

Ondansetron for Prophylaxis of Spinal Morphine Induced Nausea during Early Rooming in Breastfeeding: A Randomized Placebo Controlled Trial

Ketchada Uerpairojkit MD*, Arada Chesoh MD**, Dasinee Budcharoentong MD*

* Department of Anesthesia, Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand

** Department of Anesthesia, Yala Regional Hospital, Yala, Thailand

Background: After cesarean delivery under spinal anesthesia with morphine, postoperative nausea and vomiting (PONV) may disturb maternal activity during breastfeeding and consequently reduce the successful rate of lactation. Prophylactic ondansetron may reduce the symptoms during 24 hours postdelivery.

Objective: We conducted the present study to evaluate if ondansetron can reduce the incidence of nausea and vomiting after spinal morphine during early rooming in breastfeeding. The present study also investigated the associated factors of nausea and vomiting, occurring in post-anesthesia care unit (PACU) and during breastfeeding.

Material and Method: In a randomized, double-blinded study, 158 healthy patients having cesarean delivery under spinal anesthesia with morphine 0.2 mg were randomized to have ondansetron 4 mg (ondansetron group) or normal saline (control group) intravenously immediately after delivery. The primary outcome was the incidence of nausea during the first rooming-in breastfeeding. The incidence within 24 hours, the score of severity by a four-point Likert Scale, the incidences of vomiting, and itching were also compared.

Results: Comparing the incidence of nausea between ondansetron and control groups, they were similar during the first breastfeeding (24.2% vs. 37.5%) and 24 hours postdelivery (3.8% vs. 10.0%), ($p = 0.07$ and 0.13). The number required the rescued antiemetic in the PACU in the ondansetron group was less (5.1% vs. 16.3%, $p = 0.02$), but the other observed incidences and severity of nausea were similar to the control group. By regression analyses, the factors that reduced the nausea incidence in the PACU were ondansetron administration ($p = 0.04$, adjusted OR 0.28, 95% CI 0.08 to 0.96), and the history of previous cesarean delivery ($p = 0.04$, adjusted OR 0.29, 95% CI 0.09 to 0.98). By contrast, postdelivery methylergometrine administration increased the incidence ($p = 0.04$, adjusted OR 3.24, 95% CI 1.01 to 10.40). At 24 hours postdelivery, only the history of PONV increased the incidence ($p = 0.04$, adjusted OR 2.72, 95% CI 1.04 to 7.12).

Conclusion: The incidence of nausea was reduced by prophylactic ondansetron in the PACU, but was not significantly different during breastfeeding on the same day and 24 hours postoperatively. Therapeutic ondansetron may be appropriate and an economical practice.

Keywords: Breastfeeding, Cesarean, Nausea, Ondansetron, Prophylaxis

J Med Assoc Thai 2017; 100 (12): 1283-9

Website: <http://www.jmatonline.com>

Cesarean birth has negative impact on the successful breastfeeding. Many common causes are the various medical interventions including technique of anesthesia, surgical conditions, and their adverse effects, which affects the mother's recovery and readiness to have the baby for the first rooming-in breastfeeding^(1,2). Spinal anesthesia is the most common anesthetic technique for cesarean section in Thailand. Postoperative analgesia of 0.2 mg of spinal morphine effectively covers a period of 8 to 24 hours, which has very minimal maternal blood level and is safe for

lactation. The optimal dose of 0.2 mg of morphine has been studied and widely used for spinal anesthesia in Thailand for its acceptable VAS pain score of the first postoperative day after cesarean section; while other parenteral or enteral analgesic supplements are seldom needed⁽³⁾. However, postoperative nausea and vomiting (PONV) and itching are two common unpleasant symptoms throughout its analgesic duration. These postoperative unpleasant conditions may affect the successful rate of early breastfeeding and delay lactation onset. Suwannarurk reported the incidence of PONV at 60% to 80% after 0.2 mg spinal morphine, which is significantly higher when comparing to the prophylaxis group⁽⁴⁾. Ondansetron has been commonly used for its good efficacy and less side effect on

Correspondence to:

Uerpairojkit K. Department of Anesthesia, Faculty of Medicine, Chulalongkorn University, Bangkok 10303, Thailand.
Phone: +66-2-2564295, Fax: +66-2-2564294
E-mail: Ketchada.U@chula.ac.th

consciousness comparing to metoclopramide. However, no study confirmed its effective prophylaxis covering the period of breastfeeding activity. We conducted the present study to learn if ondansetron can reduce the incidence of nausea and vomiting after spinal morphine during early rooming in breastfeeding. The present study also investigated the associated factors of nausea and vomiting, occurring in post-anesthesia care unit (PACU) and during breastfeeding.

Material and Method

Approval was obtained from the Ethical Committee, Faculty of Medicine, Chulalongkorn University and Yala Regional Hospital, and was registered in the Thai Clinical Trial Registry (TCTR20160216003). The information of the study was explained to the parturient on the night before the surgery about the technique of anesthesia, intraoperative procedures, and the within 8-hour rooming in breastfeeding. The informed consent was received before the study was started. We enrolled 160 parturient, 68 from King Chulalongkorn Memorial Hospital and 92 from Yala Regional Hospital (between 2012 and 2015); who matched the following inclusion criteria: aged 18 to 50 years, The American Society of Anesthesiologists (ASA) physical status I-II, singleton, gestational age over 37 weeks and scheduled for elective cesarean section under successful spinal anesthesia. Exclusion criteria were allergy to any study medication, cardiovascular and neurological diseases, renal impairment, or refusal to breastfeed within eight hours after delivery. Demographic data were obtained for age, body weight, the history of PONV after previous surgery, motion sickness, and previous cesarean section. On arrival in the operating room, the parturient was applied standard monitors and baseline values were taken. Then spinal anesthesia was performed by 27 gauge Quincke spinal needle. After confirmation of free flow of cerebrospinal fluid, 2.2 ml of hyperbaric Bupivacaine (Marcaine Spinal® heavy 0.5%, Astra Zeneca) and 0.2 mg morphine were injected intrathecally. Then the patient was set in supine position and rapid intravenous cohydration of either lactated Ringer's or normal saline solution was given. The flow rate was reduced after 1,000 ml was given or maintained to replace deficit or blood loss as appropriate. Electrocardiography (ECG), oxygen saturation by pulse oximeter and 1-minute interval of blood pressure were monitored. Hypotension was treated with 6 mg of ephedrine intravenously and the same doses were repeated every one minute until the

blood pressure was within 80% of baseline values. Atropine 0.6 mg was given for heart rate below 40 beats/minute or constantly below 60 combined with over 30% decrement of systolic blood pressure after ephedrine. Successful spinal anesthesia was confirmed by pin prick test for sensory loss up to T5 skin dermatome. Analgesia during surgery was supplemented by ketamine 25 to 100 mg intravenously as needed until delivery. After delivery, 4 mg ondansetron (Onsia® Siam Pharmaceutical, Thailand) (Ondansetron group), or normal saline (control group) was given slowly by the period of two minutes. The study drug was given blindly according to the corresponding codes. The randomization code was prepared by a computer random number generator to receive the study drug. The study drug was prepared in a solution of either ondansetron 2 mg/ml (ondansetron group) or normal saline (NSS group) in 2 ml by volume. The patients were also blinded to the study medication. At the PACU, standard postoperative care was applied and nauseous or vomiting symptoms were treated with 10 mg of metoclopramide (Vomitin, Nida Pharma Inc., Thailand) intravenously upon a request. Rooming-in breastfeeding was firstly encouraged within eight hours after anesthesia on the mother's bed either on the bed or chair as preference. Metoclopramide 10 mg intravenously was a rescue antiemetic medication upon a request and total dosages within 24 hours were recorded. The recorded data were as follows: medication administered during cesarean section, for example: methylergometrine, ephedrine, ketamine, and the antiemetic request in the PACU. Presence of predelivery hypotension (systolic blood pressure below 100 mmHg), bradycardia (HR below 60/minute) were recorded. Postoperative patients were allowed nothing by mouth until the following morning. D5 1/2NS were continued postoperatively to maintain intravascular volume until oral fluid were allowed. Uterotonic agent with oxytocin intravenous infusion at 5 to 10 IU/hour for 4 hours was given without loading dose.

The severity of nausea while breastfeeding on their comfort positions at the first time (within eight hours postoperatively) and about 24-hour on the following day was self-evaluated. This was based on a four-point Likert scale, with 0 = none, 1 = mild, 2 = moderate, 3 = severe. The incidences of nausea (1 to 3 Likert scale), vomiting, vertigo, and itching, and the scores of the severity of nausea evaluated during the first breastfeeding (within eight hours postoperatively) and on 24-hour postoperatively were recorded. The time of the first rooming-in breastfeeding and

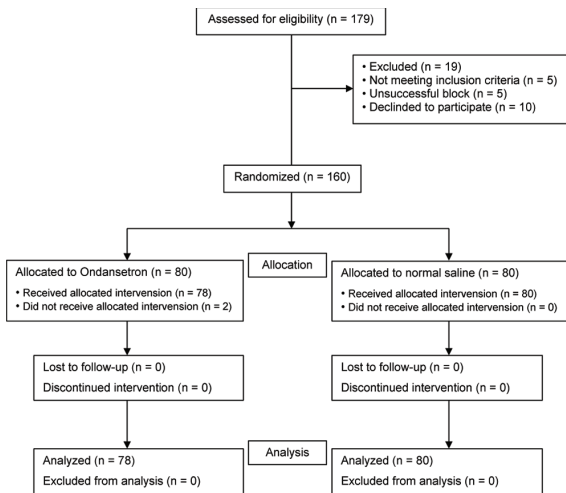


Fig. 1 CONSORT diagram showing patient recruitment and flow.

requirement of rescue antiemetic doses of metoclopramide in the PACU and within the first 24 hours were also recorded. The primary outcome measurement was the incidence of nausea during first rooming-in breastfeeding after 0.2 mg spinal morphine and local anesthetics. The previous study reported the incidence of 60%⁽⁴⁾. We calculated that the sample size of 70 parturient per group would have greater than 90% power to detect at 20% difference and increased by 10 for possible dropout. Chi-squared and Chi-squared for trend tests were used to compare the two or more categorical outcomes. Simple and multiple logistic regression were analyzed for the associated factors to the outcome of nausea in the PACU and during early rooming in breastfeeding. Analyses were performed using SPSS Statistics version 17. A *p*-value less than 0.05 was considered statistically significant.

Results

Patient recruitment and study flow were shown in Fig. 1. One hundred eighty parturient were recruited. The data were analyzed from 80 parturient in the NSS controlled group and 78 in the ondansetron group; with two that did not receive the studied drug because of the unstable blood pressure. All the data were analyzed according to their assignments. Patient's characteristics and time to the first rooming-in breastfeeding after anesthesia were shown in Table 1. The possible factors of the outcomes were summarized in Table 2. The parturient experienced of PONV, motion sickness, previous cesarean section were not different between the groups and no one had the history

of smoking. The number of the parturient who had intraoperative hypotension ($p = 0.33$), bradycardia ($p = 0.28$), received ephedrine ($p = 0.33$), methylergometrine ($p = 0.64$), ketamine ($p = 0.37$), or midazolam ($p = 0.62$) were comparable between the groups. The uncomfortable symptoms after spinal morphine were shown in Fig. 2 and 3. The numbers of mothers who had nausea during the first rooming-in breastfeeding and at 24-hour after delivery were not significantly different between the groups ($p = 0.07$ and 0.13). The incidences of nausea, vomiting, and vertigo were much lower on the following day, except itching, which continued (20% and 25% in ondansetron and control group) but all incidences were not significantly different between the two groups. The severity of the symptoms by a 4-point Likert Scale was not significant between the two groups ($p = 0.14$) (Table 3). Over half of the parturient experienced itching (52.6% and 61.3%, $p = 0.27$). There was a low incidence of vomiting (17.9% vs. 18.85%, $p = 0.90$) and vertigo (21.8% vs. 22.5%, $p = 0.92$). These incidences were comparable between the two groups. During postoperative care in the PACU, the numbers of those who requested metoclopramide were less in ondansetron [4 (5.1%)]

Table 1. Patient characteristics and time to the first breastfeeding after anesthesia

| Demographic data | Ondansetron (n = 78) | NSS (n = 80) | <i>p</i> -value |
|---|----------------------|--------------|-----------------|
| Age (year), mean (SD) | 31.5 (5.5) | 30.9 (5.4) | 0.50 |
| Weight (kg), mean (SD) | 67.4 (10.2) | 69.9 (12.8) | 0.19 |
| Time to first breastfeeding (hour), mean (SD) | 5.0 (2.5) | 4.4 (2.7) | 0.15 |

NSS = normal saline solution

Table 2. Frequencies of perioperative conditions and intraoperative medications

| Demographic data | Ondansetron (n = 78) | NSS (n = 80) | <i>p</i> -value |
|---------------------------------|----------------------|--------------|-----------------|
| Previous PONV, n (%) | 11 (14.1) | 12 (15.0) | 0.87 |
| Motion sickness, n (%) | 14 (17.9) | 15 (18.8) | 0.90 |
| Previous cesarean, n (%) | 49 (62.8) | 45 (56.3) | 0.40 |
| Perioperative medication, n (%) | | | |
| Ketamine | 1 (1.3) | 4 (5.0) | 0.37 |
| Methylergometrine | 19 (24.4) | 17 (21.3) | 0.64 |
| Midazolam | 2 (2.6) | 1 (1.3) | 0.62 |
| Ephedrine | 53 (67.9) | 60 (75.0) | 0.33 |
| Systolic BP <90 mmHg | 53 (67.9) | 60 (75.0) | 0.33 |
| HR <60 bpm | 2 (2.6) | 6 (7.5) | 0.28 |

PONV = postoperative nausea and vomiting; BP = blood pressure; HR = heart rate

Frequencies between the groups were compared by Chi-square or Fisher's exact test, significant at $p < 0.05$

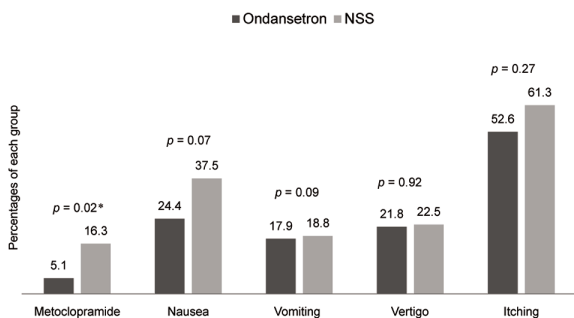


Fig. 2 Percentages of the patients who requested treatment or experienced the symptoms during early postoperative breastfeeding (Chi-squared test, * Significant at $p < 0.05$).

than the control group [13 (16.3%)] ($p = 0.02$), but were not significant for the first 24 hour postoperatively (70/7/1 vs. 69/9/2 for 0, 10, 20 mg, $p = 0.46$), Fig. 2 and 3, respectively. The factors associated with the adverse effect of spinal morphine were analyzed by simple and multiple logistic regression, and are shown in Table 4. The increased incidence of patients who required antiemetic in the PACU was associated with postdelivery methylergometrine administration ($p = 0.04$, adjusted OR 3.24, 95% CI 1.01 to 10.40), whereas the decreased were intraoperative ondansetron administration ($p = 0.04$, adjusted OR 0.28, 95% CI

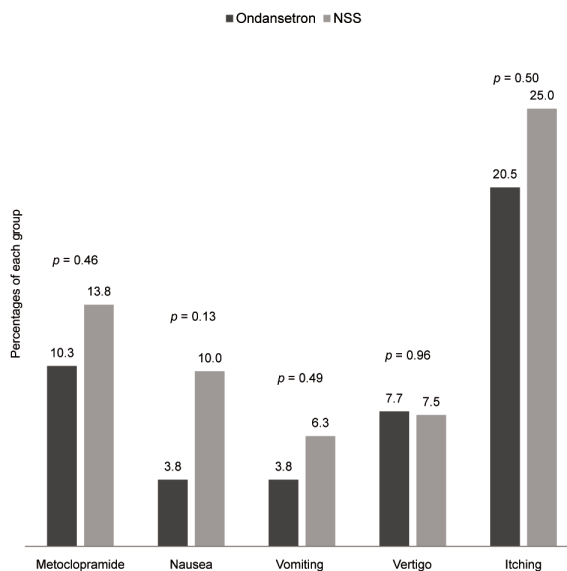


Fig. 3 Percentages of the patients who requested treatment or experienced the symptoms during 24-hour postoperative breastfeeding (Chi-squared test).

0.08 to 0.96) and history of previous cesarean delivery ($p = 0.04$, adjusted OR 0.29, 95% CI 0.09 to 0.98). When focusing on the symptom at the time of rooming-in breastfeeding, only the history of PONV significantly increased the incidence as shown in Table 5 ($p = 0.04$, adjusted OR 2.72, 95% CI 1.04 to 7.12).

Table 3. Severity of nausea during the 1st time of breastfeeding

| Severity of nausea | Ondansetron (n = 78) | NSS (n = 80) |
|--------------------|----------------------|--------------|
| 0 | 59 (75.6%) | 50 (62.5%) |
| 1 | 15 (19.2%) | 24 (30.0%) |
| 2 | 2 (2.6%) | 3 (3.8%) |
| 3 | 2 (2.6%) | 3 (3.8%) |

Chi-square for trend test $p = 0.14$

Discussion

Spinal anesthesia combined with 0.2 mg of morphine is a standard routine practice of anesthesia for cesarean section in Thailand. Minimizing the postoperative discomfort of the mothers promote the early stimulation for lactation and increase breastfeeding success. Focusing on the efficacy of ondansetron prophylaxis at the time of breastfeeding,

Table 4. The association of the factors and antiemetic request in post-anesthesia care unit (PACU)

| Variables | Coefficient β | SE | Crude OR | 95% CI | Adjusted OR | 95% CI | p-value |
|-------------------|---------------------|------|----------|---------------|-------------|---------------|---------|
| Constant | 0.73 | 3.07 | | | 2.07 | | 0.81 |
| Previous PONV | 0.41 | 0.76 | 1.37 | 0.31 to 6.16 | 1.50 | 0.34 to 6.70 | 0.59 |
| Motion sickness | 0.51 | 0.68 | 1.56 | 0.41 to 5.95 | 1.67 | 0.44 to 6.36 | 0.45 |
| Previous cesarean | -1.23 | 0.62 | 0.32 | 0.09 to 1.08 | 0.29 | 0.09 to 0.98 | 0.04* |
| HR <60 bmp | 0.66 | 0.95 | 2.09 | 0.31 to 14.12 | 1.94 | 0.30 to 12.42 | 0.48 |
| Ephedrine | 0.37 | 0.66 | 1.34 | 0.36 to 4.99 | 1.44 | 0.39 to 5.29 | 0.58 |
| Methylergometrine | 1.18 | 0.59 | 3.37 | 1.03 to 11.03 | 3.24 | 1.01 to 10.40 | 0.04* |
| Ondansetron | -1.28 | 0.63 | 0.28 | 0.08 to 0.99 | 0.28 | 0.08 to 0.96 | 0.04* |

SE = standard error

Simple and multiple logistic regression analysis, * significant at $p < 0.05$

Table 5. The association of the factors and the incidence of nausea during the 1st time of breastfeeding

| Variables | Coefficient β | SE | Crude OR | 95% CI | Adjusted OR | 95% CI | <i>p</i> -value |
|-------------------|---------------------|------|----------|---------------|-------------|--------------|-----------------|
| Constant | -4.81 | 2.51 | | | 0.01 | | -0.06 |
| Previous PONV | 1.00 | 0.49 | 2.72 | 1.04 to 7.10 | 2.72 | 1.04 to 7.12 | 0.04* |
| Motion sickness | 0.44 | 0.46 | 1.67 | 0.69 to 4.09 | 1.56 | 0.64 to 3.81 | 0.33 |
| Previous cesarean | 0.14 | 0.42 | 1.05 | 0.47 to 2.37 | 1.15 | 0.51 to 2.58 | 0.75 |
| HR <60 bmp | 0.55 | 0.81 | 2.34 | 0.46 to 12.01 | 1.74 | 0.35 to 8.51 | 0.50 |
| Ephedrine | -0.08 | 0.42 | 1.27 | 0.52 to 3.09 | 0.92 | 0.41 to 2.10 | 0.85 |
| Methylergometrine | 0.25 | 0.46 | 1.95 | 0.78 to 4.86 | 1.29 | 0.53 to 3.15 | 0.58 |
| Ondansetron | -0.51 | 0.37 | 0.60 | 0.29 to 1.26 | 0.60 | 0.29 to 1.25 | 0.17 |

Simple and multiple logistic regression analysis, * significant at $p < 0.05$

we considered two factors: the dosage and timing of drug administration. Regarding dosage, the USFDA Drug Safety Announcement (06-29-2012) offers two preliminary results. First, it cautions the dose-dependent QT prolongation of ondansetron. Second, it demonstrates that the use of 32 mg single intravenous dose causes the maximum mean difference in QTcF of 20 milliseconds, while 8 mg of the former causes 6 milliseconds of the latter from placebo. While the criterion of QT prolongation is 10 milliseconds above 450 milliseconds in females, we preferred the lower and safer dose of 4 mg intraoperative administration to avoid the incremental risk of arrhythmia during cesarean section. As for the timing of administration, we started the dose immediately after delivery to achieve intraoperative and in-PACU effect on spinal morphine-induced nausea and vomiting, as well as to eliminate drug before it passes to breast milk. Our study showed no significant difference for nausea prophylaxis of ondansetron during breastfeeding at both eight and 24 hours. Comparing to Suwannarurk's study⁽⁵⁾, the incidence of nausea during breastfeeding from the present study was half of that of 60% when the symptoms were evaluated covering postoperative period without prophylaxis. Those symptoms in the present study were in mild to moderate degree, which did not disturb breastfeeding. Psychological impact during the first breastfeeding may affect this lower incidence. The present study did not show statistical difference of the ondansetron group compared with the control. This may be explained by two factors. The first one was as our routine care, breastfeeding was delayed up to eight hours, and therefore its antiemetic efficacy was reduced along the period of time and resulted in no prophylactic coverage. The second was the physiological postpartum changes that brought them to the lower incidence and made no difference for prophylaxis administration. Oxytocin, which is

postdelivery uterotonic agent, is infused 5 to 10 IU/hour intravenously as routine practice in our institutions. This low dose minimized the risk of adverse hemodynamic changes, which induces unpleasant side-effect of nausea⁽⁶⁾. Additionally, the physiological release of oxytocin during postpartum period is known to have an effect on neuroendocrine stress signaling, anxiety, and depression and has important role in lactation, parturition, and maternal behavior⁽⁷⁾. The surge of oxytocin during breastfeeding appears to buffer subsequent stress-induced corticosteroid secretion^(8,9). This might reduce the incidence and severity of nausea and vomiting in spite of the motion during the activity of breastfeeding. By contrast, methylergometrine often induces nausea and vomiting as it is a serotonin (5HT₂) receptor agonist. In the PACU, the present study showed that methylergometrine administration was associated with higher incidence of antiemetic requests ($p = 0.04$). Intraoperative ondansetron (5HT₃ antagonist), which has a duration of around six hours, reduced this incidence in the PACU ($p = 0.04$) but did not continue its prophylactic action on nausea, vomiting, and vertigo through the time of breastfeeding. Contrary to Charuluxananan et al's study⁽¹⁰⁾, our result agreed with that by Sarvela et al⁽¹¹⁾, which did not find its protective effect on itching after spinal morphine. The experience of previous cesarean section also decreased the incidence in the PACU ($p = 0.04$). This experience might be a psychological factor on stress; however, the explanation of this is not confirmed without the psychometric measures or other psychological evaluation that might be associated with the outcome. The risk scores by Apfel et al consisted of four predictors, female gender, history of motion sickness or PONV, nonsmoking, and the use of postoperative opioids⁽¹²⁾. The present study confirmed that the history of PONV corresponds to those higher incidences during breastfeeding ($p = 0.04$). We

suggested using ondansetron individually according to these associated risk factors. The first breastfeeding in our institutes were started after discharge from the recovery room and full recovery from the anesthesia, therefore, this incidence of nausea with or without prophylaxis may be different from those which breastfeeding is earlier encouraged under the different routine mother supports.

Conclusion

Prophylactic ondansetron after cesarean delivery under spinal anesthesia with morphine reduced nausea incidence in the PACU, but was not established as effective in preventing PONV during breastfeeding. We suggest physical support during the activity and therapeutic antiemetic is an appropriate and economical practice.

What is already known on this topic?

Postoperative nausea and vomiting, induced by spinal morphine for postoperative analgesia, are found to be of high incidence, 60% to 80%. Prophylactic ondansetron is reported to be an effective decrement of PONV incidence. However, no prophylactic result has been proven with this spinal analgesic technique for cesarean section at the time of mother's rooming-in breastfeeding. The result may have influenced early breastfeeding success rate and impacted on economic practice.

What this study adds?

Prophylactic ondansetron reduced the incidence of nausea in the PACU when compared to the non-prophylactic group (OR 0.28, 95% CI 0.08 to 0.96, $p = 0.04$). In contrast with the PACU period, there was no significant difference when compared during breastfeeding on the same day and 24 hours postoperation. This study suggests that therapeutic ondansetron may be a more appropriate and economical practice.

Acknowledgement

The authors would like to thank the Department of Obstetrics and Gynecology, Faculty of Medicine, Chulalongkorn University and Yala Regional Hospital, Yala, Thailand for their assistance and cooperation.

Potential conflicts of interest

None.

References

1. Lin SY, Lee JT, Yang CC, Gau ML. Factors related

to milk supply perception in women who underwent cesarean section. *J Nurs Res* 2011; 19: 94-101.

2. Zanardo V, Svegliado G, Cavallin F, Giustardi A, Cosmi E, Litta P, et al. Elective cesarean delivery: does it have a negative effect on breastfeeding? *Birth* 2010; 37: 275-9.
3. Rodanant O, Sirichotewithayakorn P, Sriprajittichai P, Charuluxananan S. An optimal dose study of intrathecal morphine in gynecological patients. *J Med Assoc Thai* 2003; 86 (Suppl 2): S331-7.
4. Nual-on S, Theangda L, Budthai S. Effect of 4 mg ondansetron on postoperative nausea and vomiting in patients received intrathecal morphine for cesarean section. *Udonthani Hosp Med J* 2009; 17: 95-100.
5. Suwannarurk L. Comparison between dexa-methasone, metoclopramide or ondansetron for the prevention nausea and vomiting following intrathecal morphine for cesarean section. *Thammasat Med J* 2009; 9: 242-50.
6. Stephens LC, Bruessel T. Systematic review of oxytocin dosing at caesarean section. *Anaesth Intensive Care* 2012; 40: 247-52.
7. MacKinnon AL, Gold I, Feeley N, Hayton B, Carter CS, Zelkowitz P. The role of oxytocin in mothers' theory of mind and interactive behavior during the perinatal period. *Psychoneuroendocrinology* 2014; 48: 52-63.
8. Cox EQ, Stuebe A, Pearson B, Grewen K, Rubinow D, Meltzer-Brody S. Oxytocin and HPA stress axis reactivity in postpartum women. *Psychoneuroendocrinology* 2015; 55: 164-72.
9. Acevedo-Rodriguez A, Mani SK, Handa RJ. Oxytocin and Estrogen Receptor beta in the Brain: An Overview. *Front Endocrinol (Lausanne)* 2015; 6: 160.
10. Charuluxananan S, Kyokong O, Somboonviboon W, Narasethakamol A, Promlok P. Nalbuphine versus ondansetron for prevention of intrathecal morphine-induced pruritus after cesarean delivery. *Anesth Analg* 2003; 96: 1789-93, table.
11. Sarvela PJ, Halonen PM, Soikkeli AI, Kainu JP, Korttila KT. Ondansetron and tropisetron do not prevent intraspinal morphine- and fentanyl-induced pruritus in elective cesarean delivery. *Acta Anaesthesiol Scand* 2006; 50: 239-44.
12. Apfel CC, Läärä E, Koivuranta M, Greim CA, Roewer N. A simplified risk score for predicting postoperative nausea and vomiting: conclusions from cross-validations between two centers. *Anesthesiology* 1999; 91: 693-700.

Ondansetron กับการป้องกันอาการคลื่นไส้อาเจียนในขณะให้นมบุตรหลังการผ่าตัด cesarean section โดยการระงับความรู้สึกด้วยวิธีฉีดยาชา bupivacaine ร่วมกับ morphine เข้าช่องน้ำไขสันหลัง

เกษชาติ เอื้อไพโรจน์กิจ, อารดา เจ๊ะโซะ, ดาสนี พุทธเจริญทอง

ภูมิหลัง: หลังการผ่าตัดคลอดบุตรภายใต้การระงับความรู้สึกโดยการฉีดยาชาเฉพาะที่เข้าช่องน้ำไขสันหลังที่มียามอร์ฟินผสม ทำให้เกิดอาการคลื่นไส้อาเจียน ซึ่งก่อให้เกิดความไม่สบายในขณะให้นมมารดาแก่ทารกแรกคลอด และอาจมีผลกระทบต่ออัตราความสำเร็จของการเลี้ยงลูกด้วยนมมารดา การให้ ondansetron อาจลดอาการดังกล่าวได้

วัตถุประสงค์: เพื่อศึกษาว่า ondansetron สามารถลดโอกาสการเกิดอาการคลื่นไส้อาเจียน ในขณะกำลังให้นมมารดาในระยะแรกหลังการคลอดหรือไม่ หลังได้รับมอร์ฟินเข้าช่องน้ำไขสันหลังเพื่อระงับปวดหลังการผ่าตัดคลอด รวมทั้งศึกษาปัจจัยที่มีผลต่ออาการดังกล่าวในระยะพักฟื้น และขณะให้นมบุตร

วัสดุและวิธีการ: เป็นการศึกษาโดยวิธีสุ่มและปกปิดสองทางในมารดาที่มารับการผ่าตัดคลอดบุตร ภายใต้การฉีดยาชาเข้าช่องน้ำไขสันหลังร่วมกับมอร์ฟิน 0.2 มก. จำนวน 158 ราย โดยแบ่งเป็นกลุ่มทดลอง ซึ่งได้รับยา ondansetron 4 มก. และกลุ่มควบคุมได้รับน้ำเกลือ normal saline (NSS) ที่เวลาหลังการคลอดทันที โดยวัดผลการศึกษาหลักเป็นอุบัติการณ์อาการคลื่นไส้ขณะให้นมมารดาแก่บุตรในระยะแรกที่ห้องพัก รวมทั้งเปรียบเทียบอุบัติการณ์และความรุนแรงของอาการดังกล่าวโดย four-point Likert Scale และอาการอาเจียนและคันตามตัวระหว่าง 2 กลุ่ม ภายใน 24 ชั่วโมงหลังคลอด

ผลการศึกษา: เมื่อเปรียบเทียบระหว่างกลุ่มที่ได้ ondansetron กับ NSS ไม่พบความแตกต่างทางสถิติของอาการคลื่นไส้ขณะให้นมมารดาแก่บุตร (24.2% vs. 37.5%) และภายใน 24 ชั่วโมงหลังคลอด (3.8% vs. 10.0%), ($p = 0.07$ และ 0.13 ตามลำดับ) จำนวนผู้ที่ขอยาแก้อาการคลื่นไส้ในห้องพักฟื้นในกลุ่ม ondansetron น้อยกว่า NSS อย่างมีนัยสำคัญทางสถิติ (5.1% vs. 16.3%, $p = 0.02$) สำหรับอาการอื่น ๆ ไม่พบความแตกต่างกันทางสถิติ เมื่อพิจารณาโดยใช้ regression analysis พบว่าอาการคลื่นไส้ในระยะพักฟื้นในกลุ่ม ondansetron น้อยกว่ากลุ่ม NSS ($p = 0.04$, adjusted OR 0.28, 95% CI 0.08-0.96) และประวัติเคยผ่าตัดคลอดมาก่อนก็มีผลต่ออุบัติการณ์ที่ต่ำลง ($p = 0.04$, adjusted OR 2.29, 95% CI 0.09-0.98) สำหรับปัจจัยที่มีผลเพิ่มอุบัติการณ์ ได้แก่ การได้รับยา methylergometrine ($p = 0.04$, adjusted OR 3.24, 95% CI 1.01-10.40) และเมื่อผ่านพ้นไปถึงระยะ 24 ชั่วโมง ปัจจัยที่มีผลคือประวัติคลื่นไส้อาเจียนเดิมของผู้ป่วย ($p = 0.04$, adjusted OR 2.72, 95% CI 1.04-7.12)

สรุป: อุบัติการณ์ของอาการคลื่นไส้ลดลงในระยะพักฟื้นจากการป้องกันด้วย ondansetron แต่ไม่พบความแตกต่างทางสถิติในขณะให้นมมารดาทั้งระยะแรก และ 24 ชั่วโมงหลังคลอด จึงควรพิจารณาให้ ondansetron เพื่อการรักษามากกว่าเพื่อป้องกันและเพื่อให้ใช้อย่างมีประสิทธิภาพและคุ้มค่า
