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Prophylaxis against Postoperative Nausea and Vomiting in Patients undergoing Laparoscopic Abdominal Surgeries with Gabapentin alone and Gabapentin-Dexamethasone and their Comparison with Ondansetron

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Abstract: ***Postoperative nausea and vomiting (PONV) is frequently encountered after laparoscopic abdominal surgeries done under general anaesthesia. The available prophylactic agents against PONV have various side effects and have no analgesic property. Therefore we aimed to study the antiemetic effect of Gabapentin and its combination with Dexamethasone against Ondansetron. 120 patients were randomly divided into three groups . Group A received Gabapentin orally, Group B received i.v.dexamethasone in addition to oral Gabapentin and Group C received Ondansetroni.v. as control. Incidence of nausea and vomiting, requirement of rescue antiemetic and analgesic were noted in the first 24 hours of postoperative period. Group B and C had less incidence of PONV than group A. There was less requirement of additional analgesic requirement in Group A and B than in Group C. So combination of Gabapentin and Dexamethasone can be an effective and safe alternative of Ondansetron for the management of PONV.***

Keywords: postoperative nausea and vomiting, gabapentin, dexamethasone, ondansetron

1. Introduction

Postoperative Nausea & Vomiting (PONV) is often the most common and distressing complication following anaesthesia and surgery. The general incidence of vomiting is about 30%, the incidence of nausea is about 50% and in a subset of high risk patients, PONV rate can be as high as 80%[(1)]. Its prevention and/or treatment significantly improves patient satisfaction and quality of life[(2).] Unresolved PONV can cause dehydration, electrolyte imbalance, tension on suture, pain at the site of incision, venous congestion and bleeding, thus leading to delayed recovery, patient dissatisfaction, prolonged stay in post-anaesthesia care unit(PACU), unanticipated hospital admission and delayed return to work. It is estimated that each episode of emesis delays discharge from the PACU by approximately 20 minutes. This may result in significant increase in overall health care cost. Furthermore, serious complications, including retinal detachment, aspiration, wound dehiscence, oesophageal rupture and subcutaneous emphysema, related to PONV can be prevented. Factors influencing the incidence of PONV includes age, gender, smoking status, volatile anaesthetics, nitrous oxide, postoperative factors like opioid analgesics, pain, dizziness, oral intake and ambulation[(1,3)].

Abdominal surgeries, particularly laparoscopic, is one condition, where risk of PONV is very high. This increased risk of PONV is attributed to pneumoperitoneum causing stimulation of mechanoreceptors in the gut. Furthermore, intestinal ischemia induced by pneumoperitoneum may release serotonin and other neurotransmitter which could lead to PONV. Several receptor types - including serotonin 5 –HT3, 5-HT4, dopamine D2, histamine H2, α-2 adrenergic, muscarinic cholinergic, neurokinin 1 and GABA mediated receptors are involved in the initiation and co-ordination of the vomiting reflex in patients with PONV.

The currently used pharmacological antiemetics for PONV prophylaxis have many undesirable side effects such as excessive sedation, hypotension, dryness of mouth, dysphoria and hallucinations. 5-HT3 antagonists and 5-HT4 agonists are easily available and thus most commonly used for PONV prophylaxis, but they are known to produce side effects : 5-HT3 antagonists can cause ECG changes (QTc prolongation)[(4)] whereas Metoclorpramide causes extrapyramidal side effects[(5)].

Gabapentin, a structural analogue of gamma amino butyric acid (GABA), originally an antiepileptic drug had shown some antiemetic and analgesic effect in some recent studies[(6,7)]. Dexamethasone is a corticosteroid, anti-inflammatory drug with an established role for the prevention of postoperative nausea and vomiting (PONV).

2. Methods

This is a prospective, randomized, single blind, controlled, parallel group study. After obtaining approval of the institutional research and ethics committee, 120 patients of either sex aged 18-60 yrs (ASA physical status I & II), scheduled for elective laparoscopic abdominal surgery under general anaesthesia were enrolled in the study. All patients

were randomly allocated into three groups [group A- received Gabapentin 600 mg orally 2 hrs prior to induction, group B received Dexamethasone 8 mg i.vintraoperatively in addition to preoperative oral Gabapentin, group C received Ondansetron 4 mg i.v. intraoperatively] with 40 patients in each group through a computer generated random number table.

Patient exclusion criteria were : history of gastro intestinal disease, hormonal therapy, evidence of uncontrolled (clinically important) neurological, renal, hepatic, cardiovascular, metabolic or endocrine dysfunction, prior history of allergy to any of the drugs used in the study or drug abuse, patients who have received antiemetics, steroids or psychoactive medications within 24 hrs of study initiation, pregnant and lactating women and if the laparoscopic surgery is converted into open surgery.

Anaesthetic management was standardized for all patients. Following overnight fasting, all the patients were premedicated with oral alprazolam 0.25 mg, 2 hours prior to induction. At the same time, a single oral dose of Gabapentin 600 mg were given to patients of Group A and B. On arrival in the operating room baseline parameters (heart rate, 5-lead ECG, NIBP, SpO_2) were attached. After preoxygenation, patients were induced with propofol 2mg/kg, intubated after giving rocuronium0.6 mg/kg and maintained with O_2, N_2O and isoflurane. Patients of group B and C were given Dexamethasone 8mg i.v. and Ondansetron 4 mg i.v. respectively. At the end of surgery, residual neuromuscular blockade was reversed with 50mcg/kg neostigmine and 10mcg/kg glycopyrrolate after fulfilling the criteria of extubation.

3. Statistical Analysis

Sample size was calculated by a power analysis while designing the study- allowing an α-error of 5% and a β-error of 20%, it was estimated that a minimum of 38 patients per group would be required to show a 30% difference in the incidence of PONV. All statistical analyses were performed using SPSS software, version 22.0.0.0, and Microsoft Excel 2010 version for windows. Numerical variables like the patients' age, weight, anesthesia duration and baseline vital parameters were compared between groups by Analysis of Variance (ANOVA) test between the three groups. $\chi 2$ with Yates' correction or Fisher's exact test was employed for intergroup comparison of categorical variables.All analyses were two tailed. Statistically significant implied $p < 0.05$.

4. Results

Data from 120 patients were collected and analyzed. Patients were randomly allocated into three groups each having 40 participants. The patients were similar in all the three groups in relation to age, body weight and the duration of anaesthesia (Table 1).

Table 1: Characteristics of the patients (mean ± SD)

	Group A	Group B	Group C	p value
No. of patients	40	40	40	
Age (yrs)	41.2 ± 7.771	40.8 ± 8.043	42.63 ± 8.863	0.470
Weight (kg)	54.38 ± 5.499	55.68 ± 5.613	56.33 ± 5.493	0.140
Duration of anaesthesia(min)	100.88 ± 7.393	99.65 ± 7.295	99.82 ± 6.312	0.802

The comparison of the incidence of PONV in the first 24 hrs of postoperative period is presented in Table 2.

Table 2: Incidence of Nausea and Vomiting in first 0-24 hours of postoperative period

	Group A	Group B		Group B	Group C		Group A	Group C
Nausea	25 (62.5%)	8 (20%)		8 (20%)	9 (22.5%)		25 (62.5%)	9 (22.5%)
P- VALUE	**0.0003**			**1**			**0.0007**	
Vomiting	17 (42.5%)	4 (10%)		4 (10%)	4 (10%)		17 (42.5%)	4 (10%)
P- VALUE	**0.0023**			0.708			**0.0023**	

Table 2 shows that the difference in the incidence of PONV is statistically significant in Group A& B ($p < 0.05$) and Group A & C ($p < 0.05$), while it is non-significant between Group B & C ($p > 0.05$).

Patients who experienced troublesome Nausea or Vomiting or both in the 0-24 hours of the postoperative period were given Ondansetron, 4 mg, intravenously as Rescue Anti-emetic. Patients who experienced pain in the 0-24 hours of the postoperative period were given inj. Diclofenac, 75 mg, intravenously.

Patients who required rescue antiemetic and additional dose of analgesic is mentioned in Table 3.

Table 3: Need of Rescue antiemetic and additional analgesic

	Group A	Group B		Group B	Group C		Group A	Group C
No. of patients who received Rescue Antiemetic	8 (20%)	2 (5%)		2 (5%)	2 (5%)		8 (20%)	2 (5%)
P- VALUE	**0.044**			1			**0.044**	
No. of patients who received IV Diclofenac postoperatively	18 (45%)	14 (35%)		14 (35%)	32 (80%)		18 (45%)	32 (80%)
P- VALUE	0.25			**0.0004**			**0.002**	

Table 3 shows thatthe difference in the no. of patients who received rescue antiemetic is statistically significant between Group A & B and Group A & C while it is non-significant between Group B & C. Also the number of patients who

required additional dose of analgesic is significantly less in group A and B (those who received gabapentin).

5. Discussion

Gabapentin effectively suppresses nausea and vomiting in laparoscopic cholecystectomy and post-operative rescue analgesic requirement. These findings in the present study is in accordance with the findings of **Pandey CK et al[8],** who in 2006, in the study on 250 patients scheduled for laparoscopic cholecystectomy, found thatincidence of post-operative nausea and vomiting within 24 hrs after laparoscopic cholecystectomy was significantly lower in gabapentin group (46/125) than in the placebo group (75/125) (37.8% vs 60%; P =0.04). Also, there was a significantly decreased fentanyl consumption in gabapentin group (221.2+/-92.4 microg) as compared to placebo group (505.9+/-82.0 microg; P =0.01). This is further in accordance with the results of study of **Alayed N et al, 2014[9]**, who in meta-analysis on patients scheduled for abdominal hysterectomy, reported that in comparison with the control group (16.1-96.7%), the rate of nausea was less in the gabapentin group (11.6-70%). Also there was a significant decrease in morphine consumption at 24 hours when gabapentin was administered before surgery (from 24.3-55.9 mg to 13.2-42.7 mg, standardized mean difference -0.69) as well before and after surgery (from 25.7-80 mg to 20.3-55 mg, standardized mean difference -1.45), respectively.

The impact of adding iv dexamethasone as an adjuvant on overall incidence of PONV observed in this study is similar to the results of study by **Misra S et al, 2013**[10] on patients undergoing craniotomy for intracranial tumours, who concluded that there is significant difference between the groups in the incidence of nausea (P=0.02), PONV (P=0.02), and the requirement for antiemetics (P=0.03). The number of emetic episodes were also reduced in group GD, but this did not assume statistical significance (P=0.06).

6. Conclusion

It is concluded that Gabapentin-Dexamethasone combination can be used as a safe antiemetic agent for the prophylaxis of Postoperative Nausea & Vomiting with results comparable to Ondansetron without any proven cardiac toxicity.

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