Original Article

Single Dose of Dexamethasone for Prevention of Nausea and Vomiting After Major Gynaecological Surgery

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ABSTRACT

BACKGROUND: Post-operative nausea and vomiting (PONV) is a common complications following general anaesthesia and is a leading cause of morbidity following surgery . The mainstay of management them is by the use of antiemetic.

METHOD: It was a randomized double blind placebo controlled study. The sample size was calculated as 90 from previous study with 10% attrition to make the 100. They were randomly divided into two groups; group B received dexamethasone prophylactically at induction while group A received placebo also at induction. All patients had balanced general anaesthesia and were taken to the recovery room postoperatively where incidences of postoperative nausea and vomiting were recorded. Patients with incidences of nausea and vomiting were treated with 10mg metoclopramide intravenously while postoperative complications that may be associated with dexamethasone prophylaxis were also noted.

RESULTS: The groups were comparable with respect to demographic characteristics. More patients in group A(placebo group)) had incidence of nausea than group B (dexamethasone group) with p value of 0.01 and also more patients in group A had vomiting than group B with p value of 0.02; which was significant. The duration of stay in the recovery room for both groups A and B were however comparable with no statistical difference.

CONCLUSION: Dexamethasone when given prophylactically at induction reduces incidence of postoperative nausea and vomiting after gynaecological surgeries.

KEYWORDS: Postoperative nausea (PONV), Dexamethasone, prophylaxis, gynaecology.

Date Accepted for publication: 8th July, 2013
NigerJMed 2013: 207-211

INTRODUCTION

Post-operative nausea and vomiting (PONV) is one of the commonest complications following general anaesthesia and is a leading cause of morbidity following surgery. It can also result in morbidities such as wound dehiscence, bleeding, pulmonary aspiration of gastric contents, fluid and electrolyte disturbances, oesophageal tear (Mallory Weiss syndrome), delayed hospital discharge, unanticipated hospital admission following day case surgery, and patient dissatisfaction post surgery[1]. Studies and meta-analysis of PONV show high variability in PONV rates. Overall incidences of postoperative vomiting range from 12% -26%[1].

Dexamethasone is a synthetic glucocorticoid whose antiemetic mechanism is not known. Dexamethasone prevents the development of the inflammatory process by suppression of neutrophil migration, decreased production of inflammatory mediators and reversal of increased capillary permeability[2].There is no singular aetiology for PONV. It is multifactorial in nature; however contribution of each factor may differ depending on the clinical situation. Some are related to patient factors, surgical procedures and/or the anaesthetic technique used. It includes age; Amponsah[3] in a study of postoperative nausea and vomiting in children between ages of a month and 16years reported the incidence to be 18 %.. Cohen et al[4] showed that incidence of vomiting is no doubt higher in paediatric age group when compared to adults. Women because of the high serum gonadotrophin level have three times the risk for PONV compared to men[5]. The risk of PONV is increased if anaesthesia is induced in a patient with recently ingested food and in those with delayed gastric emptying [6]. In obese patients, the larger adipose tissue is a reservoir for inhaled anaesthetic agents and may contribute to PONV even when their administration has been discontinued[1].

Patients with history of motion sickness and/or PONV in previous surgery are more susceptible to PONV than those without history[1]. Some factors predisposing to PONV that are surgical related includes the following conditions e.g. raised intracranial pressure, upper gastro-intestinal obstruction, pregnancy may be associated with PONV[1]. The incidence of PONV after general anaesthesia is influenced by the type of surgical procedure, irrespective of the anaesthetic technique used [6]. others includes duration of surgery, Oduntan et al[7] in Ibadan reported that patients with surgery lasting for more than three hours had a 5.1% incidence of PONV. Anaesthesia related factors predisposing to PONV includes opioids, inhalation agents notably halothane, nitrous oxide, neostigmine and intravenous induction agents like ketamine. The potential risk of PONV after regional technique is lower when compared to general anaesthesia except when intraoperative and

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postoperative opioids are administered, and then the difference is narrowed[8].

METHODOLOGY

This was a randomized double blind placebo control study over a 6 months period. Following approval of the hospital ethics committee consecutive patients aged 18-65 years ASA 1 and 11 scheduled for elective gynaecological procedures under general anaesthesia were studied after signing informed consent. Patients requiring insertion of nasogastric tubes intra or postoperatively were excluded from the study. The sample size was calculated as 90 from previous study with 10% attrition to make 100.The patients were randomly assigned into two groups for the treatment of PONV by using table of random numbers. Group A received placebo (2mls of 0.9% normal saline), while group B received dexamethasone at a dose of 4mg/2mls. An anaesthesia resident and a pharmacist in the hospital prepared the medications in 2mls syringes, A containing 2mls normal saline and B containing 2mls of 4mg of dexamethasone while the researcher was blinded. At induction of anaesthesia the contents of the labelled syringes were administered to patients by the researcher according to the alphabets A and B assigned to the patients. All patients had balanced general anaesthesia and were transferred to the recovery room. Postoperative analgesia was with 100mg tramadol and the incidence of PONV was recorded in the first three hours postoperatively. Patients were discharged from recovery room when vital signs were stable and neither nausea nor vomiting was experienced. Information on postoperative nausea and vomiting was also taken from patients using the questionnaire design. Patients were subsequently assessed by the blinded investigator with vomiting classified as mild if it is occurs once, moderate if the incidence is between one and three and severe if more than three.

Patients who experienced nausea and vomiting were treated with 10mg metoclopramide intravenously as a rescue medication, while postoperative complications resulting from dexamethasone prophylaxis were also noted.

STATISTICAL ANALYSIS

The data were analysed using Statistical Package for Social Sciences (SPSS) version 16 . Data description was by use of means and standard deviation for continuous variables; frequency and percentages for categorical variables. Measure of association was determined using the chi-square test for categorical variables and the ANOVA and student t test for continuous variables. Where appropriate data was presented using tables and bar charts. A two sided p-value of less than 0.05 was considered significant.

RESULTS

One hundred patients participated in this study but four were disqualified for the following reasons: two had severe postoperative haemorrhage which required re-exploration, one had failed intubation and surgery was cancelled while the fourth had severe hypertension postoperatively necessitating the use of hydralazine intravenously in the postoperative period. Therefore only data from ninety six patients were analyzed.

Assessment of incidence of nausea and vomiting

Patients in group A (placebo) had more incidence of nausea than those in group B (dexamethasone) 31 vs. 2 (p =0.01). Also group A had more incidence of vomiting than B; 27 vs 4 (p =0.02).

TABLE 1: COMPARISON OF INCIDENCE OF NAUSEA BETWEEN STUDY GROUPS

INCIDENCE OF NAUSEA	GROUP A	GROUP B	P value
Incidence of nausea. Mean (%)	31(67.4)	2(4.2)	0.01

TABLE 2: COMPARISON OF INCIDENCE OF VOMITING BETWEEN STUDY GROUPS

INCIDENCE OF VOMITING	GROUP A	GROUP B	P value
Incidence of vomiting. Mean (%)	27(57.4)	4(8.3)	0.02

Assessment of severity of vomiting between study groups

In group A, 25 patients had mild vomiting, one had moderate while none had severe vomiting while in group B only 4 patients had mild vomiting while none had moderate or severe vomiting (Table 3).

TABLE 3: COMPARISON OF SEVERITY OF VOMITING BETWEEN STUDY GROUPS

SEVERITY	GROUPA	GROUPB	P VALUE
NONE	22	44	0.001
MILD	25	4	
MODERATE	1	0	
SEVERE	0	0	

Comparison of surgical procedures between study groups

A total of 22 and 15 patients in groups A and B respectively had total abdominal hysterectomy while 26(group A) and 33(group B) had myomectomy. The surgical procedures were comparable in both groups with no significant difference. (Table 4)

TABLE 4: COMPARISON OF SURGICAL PROCEDURES BETWEEN STUDY GROUPS

TYPE OF SURGERY	GROUP A	GROUP B	P VALUE
TOTAL ABDOMINAL HYSTERECTOMY	22	15	0.21
MYOMECTOMY	26	33	0.24
TOTAL	48	48	

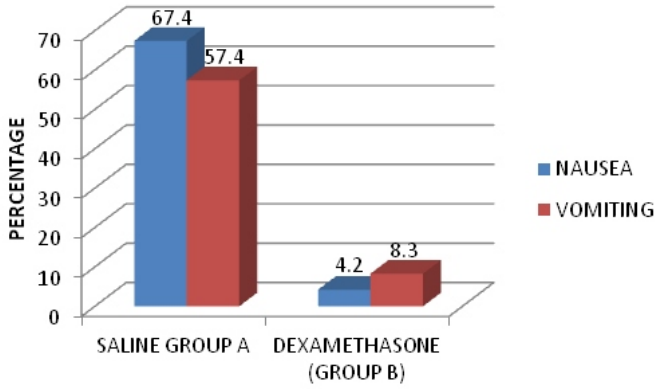
Comparison of duration of surgery and stay in the recovery room

Table 5 shows that the duration of surgery and duration of stay in the recovery room was comparable in both groups.

TABLE 5: COMPARISON OF DURATION OF SURGERY AND STAY IN THE RECOVERY ROOM

DURATION OFSURGERY	GROUP A	GROUP B	P value
DURATION OFSURGERY	2.72(0.23)	2.6(0.3)	0.08
STAY INRECOVERY	2.90(0.19)	2.84(0.28)	0.29

FIGURE 1: BAR CHART SHOWING INCIDENCES OF NAUSEA AND VOMITING



DISCUSSION

This study has shown that dexamethasone is an effective prophylactic agent for postoperative nausea and vomiting in patients undergoing gynaecological surgery. From the onset of this study, a high incidence of PONV was anticipated considering the tetrad of female gender, gynaecological surgery and intraoperative use of halothane and tramadol, these being the predisposing factors[2, 3, 4]. This setting was therefore provided to test clinical efficacy of dexamethasone in preventing PONV. The incidence of post operative nausea and vomiting was higher in the saline group than the dexamethasone group.

The above finding is in keeping with that of Guptal[9] et al and Rimaitis [10]et al in two different studies where they found the incidence of postoperative nausea and vomiting to be low in patients who had pretreatment with dexamethasone before gynaecological procedures. Zhang et al[11] also in their study that investigated the incidence and influential factors of PONV following gynaecologic surgery found out that previous PONV will increase the risk of recurrence . They also found out that perioperative opioids administration will intensify the risk for the development of PONV within 24hours following surgery, while general anaesthesia and postoperative shivering increases the risk within 6 hours after surgery.

They concluded that perioperative dexamethasone decreases the incidence of PONV within 6hours or 24hours following gynaecologic procedures.[12] This is also in agreement with other multicentre studies[13, 14] and a systematic review[15] which demonstrated that this drug is effective in preventing PONV and also in patients receiving cancer chemotheraphy[16].

Several dose response studies have also been carried out to determine the minimum effective dose of dexamethasone needed for anti-emetic prophylaxis. The various peri-operative doses of dexamethasone that have been tried so far are 2.5mg, 5mg, 4mg and 8mg[14]. The last two doses are the commonly used[11] hence the rationale for employing dose of 4mg in our study. Kiu et al[17] in their study observed 2.5 mg to be the minimum effective dose for preventing PONV in patients undergoing major gynaecological surgery, and in patients experiencing nausea and vomiting associated with epidural morphine[18]. The timing of dexamethasone administration has been shown to have some association with its effectiveness as a prophylactic anti-emetic. Wang et al observed that dexamethasone is most effective for preventing PONV when it is administered immediately before induction of anaesthesia rather than near the end of anesthesia[19]. Our study like that of Wang pre-induction administration of dexamethasone had similar result like that of Thomas et al where dexamethasone was administered after induction[20].

In this study a placebo was used as a comparator, but there exists the options of using either a contemporary standard drug and or placebo as a comparator. Thomas et al argue that it is unethical to protect a group when all patients are actually exposed to the same high risk procedure [20]; the risk here being nausea and vomiting. However one of the contemporary drugs in our setting that may be considered as a standard anti-emetic is metoclopramide. Beattie et al [21] and Huang et al[12] independently found that metoclopramide is not effective as an anti-emetic at its current peri-operative dose of 10mg IV. Henz and Tramer in one of their meta-analysis also confirmed this but they say at this dose, it is only effective as an anti-nauseant[22]. They declared that metoclopramide is unfit to be used either as a control or a comparator in clinical trials[22].W Beattie in its editorial declared that until its effective peri-operative dose is determined, it cannot be considered a fair comparator in research trials[21].

Halothane was used as the maintenance agent because it is the most readily available inhalational agent in our

environment, though it causes more emesis than Desflurane and sevoflurane which are not readily available[9].

Though tramadol an opioid was used as postoperative analgesic in the present study it could not have accounted for the high incidence of vomiting in the control group as both groups were given the same dose of tramadol. A retrospective analysis of 492 patients who had gynaecological surgeries identified history of PONV and peri-operative opioid administration as significant predictors of PONV within 24 hours following gynaecologic surger[11].The analysis also found history of PONV, general anaesthesia, and postoperative shivering to be predictors of PONV within 6 hours of surgery, and the preoperative administration of dexamethasone consistently protective against PONV within 6 hours or 24 hours following gynaecological surgeries[11].

This study did not identify any complication associated with dexamethasone use; it is in keeping with other studies that concluded that most of the complications following dexamethasone use occur as a late complication usually after 24 hours post surgery. Postoperative infection is one of the complications following use of dexamethasone though this was refuted by Corcoran et al [23] where they were not able to demonstrate an association between anti-emetic doses of dexamethasone and postoperative infection in 439 patients studied. The risk of postoperative infection could however not be ascertained with the present design because it is limited to only 3 hours postoperative period.

Other documented complications like headache, dizziness, drowsiness, constipation, sedation and muscle pain[23, 24] were not also observed in our study for similar reasons.

CONCLUSION

This study has shown that compared to placebo a single intravenous dose of 4mg dexamethasone given at induction of anaesthesia is clinically effective in preventing postoperative nausea and vomiting in women who had gynaecological surgeries under general anaesthesia. The incidence of postoperative nausea and vomiting was therefore high in those who did not have dexamethasone prophylaxis. It has also shown that dexamethasone prophylaxis does not increase the duration of stay in the recovery room.

RECOMMENDATIONS

Based on the finding from this study and some other multicenter studies that dexamethasone has clinically important peri-operative anti-emetic effects . Its use for prophylaxis against PONV in patients undergoing gynaecological surgeries under general anaesthesia should be encouraged. In addition it is cost effective and not associated with hangover effects . It can be given pre-induction as an anaesthetic premedicant or as an overnight dose since its biological half life is about 36-72hours[15]. No complication associated with dexamethasone was noted in this study, however since most of its complications occur latter than 3hours, a study with longer duration is recommended to ascertain this.

LIMITATION/STRENGTH OF THIS STUDY

Some of the limitations of this study include the study period (3hours) which only captured patients with early postoperative nausea and vomiting and the use of dexamethasone in patients who had regional anaesthesia were not studied . The incidence of PONV may have been higher than obtained if this period was more than 3hours. Also most of the patients had difficulty in classifying the severity of nausea. Tramadol; a proemetic agent was used as analgesic for all patients thereby increasing the strength of this study in evaluating the effectiveness of dexamethasone in preventing PONV considering this pro-emetic milieu.

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