A COMPARATIVE STUDY BETWEEN METOCLOPRAMIDE AND DEXAMETHASONE FOR PREVENTION OF POST OPERATIVE NAUSEA AND VOMITING IN LAPAROSCOPIC CHOLECYSTECTOMY

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ABSTRACT

Objective: To compare the prophylactic antiemetic effect of intravenous (IV) metoclopramide with dexamethasone.

Material and Methods: A prospective study of 150 patients undergoing “Laparoscopic Cholecystectomy” was carried out in the Department of Anaesthesiology, Khyber Teaching Hospital, Peshawar, from April 2009 to October 2009. Patients were divided into two groups. One group received metoclopramide 10 mg IV, while the second group received dexamethasone 8 mg IV. The anaesthetic regime and surgical procedure were standardized for all patients. Nausea and vomiting were assessed immediately after operation, at hourly intervals for 4 hours, in the recovery room, and from 4 to 24 hours in the ward.

Results: The incidence of post operative nausea and vomiting (PONV), in the metoclopramide group was 20% after 0-4 hours, 50% after 4-24 hours and 70% after 0-24 hours of surgery. The incidence of PONV in dexamethasone group was 16% after 0-4 hours, 12% after 4-24 hours and 28% after 0-24 hours surgery. A statistically significant difference was observed in both groups in respect of postoperative nausea and vomiting in 4-24 hours and 0-24 hours with a p-value 0.000 each.

Conclusion: Dexamethasone was found superior to metoclopramide as a prophylactic antiemetic in patients undergoing laparoscopic cholecystectomy.

Key Words: Postoperative, nausea, vomiting, metoclopramide, dexamethasone, laparoscopic cholecystectomy.

INTRODUCTION

Laparoscopic cholecystectomy is now considered as a method of choice for gall stones (the gold standard)1,2,3 with multiple benefits as it can provide substantial medical and economic advantages. Its rate has increased by an average of 20% since the introduction of this procedure.4 However one of the most common adverse effects of laparoscopic cholecystectomy is PONV,5,6 with a high incidence of 53 to 70%.7,8 PONV results in profound distress to the patient specially in the early hours of surgery with increased risk of aspiration and postoperative morbidity such as (wound disruption, delayed oral food intake, dehydration, electrolyte imbalance and restricted mobilization). Thereby it leads to prolonged convalescence, increased hospital stay and cost.

The risk factors for PONV may be patient related, procedure related, due to anaesthetic drugs or post operative factors. Among the patient risk factors, female gender (M:F=1:3)9, young age (6-16 years with incidence of 38-51%)10, obesity (due to accumulated fat soluble anaesthetics in adipose tissue)11, patients with history of PONV or motion sickness and patients with delayed gastric emptying (gastroparesis), contribute to PONV. Procedure related risk factors include surgical site (abdominal, gynaecological procedures, ENT and Eye surgeries), extended duration of surgery and laparoscopic procedures as both position of the body (trendelenburg position) and CO2 insufflation in abdominal cavity pushes the diaphragm upwards and increases chances of aspiration and PONV.12 Premedication with narcotic analgesics (Morphine, Pethidine, Synthetic Opioids) cause PONV. Almost all anaesthetic agents except Propofol13 lead to increased frequency of PONV. Moreover general anaesthesia has a high incidence for PONV than spinal anaesthesia. Post operative risk factors include pain, early ambulation14, hypotension or premature oral intake.

Metoclopramide is an antiemetic with multi model action i.e. it binds to dopamine, serotonin and histamine receptors. Initially metoclopramide was used for the treatment of nausea and vomiting in migraine...
Anaesthesia was maintained with 1% (inspired concentration) halothane in oxygen and nitrous oxide (50:50) and mechanical ventilation was started. During surgery, the patients were placed in a trendelenburg position and the abdomen was insufflated with carbon dioxide with an intra-abdominal pressure of 1.3-1.8 Kpa. The patients were given intravenous Ringers lactate infusion at a rate of 4 ml / kg / hour. At the cessation of surgery neuromuscular block was reversed with neostigmine 2.5 mg + atropine 1 mg. Prior to extubation of the trachea the nasogastric tube was suctioned and removed. Injection toradal (30 mg) intravenously was given routinely for the prevention of postoperative pain.

Nausea and vomiting were assessed immediately after operation and at one hour intervals for 4 hours in the recovery room. Nausea and vomiting were evaluated on a 3-point ordinal scale (0 = none, 1 = nausea, 2 = vomiting). In the present study, no distinction was made between vomiting and retching (i.e. a retching event was considered as a vomiting event). The patients were asked about any side effects e.g. headache, seizures, dizziness, abdominal pain, tremors at hourly interval during their stay in the recovery room. Episodes of PONV and rescue antiemetics used were recorded on case files by the nurse or doctor in the ward for 24 hours, who were blinded to preoperative antiemetics used. Any adverse event was also recorded. Gravinate (dimenhydrinate) was given on patient request or when vomiting occurred. The data was collected on a proforma.

RESULTS

The data was analyzed using SPSS software statistical package version 10. Comparison is given for all variables like age, sex, ASA class, weight and duration of surgery which are non significant in both the groups and shows that patients are equally distributed among both the groups (Table 1).

For purpose of comparison between the two groups Chi square test was applied to see the statistically significant difference in two groups in nausea and vomiting. In the 0-4 hours postoperatively, no statistical significant difference (P>0.05) was observed in respect of nausea and vomiting between the two groups. While in the 4-24 hours and 0-24 hours postoperatively, a significant difference was found in nausea and vomiting between the two groups. Similarly, efficacy in terms of prevention of postoperative nausea and vomiting was observed, and found that dexamethasone has significantly higher efficacy than metoclopramide (p-value = 0.000). When the side effects of both the treatments were compared, it was found that dexamethasone has no side effect whereas about in 7% of the patients in metoclopramide group headache, hypotension, dizziness and tachycardia was observed.

and in radiotherapy and chemotherapy. Today it is probably one of the most popular antiemetic drugs in anaesthetic practice for prevention of PONV. In high doses, side effects for example restlessness, dry mouth, tachycardia, headache, dizziness and extrapyramidal symptoms occur with its use.

Since 1981, dexamethasone has been reported to be effective in chemotherapy induced nausea and vomiting. Its mode of action is due to inhibition of postoperative synthesis and decrease in 5HT3 levels in CNS and also by its anti-inflammatory action at the operative site. Recently dexamethasone has also been reported to be effective in PONV particularly in paediatric and female patients. As dexamethasone has an antiemetic effect in various situations we thought that it may also be more effective in the prevention of nausea and vomiting after laparoscopic cholecystectomy than the conventionally used metoclopramide with fewer side effects.

MATERIALS AND METHODS

This comparative cross sectional study was carried out in the Anaesthesia Department of Khyber Teaching Hospital, Peshawar from April 2009 to October 2009. A total of 150 patients, belonging to American Society of Anaesthesiologists (ASA) class I and II, between age groups 15-50 years, with no gender discrimination were included. Those patients falling into ASA class III and IV or with predisposing factors for delayed gastric emptying (such as diabetes, neuro muscular disorders) or receiving regular narcotics/antiemetics, were excluded from the study. These 150 patients were randomly divided into two groups. Group A were given metoclopramide 10mg I/V and Group B were given dexamethasone 8mg I/V.

After a thorough preoperative evaluation of patients to assess their fitness for anaesthesia, the laparoscopic operative procedure was explained to them and a written informed consent was taken. A standard preoperative essential protocol was followed for each patient and data was collected on separate proformas. On the day of surgery, patients were kept nil orally for at least 6 hours prior to surgery and given tablet Bromazepam 3mg, one night before surgery to relieve anxiety. Shortly before the induction of anaesthesia every patient was asked to void urine in order to ensure an empty urinary bladder.

At the time of induction one group of patients received metoclopramide 10 mg I/V and the other group received dexamethasone 8 mg I/V by double blind method. The anaesthetic regimen and surgical procedure were standardized for all patients. Anaesthesia was induced with thiopental sodium 5 mg kg⁻¹, dormicium 0.02 mg kg⁻¹ and fentanyl 2 µg kg⁻¹. Tracheal intubation was facilitated with pancuronium 0.1 mg kg⁻¹ intravenously and nasogas-tric tube was also inserted. Nitrous oxide (50:50) and mechanical ventilation was started. During surgery, the patients were placed in a trendelenburg position and the abdomen was insufflated with carbon dioxide with an intra-abdominal pressure of 1.3-1.8 Kpa. The patients were given intravenous Ringers lactate infusion at a rate of 4 ml / kg / hour. At the cessation of surgery neuromuscular block was reversed with neostigmine 2.5 mg + atropine 1 mg. Prior to extubation of the trachea the nasogastric tube was suctioned and removed. Injection toradal (30 mg) intravenously was given routinely for the prevention of postoperative pain.

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and vomiting.15,16 Due to its short duration of action its interesting drug for preventing postoperative nausea and vomiting.15,16,17 In our study also, it was found that it decreased PONV by 80% in the early postoperative period and by 50% in the late phase. Ivanov et al18 observed 45% incidence of PONV with metoclopramide group, compared to 50% in our study.

Various doses of metoclopramide have been studied for preventing PONV and chemotherapy induced nausea and vomiting. These are 10 mg, 25 mg and 50 mg. Though the effectiveness of metoclo-pramid increases with increasing dose but the frequency of adverse reactions also increases.29 Therefore we have used a low dose i.e. 10 mg, with the result that serious side effects did not occur in any of our patients but a few side effects e.g. headache, hypotension, dizziness and tachycardia occurred with a frequency of 7% in our patients. Metoclopramide has also been used in combination with other antiemetics such as dexamethasone and 5-Hydroxy tryptamine antagonists and studies have shown that the combination increases its antiemetic efficacy.18,20,21

Dexamethasone has been found effective in laparoscopic cholecystectomy, shown by various randomized, placebo controlled studies by different researchers.22-27 A dose range of 8-10 mg has been used most frequently, for PONV in different surgical procedures.25,27,28,29 Therefore 8 mg dose was chosen for the present study. Our study showed an effective control of PONV at 0-24 hours as 72%, which is comparable to 70% observed by Farhat et al25 and 77% by Ivanov et al.18 However 66% incidence was reported by Wang et al30 because a slightly higher dose of 10mg dexamethasone was used. Side effects from brief duration of treatment (24-48 hours), even of high dose corticosteroid treatment, are rare.29-31 After conducting an extensive research of literature we were unable to find a report of side effects associated with the use of a single dose of dexamethasone. Therefore dexamethasone for prevention of PONV, is more potent than metoclopramide and is devoid of any of the adverse effects associated with metoclopramide in laparoscopic cholecystectomy.25-31

CONCLUSION
We concluded that dexamethasone (8mg) intravenously given, significantly decreased the incidence of postoperative nausea and vomiting as compared to IV metoclopramide (10mg).

REFERENCES

Table 1: Patient characteristics

<table>
<thead>
<tr>
<th>Variables</th>
<th>Groups</th>
<th>P-value</th>
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<tr>
<td>Age (Years)</td>
<td></td>
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<tr>
<td>Less than 40</td>
<td>32(42.7%)</td>
<td>0.687</td>
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<tr>
<td>Greater than 40</td>
<td>43(57.3%)</td>
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<tr>
<td>Sex</td>
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<tr>
<td>Female</td>
<td>52(69.3%)</td>
<td>0.488</td>
</tr>
<tr>
<td>Male</td>
<td>23(30.7%)</td>
<td></td>
</tr>
<tr>
<td>ASA Class</td>
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<td></td>
</tr>
<tr>
<td>ASA I</td>
<td>57(76%)</td>
<td>0.577</td>
</tr>
<tr>
<td>ASA II</td>
<td>18(24%)</td>
<td></td>
</tr>
<tr>
<td>Weight (kg)</td>
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<tr>
<td>50-60</td>
<td>25(33.3%)</td>
<td>0.258</td>
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<tr>
<td>61-70</td>
<td>23(30.7%)</td>
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</tr>
<tr>
<td>71-80</td>
<td>27(36%)</td>
<td></td>
</tr>
<tr>
<td>Duration of surgery (min)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>30-45</td>
<td>13(17.3%)</td>
<td>0.178</td>
</tr>
<tr>
<td>46-60</td>
<td>29(38.7%)</td>
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</tr>
<tr>
<td>61-120</td>
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DISCUSSION
In our study, we have compared the efficacy of metoclopramide with that of dexamethasone for prevention of PONV. All risk factors were controlled by the study design. The duration of surgery, anaesthesia and anaesthetics used were similar among the groups. Therefore it is likely that the differences in the incidence of PONV among the groups can be attributed to the study drugs rather than to any confounding variables. Data on metoclopramide as an antiemetic after surgery are contradictory. A metanalaysis found that an intravenous dose of 10 mg had only a marginal effect but because of its complex mode of action, metoclopramide remains an interesting drug for preventing postoperative nausea and vomiting.15,16 Due to its short duration of action its antiemetic effect is present only during the first 6 hours after administration.15,16,17 In our study also, it was found that it decreased PONV by 80% in the early postoperative period and by 50% in the late phase. Ivanov et al18 observed 45% incidence of PONV with metoclopramide group, compared to 50% in our study.

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