Original Research Article

Randomized study for evaluation of timing of injection dexamethasone on its efficacy as prophylactic antiemetic in laparoscopic surgery

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Abstract

Background:-Patients undergoing laparoscopic surgeries are highly susceptible for postoperative nausea and vomiting (PONV). PONV prophylaxis is must for these patients.Many drugs are used for prophylaxis of PONV in these patients and dexamethasone is one of the cost effective drug amongst all.**Aim and objectives:-** To asses effect of timing of injection dexamethasone administration on its efficacy as prophylactic antiemetic for post operative nausea and vomiting in patients undergoing laparoscopic surgery.**Material and methods**:- 240 patients of ASA grade I were posted for laparoscopic surgeries under general anaesthesia.These patients were randomly allocated in group 1(pre induction) and group 2 (post extubation)of 120 each.group 1 received inj.dexamethasone 8 mg 30 minutes before induction while group 2 received inj. Dexamethasone 8 mg after extubation.Patients were observed for 24 hrs for episodes of nausea, vomiting and need for rescue antiemetic and for 48 hrs for side effects of steroid. Study results were analyzed by Unpaired "t" test and categorical data was analyzed by chi-square test. A p-value of less than 0.05 was considered for statistical significance.**Results:-**It was found that in the first 2 hours as well as beween 2-6 hours after surgery ,incidence of nausea and vomiting was significantly less in group 1 as compared to group 2. Beween 6-24 hours after surgery , incidence of nausea was significantly less in group 1 than group 2 but there was no significant difference in the incidence of vomiting between the two groups.Rescue antiemetic was needed in 25% of patients in group 1 and 63.33% patients in group 2 (p=0.001). No adverse effects was seen in either of the groups.**Conclusion:-**This study results show that prophylactic therapy with inj. Dexamethasone (8mg) given before induction significantly reduces early as well as late post operative nausea and vomiting in patients undergoing laparoscopic surgeries.

Keywords:Postoperative Nausea And Vomiting ;Adverse Effects;Rescue antiemetic

Introduction

Postoperative nausea and vomiting (PONV) is one of the most common complications after anesthesia and occurs after both general and regional anesthesia. The incidence of postoperative emesis have been reported to be in 20-30% of the cases.[1,2] Persistence of nausea and vomiting in the postoperative patient who is fasting can result in dehydration, electrolyte imbalance, and delay in discharge especially after ambulatory surgery.[1] Persistent retching and vomiting can cause tension in suture lines, venous hypertension, bleeding under skin flaps and increased risk of pulmonary aspiration of vomitus if airway reflexes are depressed from the residual effects of anesthetic and analgesic drugs. [1-3] Certain procedures such as gynecological surgeries, laparoscopies,middle ear surgeries,strabismus surgeries are associated with higher incidence of PONV.[1,2] Patients undergoing laparoscopic surgeries are at moderate to high risk (70%-80%) for post operative nausea vomiting.[1] It has been suggested that PONV prophylaxis is cost effective with the older, less expensive drugs when patients have a 10% or more risk of emesis[4,5]. Therefore many anesthetists like to give PONV prophylaxis to even patients at low risk of PONV.The preferred option of antiemetic should be inexpensive and with minimal side effects. For patients with moderate risk of PONV single agent antiemetic or combination therapy is recommended for prophylaxis depending upon the level of risk.[4]Dexamethasone has been found to have a prophylactic effect on PONV in patients undergoing thyroidectomy,major gynaecological surgeries and ambulatory laparoscopic surgeries.[6-11]. Wang JJ et al and Ali Z et al did a study to determine its time of administration as an prophylactic antiemetic in laparoscopic surgeries.[6,8] So we decided to study effect of timing of administration of inj. Dexamethasone on its efficacy as an antiemetic in laparoscopic surgeries.The exact mechanism of the antiemetic action of dexamethasone is not known. However, there have been some suggestions,such as central or peripheral inhibition of the synthesis of prostaglandins, in the production or secretion of serotonin or changes in the permeability of the blood–brain barrier to serum proteins.[7] Aim of the study was to evaluate the effect of timing of injection dexamethasone administration on its efficacy as prophylactic antiemetic for post operative nausea and vomiting in patients undergoing laparoscopic surgery. Other objective was to

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note any side effects of steroid administration, mainly delayed wound healing and wound infection.

Material and methods

The present study was conducted in 240 adult patients undergoing elective laparoscopic surgeries under general anesthesia in our hospital during the period of DEC 2009- MARCH 2011 in Dept. of Surgery of KEM Hospital, Mumbai. To calculate Sample size SPSS software version 21 (SPSS inc, Chicago, II,USA),keeping 80% power and 95% of confidence interval was used. After institutional committee approval (KEM/IEC/103/09) Dated 20/11/2009 and written informed consent, patients posted for Laparoscopic surgeries requiring general anesthesia were selected. The study population was randomized and divided into 2 groups of 120 patients each using computer generated software.

Group 1 : Group which received injection dexamethasone 8 mg diluted with 3 cc of normal saline, given intravenously slowly before the induction.

Group 2 : Group which received injection dexamethasone 8 mg ,diluted with 3 cc of normal saline given intravenously slowly within 10 minutes after extubation.

Selection of patients

Inclusion criteria

- Patients aged between 18-50 years.
- Patients belonging to ASA I grade.
- Patients undergoing laparoscopic surgeries under general anesthesia.

Exclusion criteria

- Patients refusal for the study
- Patients with major hepatic or cardiac disease and diabetics
- Pregnant and lactating patients
- Patient taking medicine with known antiemetic activity

After taking written informed consent for participation in the study, pre-operative baseline values of heart rate and blood pressure etc. were recorded five minutes before the surgery. An intravenous access with an appropriate size cannula was obtained. Patients were premedicated with inj. Midazolam 0.03mg/kg, inj. pentazocine 0.3mg/kg, inj.glycopyrrolate 0.2 mg. Patients were given inj Dexamethasone 8 mg, 30 minutes before induction in group 1 and after extubation within 10 minutes in group 2. After preoxygenation for 3 minutes, general anaesthesia was induced with injection Propofol (1%) 2mg/kg i.v. and subsequent relaxation and intubation in both groups were accomplished with injection succinyl choline 2 mg/kg i.v. and orotracheal intubation with an appropriate sized cuffed portex tube was done.Anaesthesia was maintained with O_2:N_2O (40:60) and isoflurane (MAC of 1 to 1.5). Inj.vecuronium was used as muscle relaxant.Inj Paracetamol 15 mg/kg was used as analgesic intraopearatively. Once the surgery was completed, duration of surgery was noted. Neuromuscular blockade was reversed with inj. neostigmine 0.05 mg/kg and injection glycopyrrolate 8 mcg/kg i.v. The patient was extubated and Duration of anesthesia was noted as starting from induction to reversal of muscle relaxant. Patients were observed for 48 hours postoperatively. Nausea and vomiting were recorded at the time period of 0-2 hour, 2-6 hour and 6- 24 hour.VAS (Visual analogue score) was maintained below 6 by giving adequate analgesia. First line analgesic was inj. Paracetamol 15mg/kg IV given 8 hourly. Inj. Tramadol 1mg/kg as per necessity was given as add on analgesic to maintain VAS below 6. Patients were observed for side effects like delayed wound healing , wound infection till 48 hours post operatively.

Assessment : The number of episodes of vomiting were recorded and the data was recorded as follows- 0 episode - V0; 1 episode- V1; 2 episode – V2 ; 3 episode –V3

If total number of vomiting episodes in 24 hour period were 4 or more then it was called as severe vomiting.

The number of episodes of nausea were also recorded, and the data was recorded as follows-

0 episode-N0; 1 episode- N1; 2 episode- N2; 3 episode-N3

If total number of nausea episodes in 24 hour period were 4 or more then it was called as severe nausea. Rescue antiemetic consisted of injection Ondansetron 4mg given intravenously. It was given if patient had even a single episode of vomiting. Complete response was defined as no episode of vomiting in 24 hours post operatively.

Statistical Analysis: The data was expressed as distribution of cases with corresponding number of episodes of nausea, vomiting and need for rescue antiemetic. Continuous variables were analyzed by Unpaired "t" test and categorical data was analyzed by chi-square test.A p-value of less than 0.05 was considered for statistical significance. SPSS software version 21 (SPSS inc, Chicago, II,USA) was used for statistical analysis.

Results

All the study participants(n=240)were comparable in terms of demographic profile, baseline hemodynamic parameters and duration of surgery as well as anaesthesia.

Table 1: Demographic profile and other variables of study population

Demographic Profile	Group 1 (N=120)(mean ± SD)	Group 2(N=120) (mean ± SD)	P Value
Age (years)	37 ± 9.747	38 ± 7.584	0.368
Sex (m/f)	37/83	35/85	0.778
Weight (kg)	71.67±5.66	72.9±5.92	0.413
Height (cm)	157±15.5	152±14.14	0.192
Systolic BP (mm of Hg)	115± 4.60	117±3.61	0.255
Diastolic BP(mm of Hg)	71±2.42	73±8.40	0.962
Pulse Rate (beats/min)	86±6.90	84±6.70	0.782
Respiratory Rate (breaths/min)	16±1.10	18±1.20	0.224
Mean anesthesia time (Minutes)	95.87 ± 12.92	98 ± 14.43	0.229
Mean surgery time(Minutes)	69.78 ± 12.74	72.95 ± 14.52	0.073
Patients receiving tramadol (n)	13	11	0.741
(Data expressed as mean ± standard deviation) ; unpaired t test is used for statistical significance.			

Table 2:Showing patients experiencing nausea

Time interval	Group 1	Group 2	P value (chi-square test)
0-2 hours	36	84	0.001
2-6 hours	36	83	0.001
6-24 hours	20	62	0.0001

Table 2 shows that over the observation period of 24 hours , number of patients experiencing nausea in group 1 differs significantly compared to group 2

Table 3:showing patients experiencing vomiting

Time interval	Group 1	Group 2	P value(chi-square test)
0-2 hours	30	76	0.001
2-6 hours	13	42	0.0001
6-24 hours	6	13	0.254

Table 3 shows that there was significant difference in the number of patients experiencing vomiting within first 6 hours between two groups. There was no significant difference in the number of patients experiencing vomiting in 6-24 hours between two groups

Table 4: showing patients with severe nausea and vomiting

Severe nausea or vomiting	Group 1	Group 2	P value(chi-square test)
Severe Nausea	19	54	0.0001
Severe Vomiting	5	12	0.078

Table 4 shows that there was significant difference in number of patients experiencing severe nausea between two groups. There was no significant difference between two groups in terms of patients having severe vomiting.

It was found that rescue antiemetic was needed in 30(25 %) of patients in group I and 76(63.33%) of patients in group 2(p=0.001).

Discussion

Postoperative nausea and vomiting (PONV) is of multifactorial origin. Factors affecting PONV include patient related (age, sex, phase of the menstrual cycle) , anesthesia related (use of volatile anaesthetic agents, N_2O,Opioid) and surgery related factors.[1] Female gender has been associated with higher incidence of PONV compared to male patients.[1,2] Patients undergoing laparoscopic surgeries are moderate to high risk for PONV, with incidence of 70-80%.[1] For patients which are at moderate risk for PONV, a single antiemetic agent should be given as prophylactic antiemetic. For patients with high risk of PONV, two or three antiemetic agents as prophylaxis or multimodal approach should be used.[4] In the IMPACT trial , it was found that Ondansetron 4 mg , droperidol 1.25 mg and dexamethasone 4 mg were equally effective and each independently reduced PONV risk by approximately 25%.[4] Out of these three drugs dexamethasone is inexpensive and with very few side effects .So we decided to study inj. Dexamethasone for prophylaxis of PONV. There are very few studies which correlate the efficacy of Dexamethasone as an prophylactic antiemetic with its time of administration.[6,8] This study was aimed to evaluate the effect of timing of Dexamethasone administration on its efficacy as prophylactic antiemetic in patients undergoing laparoscopic surgeries.Most commonly used dose of Dexamethasone is 8-10 mg but the minimum effective dose is suggested to be 5 mg as reported by Huang JC et al.[11] A study done by Wang JJ et al demonstrated that prophylactic Dexamethasone 8 mg significantly reduced the incidence of nausea and vomiting after laparoscopic cholecyst-ectomy.[12]That is the reason why it was decided to use 8 mg as a dose of dexamethasone in this study. In this study there was no statistically significant difference in the hemodynamic parameters. It was ensured to maintain adequate hydration, optimum pain relief, adequate oxygenation.There was avoidance of hypotension , easy ambulation and gentle handling of patients in the postoperative period. All of the above factors have been found to decrease the incidence of PONV as per study done by Lerman J.[13] In this study, Ondansetron 4mg intravenously was used as a rescue antiemetic. This was decided as per Guidelines of society for ambulatory anesthesia for management of PONV .[4] It was suggested that when PONV occurs, treatment antiemetic must be from different pharmacological class than that of prophylactic antiemetic. [4] In this study,it was found that there was significantly less incidence of nausea in 0-24 hrs of post operative period in group 1(preinduction) compared to group 2 (postext-ubation). In the study conducted by Wang JJ et al. incidence of nausea in the first 2 hours of postoperative period in preinduction group was 10% while in the postextubation group was 25% ($p<0.05$).[6] But Wang JJ et al didn't find significant difference in the incidence of nausea in the time period of 2 to 24 hours between two study groups.[6] The difference in the incidence of nausea between 2-24 hours postoperatively may be due to onset of antiemetic action of dexamethasone being more than 2 hours. In this study it was found that the incidence of vomiting within first 2 hours as well as in 2-6 hours of post operative period in group 1 (preinduction) was significantly less than group 2 (postextubation) . In the study conducted by Wang JJ et al. Incidence of vomiting in the first 2 hours of postoperative period in preinduction group was 5% while in the postextubation group it was 20%.[6] In the present study, they didn't find significant difference in the incidence of vomiting in the time period of 6 to 24 hours. Wang J J et al didn't find significant difference in the incidence of vomiting in the time period of 2 to 24 hours between two study groups.[6] This may be because the time of onset of antiemetic action of dexamethasone is more than 2 hours. Hence we found significant difference in the incidence of nausea and vomiting between 2-6 hours In this study, they found the incidence of severe nausea within 24 hours of post Operatively was significantly less in group 1 when compared to group 2. It is similar to findings of study conducted by Worni M et al.[14] In their study they evaluated nausea and vomiting on 4 point scale and they found that the severity of nausea in a dexamethasone group was less as compared to other group. In this study,it was found that there was no significant difference in the incidence of severe vomiting between two groups over 24 hours of postoperative period. Two studies which are conducted by Liu K et al [15] and Wang JJ et al[10] have described episodes of severe vomiting as four or more episodes of vomiting within 24 hours of post operative period. In their study Wang JJ et al found the incidence of severe vomiting to be 2% in 10mg and 5mg group ,which is similar to present study with incidence of 4.2% in preinduction group. While Liu K et al found no severe vomiting in their study population of 30 patients receiving dexamethasone before induction.[15]In present study population, number of patients requiring rescue antiemetic in group 1 (25%) were significantly less than group 2 (63.33%) over total observation period of 24 hours($p=0.001$). In a study conducted by Subramanian et al no. of patients who needed rescue antiemetic was 17% over 24 hours.[16]Wang JJ et al found that number of patients requiring rescue antiemetic in group 1(preinduction) was 21% in 24 hours of postoperative period, while in group 2 (postextubation) about 45% in the postoperative time period of 24 hours. [6] In this study they didn't find delayed wound healing or increase in infection rate in the postoperative period of 48 hours in either group. Adverse effects related to a single dose of Dexamethasone are extremely rare as suggested by previous study done by Wang JJ et al. They too were unable to find any report on side effects associated with a single dose of dexamethasone.[12]

Hyperglycemia is one of the prominent side effect of dexamethasone administration.[17,18] They didn't check for hyperglycemia in either of the groups due to limitation of manpower. Less than 24 hour of Dexamethasone therapy is considered safe and almost without adverse effects.[19]

Limitations:-This study was single blinded study due to limitation of manpower.Patients were observed only for 48 hrs for side effects.ASA II patients, oncosurgical patients , patients with prolonged surgery were excluded from the study.One of the main side effect of steroid administration i.e hyperglycemia was not studied.

Conclusion

Study results show that prophylactic therapy with inj. Dexamethasone (8mg) given before induction significantly reduces early as well as late post operative nausea and vomiting in patients undergoing laparoscopic surgeries. Its efficacy as antiemetic is comparable to established antiemetics.

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