

Original Article**COMBINED USE OF METOCLOPRAMIDE AND GLYCOPYRROLATE AS A PROPHYLACTIC ANTIEMETIC IN ELECTIVE CESAREAN SECTION UNDER SPINAL ANESTHESIA****Dinesh Thakur¹, Mihir Goswami², Himanshu Shah³**

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ABSTRACTS

Objective: To compare the combined effect of two traditional antiemetic drugs (metoclopramide and glycopyrrolate) against published data of effect of single antiemetic drug for prevention of nausea and vomiting in women undergoing lower section caesarean section under spinal anaesthesia
Methods: Seventy eight full term parturient women undergoing lower segment cesarean section under spinal anaesthesia (using 5% lignocaine) were injected metoclopramide 10mg & glycopyrrolate 0.2mg intravenously at the time of abdominal incision. The frequency of nausea and vomiting and Apgar scores of neonates were noted. **Results:** Incidence of nausea was noted in 3.84% during operative and post operative period. No incidence of vomiting and any other adverse effects were observed. Apgar scores were ≥ 8 in all neonates at one and five minutes. **Conclusion:** Incidence of vomiting is low (zero case) in current study group compared to groups (data from published research) with either metoclopramide or glycopyrrolate or ondansetron but observed differences are statistically insignificant, however the upper class interval limit of Z value falling above significance level (>1.96) in all groups suggesting that it might significant and required further studies to prove or disprove significantly lower incidences of nausea and vomiting if combine use of two drugs (glycopyrrolate plus metoclopramide) as a prophylactic antiemetic in elective cesarean section under spinal anaesthesia.

Key Words: nausea, vomiting, spinal anaesthesia, cesarean section, metoclopramide, glycopyrrolate

INTRODUCTION

The incidences of emetic symptoms are high during the pregnancy because of increased concentration of progesterone in the system. Progesterone decreases gastrointestinal motility and reduces lower oesophageal pressure. These physiological and anatomical changes may predispose the pregnant women to develop emetic tendency.

Intra-operative emetic symptoms during abdominal surgery under regional anaesthesia have a multi-factorial origin and factors such as psychological changes (anxiety), arterial hypotension, hypo-perfusion of the central

nervous system, abrupt visceral movements, and concomitant opiate administration¹ may have an influence on them. Additionally, there is a higher predisposition to intra operative nausea vomiting among patients at the end of their pregnancies, as a consequence of increased intra-abdominal pressure.

The reported incidence of nausea and vomiting during cesarean section performed under regional anaesthesia varies from 50% to 80% when no prophylactic antiemetic is given.²⁻⁸

A number of treatments have been introduced in order to reduce post operative nausea and vomiting (PONV), such as 5-HT₃ antagonists

(ondansetron and granisetron), dopamine receptor antagonists, and antihistamine drugs. However, each of these treatments is associated with critical limiting factors, namely cost with 5-HT₃ antagonists, extrapyramidal symptoms with dopamine receptor antagonists, excessive sedation and tachycardia with antihistamine drugs.⁹⁻¹¹

Almost all previous researches on PONV prevention were using single prophylactic antiemetic drug. The purpose of present study was to compare the combined effect of two traditional antiemetic drug i.e. metoclopramide and glycopyrrolate against published research data of single antiemetic drug for prevention of nausea and vomiting in women undergoing cesarean section under spinal anaesthesia.

MATERIALS AND METHODS

Seventy eight full term parturient women of ASA I & II (American Society of Anesthesiology Grade I & II), aged between 19 and 35 years scheduled for elective lower segment cesarean section under spinal anaesthesia were subjects of the study. Patients with preeclampsia, arterial hypertension, chronic utero-placental insufficiency, history of acid peptic disease or fasting for less than 6 hours were excluded. The study period was between January 2010 and December 2010.

Each patient received 20 ml per kilogram of lactated Ringer's solution before administration of spinal anaesthesia to prevent hypotension. All patients received oxygen via a face mask at a flow rate of 3 liters per minutes since induction of spinal anaesthesia. Patients were positioned in the right/left lateral decubitus or sitting

position and a 22 gauge spinal needle was introduced through mid line approach at the L3-L4 inter-space. Patients received 2 ml of 5% lignocaine (hyperbaric) subarachnoid injection and turned in supine position with left uterine displacement to avoid aorto-caval compression. Surgery was started when a sensory block up to T5 dermatome was obtained. Each patient received 10 mg of metoclopramide and 0.2 mg of glycopyrrolate intravenously when surgery started.

Hypotension was defined as a reduction of more than 20% from baseline pressure or if systolic blood pressure was less than 90 mmHg and managed with bolus intravenous lactated Ringer's solution and ephedrine in 10-mg increments.

Each patient was observed and asked for the intra-operative occurrence of nausea and vomiting. Apgar scores were obtained at 1 and 5 minutes. Each patient remained in the recovery room for 4 hours and was observed by the nursing staff for the postoperative occurrence of nausea and vomiting.

Results are analyzed manually by suitable statistical tests.

OBSERVATIONS AND RESULTS

Incidence of nausea was noted in 3(3.84%) of total 78 studied subjects during operative/post-operative period. No incidence of vomiting was observed. Noticeable side effects of metoclopramide and glycopyrrolate were not found in any studied subjects. Apgar scores were ≥ 8 in all neonates at one and five minutes.

Table 1: Published researches showing effect of antiemetic drugs during operative and post operative period of cesarean section under spinal anaesthesia in American Society of Anesthesiology grade I & II full term parturient women

Antiemetic drugs →	Metoclopramide (10mg)			Ondansetron(4mg)	
	Biswas et al ¹² (n=20)	Ali Shahriari at al ¹³ (n=40)	Garcia-Miguel FJ at al ¹⁴ (n=48)	A K Pan at al ⁸ (n=20)	Garcia-Miguel FJ at al ¹⁴ (n=49)
Nausea (%)	4(20)	21(52.5)	3(6.25)	2(10)	4(8.16)
Vomiting (%)	2(10)	0	1(2.08)	1(5)	0

DISCUSSION

Great care had been taken to design methodology such a way that made possible to compare findings with previous researches.

Present study found no side effects of combination of metoclopramide (10mg) and glycopyrrolate (0.2mg) on parturient women and neonates. The Apgar scores were acceptable

range of 8-10 at one and five minutes suggesting safety of drugs. Similar drug safety of Metoclopramide was observed by Lussos SA at al³, Biswas et al¹² and Ali Shahriari at al¹³. Similarly, Biswas et al¹² and Ure D at al¹⁵ found that Glycopyrrolate was safe to neonates and no adverse effects found in patients.

Study results were compared with Glycopyrrolate alone shows lower in incidence of nausea and vomiting but statistically insignificant at 95% significance level (Table 2).

Table 2: Comparison of antiemetic effect of metoclopramide plus glycopyrrolate to glycopyrrolate alone during operative and post operative period of cesarean section under spinal anaesthesia in American Society of Anesthesiology grade I & II full term parturient women

Observation	Metoclopramide(10mg) + Glycopyrrolate(0.2mg) % (n=78)	Glycopyrrolate (0.2mg) ¹² % (n=20)	Z value (Class Interval) at 95% CL	P value (95% C.L.)
Nausea	3.84	10	0.87 (-1.08, 2.83)	0.38
Vomiting	0	5	1.02 (-0.93, 2.98)	0.30

Table 3: Comparison of antiemetic effect of metoclopramide plus glycopyrrolate to metoclopramide alone during operative and post operative period of cesarean section under spinal anaesthesia in American Society of Anesthesiology grade I & II full term parturient women

Observation	Metoclopramide(10mg) + Glycopyrrolate(0.2mg) % (n=78)	Metoclopramide (10mg) % (n=108)*	Z value (Class Interval) at 95% CL	P value (95% C.L.)
Nausea	3.84	25.92	4.65 (2.67, 6.61)	<0.001
Vomiting	0	2.77	1.75 (-0.020, 3.70)	0.08

*combine data, incorporated from studies by Biswas et al¹², Ali Shahriari¹³ & Garcia-Migual FJ at al¹⁴

Study results were compared with Metoclopramide alone shows lower in incidence of nausea and vomiting but the incidence of

vomiting is statistically insignificant at 95% confidence limits (Table 3).

Table 4: Comparison of antiemetic effect of metoclopramide plus glycopyrrolate to ondansetron during operative and post operative period of cesarean section under spinal anaesthesia in American Society of Anesthesiology grade I & II full term parturient women

Observation	Metoclopramide(10mg) + Glycopyrrolate(0.2mg) % (n=78)	Ondansetron(4mg) % (n=69) [#]	Z value (Class Interval) at 95% CL	P value (95% C.L.)
Nausea	3.84	8.69	1.20 (-0.75, 3.16)	0.22
Vomiting	0	1.44	1.00 (-0.95, 2.96)	0.31

[#] combined data, incorporated from studies by A K Pan at al⁸ & Garcia-Migual FJ at al¹⁴

Study results were compared with ondansetron shows lower in incidence of nausea and vomiting in current study group but statistically insignificant at 95% confidence limits (Table 4).

Although, incidence of nausea was low and statistically significant ($p < 0.001$) when study group compared to group with metoclopramide alone drug (Table 3) have comparatively moderate value as nausea is discomfort, not complication. Again, nausea is a subjective

sensation which interfering in valid comparisons.

CONCLUSION AND RECOMMENDATION:

Incidence of vomiting is low (zero case) in current study group compared to groups with either metoclopramide or glycopyrrolate or ondansetron. However, observed differences are statistically insignificant, the upper class interval limit of Z value falling at significant level (>1.96)

in all groups. It suggest, observed lower incidence of nausea and vomiting in current study group (glycopyrrolate + metoclopramide) may be significant in future studies or if sample size increased. So we recommended further studies to prove or disprove our findings of lower incidences of nausea and vomiting if combine two drugs (glycopyrrolate plus metoclopramide) as a prophylactic antiemetic in elective cesarean section under spinal anesthesia.

REFERENCES:

1. Kestin IG. Spinal anaesthesia in obstetrics. *Br J Anesth* 1991;66:596-607.
2. Kovac AL. Prevention and treatment of postoperative nausea and vomiting, *Drugs* 2000; 59: 213-43.
3. Lussos SA, Bader AM, Thornhill ML, Datta S. The antiemetic efficacy and safety of prophylactic metoclopramide for elective caesarean section delivery during spinal anaesthesia. *Reg Anesth* 1992; 17: 126-30.
4. Pan PH, Moore CH. Intraoperative antiemetic efficacy of prophylactic ondansetron versus droperidol for cesarean section patients under epidural anesthesia. *Anesth Analg* 1996;83:982-6
5. Kang YG, Abouelish E, Caritis S. Prophylactic intravenous ephedrine infusion during spinal anesthesia for cesarean section. *Anesth Analg* 1982;61:839-42.
6. Santos A, Datta S. Prophylactic use of droperidol for control of nausea and vomiting during spinal anaesthesia for caesarean delivery. *Anesth Analg* 1984; 63: 85-87.
7. Chestnut DH, Vandewalker GE, Qwen CI et al. Administration of metoclopramide for prevention of nausea and vomiting during epidural anaesthesia for elective caesarean delivery. *Anesthesiology* 1987; 66: 563-566.
8. A K Pan, A Rudra. Prophylactic single dose intravenous administration of ondansetron in the prevention of postoperative emetic symptoms during spinal anaesthesia for caesarean delivery. *Indian J. Anaesth.*2003;47(3):178-180.
9. Gan TJ. Postoperative nausea and vomiting-can it be eliminated? *JAMA* 2002; 287: 1233-6.
10. 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: 1370-9.
11. Fujii Y, Tanaka H, Kobayashi N. Prevention of nausea and vomiting after middle ear surgery: granisetron versus ramosetron, *Laryngoscope* 1999; 109: 1988-90.
12. B N Biswas, A Rudra, S K Das, S Nath et al. A Comparative Study of Glycopyrrolate, Dexamethasone and Metoclopramide in Control of Post-Operative Nausea and Vomiting after Spinal Anaesthesia for Caesarean Delivery. *Indian J. Anaesth.* 2003; 47 (3) : 198-200.
13. Ali Shahriari, K Maryam, M H Heidari. Prevention of nausea and vomiting in caesarean section under spinal anaesthesia with midazolam or metoclopramide? *Journal of the Pakistan Medical Association* 2009;43:756-759.
14. García-Miguel FJ, Montaña E, Martín-Vicente V, Fuentes AL, Alsina FJ, San José JA: Prophylaxis Against Intraoperative Nausea And Vomiting During Spinal Anesthesia For Cesarean Section. A Comparative Study Of Ondansetron Versus Metoclopramide. *The Internet Journal of Anesthesiology* 2000; Vol4N2: <http://www.ispub.com/journals/IJA/Vol4N2/nvpo.htm>; Published April 1, 2000; Last Updated April 1, 2000.accessed on 1st March 2011.
15. Ure D, James KS, McNeill M, Booth JV. Glycopyrrolate reduces nausea during spinal anaesthesia for caesarean section without affecting neonatal outcome. *Br J Anaesth.*1999;82(2):277-9.