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Original Article

METOCLOPRAMIDE ALONE AND WITH DEXAMETHASONE FOR PROPHYLAXIS OF POST-OPERATIVE NAUSEA VOMITING IN DAY CARE BREAST SURGERY PATIENTS.

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ABSTRACT:

Objective: The objective of this study was to find out the anti-emetic efficacy of Metoclopramide alone and in combination with Dexamethasone. **Material and Method:**One hundred twenty eight female patients undergoing breastsurgery were randomized to receive Metoclopramide alone and Metoclopramide and Dexamethasone (combination group) in a double-blind manner. Metoclopramide 0.15mg/kg in (10ml) and the combination ofdrugs (metoclopramide0.15mg/kg & dexamethasone0.1mg/kg) in (10ml) were administered after induction of anesthesia. General anesthesia included Propofol,sevoflurane in N_2O/O_2 Nalbuphine 0.15mg/kg as analgesia .Episodes of nausea &vomiting and the need for additional antiemetic were recordedfor 6 hours. **Results:** The incidence of patients free from post-operative nausea vomiting (PONV) was 78.1% in metoclopramide-groupand free from vomiting95.3% in combination-group ($P = 0.042$). **Conclusion:** There was a high incidence of postoperative nausea and vomiting in breast surgery patients with Metoclopramide alone, however the combination of Metoclopramide and Dexamethasone drugs revealed additive effect. PONV was reduced from78.1% in metoclopramide group to 95.3% in combination group.

Keywords: Metoclopramide, Dexamethasone, PONV, Breast surgery

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INTRODUCTION

Post-operative nausea vomiting (PONV) is still a frequent complication of anaesthesia and surgery with 8-45% in day care patients.[1]This is a major concern for the patients undergoing day care surgery under general anaesthesia.[2]Pain, nausea vomiting are frequently listed by the patients as their most important postoperative concern. Some patients report greater concerned then postoperative pain. PONV can lead to wound dehiscence, bleeding, aspiration of gastric contents, water and electrolyte abnormalities, prolonged hospitalization,rehospitalization and patients' low satisfaction with postoperative care [3].It is so unpleasant that most patientswould prefer

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to experience postoperativepain rather than nausea and vomiting. Occurrence of PONV is influenced by various factors such as duration of anaesthesia, type of surgery, use of narcotics, patient's age and sex, and history of PONV, motion sickness or smoking [4]. Female patients have 3 times greater incidence of emetic symptoms than males, due to increased gonadotropin, estrogen, and plasma progesterone levels during their menstrual cycles [5]. Fat soluble anaesthetic agents accumulate in adipose tissue, which later on release may cause post-operative nausea vomiting. The etiology of PONV is still not clearly understood but is known to be multi factorial and includes factors like patients characteristic, type of surgery, anaesthetic techniques and postoperative care.[6] Nausea vomiting can delay discharge from day care surgery and shown to be a major cause of unplanned admission to the hospital and increased cost related to length of hospital stay[7].Studies indicated that Dexamethasone may effectively decrease the incidence of PONV [8]. Dexamethasone, a corticosteroid exact mode of action as anti-emetic still not known.It has anti-inflammatory effects that may decrease postoperative tissue injury, edema and pain. It has an elimination half-life of 3hours.Metoclopramide is a medication that has been used for 40 years in the prevention of postoperative emesis [9]. It is a very low-cost drug, and doseof 10 mg IV, has a low incidence of adverse events [10].Metoclopramide blocks dopamine receptor in the chemoreceptor trigger zone and vomiting Centre. Post-operative nausea vomiting is often managed with single prophylactic anti emetic given during surgery but there is a growing trend towards the use of combination anti emetics therapy in moderate to high risk patients [11,12,13].Better results can be obtained by combining antiemetic's, because they have different sites of action. Combination anti emetics therapy is often effective for preventing PONV after breast surgery. We want to compare effectiveness of metoclopramide alone and combine with dexamethasone for preventing post-operative nausea vomiting in day care breast surgery patients.

MATERIALS AND METHODS

This study was conducted at department of Anaesthesia Liaquat National Hospital and Medical College from January 2015 to October 2015.A sample size estimate is performed prospectively which revealed that 64 patients in each group were necessary (?0.05, 1-?-80, P1 0.62 and P_2 0.85)[15].After taking verbal consent from the patients, a total of 128 patients undergoing breast surgery were enrolled. Women who were pregnant, breast feeding, receiving anti emetic, known allergy to one of drugs, American society of anesthesiology (ASA) class>3 and predicted difficult intubation were excluded from the study. All patients included were adult, female ASA class I-II.All patients divided into two groups' Metoclopramide group and combination group. These patients were nil per oral for six hours preoperatively and intravenous line was secured with 20 gauge cannula. Ringer solution was infused intravenously for replacement of deficit and maintenance fluids. General anaesthesia was given. Propofol 2mg/kg was used for induction of anaesthesia .After induction of anaesthesia laryngeal mask airway (LMA) size3 was inserted. Patient randomly received in a double blind fashion Metoclopramide 0.15mg/kg in (10ml) or Metoclopramide 0.15mg/kg /Dexamethasone0.1mg/kg in (10ml) by anaesthesia resident who was unaware of drug preparation. Anaesthesia was maintained with sevoflurane 2-8% and nitrous oxide 60% in oxygen 40% via a Bain circuit. Nalbuphine 0.15mg/kg was given as I/V analgesia .The patient's radial pulse was maintained by regular palpation for rate rhythm and volume. Blood pressure was monitored every five minutes .Standard lead II was used for continuous ECG display. The respiration of the patients was monitored clinically by observation of the respiratory rate, chest expansion and auscultation of chest for breath sound. Oxygen saturation and pulse rate were also continuously displayed by the pulse oximeter using a finger probe. At the completion of surgery the anaesthesia was turned off and patient was shifted to recovery.LMA was removed in the recovery when patients followed the verbal commands. A trained anaesthesia resident unaware of the nature of the study drugs observed the patients and maintained data for the frequency of nausea &vomiting or any side effects of drugs for six hours in the postoperative periods. A rescue anti emetic Ondansetron I/V given if patient remained nauseous for more than 15 minutes or experienced vomiting two or more than two episodes

Statistical analyses were performed using SPSS (Statistical Package for Social Sciences) version 20. Quantitative variables were expressed as mean + SD (standard deviation), while qualitative variables were expressed as percentage. Age, weight and duration of surgery were analyzed by using student t-test, while ASA physical status, frequency of nausea and vomiting

TABLE 1.
DEMOGRAPHIC DATA

Variables	Metoclopramide group (Mean ±SD)	Combination group(Mean ±SD)	p value
Age(years)	24.42±6.64	24.63±7.19	0.609
Weight (kg)	53.88±6.98	50.89±8.76	0.887
Duration of surgery(mints)	27.61±9.19	30.19±8.76	0.525
Time to recovery(mints)	6.37±1.34	10.91±1.36	0.762

TABLE 2.
COMPARISON OF RESULTS

PONV	Metoclopramide group (n=64) Number of patients& percentage	Combination group (n=64) Number of patients &percentage(n=64)
No nausea and vomiting	50 (78.1%)	61 (95.3%)
Vomiting	8 (12.5%)	1 (1.6%)
Nausea	4 (6.2%)	2 (3.1%)
Nausea and vomiting	2 (3.1%)	0 (0%)

TABLE 3.
COMPARISON OF COMPLICATIONS

Complications	Metoclopramide group (n=64) (number of patients & percentage)	Combination group (n=64) (number of patients & percentage)
No complication	48 (75%)	52 (81.2%)
Headache	6 (9.4%)	4 (6.2%)
Dizziness	6 (9.4%)	5 (7.8%)
Sedation	0 (0%)	1 (1.3%)
shivering	2 (3.16%)	0 (0%)
restlessness	2 (3.1%)	2 (3.1%)

were analyzed by using chi-square test. P-value less than 0.05 were considered significant.

RESULTS

There were no significant difference between the two groups with regards to mean age, weight, length of surgical procedure and time to recovery. (Table1)

Out of 64 patients in Metoclopramide group (n=50) 78.1 % did not have nausea vomiting postoperatively while (n=4) 6.2% experienced nausea, (n=8) 12.5% vomiting and(n=2) 3.1% both nausea and vomiting

Out of 64 patients in combination group (n=61) 95.3 % did not have nausea vomiting postoperatively while (n=2) 3.1% experienced nausea, (n=1)1.6% vomiting

P value for two tailed asymptotic test was <0.016

for Metoclopramide vs. combination group. Reduction of PONV induced by Metoclopramide vs. combination group was statistically significant.

Ondansetron was used as rescue antiemetic. 5 patients 7.8% in Metoclopramide group received anti emetic while one patient 1.6% in combination group. This was found to be statistically significant. P value 0.042(Table2)

48 patients were free from side effect in Metoclopramide group and 52 patients were free from side effect in combination group. Incidence of side effect in Metoclopramide group headache (n=6) 9.4% dizziness (n=6)9.4%, shivering (n=2) 3.1%and restlessness (n=2) 3.1%.In combination group headache (n=4) 6.2%, dizziness (n=5)7.8%sedation (n=1) 1.3%and restlessness (n=2)3.1%. (Table3)

DISCUSSION

The corticosteroid Dexamethasone effectively prevents nausea and vomiting in postoperative patients. A prophylactic dose of 4 to 5 mg IV for patients at increased risk for PONV is recommended after anesthesia induction rather than at the end of surgery.[16] For PONV prophylaxis, the efficacy of Dexamethasone 4 mg IV is similar to Ondansetron 4 mg IV and droperidol 1.25 mg IV. Mechanism of antiemetic action of Dexamethasone is not exactly known till yet but it may involve central inhibition of prostaglandin and it also reduces the level of 5- hydroxyl tryptophan in neural tissue by depleting its precursor tryptophan. In our study 78.1% patient was free from nausea and vomiting and in combination group 95.3% patients was free from nausea and vomiting in day care breast surgery. In comparison combination of Metoclopramide and Dexamethasone is found superior to Metoclopramide (free from PONV are 95.3% vs 78.1).Usha Daria et al [17]also did study on Metoclopramide and combination with Dexamethasone. He also found that combination of Metoclopramide and Dexamethasone is superior to Metoclopramide (free from PONV are 73.3% vs 36.7%) but their result is low as compared to our result. Combination of Ondansetron & Dexamethasone found superior to Ondansetron alone (no PONV is 90% vs 63.7%) as studied by Rajeev et al[18] and Lopez-Olando L.et al[19]. Similarly combination of Granisetron & Dexamethasone is also found superior to Granisetron alone (success rate is 90% vs 67.7%) Splinter and Roberts[20] evaluated the effect of Dexamethasone on vomiting after elective tonsillectomy and found that Dexamethasone reduced the overall incidence of vomiting from 72% (placebo) to 40%. Biswas et al[21] reported only 20% incidence of PONV with Dexamethasone alone. Frikha et al [22] used Metoclopramide alone and in combination with Dexamethasone as a prophylactic antiemetic in elective cesarean section, found 83% of patients free from nausea and vomiting Metoclopramide group and 86% of a patients was free from nausea and vomiting in combination group.Entezariasl.M et al [23] used Dexamethasone and Metoclopramide and he found the incidence of nausea with metoclopramide plus dexamethasone was 8% versus 44% with placebo. Essam. M et al [24] used Metoclopramide alone and in combination with Dexamethasone in maxillofacial procedures, the number of patients with complete response to prophylactic antiemetic medication was significantly higher in in combination group 90.4% vs75%.The results from Frikha, Entezariasl and Essam are more or less same as compare to our result.

CONCLUSION

Breast surgery is associated with a high incidence of post-operative nausea & vomiting and it is not effectively reduced by using prophylactic Metoclopramide alone. Combining Metoclopramide with Dexamethasone is more effective in reducing PONV as compared to Metoclopramide alone and therefore combination can be recommended as a prophylaxis for PONV in females undergoing breast surgery.

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Authors contribution:
* Study design, proforma design, data assesment , manuscript writing, references
** Data collection, patients monitoring

Conflict of interest: The authors declare no conflicts of interest.