

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%.⁵⁻⁸ Postoperative 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

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, age 33 to 65 years, ASA (American Society of Anesthesiologists) physical status I and II, scheduled for elective craniotomy under general anaesthesia were included 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.

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

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

1981⁹. The incidence of postoperative nausea and vomiting has been significantly decreased by pre-operative 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 opioids¹³.

Table 3: Use of Rescue Anti-Emetic.

Group	No. of Patients	Percentage	P-Value
A	2	(04%)	0.014
B	10	(20%)	

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

Table 2: Frequency of Postoperative Nausea and Vomiting.

Time	Event	Group A	Group B	P-Value	
0 – 02 Hours	Nausea	5 (10%)	11 (22%)	0.032	
	Vomiting	1 (02%)	03 (06%)		
02 – 04 Hours	Nausea	3 (06%)	04 (08%)		
	Vomiting	0	02 (04%)		
04 – 24 Hours	Nausea	0	02 (04%)		
	Vomiting	0	0		
First 24 Hours	Nausea	8 (16%)	17 (34%)		0.028
	Vomiting	1 (02%)	05 (10%)		

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

REFERENCES

1. Gan TJ, Meyer T, Apfel CC, et al. Consensus guidelines for managing postoperative nausea and vomiting. *Anesth Analg* 2003; 97: 62–71.
2. Watcha MF. Postoperative nausea and emesis. *Anesthesiol Clin North America* 2002; 20: 709–22.
3. Ziauddin AK, Zainab S, Saeeda H. Injection dexamethasone in preventing postoperative nausea and vomiting: A comparison with placebo in the patients undergoing Laparoscopic Cholecystectomy. *J Coll Physicians Surg Pak* 2006; 16 (11): 689-92.
4. Nasreen L, Mohammad NK, Fayyaz AQ, Shahid K, Akbar SJ. Dexamethasone as antiemetic during Gynecological Laparoscopic surgery. *J Coll Physicians Surg Pak* Dec 2005; 15 (12): 778-81.
5. Fabling JM, Gan TJ, El – Moalem HE, et al. A randomized, double – blind comparison of ondansetron versus placebo for prevention of nausea and vomiting after infratentorial craniotomy. *J Neurosurg Anesthesiol* 2002; 14: 102–7.
6. Fabling JM, Gan TJ, El – Moalem HE, et al. A randomized, double – blinded comparison of ondansetron, droperidol, and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. *Anesth Analg* 2000; 91: 358–61.
7. Madenoglu H, Yildiz K, Dogru K, et al. Randomized, double – blinded comparison of tropisetron and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. *J Neurosurg Anesthesiol* 2003; 15: 82–6.
8. Kathirvel S, Dash HH, Bhatia A, et al. Effect of prophylactic ondansetron on postoperative nausea and vomiting after elective craniotomy. *J Neurosurg Anesthesiol* 2001; 13: 207–12.
9. Italian Group for antiemetic research. Dexamethasone, granisetron or both for prevention of nausea and vomiting during chemotherapy for cancer. *N Eng J Med* 1995; 332: 1-5.
10. Callery MP. Preoperative steroids for laparoscopic surgery. *Ann Surg* 2003; 238: 661-2.
11. Wang JJ, Ho ST, Liu HS, Ho CM. Prophylactic antiemetic effects of dexamethasone in woman undergoing ambulatory laparoscopic surgery. *BJA* 2000; 84: 459-62.
12. Wattwil M, Thorn SE, Lovqvist A, Wattwil L, Gupta A, Liljegren G. Dexamethasone is as effective as ondansetron for the prevention of postoperative nausea and vomiting following breast surgery. *Acta Anaesthesiol Scand* 2003; 47: 823-7.
13. Sapolsky RM, Romero LM, Munck AV. How do glucocorticoids influence stress response? Integrative, permissive, suppressive stimulatory and preparatory action. *Endocr Rev* 2000; 21: 55-89.
14. Domino KB, Anderson EA, Polissar NL, Posner KL. Comparative efficacy and safety of ondansetron, droperidol and metoclopramide for preventing postoperative nausea and vomiting: a meta – analysis. *Anesth Analg* 1999; 88: 1370-1379.
15. Huang JC, Shieh JP, Tang CS, Tzeng JI, Chu KS, Wang JJ. Low – dose dexamethasone effectively prevents postoperative nausea and vomiting after ambulatory laparoscopic surgery. *Can J Anesth* 2001; 48: 973–977.
16. Tzeng JI, Hsing CH, Chu CC, Chen YH, Wang JJ. Low – dose dexamethasone reduces postoperative nausea and vomiting after epidural morphine: comparison of metoclopramide with saline. *J Clin Anesth* 2002; 14: 19–23.
17. Biswas BN, Rudra A. Comparison of granisetron and granisetron plus dexamethasone for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Acta Anaesthesiol Scand* 2003; 47: 79–83.
18. Lopez – Olaondo L, Carrascosa F, Pueyo FJ, Mondero P, Busto N, Saez A. Combination of ondansetron and dexamethasone in the prophylaxis of postoperative nausea and vomiting. *Br J Anesth* 1996; 76: 835–840.
19. McKenzie R, Tantisira B, Karambelker DJ, Riley TJ, Abdelhady H. Comparison of ondansetron with ondansetron plus dexamethasone in the prevention of postoperative nausea and vomiting. *Anaesth Analg* 1994; 79: 961–964.
20. Bano F, Zafar S, Aftab S, Haider S. Dexamethasone plus ondansetron for prevention of post-operative nausea and vomiting in patients undergoing laparoscopic cholecystectomy: A comparison with dexamethasone alone. *J Coll Physicians Surg Pak* 2008; 18: 265-9.
21. Fujii Y, Tanaka H, Toyooka H. The effects of dexamethasone on antiemetics in female patients undergoing gynaecologic surgery. *Anesth Analg* 1997; 85: 913–917.
22. Maddali MM, Mathew J, Fahr J, Zarroung AW. Postoperative nausea and vomiting in diagnostic gynaecological procedure : comparison of the efficacy of the combination of dexamethasone and metoclopramide with that of dexamethasone and ondansetron. *J Postgrad Med* 2003; 49: 302–306.
23. Wallenborn J, Gelbrich G, Bulst D, Behrends K, Wallenborn H, Rohrbach A et al. Prevention of post-operative nausea and vomiting by metochlorpromide combined with dexamethasone : randomized double blind multi-centre trial. *Br Med J* 2006; 333 (7563): 324.
24. Nesek – Adam V, Grizelj – Stojcic E, Rasic Z, et al. Comparison of dexamethasone, metoclopramide, and their combination in the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. *Surg Endosc* 2007; 21: 07-12.