 30% with the advent of halothane in the mid 1950's. There is now evidence that the use of propofol is associated with an incidence of less than 10%. Addition of nitrous oxide to general anaesthesia, use of opioids as anaesthesia supplement and as analgesic, reversal of residual effects of non-depolarizing muscle relaxant at the end of surgery with neostigmine and operation like strabismus surgery, laparatomy and throat surgery are associated with higher incidence of PONV. The routine prophylactic use of antiemetics to prevent PONV is hard to justify. However it is lucid to give a prophylactic antiemetics drug to patients, high risk for emesis and aspiration.[1] Much information has been published on the efficacy and side effects of various antiemetic drugs. However there is a continued search for an ideal antiemetic that is effective, safe, cheaper and easily available. This study was designed as a part of these efforts to search out a solution for minimizing the occurrence of postoperative emetic sequelae.

The frequency of PONV in groups A, B and C was 18%, 16% and 24% respectively. The

frequency of PONV in group B (16%) is less as compared to group A (18%) and group C (24%), but the difference did not reach statistical significance (P>0.05). The frequency of PONV in the group C is similar to 24% reported by Khan et al.[18] The frequency of vomiting in groups A and C was 14% and 10% respectively, which is comparable to each other. It was 4% in groups B which is less as compared to the other groups, but the difference did not reach statistical significance (P>0.05).

Mckenzie et al[19] reported vomiting 54% in placebo group. They studied woman undergoing laparoscopic gynaecological surgery under local and general anesthesia, their result is much higher than my result. The frequency of nausea in my study in groups A, B and C was 4%, 12%, and 14% respectively. This difference did not reach statistical significance (P>0.05).

Bone et al[16] and Raphael and Norton[20] have reported the incidence of nausea as 28% and 53% respectively in their patients who received a similar dose of metoclopramide (0.1 – 0.2 mg kg^{-1}) as in my study. The result of my study is much lower than their results. This is because they have performed their study on woman undergoing major gynaecological surgery and followed up their patients postoperatively for 12 hours. Similarly Bone et al[16] had reported the incidence of emetic sequelae as 70% in the placebo group and 45% and 50% in the ginger root and metoclopramide groups respectively. These results are also higher than those of my study.

Madej and Simpson[11] and Raphael and Norton[20] have reported the incidence of vomiting in their female patients undergoing major gynaecological surgeries as 51% and 53% respectively. They received metoclopramide as a prophylactic antiemetic.

Madej and Simpson[11] have reported the incidence of nausea in the placebo group as 30% and in the metoclopramide group as 20%. The incidence of nausea in their patients is also higher than in my patients. The incidence of vomiting in placebo and metoclopramide groups was 18% and 6% respectively. Their studies were performed on women undergoing minor gynaecological procedures and were followed up for 4 hours.

The study of Rudra[21] shows the incidence of PONV 15% in ondansetron group, 50% in metoclopramide group and 85% in the placebo group. 20% of patients in the ondansetron and metoclopramide group needed rescue antiemetic. Thus the incidence and severity of PONV in the study of A Rudra is considerably higher than that of my study. This is due to the fact that Rudra performed study on female patients who underwent upper abdominal surgery (Cholecystectomy), they also received pethidine IM 6 hourly for analgesia and they were followed up for 24 hours postoperatively.

VandenBerg[14] compared the efficacy of ondansetron 0.06 mg kg^{-1} IV and Prochlorperazine 0.2 mg kg^{-1} IM and Prochlorperazine 0.1 mg kg^{-1} IV, given during induction of general anaesthesia to patients undergoing adenotonsillectomy. Nausea perse occurred with similar frequency in-between 6% and 11% of patients in each test drug group. Vomiting perse without accompanying complaints of nausea also occurred with similar frequency in between 11% and 19% of patients in each group. The incidences of the dual complaints of nausea and vomiting were also similar in those given placebo and prochlorperazine IV 29% and 21% respectively, but greatly reduced to 3% and 2% respectively in those given prochlorperazine IM and on dansetron IV. The frequency of nausea and vomiting in my study is comparable to that of Vanden Berg study. But the frequency of vomiting in group B (Prochlorperazine) in my study is lower 4%, than that reported by Vanden Berg. This may be due to the following reason that many young children were included in the study of Vanden Berg, adenoidectomy in addition to tonsillectomy was performed on these children, they received nondepolarizing muscle relaxants that needed reversal with neostigmine at the end of surgery, they also received Parenteral opioids for analgesia postoperatively and the the observation time was longer (24 hours) than in my study.

CONCLUSION

This study has demonstrated that the occurrence of PONV is comparable in metoclopramide group (18%) and prochlorperazine group (16%). While the occurrence of PONV is higher in the control group. But these differences are not statistically significant (P>0.05). The need for rescue antiemetic was least in the prochlorperazine group (2%) as compared to the metoclopramide group (8%) and control group (12%). These differences also did not reach statistical significance.

However, either prochlorperazine or metoclopramide can be safely administered as prophylactic antiemetic till the availability of more efficacious and safe antiemetic drug. Their does of 0.1-0.2mg kg^{-1} are also effective for the prophylaxis of postoperative nausea and vomiting. More experimental work is required to explore the various aspects of the problem of PONV. This may include the proper patient preparation, anaesthetic techniques, doses of drugs and comparative studies regarding efficacy, safety and cost benefit ratio of various antiemetic drugs.

REFERENCES

1. Watch MF, White PF. Postoperative nausea and vomiting, its etology, treatment and prevention Anesthesiology 1992; 77; 162-84.
2. Beattie WS, Lindblad T, Buckley DN, Forrest JB. Mensturation increases the risk of nausea and vomiting after laparoscopy, a prospective randomized study Anesthesiology 1993;78; 272-76.
3. Lerman J. Surgical and patient factor involved postoperative nausea and vomiting Br J Anaesth 1992;69(suppl-1);24S-32S.
4. Kamath B, Curran J, Hawkey C. Anaesthesia, movement and emesis. Br J Anaesth 1990; 64; 728-30.
5. Andrews PLR. Physiology of nausea and vomiting Br J Anaesth 1992; 69 (Supply -1); 2S-19S.
6. Bremner WGM, Kumar CM. Delayed surgical emphysema Pneumomediastinum and bilateral pneumothoraces after postoperative vomiting Br J Anaesth 1993; 71:296-7.
7. Capouet V, De Pauw C, Vernet B. Single dose i, v tropisetron in the prevention of postoperative nausea and vomiting after gynecological surgery, Br J Anaesth 1996;76:54-60.
8. Shenkman Ze' EV, Holzman RS, Kim E. Acupressure-Acupuncture Antiemetic prophylaxes in children under going Toxsillectomy Anesthesiology 1999; 90; 1311-6.
9. Florio TD. The use of midazolam for persistent postoperative nausea and vomiting Anaesth Intensive Care 1992; 20; 383-86.
10. Bowhayar, Mayha, Rudnicka AR. A randomized controlled trail of the antiemetic effect of three doses of ondansetron after strabismus surgery in children. Paed Anaesth 2001; 11; 215-21.
11. Madej TH, Simpson KH. Comparison of the use of domperidone, droperidol and metoclopramide in the prevention of nausea and vomiting following major metoclopramide surgery. Br J Anaesth 1986;58;884-7.
12. Tramer M, Moore A, McQuay H. Prevention of vomiting after paediatirc strabismus surgery, a systematic review using review using the numbers needed to treat method. Br J Anaesth 1995;75:556-61.
13. Buther M, Walder B, Elm Fvetal. Is lower dose haloperidol a useful antiemetic. A Meta-analysis of published and unpublished Randomized trials. Anesthesiology 2004;104:1454-63.
14. Van den Berg AA. Comparison of ondansetron and prochloperazine for the prevention of nausea and vomiting after adenotosillectiomy. Canjanaesth 1996;76; 449-51.
15. Knapp MR, Beecher HK. Postanaesthetic nausea, vomiting and retching. JAMA 1956;160;376-85.
16. Bone Me, Wilkinson DJ, Young JR, McNeil J, Charltron S. Ginger root a new antiemetic. The effect of ginger root on postoperative nausea and vomiting after major Gyneacological surgery. Anaesthesia 1990;45:669-71.
17. Honkavaara P. Effect of transdermal hyoscine on nausea and vomiting during and after ear surgery under local anesthesia. Br J Anaesth 1996;76:49-53.
18. Khan FA. Soomro NA, Kamal RS. A review of 6978 consecutive admission to the recovery room at a university hospital J Pak Med Assoc 1991;41:2-6
19. Mckenzie R, Kovac A, Connor TO. Comparison of ondansetron versus placebo to prevent postoperative nausea and vomiting in woman undergoing ambulatory gynaecologic surgery. Anesthesiology 1993;78:21-8.
20. Raphael JH, Norton AC. Antiemetic efficacy of prophylactic ondansetron in laparoscopic surgery. Randomized, double-blind comparison with metoclopramide. Br J Anaesth 1993;71:845-8.
21. Rudra A. Comparison of ondansetron, metoclopramide and placebo in the prevention of emetic episodes following Cholecystectomy. Anesthesiology 1993; XVII:14-17

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