ORIGINAL ARTICLE

Prophylactic use of gabapentin to reduce postoperative nausea and vomiting in patients undergoing diagnostic gynecological laparoscopy

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ABSTRACT

Introduction: Postoperative nausea and vomiting (PONV) occurs in patients during the first 24 hours of the surgery. Many drugs have been used for the prevention and treatment of PONV. In this trial, we used gabapentin to evaluate its prophylactic effect in reducing the severity and incidence of PONV in patients undergoing diagnostic laparoscopic gynecological surgery.

Methodology: This, double blind randomized controlled trial, was done in operation theatre complex over a period of six months.140 patients undergoing diagnostic gynecological laparoscopic surgery were selected. Two groups were formed and 70 patients were recruited in each group using lottery method as method of randomization. Group C (control group) was given placebo medication orally two hours before surgery and group G (gabapentin group) received 600 mg of gabapentin orally two hours before the procedure. Standard general anesthesia technique was used in all patients and incidence and severity of postoperative nausea and vomiting (PONV) was recorded in these patients till 24 hours of laparoscopy.

Results: Severity of PONV was graded from mild to severe. There was no PONV in 25 patients (35.7%) in group C and 47 patients (67.1 %) in group G. It was mild in severity in 8 patients (11.4 %) in group C and 5 patients (7.1 %) in group G, moderate in 31 patients (44.3 %) in group C and 15 patients (21.4 %) in group G and severe PONV was seen in 6 patients (8.6%) in group C and 3 patients (4.3 %) in group G (P=0.003). Postoperative nausea and vomiting within 24 hours after procedure was present in 45 patients (64.3%) in group C and 23 patients (32.9%) in group G. Results were significant between two groups after statistical analysis with p value of 0.001.

Conclusion: Administration of 600 mg of gabapentin two hours before diagnostic gynecological laparoscopy decreases the frequency and severity of PONV.

Key words: Postoperative nausea and vomiting, Gabapentin, Diagnostic Gynecological Laparoscopy.

Citation: Khan MA, Siddiqi KJ, Khan MS. Prophylactic use of gabapentin to reduce postoperative nausea and vomiting in patients undergoing diagnostic gynecological laparoscopy. Anaesth Pain & Intensive Care 2017;21(1):19-24

Received: 30 Jan 2017; **Reviewed:** 9 Mar 2017; **Corrected:** 12 Mar 2017; **Accepted:** 20 Mar 2017

INTRODUCTION

Postoperative nausea and vomiting (PONV) is commonly seen in operated patients in first 24 hours of surgery and anesthesia. It is a complex problem and its rate is increasing in surgical patients.[1] Despite the use of better anesthetics and perioperative medications[2] and improvement in operative technique,[3] there is still an unacceptable frequency of PONV with an incidence up to 85 % reported in some studies.[4] The incidence is more than 50% after day case gynecological laparoscopy.[5] Laparoscopy is considered an important risk factor for PONV. Fe-

male gender,use of opioids in perioperative period and history of previous PONV, motion sickness and smoking are also considered important aetiological risk factors.[6-8] PONV has various adverse effects on outcome of the patients. It can aggravate pain and can result in unplanned hospital admission. It can increase the risk of pulmonary aspiration leading to aspiration pneumonia and recurrent vomiting can cause dehydration and electrolyte imbalance.[5] Due to all these hazardous effects, PONV in patients undergoing day case surgeries can cause severe economic problems by delaying their hospital discharge.[9]

Various strategies are used to reduce the occurrence of PONV. These include use of single or multiple prophylactic antiemetic agents, modifying anesthetic technique or applying all of them in a multimodal approach to achieve maximum protection.[4,10]

Prophylaxis of PONV means administration of an antiemetic drug before the start of surgery or during the surgery. Commonly used antiemetic drugs are metoclopramide, cyclizine, droperidol, ondansetron and dexamethasone. These drugs decrease the incidence of PONV by 50%.[11-15] However, despite use of all these agents, many anesthetists still face this problem in their patients.

Gabapentin, an antiepileptic drug, was introduced in clinical practice in 1993. It is similar in structure to gamma amino butyric acid (GABA).[16] Antiemetic effect of gabapentin was indicated by a clinical trial in which it was used for treatment of chemotherapy induced nausea and vomiting in patients of breast cancer.[17] In another study, it was used as prophylactic antiemetic in patients undergoing laparoscopic cholecystectomy. This study showed that the incidence of PONV was significantly lower in patients of gabapentin group versus in patients receiving placebo.[18]

In our study, we hypothesized that prophylactic use of 600 mg of gabapentin two hours before anesthesia would decrease the incidence and severity of PONV in high risk group of patients undergoing elective gynecological laparoscopic surgery.

Primary objectve was to determine the efficacy of gabapentin as prophylactic antiemetic to reduce the rate and severity of postoperative nausea and vomiting (PONV) in patients undergoing elective diagnostic laparoscopy for gynecological problems. Secondary objective was to determine the frequency of use of rescue antiemetic (Ondansetron) for management of PONV and consumption of opioids for treatment of postoperative pain.

METHODOLOGY

This randomized double-blind controlled trial was done in operation theatre complex of hospital over a period of almost six months. Approval from institutional review board was obtained and 140 female patients of ASA I & ASA II physical status, aged 20-40 years, scheduled for elective diagnostic gynecological laparoscopy for problems of infertility, chronic pelvic pain and ectopic pregnancy were included in the study. Two groups were formed having 70 patients in each group. Study group was labelled as Group G and control group was labelled as group C. All patients were explained about the study and consent was obtained from them. The calculated sample size, with 10% margin of error and 80% power of study with magnitude of prevention of PONV by gabapentin in previous studies (i.e. 62.2%) , was 140 patients. The patients having history of cardiovascular diseases, acid peptic disease, epilepsy, renal or hepatic diseases, coagulopathy and patients on antidepressants or calcium channel blockers were excluded from the study. The patients sensitive to any drug and not willing for study were also not included. Lottery method was used as method of randomization to allot 70 patients to each group and a randomization list was generated. The capsules containing gabapentin and placebo were identical and were prepared by the pharmacy. Study group G (70 patients) received 600 mg of gabapentin orally two hours before induction of anesthesia and control group C (70 patients) received capsules containing placebo (starch powder) orally two hours before anesthesia. Patients, researcher and staff nurse in postanesthesia care unit (PACU) were all blinded to treatment groups.

Following were the variables in this study; Ages and weights of the all patients to be recorded in data forms. Following were the dependent variables which were to be recorded by designated staff nurse of PACU till 24 hours of anesthesia. She was blinded of treatment groups.

1- Incidence and severity of PONV was graded as;

Absent = Absence of any episode of nausea or vomiting

Mild = One episode of Vomiting with short lasting nausea of less than 10 minutes and no antiemetic required.

Moderate = 1-2 episodes of Vomiting with moderate nausea and one-time antiemetic used for this.

Severe = More than 2 episodes of Vomiting with severe nausea and antiemetic used for each episode.

2- Use of rescue antiemetic (ondansetron 0.1 mg/Kg).

3- Use of rescue analgesia for postoperative pain (nalbuphine 0.05 mg/Kg).

Anesthetic technique was standardized for both the groups. Standard general anesthesia was administered to all patients. Induction of anesthesia was achieved with Propofol 2 mg/kg and nalbuphine 0.15 mg/kg intravenously (IV). Atracurium besylate 0.5 mg/kg was given intravenously to achieve muscle relaxation for tracheal intubation. Bag mask ventilation continued for three minutes with 50% oxygen in nitrous oxide and isoflurane 0.6% through closed circuit with fresh gas flow at 6 lit/min. Tracheal intubation was done with 7.5 mm endotracheal tube. 40% oxygen in nitrous oxide, isoflurane 0.6 - 1.0 % and fresh gas flow rate @ 3 liters per minute was used for maintenance of anesthesia. Intermittent boluses of 10 mg of atracurium besylate were given to maintain muscle relaxation. Maintenence and deficit fluid was replaced using Ringer's lactate according to weight of the patients. When laparoscopic procedure finished and there were two twitches on train of four on nerve stimulator, the patients were reversed with neostigmine 2.5 mg and glycopyrrolate 0.4 mg intravenously. ECG, pulse oximetry, noninvasive blood pressure, end tidal capnography and neuromuscular function monitor were used for monitoring of all patients. Nalbuphine 0.05 mg/kg two hourly was used intravenously for treatment of postoperative pain. Ondansetron 0.1 mg/kg intravenously was used as rescue antiemetic for any episode of PONV within 24 hours of surgery.

In PACU, patients were assessed 4 hourly by the staff nurse who was blinded of groups and information of incidence and severity of PONV (no, mild, moderate & severe) , use of rescue antiemetic and supplemental analgesic requirements were recorded by her in data forms till 24 hours.

Statistical Analysis: At the end of study, all the information collected was entered and processed in SPSS 10.0 for statistical results. The qualitative variables such as postoperative nausea and vomiting and rescue antiemetic use were presented as percentages and frequencies. Quantitative variables such as age, weight and number of times rescue analgesia used were presented as mean and standard deviation. Chi-square test was applied as test of significance and a p-value of < 0.05 was considered significant.

RESULTS

All 140 patients undergoing diagnostic gynecological laparoscopy completed the study with 100% participation from both groups (Table 1).

All the patients were 20 to 40 years of age with means of 28.56 ± 4.15 years in group C and 28.59 ± 4.18 years in group G. Weights of patients were from 45 to 77 kg and mean weight was 60.16 ± 7.14 kg in group C and 57.30 ± 6.7 kg in group G (Table 2).

PONV was absent in 25 (35.7%) patients in group C and 47 (67.1%) patients in group G. It was mild in severity in 8 (11.4%) patients in group C and 5 (7.1%) patients in group G. Moderate PONV was observed in 31 (44.3%) patients in group C and 15 (21.4%) patients in group G. It was severe in 6

Table 1: Distribution of patients according to groups

*Group	Frequency (n)	Valid Percentage	Cumulative Percentage
G	70	100	100
C	70	100	100
Total	140	100	

*G= Gabapentin Group, C= Control Group

Table 2: Demographic data of patients

Parameter	Group C (Placebo)			Group G(Gabapentin)		
	Minimum Value	Maximum Value	Mean ± SD	Minimum Value	Maximum Value	Mean ± SD
Age (years)	20	40	28.56 ± 4.15	20	40	28.59 ± 4.18
Weight(Kg)	45	77	60.16 ± 7.14	45	77	57.30 ± 6.7

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Table 3: Distribution of cases by severity of PONV

Grade of Severity	Group C (Placebo) n (%)	Group G (Gabapentin) n (%)	Statistical analysis
No	25 (35.7)	47 (67.1)	Chi Square = 13.980, df = 3 , P value = 0.003
Mild	08 (11.4)	05 (7.1)	
Moderate	31 (44.3)	15 (21.4)	
Severe	06 (8.6)	03 (4.3)	

Table 4: Use of rescue antiemetic, PONV within 24 hours and Rescue analgesia used

Variables	Group C n (%)	Group G n (%)	Chi- Square	P Value
Rescue Antiemetic used	37 (52.9)	17 (24.3)	12.05	0.001
PONV within 24 hours	45 (64.3)	23 (32.9)	13.84	0.001
Times rescue analgesia used 1-2 Times	15 (21.4)	63 (90)	66.70	≤ 0.001
3-4 Times	55 (78.6)	07 (10)		

(8.6%) patients in group C and 3 (4.3%) patients in group G. Results were significant as p value was 0.003 (Table 3).

The rescue antiemetic (ondansetron) was used in 37 (52.9%) patients in group C and 17 (24.3%) patients in group G. So results were statistically analyzed and found significant with p value of 0.001 (Table 4).

Postoperative nausea and vomiting within 24 hours was present in 45 (64.3%) patients in group C and 23 (32.9%) patients in group G with p value of 0.001 (Table 4).

Rescue analgesia was used 1-2 times in 15 (21.4%) patients in group C and 63 (90%) patients in group G. In group C, rescue analgesia was used 3-4 times in 55 (78.6%) patients. While 7 (10%) patients in group G received rescue analgesia 3-4 times. So results were significant with p value of 0.001 (Table 4).

DISCUSSION

Laparoscopic surgery is commonly performed, especially for diagnostic purposes in gynecological patients. Most of these gynecological laparoscopic procedures are done routinely on day case basis and are short in duration. However, certain postoperative problems like nausea & vomiting and pain can delay the discharge of these day case patients from the hospital. The trials have proved that postoperative nausea and vomiting (PONV) is common after anesthesia and surgery and its overall incidence is from 28-30%.[19]

Our study also showed a lower incidence and severity of postoperative nausea and vomiting in diagnostic laparoscopy in gynecological patients who received 600 mg of gabapentin two hours before anesthesia than those who received placebo (32.9% vs 64.3%).

Causes of postoperative nausea and vomiting after gynecological laparoscopy are not clear but might be associated with operative factors. The most important factor is intraperitoneal CO2 insufflation which causes peritoneal stretching and irritation.[20] Other factors having affect on PONV are age, female gender, obesity, technique of anesthesia, presence of pain, use of opioid for pain management and type and duration of surgery.[21] In our study, the duration of surgery was also short which might decrease the incidence of PONV and mean ages were 28.56±4.15 in group C and 28.59±4.18 in group which indicated that our patients were from high risk group as incidence of PONV is maximum in this young age group. Apfil et al demonstrated in a study that female gender, previous history of motion sickness & PONV, smoking and use of opioids for treatment of postoperative pain increased the incidence of PONV by 10-21%, 39%, 61% and 79% respectively.[22]

In our study all patients were nonsmokers and there was no history of motion sickness and there was no gender difference. So both groups were comparable regarding this.

In a trial, Guttuso et al used gabapentin as antiemetic for treatment of acute and delayed onset nausea and vomiting induced by chemotherapy. They used oral 300 mg of gabapentin twice daily in nine patients who were receiving chemotherapy for breast cancer. Six patients showed great improvement on incidence of nausea and vomiting while there was complete resolution in three patients.[16]

Pandey et al conducted a randomized control trial in which 600 mg of gabapentin was used two hours before anesthesia for prevention of postoperative nausea and vomiting in patients undergoing for laparoscopic cholecystectomy. It was seen that patients of gabapentin group had quite lower incidence of PONV within 24 hours than placebo group (37.8% vs 64%).[17]. Our study also showed similar results with decrease in incidence of PONV within 24 hours in gabapentin group as compared to placebo group (32.9% vs 64.3%) but we used same dose of gabapentin in young female patients of diagnostic gynecological laparoscopy who were high risk group for PONV. This fact further encouraged its use in day case young patients because effective control of PONV would help in timely discharge of these patients from the hospital.

Apart from its antiemetic effect, different studies have shown that gabapentin reduced the pain scores and opioids requirements in surgically operated patients.[23,24] Our study also showed that opioids requirements were quite less in gabapentin group as compared to control group. As use of opioids for postoperative pain is an important risk factor for PONV, so less opioid use in gabapentin group might also decrease the occurrence and severity of PONV in these patients. Our study also showed that there was no discernible effect on somnolence in gabapentin group. So due to all these reasons, it can be used safely in day case young patients.

CONCLUSION

Prophylactic use of 600 mg of gabapentin two hours before diagnostic gynecological laparoscopy decreases the incidence and severity of postoperative nausea and vomiting and it also decreases the opioids requirements. Therefore, gabapentin can be given preoperatively for its antiemetic and analgesic effects as it was well tolerated by all patients in this study.

Conflict of interest: Nil

Author contribution: All authors took part in design, planning, conduct of the study and data collection, literature review and manuscript preparation

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