Comparison of Dexamethasone Plus Metoclopramide, with Dexamethasone Alone in The Prevention of Postoperative Nausea and Vomiting in Patients Undergoing Elective Craniotomy

MOHAMMAD ABBAS TARIQ,1 MOHAMMAD KAMRAN,1 MUMTAZ ALI2
Departments of Anaesthesia1 and Neurosurgery,2 Hayatabad Medical Complex, Peshawar

ABSTRACT
Objective: To compare the efficacy of combination of dexamethasone plus metoclopramide with dexamethasone alone for control of postoperative nausea and vomiting in patients undergoing elective craniotomy.

Study Design: Double blinded randomized controlled clinical trial.

Material and Methods: One hundred ASA I – II patients listed for elective craniotomy were randomized to two groups of 50 patients each. Group A received dexamethasone 8 mg (2 ml) plus metoclopramide 10 mg (2 ml) prepared in two different syringes, and group B received dexamethasone 8 mg (2 ml) and normal saline (2 ml), prepared in two separate received syringes just before induction of anaesthesia. Anaesthesia was standardized. All episodes of Postoperative Nausea and Vomiting (PONV) during the first 24 hours postoperatively were evaluated at 3 time periods: 2, 4, and 24 hours. The presence or absence of nausea and vomiting (by simply yes or no) was assessed by research nurses aware of the study but blinded to the group to which the patient belonged. The rescue antiemetic IV ondansetron 4 mg was given, if patient remained nauseous for more than 15 minutes, or experience retching or vomiting during study period.

Results: The frequency of nausea and vomiting was clinically and statistically lower in dexamethasone plus metoclopramide group as compared to dexamethasone alone p-value 0.032 and 0.028 for nausea and vomiting respectively.

Conclusion: Combination of dexamethasone plus metoclopramide is more effective in preventing postoperative nausea and vomiting than dexamethasone alone when used for prophylaxis of Post-operative Nausea and Vomiting (PONV) before the induction of anaesthesia in patients undergoing elective craniotomy.

Keywords: Nausea, Vomiting, Postoperative, Metoclopramide, Dexamethasone.

INTRODUCTION
Postoperative nausea and vomiting (PONV) continues to be a cause of morbidity after all types of surgeries, despite the introduction of new antiemetic drugs, and new anesthetics techniques, and minimally invasive surgical techniques.1,2 The current overall incidence of Postoperative Nausea and Vomiting (PONV) for all surgeries is estimated to be 20% – 33%,3,4 whereas the incidence of Postoperative Nausea and Vomiting (PONV) after craniotomies is more than 50%.5,6 Post-operative vomiting is not only unpleasant but is likely to increase arterial blood pressure and intracranial pressure with a consequently increased risk of intracranial hemorrhage. PONV also results in delay in oral food intake, dehydration, electrolyte imbalance and restricted mobilization. Thereby, it leads to delayed time to convalescence and increases hospital stay and cost. We therefore designed a prospective study to evaluate the effect of dexamethasone in combination with metoclopramide with dexamethasone alone on the incidence of PONV, We hypothesized that the combination of dexamethasone and metoclopramide would
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decrease the incidence of PONV compared to dexamethasone used alone.

MATERIAL AND METHODS

It was a double blind randomized clinical trial. One hundred patients, both male and female, aged 33 to 65 years, ASA (American Society of Anesthesiologists) physical status I and II, scheduled for elective craniotomy under general anaesthesia were enrolled in this study. Patients who received antiemetic within 24 hours, steroids or gave a preoperative history of motion sickness were excluded. Patients were randomly allocated into two groups (50 patients in each).

Group A to receive dexamethasone 8 mg (2 ml) plus metoclopramide 10 mg (2 ml) prepared in two different syringes, and group B to receive dexamethasone 8 mg (2 ml) and normal saline (2 ml), prepared in two separate syringes. In the operation theater after establishing standard monitoring, all the patients were preoxygenated for 5 minutes. The study agents were injected according to group of patient, just before the induction of anaesthesia. Anaesthesia was induced with propofol (2.0 mg/kg) and nalbuphine (0.1 mg/kg). Muscle relaxation was achieved with atacurium (0.5 mg/kg). 3 minutes later trachea was intubated with appropriate size endotracheal tube. Ventilation was controlled mechanically and adjusted to keep end-tidal carbon dioxide between 30–40 mm of Hg. Anaesthesia was maintained with isoflurane, 50% oxygen in nitrous oxide. At the end of surgery, volatile agent and nitrous oxide were turned off; ketorolac 30 mg was given for postoperative pain control and Neostigmine 2.5 mg with glycopyrrolate 0.5 mg was given for reversal of neuromuscular block and trachea was extubated on regaining spontaneous breathing and opening of the eyes.

All episodes of PONV (Postoperative Nausea and Vomiting) in the first 24 postoperative hours were evaluated at 3 time periods: 2, 4, and 24 h. The presence or absence of nausea and vomiting (by simply yes or no) was assessed by research nurses aware of the study but blinded to the group to which the patient belonged. Patients who remained nauseous for more than 15 minutes, or experience retching or vomiting during study period were treated with IV ondansetron 4 mg as a rescue antiemetic. Statistical analyses were performed using SPSS (Statistical Package for Social Sciences) Quantitative variables were expressed as mean ± SD (standard deviation), while qualitative variables were expressed as percentage. Age, weight, duration of surgery and duration of anaesthesia were analyzed by using student t-test, while gender, frequency of nausea and vomiting and use of rescue antiemetic were analyzed by using chi-square test. P-value less than 0.05 were considered significant.

RESULTS

There were no statistically significant differences among the groups regarding age, weight, sex ASA physical status, duration of surgeries and duration of anaesthesia (Table 1).

Table 1: Demographic Data.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Group A</th>
<th>Group B</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>45 ± 16</td>
<td>38 ± 17</td>
<td>0.918</td>
</tr>
<tr>
<td>Sex (M : F)</td>
<td>28 : 22</td>
<td>26 : 24</td>
<td>0.841</td>
</tr>
<tr>
<td>Weight (Kg)</td>
<td>55 ± 17</td>
<td>50 ± 15</td>
<td>0.595</td>
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<tr>
<td>Duration of surgery (minutes)</td>
<td>2 ± 0.4</td>
<td>2 ± 0.6</td>
<td>0.858</td>
</tr>
<tr>
<td>Duration of anaesthesia (minutes)</td>
<td>15 ± 3</td>
<td>15 ± 4</td>
<td>0.452</td>
</tr>
</tbody>
</table>

In group A out of 50 patients, 41 (82%) did not have nausea or vomiting postoperatively. 8 (16%) patients had nausea, while only 1 (2%) patient had vomiting in the first 24 hours. In group B, 17 (34%) patients had nausea, 5 (10%) had vomiting, while 28 (56%) did not complain of either nausea or vomiting. The frequency of nausea and vomiting was clinically and statistically lower in dexamethasone plus metoclopramide group as compared to dexamethasone alone p-value 0.032 and 0.028 for nausea and vomiting respectively.

Two patients in group A had to be given IV ondansetron 4 mg as a rescue antiemetic, while 10 patients in group needed the rescue antiemetic. Use of rescue antiemetic shown in Table 3, was significantly higher in dexamethasone group (p = 0.014).

DISCUSSION

This study compared the efficacy of the combination of dexamethasone and metoclopramide with dexamethasone alone in patients undergoing elective craniotomy.

Dexamethasone was reported as an effective antiemetic in patients receiving cancer chemotherapy in
The incidence of postoperative nausea and vomiting has been significantly decreased by preoperative single dose steroid administration in several studies.10,11

As an immune modulation strategy, Dexamethasone appears to shift the balance of inflammation, in favor of anti-inflammatory mediators. The incidence and severity of PONV have been significantly decreased as shown in several studies.12

The exact mechanism by which glucocorticoids decrease the incidence of nausea / vomiting is not fully understood, but probably can be explained by centrally mediated anti-emetic action via inhibition of prostaglandin synthesis, or inhibition of release of endogenous opioids.13

<table>
<thead>
<tr>
<th>Table 3: Use of Rescue Anti-Emetic.</th>
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<tr>
<td><strong>Group</strong></td>
</tr>
<tr>
<td>A</td>
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<tr>
<td>B</td>
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Table III: Num with Post-operative Nausea and V.

Metoclopramide is a central dopaminergic D2 receptor antagonist and a prokinetic drug that increases gastric emptying and shortens bowel transit time. The meta-analysis by Domino et al14 has shown that metoclopramide is not as effective as ondansetron and droperidol in preventing postoperative vomiting. Several studies compared a single dose of dexamethasone with a single dose of metoclopramide in the prophylaxis and treatment of PONV and found dexamethasone to be superior in the control of nausea and vomiting.15,16

However, current opinion questions the role of monotherapy, and combinations of dexamethasone with some other antiemetics have been found to be more effective than any drug alone.17-19 Biswas et al17 demonstrated that granisetron plus dexamethasone reduced the incidence of PONV after laparoscopic cholecystectomy more effectively than granisetron alone. Bano and colleagues compare the efficacy of combination of dexamethasone plus ondansetron with dexamethasone alone for postoperative nausea and vomiting in patients undergoing laparoscopic cholecystectomy, and the results showed the combination to be more effective than dexamethasone alone.20

Because of the high cost of these agents, we decided to use the less expensive metoclopramide in our study. Although some studies have described the combination of metoclopramide and dexamethasone as an inefficient combination for the prevention of postoperative nausea and vomiting.21,22 However Wallenborn and colleagues in a multicenter trial concluded that intraoperative administration of metoclopramide and dexamethasone is effective, safe, and cheap in preventing postoperative nausea and vomiting.23 Nasek et al24 also demonstrated that combination of dexamethasone plus metoclopramide is superior to metoclopramide and placebo in preventing PONV. Our study found this combination to be effective when compared to dexamethasone alone. The total incidence of PONV after laparoscopy was only 16% in patients administered the combination of dexamethasone plus metoclopramide. Furthermore only two patients from the dexamethasone and metoclopramide group required a rescue antiemetic, pointing to the high efficacy of this drug combination in the prevention of postoperative nausea and vomiting.

**CONCLUSION**

The present study demonstrated the combination of dexamethasone plus metoclopramide is superior to dexamethasone alone in preventing postoperative nausea and vomiting in patients undergoing elective craniotomy.

**Address for Correspondence**
Dr. Mohammad Abbas Tariq
Department of Anaesthesia, Institute of Kidney Diseases, Hayatabad Medical Complex, Peshawar
E-mail: drabbastariq@hotmail.com
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REFERENCES