A COMPARATIVE STUDY OF INTRAVENOUS ONDANSETRON, GRANISETRON AND RAMOSETRON FOR PREVENTION OF POSTOPERATIVE NAUSEA AND VOMITING IN PATIENTS UNDERGOING CAESAREAN SECTION

Bansal Suman R[1], Ramtani Umesh[2], Bansal Rohan[3]

[1]Senior Resident, Department of Anaesthesiology, Indira Gandhi Government Medical College, Nagpur, Maharashtra, Affiliated to Maharashtra University of Health Sciences, Nashik.
[2]Assistant Professor, Department of Anaesthesiology, Indira Gandhi Government Medical College, Nagpur, Maharashtra, Affiliated to Maharashtra University of Health Sciences, Nashik.
[3]Assistant Professor, Department of Orthopaedics, Indira Gandhi Government Medical College, Nagpur, Maharashtra, Affiliated to Maharashtra University of Health Sciences, Nashik.

ABSTRACT

BACKGROUND

Nausea and vomiting after regional anaesthesia for caesarean delivery are common occurrences. Despite of high incidence of PONV in caesarean section, there are limited studies to compare antiemetic drugs. This study compares intravenous ondansetron, granisetron, ramosetron in patients undergoing LSCS with respect to efficacy in preventing PONV.
Study Design- Prospective, observational study.

MATERIALS AND METHODS

A prospective, observational study with sample size -150 patients conducted with 50 patients in each group. A standard regional anaesthetic for caesarean section given. Group-O received intravenous Ondansetron, Group-G received intravenous Granisetron and Group-R received intravenous Ramosetron. Presence of nausea and vomiting & haemodynamic parameters were recorded during and after surgery. Incidence of PONV was studied over a period of 24 hours and was divided into early (0-6) and late (6-24) postoperative period. If nausea and/or vomiting were present, VAS score and need for rescue antiemetics were noted.

RESULTS

Incidence of nausea and vomiting and rescue antiemetic requirement was maximum in group O and minimum in group R during both early and late postoperative period. Mean VAS score was highest in group O & lowest in group R. Incidence and severity of adverse effects were statistically comparable in all 3 groups.

CONCLUSION

Ramosetron is best followed by Granisetron and both are comparably better than Ondansetron for prophylaxis of PONV after caesarean section.

KEYWORDS

Postoperative Nausea & Vomiting, Caesarean Section, Antiemetic.

HOW TO CITE THIS ARTICLE: Suman BR, Umesh R, Rohan B. A comparative study of intravenous ondansetron, granisetron and ramosetron for prevention of postoperative nausea and vomiting in patients undergoing caesarean section. J. Evolution Med. Dent. Sci. 2017;6(7):575-580, DOI: 10.14260/Jemds/2017/123

BACKGROUND

Nausea, retching and vomiting during and after regional anaesthesia for caesarean delivery are a common occurrence (Incidence is extremely variable, up to 80%).[1] These symptoms are distressing and uncomfortable for the parturient and may interfere with the surgical procedure.[2] Emetic symptoms during caesarean delivery have a multifactorial origin such as psychological (anxiety), hypotension, hypoperfusion of the CNS, surgical stimuli (abrupt visceral movements, exteriorisation of the uterus, intra-abdominal manipulation or exploration and peritoneal traction during closure), concomitant opiate administration, increased intra-abdominal pressure and hormonal changes. Apart from these, a number of factors including age, gender, smoking habit, history of motion sickness, previous postoperative emesis, pain, operative procedure, and anaesthetic technique, are all considered to affect the occurrence of nausea, retching and vomiting.[1,2]

Many drugs like Prochlorperazine, Metoclopramide and Promethazine have so far been tried to prevent or alleviate this problem. But these drugs have varying effectiveness and their use is limited because of delayed recovery, sedation and sometimes distressing side effects like dry mouth, dysphoria, restlessness and extrapyramidal symptoms.[3,4,5] A potential new entry (in the early 1990s) into the antiemetic pharmacopoeia is selective 5-hydroxytryptamine receptor antagonist, {Ondansetron, Granisetron, Ramosetron, Dolasetron, Palonosetron (intravenous use only) and Tropisetron} which lacks the effect at cholinergic, adrenergic, dopaminergic and histaminic receptors. Since their introduction the 5-HT_3-receptor antagonists have become the most widely used drugs for chemotherapy-induced emesis.[6,7,8] The use of these agents has been shown to

Financial or Other, Competing Interest: None.
Submission 15-12-2016, Peer Review 07-01-2017,
Acceptance 14-01-2017, Published 23-01-2017.
Corresponding Author:
Dr. Ramtani Umesh,
"Utkarsh", 97, Roopam Society,
Near Lahanuji Nagar,
Jaripatka-440014,
Nagpur.
E-mail: drumesh08@gmail.com
DOI: 10.14260/jemds/2017/123

improve patient satisfaction, decrease recovery and discharge times, and reduce an unanticipated hospital admission.[9]

There are a lot of studies comparing 5-HT_3 antagonist in laparoscopic surgeries and gynaecological surgeries.[10,11,12,13,14,15] Despite of very high incidence of PONV in caesarean section, there are limited studies to compare these drugs, thus we conducted a study to compare intravenous Ondansetron, Granisetron and Ramosetron in patients undergoing LSCS with respect to efficacy in preventing nausea and vomiting intra-operatively and during first 24 hours after surgery, to determine whether these agents alone are effective for prevention of PONV following elective caesarean section, need for rescue antiemetic, severity of nausea using VAS score, overall patient satisfaction, effect on haemodynamics and incidence of adverse effects.

MATERIALS AND METHODS

After receiving ethical committee clearance, written and informed consent from patients, this prospective, observational study was conducted with sample size of 150 patients (ASA grade I or II) aged 18-40 yrs. Exclusion criteria included incapable or refusing to be enrolled, allergy to study drugs, previous history of PONV, history of motion sickness, patient who received antiemetic drug within 24 hours prior to surgery, significant renal, hepatic, cardiac and coagulation abnormalities, known contraindication to SAB and history of drug or alcohol abuse.

Parturients were randomly allocated into three groups, fifty in each (n=50) by card sampling. Every parturient included in the study was allowed to choose a card in the preoperative period. A randomisation list was generated, and syringes containing each drug were prepared by personnel not involved in this study. Test drug was given after clamping of umbilical cord. Group-O received IV Ondansetron (4 mg, 2 mL), Group-G received IV Granisetron (3 mg, 3 mL) and Group-R received IV Ramosetron (0.3 mg, 2 mL).

After shifting patient on operation table, all preoperative vital parameters (BP, Pulse, SpO_2, RR, $EtCO_2$, Urine output) were recorded. Pre-hydration was done with 10-15 mL/kg body weight- IV Ringer lactate solution within 20 minutes. Under all aseptic precautions lumbar puncture was performed with 25/26 gauge Quincke needle in the L3-L4 or L4-L5 space in sitting or left lateral position using midline technique. After confirming free flow of CSF, 0.5% hyperbaric bupivacaine 2 mL (10 mg) injected at a rate of 0.25 mL/sec, time of injection noted & immediately patients were placed in supine position to achieve block height up to T_6. A wedge of 15^0 was placed under the right hip. All patients received supplemental Oxygen (4 litre/min.) via nasal prong. Injection Oxytocin 10 units was given slowly to mother. Injection Diclofenac 3 mL (75 mg) IM given (2 hours after completion of surgery and further advised as twice a day dose or on patient request) for postoperative analgesia.

Presence of nausea and vomiting & all the haemodynamic parameters were recorded during and after surgery. Incidence of PONV was studied over a period of 24 hours after surgery and was divided into intra-operative, early (0-6) and late (6-24) postoperative period. If nausea and/or vomiting were present, VAS score and need for rescue antiemetics were noted. We also observed for any adverse effects and finally asked the patient for overall satisfaction at the end of 24 hours.

Vital parameters (ECG, Heart rate, MBP, Respiratory rate, SpO_2, $EtCO_2$) were recorded (baseline measurements, every 5 minute intervals till 20 min., every 10 minute intervals till end of procedure, one hourly for the first 3 hours, at 12 hours & at 24 hours postoperatively).

The intensity of nausea and vomiting was assessed during intra-operative period, from end of surgery till 6 hours (early postoperative period) and from 6 hours to 24 hours (late postoperative period) by Nausea and Vomiting Score (0-complete response, 1-nausea only, 2-nausea and vomiting).[13] The intensity of nausea episode was assessed using a 100 mm Visual Analogue Scale (VAS) (0 = No nausea, 100 = Severe nausea). Rescue antiemetic of metoclopramide 10 mg IV was given if vomiting occurred once or nausea of VAS score >40 or at the patient request.[14]

The degree of overall satisfaction with management of nausea and vomiting was assessed and asked by patient at the end of observation period (24 hours) by Patient Satisfaction Score (Grade 0 = Poor, Grade 1 = Adequate, Grade 2 = Good, Grade 3 = Excellent).[13,14]

Patients were carefully observed for any adverse effects like headache, dizziness, constipation, flushing, drowsiness or any other symptoms. Apgar score was not recorded in our study because study drugs were given after clamping of umbilical cord.

The collected data were analysed by various statistical techniques like percentage, mean and standard deviation. Significance of difference between means of the groups was found out by paired t- test.

RESULTS

In our study, the mean age of patients was 23.92±3.34 years in Group O, 26.46±3.58 years in group G and 23.88±2.21 years in Group R. The average weight was 54.84±8.23, 50.16±5.12 and 49.12±16.35 whereas the mean duration of surgery was 50.1±7.52 minutes, 48±6.30 minutes and 50.1±7.52 minutes in Group O, G and R respectively. The difference was statistically insignificant among all the three groups ($p>0.05$) for the demographic parameters including age, weight and duration of surgery (Table 1).

In early postoperative period, complete response was seen in 40 patients (80%), 43 patients (86%) and 47 patients (94%) in Group O, G and R respectively. Nausea was seen in 7 patients (14%), 5 patients (10%) and 3 patients (6%) whereas both nausea and vomiting was observed in 3 patients (6%), 2 patients (4%) and none in Group O, G and R respectively. There was statistically significant difference between group O versus R ($p< 0.05$) but no statistically significant difference was present between group O versus G & G versus R ($p>0.05$) for complete response, nausea and nausea with vomiting. Difference among all the 3 groups were statistically significant (O>G>R) in regards to rescue antiemetic given ($p< 0.05$) with 5 patients (10%) in group O and 2 patients (4%) in group G given rescue antiemetic whereas none in group R required it. PONV scores were 0.26±0.48, 0.18±0.56 and 0.06±0.23 in group O, G and R

respectively whereas VAS scores were 16.8±13.59, 10.6±12. 34 and 8.5±11.21 in group O, G and R respectively which was statistically significant (p< 0.05) between the three groups.

In late postoperative period, complete response was seen in 33 patients (66%), 40 patients (80%) and 45 patients (90%) in Group O, G and R respectively. Nausea was seen in 12 patients (24%), 8 patients (16%) and 5 patients (10%) whereas both nausea and vomiting was observed in 5 patients (10%), 2 patients (4%) and none in Group O, G and R respectively. There was statistically significant difference between group O versus R (p< 0.05) but no statistically significant difference was present between group O versus G & G versus R (p>0.05) for complete response, nausea and nausea with vomiting. Difference among all the 3 groups were statistically significant (O>G>R) in regards to rescue antiemetic given (p< 0.05) with 10 patients (20%) in group O and 2 patients (4%) in group G given rescue antiemetic whereas none in group R required it. PONV scores were 0.44±0.67, 0.24±0.57 and 0.1±0.30 in group O, G and R respectively whereas VAS scores were 26.9±23.79, 12.8±23.31 and 4.9±9.31 in group O, G and R respectively which was statistically significant (p<0.05) between group O versus group G, group O versus group R and group G versus group R.

The results obtained after Ramosetron administration were superior as compared to Ondansetron and Granisetron administration with a statistically significant difference for VAS scores, patient satisfaction and requirement of rescue antiemetic.

No serious side effect was noted in any group. Headache was most common in all 3 groups (10%, 10% and 6% in Group O, G and R respectively) followed by constipation (4%, 2% and 4% in Group O, G and R respectively) & dizziness (4% in all 3 groups). None of the patients showed extra-pyramidal side effect, allergic reactions or any other side effect due to drugs. Incidence of overall side effects was low & statistically comparable in all 3 groups (p>0.05) [Table 3].

Sl. No.	Variables	Range	Group O (Mean±SD)	Group G (Mean±SD)	Group R (Mean±SD)	P Value
1.	Age (years)	18-40	23.92±3.34	26.46±3.58	23.88±.21	>0.05
2.	Weight (kg)	45-65	54.84±8.23	50.16±5.12	49.12±16.35	>0.05
3.	Duration of surgery(min.)	45-75	50.1±7.52	48±6.30	50.1±7.52	>0.05

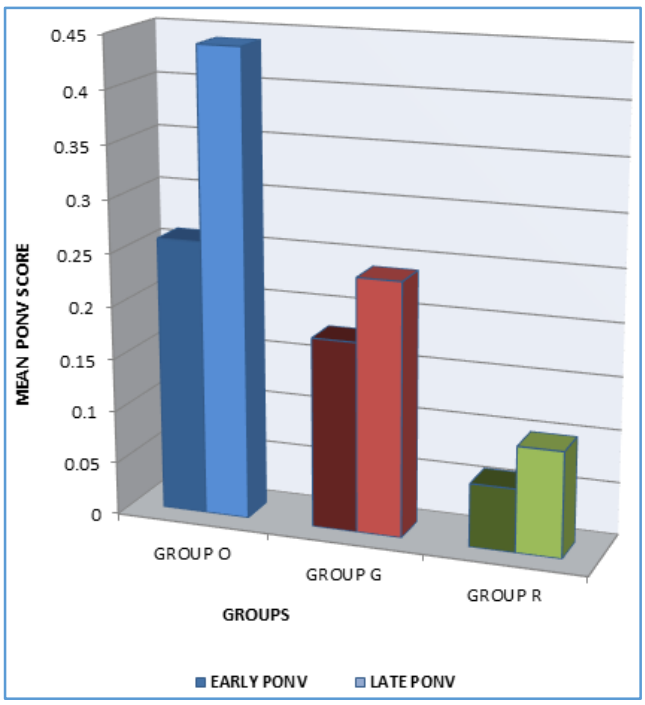
Table 1. Demographic Profile

Early Postoperative		Group O	Group G	Group R
1.	Complete response n (%)	40(80)	43(86)	47(94)
2.	Nausea n (%)	7(14)	5(10)	3(6)
3.	Nausea & Vomiting n (%)	3(6)	2(4)	0
4.	Rescue antiemetic n (%)	5(10)	2(4)	0
5.	PONV score mean± SD	0.26±0.48	0.18±0.56	0.06±0.23
6.	VAS score for nausea mean± SD	16.8±13.59	10.6±12..34	8.5±11.21
Late Postoperative				
1.	Complete response n (%)	33 (66)	40 (80)	45 (90)
2.	Nausea n (%)	12 (24)	8 (16)	5 (10)
3.	Nausea & Vomiting n (%)	5 (10)	2 (4)	0
4.	Rescue antiemetic n (%)	10 (20)	2 (4)	0
5.	PONV score mean± SD	0.44±0.67	0.24±0.57	0.1±0.30
6.	VAS score for nausea mean± SD	26.9±23.79	12.8±23.31	4.9±9.31

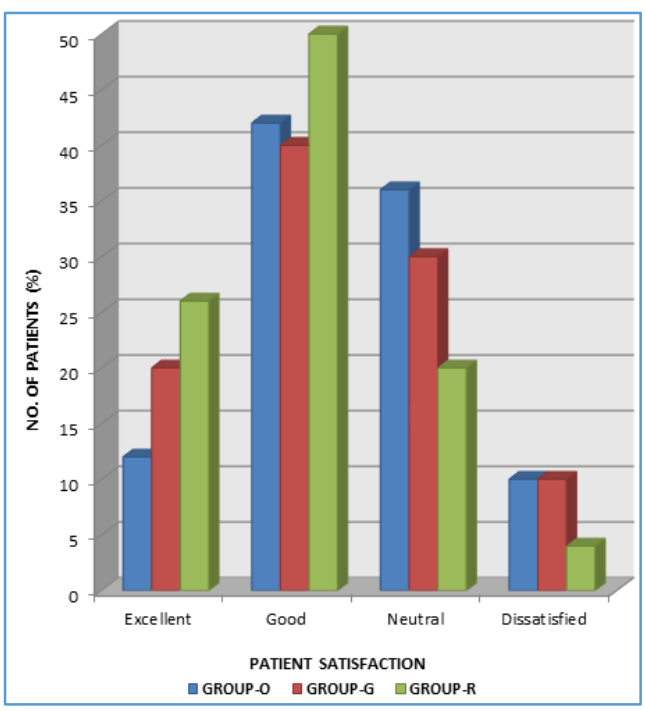
Table 2. Incidence of Nausea and Vomiting in Three Treatment Groups over 24 Hours

Sl. No.	Adverse Effects	O		G		R	
		N	%	N	%	N	%
1.	Headache	5	10	5	10	3	6
2.	Constipation	2	4	1	2	2	4
3.	Dizziness	2	4	2	4	2	4
4.	Others (Flushing, Diarrhoea, Hypotension, ECG changes, Extra-pyramidal reactions, Allergic reactions)	0	0	0	0	0	0

Table 3. Incidence of Adverse Effects in Three Groups



Graph 1. Comparison of Mean Early (0-6 Hours) & late (6-24 Hours) PONV Scores



Graph 2. Patient Satisfaction Score

DISCUSSION

Spinal blockade is the preferred anaesthetic for elective or emergency caesarean section. The effects of spinal anaesthesia on women during labour are different as compared to the general population due to the differential distribution of the anaesthetic drug in the cerebrospinal fluid as a result of increased spinal canal pressure,[16] changes in CSF acid-base balance,[17] and protein content.[18] Side effects, including hypotension, nausea and vomiting, and hypersensitivity to intrathecal opiates are common.[19]

Lussos et al believe that PONV after delivery is related to the surgical manipulation of the uterus, abdominal viscera and peritoneum, even in the presence of adequate sensori-motor blockade.[20] Abdominal surgery and manipulation of abdominal viscera induces the release of humoral substances including 5-HT, which may stimulate 5-HT3 receptors on the afferent vagus nerves, triggering the emetic reflex especially in awake patients. We compared intravenous Ondansetron, Granisetron and Ramosetron in patients undergoing LSCS with respect to efficacy in preventing nausea and vomiting intra-operatively and during first 24 hours after surgery, to determine whether these agents alone are effective for prevention of PONV following elective caesarean section, need for rescue antiemetic, severity of nausea using VAS score, overall patient satisfaction, effect on haemodynamics and incidence of adverse effects.

We administered the antiemetic drug after clamping of the umbilical cord because the effects of Ondansetron, Granisetron and Ramosetron on foetus and new-borns are unknown. Ondansetron has been used for hyperemesis gravidarum and no adverse foetal effects were observed.[21] The optimal dose of ondansetron to prevent PONV following ambulatory gynaecological surgery is 4 mg.[22] The optimal dose of granisetron to prevent PONV is 2 mg,[23] whereas dose for Ramosetron is 0.3 mg.[13] In the study, test drugs were given through intravenous route as it was convenient for us and it did not disturb NBM status required preoperatively though some studies compared oral vs. intravenous route.[24] Gigilo et al in their study to prevent nausea and vomiting following cancer chemotherapy concluded that both ondansetron and granisetron have similar antiemetic efficacy but dose of granisetron is much less than ondansetron.[25] Moreover ondansetron has a shorter half-life of 3 hours, whereas granisetron and ramosetron have a longer half-life of 8-9 hours and 9.3 hours respectively due to which they are more effective in preventing nausea and vomiting.

Ogata A et al conducted an analysis of Ramosetron hydrochloride, based on receptor occupancy considering its active metabolite (M-1). The average total receptor occupancy after intravenous administration of 0.3 mg of Ramosetron hydrochloride to human was calculated to be 82.9% (ramosetron, 77.8%; M-1, 5.1%), thus exhibiting a significant antiemetic activity. Furthermore, the estimated time course of 5-HT3 receptor occupancies after intravenous administration of 0.3 mg of Ramosetron hydrochloride suggested a substantial impact of the active metabolite (M-1) which contributed to the long duration of binding on the 5-HT3 receptor. Thus, ramosetron is more selective 5-HT3 receptor antagonist than ondansetron and granisetron.[26,27]

Lee J W et al compared Ramosetron's and Ondansetron's preventive antiemetic effects in highly susceptible patients undergoing abdominal hysterectomy and concluded that Ramosetron (0.3 mg) is more effective in preventing delayed PONV in highly susceptible women undergoing abdominal hysterectomy compared with Ondansetron (4 mg).[13] Fujii Y e al studied the effect of Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynaecological surgery and also compared Ramosetron and Granisetron for preventing postoperative nausea and vomiting after gynaecologic surgery and concluded that prophylactic therapy with Ramosetron is more effective than

Granisetron for the long term prevention of PONV after major gynaecologic surgery.[28] Mild headache, constipation and dizziness have been reported as side effects with all three drugs as was also seen in our study but no serious side effects were seen.

In our study, results obtained after Ramosetron administration were superior as compared to Ondansetron and Granisetron administration for PONV prophylaxis and there was a statistically significant difference for VAS scores, patient satisfaction and requirement of rescue antiemetic favouring ramosetron as the drug of choice for PONV prophylaxis in patients undergoing caesarean section.

To our knowledge, no study has compared Ondansetron, Granisetron and Ramosetron simultaneously. We have shown that the IV administration of Ramosetron followed by Granisetron are comparably better than Ondansetron for prophylaxis of PONV after caesarean section. Ramosetron and granisetron are highly effective up to 24 hours with single dose, and are devoid of many side effects associated with traditional antiemetics.

CONCLUSION

Ramosetron and granisetron appreciably and remarkably reduced PONV till 24 hours; none of the patients had vomiting in ramosetron group. Ondansetron reduced PONV significantly till 6 hours but as its half-life is short ($t_{1/2}$- 3.5 hours), it was not that effective in late postoperative period. In our study, occasional headache, constipation & dizziness were noted, but the incidence and severity of these events were similar in all 3 groups. No serious side effect was noted in any group. Thus, all the three drugs were considered to be relatively free of adverse effects for preventing PONV during caesarean section.

To conclude Ramosetron followed by Granisetron are comparably better than Ondansetron for prophylaxis of PONV after caesarean section. Ramosetron and granisetron are highly effective up to 24 hours with single dose, and are devoid of many side effects associated with traditional antiemetics.

REFERENCES

[1] Balki M, Carvalho JC. Intraoperative nausea and vomiting during cesarean section under regional anesthesia. International Journal of Obstetric Anesthesia 2005;14(3):230–41.

[2] Watcha MF, White PF. Postoperative nausea and vomiting. Its etiology, treatment, and prevention. Anesthesiology 1992;77(1):162-84.

[3] Fujii Y, Tanaka H, Toyooka H. Prevention of nausea and vomiting with granisetron, droperidol and metoclopramide during and after spinal anaesthesia for caesarean section: a randomized, double-blind, placebo-controlled trial. Acta Anaesthesiol Scand 1998;42(8):921-5.

[4] Garcia-Miguel FJ, Montano E, Martin-Vicente V, et al. Prophylaxis against intraoperative nausea and vomiting during spinal anesthesia for cesarean section, a comparative study of ondansetron versus metoclopramide. Internet Journal of Anesthesiology 2000;4N2.

[5] Gan TJ, Meyer T, Apfel CC, et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003;97(1):62-71.

[6] Pan PH, Moore CH. Comparing the efficacy of prophylactic metoclopramide, ondansetron, and placebo in cesarean section patients given epidural anesthesia. J Clin Anesth 2001;13(6):430-5.

[7] Abouleish EI, Rashid S, Haque S. Ondansetron versus placebo for the control of nausea and vomiting during caesarean section under spinal anaesthesia. Anaesthesia 1999;54(4):479-82.

[8] Bhattacharya D, Banerjee A. Comparison of ondansetron and granisetron for prevention of nausea and vomiting following day care gynaecological laparoscopy. Indian journal of Anaesth 2003;47(4):279-82.

[9] Pan AK, Rudra A. Prophylactic single dose intraoperative administration of ondansetron in the prevention of postoperative emetic symptoms during spinal anaesthesia for caesarean delivery. Indian journal of Anaesth 2003;47(3):178-80.

[10] Uddin R, Aziz L, Choudhury SNS. Comparison of ondansetron and granisetron for prevention of PONV following elective LUCS. Journal of BSA 2007;20(2):61-5.

[11] 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(1):79–83.

[12] Fujii Y, Saitoh Y, Tanaka H, et al. Ramosetron vs granisetron for the prevention of postoperative nausea and vomiting after laparoscopic cholecystectomy. Can J Anaesth 1999;46(10):991-3.

[13] Kim SI, Kim SC, Baek YH, et al. Comparison of ramosetron with ondansetron for prevention of postoperative nausea and vomiting in patients undergoing gynaecological surgery. British Journal of Anaesthesia 2009;103(4):549–53.

[14] Lee JW, Park HJ, Choi J, et al. Comparison of ramosetron's and ondansetron's preventive antiemetic effects in highly susceptible patients undergoing abdominal hysterectomy. Korean J Anesthesiology 2011;61(6):488-92.

[15] Rajeeva V, Bhardwaj N, Batra YK, et al. Comparison of ondansetron with ondansetron and dexamethasone in prevention of postoperative nausea and vomiting in diagnostic laparoscopy. Can J Anaesth 1999;46(1):40-4.

[16] Dantenhan DL, Fragraeus L. Acid-base changes of spinal fluid during pregnancy. Anesth Analg 1984;A63:204.

[17] Sheth AP, Dantenhan DL, Fragraeus L. Decreased CSF protein during pregnancy as a mechanism facilitating the spread of spinal anesthesia. Anesth Analg 1985;A64:280.

[18] Echevarría M, Caba F, Bernal L, et al. Effect of the local anesthetic on visceral pain in cesarean sections done under intradural anesthesia. Rev Esp Anesthesiol Reanim 1996;43(1):2-6.

[19] Kestin IG. Spinal anaesthesia in obstetrics. Br J Anesth 1991;66(5):596-607.
[20] Lussos SA, Bader AM, Thornhill ML, et al. The antiemetic efficacy and safety of prophylactic metoclopramide for elective cesarean delivery during spinal anesthesia. Reg Anesth 1992;17(3):126-30.
[21] Briggs GG. Teratogenicity and drugs in breast milk. In: Yee LL, Koda-Kimble MA (eds). Applied therapeutics: the clinical use of drugs. Vancouver, WA 1985:45-1.
[22] Raphael JH, Norton AC. Antiemetic efficacy of prophylactic ondansetron in laparoscopic surgery: randomized double-blind comparison with metoclopramide. Br J Anaesth 1993;71(6):845-8.
[23] Fujii Y, Tanaka H, Toyooka H. Optimal antiemetic dose of granisetron for preventing postoperative nausea and vomiting. Can J Anaesth 1994;41(9):794-7.
[24] Perez EA, Hesketh P, Sandbach J, et al. Comparison of single-dose oral granisetron versus intravenous ondansetron in the prevention of nausea and vomiting induced by moderately emetogenic chemotherapy: a multicentre, double blind, randomized parallel study. J Clin Oncol 1998;16(2):754-60.
[25] Gigillo CA, Soares H, Castro CP, et al. Granisetron is equivalent to ondansetron for prophylaxis of chemotherapy induced nausea and vomiting: results of a meta-analysis of randomized controlled trials. Cancer 2000;89(11):2301-8.
[26] Janknegt R. Clinical efficacy of antiemetics following surgery. Anaesthesia 1999;54:1059-68.
[27] Ogata A, Yamada Y, Sugiura M, et al. Analysis of 5-HT3 receptor antagonist, ramosetron hydrochloride, based on receptor occupancy considering its active metabolite. Yakugaku Zasshi 2001;121(11):793-8.
[28] Fujii Y, Saitoh Y, Tanaka H, et al. Ramosetron for preventing postoperative nausea and vomiting in women undergoing gynecological surgery. Anesth Analg 2000;90(2):472-5.