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A STUDY OF PROPHYLACTIC GABAPENTIN FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING LAPAROSCOPIC CHOLECYSTECTOMY

Anaesthesiology

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ABSTRACT

Introduction: Postoperative nausea and vomiting (PONV) has been variously described as the big little problem, the final therapeutic challenge for any anaesthesiologist.

Aims and Objectives: The main aim of this study is to evaluate and compare the antiemetic effects of gabapentin and ondansetron for prevention of post operative nausea and vomiting (PONV).

Materials and methods: This study was carried out at Command Hospital (Eastern Command), Alipore, Kolkata (operation theatre and ward) between Jan 2018 – May 2019. Patients of either sex, ASA grade I and II, age between 20 to 60 years, body weight between 45 to 85 kgs, planned for Elective laparoscopic cholecystectomy were chosen. PONV in first 12 hours was measured at 1st hour, 3rd hour, 6th hour and 12th hour, and calculation was done based on study carried out by Apfel et al[1]. Taking an alpha error of 0.05 and a power of the study as 90%, the sample size was worked out as 100 (50 in each group).

Conclusion: The results demonstrated that for decreasing the incidence of PONV, prophylactic use of 600 mg of Gabapentin two hours prior to planned laparoscopic cholecystectomy is not superior to Ondansetron (which is the standard of care).

KEYWORDS

Prophylactic Gabapentin, Laparoscopic Cholecystectomy and Ondanstron.

INTRODUCTION

Postoperative nausea and vomiting (PONV) has been variously described as the big little problem[2,3], the final therapeutic challenge for any anaesthesiologist. The commonest cause of morbidity after anaesthesia and surgery are pain and PONV. Unrelieved pain is a common cause of PONV[4,5] and opioids used for pain relief also cause PONV[6].

In spite of extensive understanding of physiology of nausea and vomiting, and abundance of antiemetic medications, certain surgical procedures are associated with unacceptably high incidence of PONV. Laparoscopic surgery is one of them, which is popular for minimal invasiveness but associated with increased morbidity due to PONV.

Factors believed to contribute are :

- Rigorous decompression of abdomen by surgeon[7]
- Irritation of parasympathetic nerve endings in the abdomen
- Effect of carbon dioxide on the emetic centre[8]

Although regarded by medical and nursing staff as minor complication of anaesthesia and surgery, nausea and vomiting are a frequent cause of great distress to the patient. In a study, approximately three quarter of the patients being questioned, they rated freedom from nausea vomiting as their most important postoperative requirement. Patients were willing to accept dysphoria, loss of mental acuity and increased pain in order to avoid nausea and vomiting. In a questionnaire analysis, nausea was second only to failure to wake up, as a reason for fear of general anaesthesia[9].

Although unpleasant and embarrassing, PONV may occasionally lead to significant morbidity from dehydration, electrolyte imbalance, aspiration of vomitus and wound dehiscence. PONV may lead to prolongation of hospital stay and therefore increased expenses for surgery.

Vomiting continues to be a major challenge in postoperative care leading to PONV being the commonly occurring complication following anaesthesia and surgery. Prevention and treatment of PONV plays an important role in well-being of the surgical patients. Several factors are responsible for the etiology of PONV including the type and site of surgery, anaesthesia technique and gender. Now-a-days, laparoscopic procedure has become more popular compared to conventional open technique. Incidence of PONV is more in laparoscopic than in open technique. It is seen that nearly 53-72% of patients require antiemetic treatment after laparoscopic surgery, whereas the incidence of PONV in patients undergoing general anaesthesia for conventional surgery is 30%. The probable cause of PONV in laparoscopic surgery is peritoneal stretching due to intraperitoneal CO_2 insufflation.

Gabapentin is an anticonvulsant which has anti-nociceptive and anti-hyperalgesic properties. It is a structural analog of gamma amino butyric acid (GABA). It does not bind with plasma proteins and is not metabolized in humans. After a single oral dose of 300 mg, mean maximum plasma concentration is attained in 2 - 3 hours. Absorption kinetics of gabapentin is dose-dependent due to a saturable transport system. The bioavailability of a single 300mg oral dose of gabapentin is 60% which decreases with increasing dose. Elimination of gabapentin is by renal clearance and elimination half-life is about 5 - 7 hours after a single oral dose of 200mg - 400mg. Recently the anti-emetic effect of gabapentin was reported in chemotherapy-induced, acute (within 24 hours) and delayed onset (2 - 5 days) of nausea and vomiting in breast cancer. In this study, we will evaluate the antiemetic effect of gabapentin on the incidence and severity of PONV in patients undergoing elective laparoscopic cholecystectomy. There are several drugs used to prevent PONV like metoclopramide, ondansetron etc. which can have some severe adverse effects like extra-pyramidal symptoms. On the other hand, they do not decrease postoperative rescue analgesic requirements. In the study by Pandey et al.[10] on 250 patients scheduled for elective laparoscopic cholecystectomy, gabapentin as premedication effectively suppresses nausea, vomiting and post-operative rescue analgesic requirement. Therefore, a comparative study to test the hypothesis that oral gabapentin 600mg as premedication would decrease the incidence and severity of PONV in elective laparoscopic cholecystectomy.

The primary aim of this study is to evaluate and compare the antiemetic effects of gabapentin and ondansetron for prevention of postoperative nausea and vomiting (PONV).

Secondary Outcome: To note any adverse effects in either group.

MATERIALS AND METHODS

Study area: Command Hospital (Eastern Command), Alipore, Kolkata (operation theatre and ward).

Study population: Patients posted for Elective Laparoscopic Cholecystectomy.

Inclusion Criteria:

- Patients of either sex, ASA grade I and II.

- Age between 20 to 60 years.
- Body weight between 45 to 85 kgs.
- Planned for Elective Laparoscopic Cholecystectomy.

Exclusion Criteria:
- Patients who have not given consent.
- Patients with Bleeding Disorders / On Anticoagulant Medication.

Study period: Jan 2018 to May 2019

Study Time: First 12 hours post-operative, PONV measured at 1st hour, 3rd hour, 6th hour and 12th hour respectively.

Sample Size: 100, calculation based on study carried out by Apfel et al[1]. Taking an alpha error of 0.05 and a power of the study as 90%, the sample size was worked out as 100 (50 in each group).

Sample and Study Design: A comparative clinical study where patients are divided into 2 groups of 50 each.

Group A: Patients in this group received 600 mg of oral gabapentin 2 hours prior to surgery.

Group B: Patients in this group received 4 mg of IV ondansetron during the time of induction.

Parameters to be recorded: The subjects are allocated into 2 groups of 50 each.

1. Duration of Antiemesis: This is the time for requirement of first rescue antiemetic in post-operative period.
2. Grading of PONV as used in the study by Pandey et al[11]

a. No PONV: Absence of any emetic episode or nausea.
b. Mild PONV: The patient has only mild nausea or one emetic episode or short lasting nausea of any severity of less than 10 minutes which is triggered by exogenous stimulus, no antiemetic drug is required.
c. Moderate PONV: The patient has 1-2 emetic episodes or moderate or severe nausea without exogenous stimulus and patient requires antiemetic therapy once.
d. Severe PONV: The patient has more than two emetic episodes or suffers nausea more than twice and administration of at least one antiemetic is required.

3. Vital Parameters:
a. Heart Rate (HR)
b. Blood Pressure (BP)
c. SpO2
d. ECG
e. EtCo2 Monitoring

4. Side Effects observed were:
a. Hypotension
b. Respiratory Depression
c. Pruritus
d. Allergic Reaction

Plan for Data Analysis:
For statistical analysis, data were entered into a Microsoft Excel spreadsheet, then analyzed by SPSS (version 25.0; SPSS Inc., Chicago, IL, USA) and Graph Pad Prism version 5. Data has been summarized as mean and standard deviation for numerical variables, count and percentages for categorical variables.

Two sample t-tests were done for a difference in mean involved in independent samples or unpaired samples. Unpaired proportions were compared by Chi- square test or Fischer's exact test, as appropriate. p-value ≤ 0.05 was considered statistically significant.

Distribution of PONV after 1hr, PONV after 3hrs, PONV after 6hrs and PONV after 12hrs

		Group-A	Group-B	Total
PONV after 1hr	**NO PONV**	31	40	71
	Row %	43.7	56.3	100.0
	Col %	62.0	80.0	71.0
	MILD PONV	12	10	22
	Row %	54.5	45.5	100.0
	Col %	24.0	20.0	22.0
	MOD PONV	0.0	0.0	0.0
	SEV PONV	7	0	7
	Row %	100.0	0.0	100.0
	Col %	14.0	0.0	7.0
	TOTAL	50	50	100
	Row %	50.0	50.0	100.0
	Col %	100.0	100.0	100.0
PONV after 3hrs	**MILD PONV**	6	1	7
	Row %	85.7	14.3	100.0
	Col %	12.0	2.0	7.0
	NO PONV	44	49	93
	Row %	47.3	52.7	100.0
	Col %	88.0	98.0	93.0
	TOTAL	50	50	100
	Row %	50.0	50.0	100.0
	Col %	100.0	100.0	100.0
PONV after 6hrs	**MILD PONV**	6	0	6
	Row %	100.0	0.0	100.0
	Col %	12.0	0.0	6.0
	NO PONV	44	50	94
	Row %	46.8	53.2	100.0
	Col %	88.0	100.0	94.0
	TOTAL	50	50	100
	Row %	50.0	50.0	100.0
	Col %	100.0	100.0	100.0
PONVafter12hrs	**MILD PONV**	6	1	7
	Row %	85.7	14.3	100.0
	Col %	12.0	2.0	7.0
	NO PONV	44	48	92
	Row %	47.8	52.2	100.0
	Col %	88.0	96.0	92.0
	SEVERE PONV	0	1	1
	Row %	0.0	100.0	100.0
	Col %	0.0	2.0	1.0
	TOTAL	50	50	100
	Row %	50.0	50.0	100.0
	Col %	100.0	100.0	100.0

Distribution of PONV after 1hr, PONV after 3hrs, PONV after 6hrs and PONV after 12hrs

RESULT AND DISCUSSION
Bhandari V et al[12] (2014) found significant reduction in PONV and antiemetic consumption in gabapentin group when compared to a placebo for a period of 24 hours. Gabapentin in the doses used was found to be ineffective in PONV in patients undergoing planned laparoscopic cholecystectomy with standardized pre-anaesthetic and anaesthetic medication.

Khan MA et al[13] (2019) found that incidence and severity of postoperative nausea and vomiting (PONV) was recorded in these patients till 24 hours of laparoscopy. 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.

Sharma JP et al[14] (2015) found that administration of gabapentin 2 hours before and 6 hours after the surgery significantly decreased the incidence of postoperative pain, nausea, and vomiting.

Grant MC et al[15](2016) found that use of gabapentin reported reduction in the side effects nausea and vomiting. Among the trials designed with PONV as a primary end point (8 trials; n = 838), preoperative gabapentin was associated with a significant reduction in PONV and vomiting at 24 hours. Among all included trials that reported on the side effects nausea and vomiting, similar reductions were noted in PONV with preoperative gabapentin administration. Preoperative gabapentin is associated with a significant reduction in PONV among studies designed to investigate this end point. Preoperative gabapentin should be considered not only as part of a multimodal approach to postoperative analgesia, but also for prevention of PONV.

We found that in Group A, the mean age (mean ± s.d.) of patients is 44.8400 ± 15.5253 years. In Group B, the mean age (mean ± s.d.) of patients is 45.0200 ± 15.3177 years. Distribution of mean age vs. study group is not statistically significant (p = 0.9536). In Group A, 41 (82.0%) patients are female and 9 (18.0%) patients are male. In Group B, 33 (66.0%) patients are female and 17 (34.0%) patients are male. Association of gender vs. study group is not statistically significant (p = 0.1105205059).

In Group A, 26 (52.0%) patients were in ASA grade I and 24 (48.0%) patients were in ASA grade II. In Group B, 29 (58.0%) patients were in ASA grade I and 21 (42.0%) patients were in ASA grade II. Association of ASA grade vs. study group is not statistically significant(p = 0.6876732594).

We found that distribution of mean temperature at different time intervals in study group is not statistically significant. Distribution of mean pulse at different time intervals in study group is not statistically significant.

We found that distribution of mean SBP, DBP and SpO2 at different time intervals in study group is not statistically significant (p = 0.9182). It was found that distribution of mean height vs. study group is not statistically significant (p=0.0793). Distribution of mean weight vs. study group is not statistically significant (p=0.4750).

In Group A, the mean EtCo2 intraoperatively (mean ± s.d.) of patients is 36.0800 ± 1.4824. In Group B, the mean EtCo2 intraoperatively (mean ± s.d.) of patients is 36.3800 ± 1.3536. Distribution of mean EtCo2 intraoperatively vs. study group is not statistically significant (p=0.2932).

We found that after 1 hour in the post-operative period in Group A, 12 (24.0%) patients had mild PONV and 7 (14.0%) patients had severe PONV. In Group B, 10 (20.0%) patients had mild PONV and no patient had severe PONV. Difference of total PONV after 1 hr in Group A 19 (38%) vs. Group B 10 (20%) was statistically significant (p=0.0156).

We found that after 3 hrs in the post-operative period in Group A, 6 (12.0%) patients had mild PONV. In Group B, 1 (2.0%) patient had mild PONV. Difference of total PONV after 3 hrs in Group A 6 (12%) vs. Group B 1 (2%) was not statistically significant (p=0.1169466834).

We found that after 6 hours in the post-operative period in Group A, 6 (12.0%) patients had mild PONV. In Group B, 50 (100.0%) patients had no PONV. Difference of total PONV after 6 hrs in Group A 6 (12%) vs. Group B 0 (0%) was statistically significant (p=0.0352593886).

We found that after 12 hours in the post-operative period in Group A, 6 (12.0%) patients had mild PONV. In Group B, 1 (2.0%) patient had mild PONV and 1 (2.0%) patient had severe PONV. Difference of total PONV after 12 hrs in Group A 6 (12%) vs. Group B 2 (4%) was not statistically significant (p=0.0932).

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