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# The efficacy of ondansetron in comparison with pethidine for prevention of shivering in pregnant patients undergoing a cesarean section with spinal anesthesia

**Ferianto[1], Pandit S[2], Bambang Suryono S[2]**
Dumai District Hospital, Riau, [2]Department of Anesthesiology and Reanimation, Faculty of Medicine, Universitas Gadjah Mada University/Dr. Sardjito General Hospital Yogyakarta

## ABSTRACT

Postanesthetic shivering (POS) is a common complication following spinal anesthesia. Several drugs have been used to prevent POS, including ondansetron and pethidine. This study was conducted to compare the efficacy of ondansetron 8 mg with pethidine 0.4 mg/kg BW for prevention of shivering in pregnant patients undergoing a cesarean section with spinal anesthesia. This is a double blind controlled trial involving 96 pregnant patients between the age 18-40 years with ASA physical status I-II, gestational age of 37-42 weeks, body weight of 40-70kg or Body Mass Index (BMI) $<30$, body height $>145$ cm who underwent a cesarean section with spinal anesthesia in Dr. Sardjito General Hospital, Yogyakarta and affiliated hospital. Exclusion criteria included patients or families who refused to participate in the study, having a history of allergy to bupivacaine, ondansetron, and pethidin, patients with a fetus known to have congenital abnormalities earlier, body temperature early $>$ 38 ºC or $<36$ ºC, pregnancy with complications (PEB, eclampsia, HELLP syndrome), and pregnant patients with heart disease (severe hypertension, heart trouble, abnormal heart valves). The patients were randomized into two groups i.e. 48 patients of group ondansentron receiving intravenous ondansetron 8 mg and 48 patients of group pethidine receiving intravenous pethidine 0.4 mg/kg BW. The patients were observed for occurence and severity of POS, postoperative nausea and vomiting. The results showed that two patients (4.2%) on the ondansetron group and six patients (12.5%) on the pethidine group experienced of POS. Moreover, the efficacy of ondansetron in the prevention of POS (95.8%) was higher than pethidine (87.5%). However, there were not significantly different ($p>0.05$). The incidence of nausea on the ondansetron group (4.2%) was lower than the pethidine group (16.7%) ($p<0.05$). However, no significant difference in the incidences of vomiting was observed between the ondansetron (0%) dan the pethidine (4.2%) groups ($p>0.05$). In conclusion, the efficacy of ondansetron 8 mg is comparable to pethidine 0.4 mg/kgBW for prevention of shivering in pregnant patients after spinal anesthesia.

## ABSTRAK

*Postenesthetic shivering* (POS) adalah komplikasi yang umum terjadi setelah tindakan anestesi spinal. Beberapa obat telah digunakan untuk mencegah POS termasuk ondansetron dan petidin. Penelitian ini dilakukan untuk membandingkan efektivitas ondanstron 8 mg dengan petidin 0,4 mg/kg BB untuk mencegah POS pada pasien hamil yang menjalani operasi sesar dengan anestesi spinal. Penelitian ini merupakan uji klinik tersamar ganda melibatkan 96 pasien berumur 18-40 tahun dengan status fisik ASA I dan II, umur kehamilan 37-42 minggu, berat badan 40-70 kg (BMI $<30$), tinggi badan $>145$ cm yang menjalani bedah sesar dengan anestesi spinal di RSUP Dr. Sardjito, Yogyakarta dan rumah sakit afiliasi. Kriteria pengeluaran adalah pasien atau keluarga menolak terlibat penelitian, mempunyai riwayat alergi bupivakain, ondansetron, dan petidin,

* corresponding author: nabil.amanah@yahoo.co.id

pasien dengan janin diketahui mempunyai kelainan kongenital sebelumnya, temperatur awal >38 °C atau <36 °C, kehamilan dengan komplikasi (PEB, eklamsia dan simdrom HELLP), dan pasien hamil dengan kelainan jantung (hipertensi berat, gangguan jantung, kelainan denyut jantung). Pasien diacak menjadi dua kelompok yaitu 48 psien kelompok ondansetron yang menerima ondanstron 8 mg intravena dan 48 pasien kelompok petidin 0.4 mg/kg BB intravena. Pengamatan dilakukan terhadap kejadian dan keparahan POS, mual dan mutah pasca operasi. Hasil penelitian menunjukkan dua pasien (4,2%) pada kelompok ondansetron dan enam (12,5%) pada kelompok petidin mengalami POS. Efikasi ondansetron dalam mencegah POS (95.8%) lebih tinggi dari petidin (87,5%). Namun demikian tidak terdapat perbedaan nyata (p>0,05). Kejadian mual pada kelompok ondansetron (4,2%) lebih rendah dari pada kelompok petidin (16.7%) (p<0,05). Namun demikian kejadian mutah tidak berbeda nyata pada kelompok ondansetron (0%) dan petidin (4,2%) (p>0,05). Dapat disimpulkan, efikasi ondansetron 8 mg sebanding dengan petidin 0,4 mg/kg BB untuk mencegah *shivering* pada psien hamil setelah tindakan anestesi spinal.

***Key words***: shivering - hypothermia - spinal anesthesia - ondansetron - pethidine

## INTRODUCTION

Postanesthetic shivering (POS) is an involuntary movement that may affect one or several muscle groups. Postanesthetic shivering is a common complication following general anesthesia and also occurs intraoperatively during moderate and deep sedation.[1-3] The incidence of POS is reported between 5 up to 60% of patients recovering from general anesthesia and up to 30% of patients receiving epidural anesthesia.[4,5] Age, gender, type of anesthesia, amount and temperature of intravenous fluids, duration of surgery and temperature of operating room seem to be determinant factors of POS.[1-5]

The body thermoregulatory system coordinates defense against temperature changes to maintain body temperature within a normal range by optimizing normal body function. The central thermoregulatory control is the hypothalamus. Spinal anesthesia induces thermoregulatory impairment and leads to hypothermia. The hypothermia results from redistribution of body heat to periphery. Normally, heat loss is regulated by cutaneous vasodilation or vasoconstriction, sweating, and shivering. Shivering is an important complication of hypothermia. Shivering is a last defense that is activated only when behavioral compensations and maximal arterio venous shunt vasoconstriction are insufficient to maintain body temperature.[1-3] It is an involuntary, oscillatory muscular activity that augment metabolic heat production up to 600% above basal level.[6,7]

The first clinical consequence of POS is the discomfort for the patients. Moreover, it is associated with number of deleterious of sequelae. These include increased oxygen consumption and carbon dioxide production, cathecolamine release, a significant increased metabolic acidosis, increased cardiac output, tachycardia and hypertension, raised intraocular and intracranial pressures, increased risk of incidental trauma, and disrupts medical devices.[6-8] Postanesthetic shivering may also decrease mix venous oxygen saturation as well as interfering with electrocardiogram and pulse oxymetri monitoring.[9,10]

A wide range of drugs have been used to prevent POS, including pethidine and other opioids suc as fentanyl, sulfentanil, and meperidine,[5,6] tramadol,[4,5] ketamine,[11] clonidine,[12] and benzoxazocine.[13] Pethidine is remarkably effective to treat POS. Pethidine 25-50 mg doses is sufficient when given intravenously for

prevention and treatment of shivering in the majority of adults. Pethidine has long been used as standard therapy to prevent and treat shivering postanesthetic action. [5-7]

Postanesthetic shivering is accosiated with stimulation of seretonin or 5-hydroxytryptamine (5-HT) receptor in the brain and spinal cord. The 5-HT receptor plays an important role in control of the heat production and loss of body heat.[14] Antagonist of 5-$HT_3$ such as ondanstron and granisetron is reported to have effect against POS. [14-16] Moreover, ondansetron has been shown to be effective in the prevention of post-operative nausea and vomiting (PONV).[17] An agent to reduce both POS and PONV will be very benefit.[18] This study was conducted to evaluate the efficacy of intravenous bolus of ondansetron 8 mg in comparison to intravenous bolus of pethidine 0.4 mg/kg BW for prevention of shivering in pregnant patients undergoing a cesarean section with spinal anesthesia.

## MATERIALS AND METHODS

### Subjects

This was a randomized double-blind clinical trial conducted after approval from the Medical and Health Research Ethic Committee, Faculty of Medicine, Universitas Gadjah Mada, Yogyakarta and obtaining a written informed consent. A total of 96 pregnant women patients between the age 18-40 years with ASA physical status I-II, gestational age of 37-42 weeks, body weight of 40-70kg or Body Mass Index (BMI) <30, body height >145 cm who underwent a cesarean section with spinal anesthesia techniques in Dr. Sardjito General Hospital, Yogyakarta and affiliated hospital i.e. Dr. Soeradji General Hospital, Klaten, Central Java, Banyumas General Hospital, Central Java and Panembahan Senopati District Hospital, Bantul, Yogyakarta for period of February to June 2011. Exclusion criteria included patients or families who refused to participate in the study, having a history of allergy to bupivacaine, ondansetron, and pethidin, patients with a fetus known to have congenital abnormalities earlier, body temperature early > 38 ºC or <36 ºC, pregnancy with complications (PEB, eclampsia, HELLP syndrome), and pregnant patients with heart disease (severe hypertension, heart trouble, abnormal heart valves). Drop out criteria included patients experienced total spinal, sensory and motor block (T4-T8) not happened 15 minutes after anesthesia, spinal anesthesia considered fail, withdrew from the research and bleeding complications (uterine atony). The patients were randomly allocated to one of two groups i.e. 48 patients of group ondansentron receiving 8 mg ondansetron as an intravenous bolus injection and 48 patients of group pethidine receiving pethidine 0.4 mg/kg BW as an intravenous bolus injection.

### Protocol of study

Preoperative visit and checkup were performed before surgery and characteristics of patients were taken. A detail operating procedure conducting was explained to all patients. The patients who were willing to be involved in the study would signed an inform consent. The patient was placed in the surgery preparation room and an intravenous line was installed using abbocath 18G on the dorsum manus vein of the hand and ringer lactate solution was infused at dosage of 2 cc/kg BW/ hour for 30 minutes. Operating room temperature was maintaines at 20-26 $^{o}$C. After shifting the patients to operation table, preoperative vital parameters like electrocardiogram (ECG), pulse rate (PR), respiratory rate (RR), non invasive blood pressure (NIBP), mean arterial pressure (MAP), heart rate (HR) and $SpO_2$ rate were monitored and recorded prior to the anesthetic procedure. Ten minutes before spinal anesthesia,

8 mg ondansetron or pethidine 0.4 mg/kg BW was given as an intravenous bolus injection. The patients were placed in sitting or lateral dicubitus position and the spinal anesthesia was performed at the L3-4 lumbar region puncturing with a 25 G needle under sterile technique. Local anesthesia was conducted using 12.5 mg of 0.5% hyperbaric bupivacaine. The patients were then placed in the modified supine position with a pillow. The level of sensory blockade was evaluated using pinprick method at the second minute after spinal induction and continued in five-minute interval for 15 minutes. Standards for patient hemodynamic monitoring during anesthesia i.e. MAP, PR and RR was performed in five-minute interval for the first 15 minutes and then in fifteen-minute interval from the time just after the anesthesia started to the end of the operation. Oxygen supplementation was given using nasal cannulae. In the case of hypotention or blood pressure dropped >20%, 5-20 mg of ephedrine was given as an intravenous bolus injection. The patients were observed for occurence and severity of POS, postoperative nausea and vomiting, axilla and tympanic membrane temperature in fifteen-minute interval from the time just after anesthesia strated to the end of the operation and then thirty-minute interval from the end of the operation to the patients were placed in the recovery room. An intravenous bolus injection of pethidine 25 mg was given to patients with shivering. Moreover, intravenous of analgesic ketorolac 30 mg was given before the end of the operation. The severity of POS was measured as conducted by Crossley and Mahajan[19] with the criteria presented in TABLE 1. Data were recorded on the predesigned data collection form.

TABLE 1. Grade of shivering

| Grade | Clinical signs |
|---|---|
| 0 | No shivering |
| 1 | Piloerection or peripheral vasoconstriction, shivering invisible |
| 2 | No muscle activity, but limited to one muscle group |
| 3 | Muscular activity occurred in more than one muscle group |
| 4 | Shivering in the whole body |

### Statistical analysis

Data were tabulated and presented as mean ± standard deviation (SD) or percent. Data of incidence and severity of shivering and the side effects of drugs of ondansetron and pethidine groups were analyzed statistically using Chi square test. Data of age, weight, hemodynamic chages, axilla and tympanic membarane temperatures, operation room temperature were analyzed statistically using independent t-test. A p value $<0.05$ was considerd statistically significant. All statistic analysis was performed using SPSS version 15 computer program.

## RESULTS

Forty eigth patients were involved in each group of this study. The characteristics of patients of both groups are presented in TABLE 2. No significant difference was observed in terms of age, weight, height, BMI, systolic and diastolic blood pressure, MAP, HR, RR, axilla and tympani temperatures, and room temperature between the groups ($p>0.05$). It was indicated that the patients characteristics of both groups were comparable.

TABLE 2. Characteristics of subjects (mean ± SD or percent) of ondansetron and pethidine groups

| Variables | Ondansetron (n=48) | Pethidine (n=48) | p |
|---|---|---|---|
| Age (years) | 29.25±4.715 | 30.31±6.701 | 0.37 |
| Weight (kg) | 61.46±5.885 | 63.29±5.805 | 0.13 |
| Height (cm) | 156.88±4.693 | 158.10±4.219 | 0.18 |
| BMI (kg/m$^2$) | 24.97±2.097 | 25.32±2.108 | 0.42 |
| Systolic blood pressure (mmHg) | 124.83±15.620 | 125.88±14.107 | 0.73 |
| Diastolic blood pressure (mmHg) | 73.08±9.987 | 74.08±9.739 | 0.62 |
| MAP (mmHg) | 90.33±8.961 | 91.35±9.591 | 0.59 |
| RR (beats/minute) | 17.67±1.562 | 17.63±1.632 | 0.90 |
| HR (beats/minute) | 91.35±11.391 | 93.25±11.470 | 0.42 |
| Axilla temperature ($^o$C) | 36.70±0.387 | 36.56±0.249 | 0.07 |
| Tympani temperature ($^o$C) | 36.90±0.491 | 36.75±0.247 | 0.07 |
| Room temperature | 23.43±2.422 | 23.25±1.889 | 0.69 |
| Mistoprostol (N/%) | | | |
| • Use | 4 (12.5%) | 4 (8.3%) | 0.50 |
| • Not use | 42 (87.5%) | 44 (91.7%) | |

The incidences of POS at different time intervals on the group of ondansetron and the group of pethidine are presented in TABLE 3, while the severity of POS are presented in TBALE 4. No significant difference in the incidences and the severity of POS between the two gropus was also also observed (p>0.05).

TABLE 3. The incidence of POS at different time intervals on ondansetron and pethidine groups

| The incidence of POS | Ondansetron (n=48) | | Pethidine (n=48) | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 15 min | | | | | |
| • Positive | 0 | 0 | 2 | 4.2 | 0.15 |
| • Negative | 48 | 100 | 46 | 95.8 | |
| 30 min | | | | | |
| • Positive | 0 | 0 | 0 | 0 | 1.00 |
| • Negative | 48 | 100 | 48 | 100 | |
| 45 min | | | | | |
| • Positive | 1 | 2.1 | 4 | 8.4 | 0.17 |
| • Negative | 47 | 97.9 | 44 | 91.6 | |
| 60 min | | | | | |
| • Positive | 1 | 2.1 | 4 | 8.4 | 0.17 |
| • Negative | 47 | 97.9 | 44 | 91.6 | |
| 75 min | | | | | |
| • Positive | 0 | 0 | 3 | 6.3 | 0.08 |
| • Negative | 48 | 100 | 45 | 93.7 | |
| 90 min | | | | | |
| • Positive | 0 | 0 | 2 | 4.2 | 0.15 |
| • Negative | 48 | 100 | 46 | 95.8 | |
| 120 min | | | | | |
| • Positive | 0 | 0 | 2 | 4.2 | 0.15 |
| • Negative | 48 | 100 | 46 | 95.8 | |

TABLE 4. The severity of POS at different time intervals on ondansetron and pethidine groups

| The severity of POS | Ondansetron (n=48) | | Pethidine (n=48) | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 15 min | | | | | |
| • 0 | 48 | 100 | 46 | 95.8 | |
| • 1 | 0 | 0 | 1 | 2.1 | |
| • 2 | 0 | 0 | 0 | 0 | 0.36 |
| • 3 | 0 | 0 | 0 | 0 | |
| • 4 | 0 | 0 | 1 | 2.1 | |
| 30 min | | | | | |
| • 0 | 48 | 100 | 48 | 100 | |
| • 1 | 0 | 0 | 0 | 0 | |
| • 2 | 0 | 0 | 0 | 0 | 1.00 |
| • 3 | 0 | 0 | 0 | 0 | |
| • 4 | 0 | 0 | 0 | 0 | |
| 45 min | | | | | |
| • 0 | 47 | 97.9 | 44 | 91.7 | |
| • 1 | 0 | 0 | 3 | 6.2 | |
| • 2 | 0 | 0 | 0 | 0 | 0.21 |
| • 3 | 1 | 2.1 | 1 | 2.1 | |
| • 4 | 0 | 0 | 0 | 0 | |
| 60 min | | | | | |
| • 0 | 47 | 97.9 | 44 | 91.6 | |
| • 1 | 0 | 0 | 2 | 4.2 | |
| • 2 | 0 | 0 | 0 | 0 | 0.23 |
| • 3 | 1 | 2.1 | 2 | 4.2 | |
| • 4 | 0 | 0 | 0 | 0 | |
| 75 min | | | | | |
| • 0 | 48 | 100 | 45 | 93.7 | |
| • 1 | 0 | 0 | 3 | 6.3 | |
| • 2 | 0 | 0 | 0 | 0 | 0.08 |
| • 3 | 0 | 0 | 0 | 0 | |
| • 4 | 0 | 0 | 0 | 0 | |
| 90 min | | | | | |
| • 0 | 48 | 100 | 46 | 95.8 | |
| • 1 | 0 | 0 | 0 | 0 | |
| • 2 | 0 | 0 | 0 | 0 | 0.15 |
| • 3 | 0 | 0 | 2 | 4.2 | |
| • 4 | 0 | 0 | 0 | 0 | |
| 120 min | | | | | |
| • 0 | 48 | 100 | 46 | 95.8 | |
| • 1 | 0 | 0 | 0 | 0 | |
| • 2 | 0 | 0 | 0 | 0 | 0.15 |
| • 3 | 0 | 0 | 2 | 4.2 | |
| • 4 | 0 | 0 | 0 | 0 | |

Notations: 0: no shivering ; 1: piloerection or peripheral vasoconstriction, shivering invisible; 2 : no muscle activity, but limited to one muscle group ; 3 : muscular activity occurred in more than one muscle group; 4 : shivering in the whole body

The patients who experienced of POS on the group of ondansetron and pethidine are presented in TABLE 5. Two patients (4.2%) on the group of ondansetron and 6 patients (12.5%) experienced of POS. Moreover, the effectivenss of ondansetron in the prevention of POS after spinal anesthesia (95.8%) was higher than pethidine (87.5%). However, ther were not significantly different (p>0.05).

TABLE 5. The patients who experienced of POS on ondansetron and pethidine groups

| POS | Ondansetron (n = 48) | | Pethidine (n=48) | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Negative | 48 | 95.8 | 42 | 87.5 | 0.14 |
| Positive | 2 | 4.2 | 6 | 12.5 | |
| Total | 48 | 100 | 43 | 100 | |

The axilla and tympani temperatures after spinal anesthesia at different time intervals on the group of ondansetron and the group of pethidine are presented in TABLE 6. The axilla temperature of patients on the group of ondansetron in the 15; 30; 45; 60 dan 75 minutes after spinal anesthesia was normally significantly higher than the group of pethidine ($p<0.05$), while in the 90 and 120 minute was not significantly different ($p>0.05$). Furthermore, the tympani termperature of patients on the group of ondansetron at different time intervals of observation was normally significantly higher than the group of pethidine ($p<0.05$), except in the 120 minute. No significant difference of the tympani temperature was observed in the 120 minute after spinal anesthesia on the both groups ($p>0.05$).

TABLE 6. The body temperature at different time intervals on ondansetron and pethidine groups

| Temperature ( $^{o}$C) | Ondansetron | Pethidine | p |
|---|---|---|---|
| 15 min | | | |
| • Axilla | 36.356±0.316 | 36.123 ±0.3 74 | 0.001 |
| • Tympani | 36. 6 31 ±0.4 11 | 36.377 ±0.4 18 | 0.003 |
| 30 min | | | |
| • Axilla | 36.39 0±0.3 21 | 36.077 ±0.432 | 0.00 1 |
| • Tympani | 36. 6 46 ±0.405 | 36.298 ±0.374 | 0.001 |
| 45 min | | | |
| • Axilla | 36.413 ±0.3 89 | 35.983 ±0.369 | 0.001 |
| • Tympani | 36.685 ±0.493 | 36.317 ±0.410 | 0.001 |
| 60 min | | | |
| • Axilla | 36. 508 ±0.3 52 | 36.204 ±0. 401 | 0.001 |
| • Tympani | 36. 763 ±0.4 39 | 36. 494 ±0.4 41 | 0.004 |
| 75 min | | | |
| • Axilla | 36.62 5±0.3 49 | 36. 358 ±0.4 17 | 0.0 01 |
| • Tympani | 36. 856 ±0. 400 | 36. 621 ±0.4 49 | 0.008 |
| 90 min | | | |
| • Axilla | 36.646 ±0.3 06 | 36. 527 ±0. 506 | 0.1 68 |
| • Tympani | 36.975 ±0. 385 | 36. 792 ±0. 429 | 0.030 |
| 120 min | | | |
| • Axilla | 36.627 ±0.3 73 | 36.68 1±0. 427 | 0. 509 |
| • Tympani | 36.969 ±0.296 | 36. 910 ±0. 354 | 0.383 |

The block heights after spinal anesthesia at different time intervals on the group of ondansetron and the group of pethidine are presented in TABLE 7. The block heigths in the minute 2 and 5 on the group of ondansetron was not significantly different compared to the group of pethidine ($p>0.05$). However, the block height on the group of ondansetron in the minute 10 and 15 was significantly different compared to the group of pethidine ($p<0.05$).

TABLE 7. The block heights after spinal anesthesia at different time intervals on on ondansetron and pethidine groups

| The block height | Ondansetron (n=48) | | Pethidine (n=48) | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| 2 min | | | | | |
| • T6 | 3 | 3.1 | 0 | 0 | 0.20 |
| • T8 | 11 | 22.9 | 15 | 31.3 | |
| • T10 | 29 | 60.4 | 25 | 52.1 | |
| • T12 | 5 | 10.4 | 8 | 16.7 | |
| 5 min | | | | | |
| • T6 | 8 | 16.7 | 7 | 14.6 | 0.89 |
| • T8 | 26 | 54.2 | 28 | 58.3 | |
| • T10 | 13 | 27.1 | 11 | 22.9 | |
| • T12 | 1 | 2.1 | 2 | 4.2 | |
| 10 min | | | | | |
| • T6 | 24 | 50.0 | 11 | 22.9 | 0.09 |
| • T8 | 20 | 41.7 | 33 | 68.8 | |
| • T10 | 4 | 8.3 | 4 | 8.3 | |
| • T12 | 0 | 0 | 0 | 0 | |
| 15 min | | | | | |
| • T6 | 30 | 62.5 | 15 | 31.2 | 0.00 |
| • T8 | 18 | 37.5 | 33 | 68.8 | |
| • T10 | 0 | 0 | 0 | 0 | |
| • T12 | 0 | 0 | 0 | 0 | |

The incidence of side effects of drugs i.e. nausea and vomiting after spinal anesthesia on ondanstron and pethidine groups are presented in TABLE 8. The incidence of nausea on the ondansetron group (4.2%) was lower than the pethidine group (16.7%) ($p<0.05$). No significant difference in the incidences vomiting was observed between the ondansetron (0%) dan the pethidine groups (4.2%) ($p>0.05$).

TABLE 8. The incidence of nausea and vomiting on ondansetron and pethidine groups

| Side effect | Ondansetron (n = 48) | | Pethidine (n=48) | | p |
|---|---|---|---|---|---|
| | n | % | n | % | |
| Nausea | 2 | 4.2 | 8 | 16.7 | 0.05* |
| Vomiting | 0 | 0 | 2 | 4.2 | 0.15 |

** p< 0.05 = statistically significant difference*

The incidence of shivering on patients who had history of misoprostol administration on the ondanstron and the pethidine groups is presented in TABLE 9. No significant difference in the incidence of shivering on patients who had history of misoprostol administration was observed between both groups (p>0.05). Among 8 patients who experienced shivering, just 1 (12.5%) patient having history of misoprostol administration, while 7 (87.5%) patients not having of history of mistoprostol administration, whereas from 88 patients who not experienced shivering, there just 9 (10.2%) patients having history of mistoprostol administration, whereas 79 (89.8%) not having of histroy of mistoprostol administration.

TABLE 9. The incidence of shivering on patients who had history of misoprostol administration on ondansetron and the pethidine groups

| Misoprostol | Shivering | | | | p |
|---|---|---|---|---|---|
| | Positive (n = 8) | | Negative (n = 88) | | |
| | N | % | N | % | |
| Use | 1 | 12.5 | 9 | 10.2 | 0.84 |
| Not use | 7 | 87.5 | 79 | 89.8 | |
| Total | 8 | 100 | 88 | 100 | |

The length of operation, fluid administration, and bleeding during spinal anesthesis on the ondansetron and the phetidine groups are presented in TABLE 10. No significant different in the length of operation, fluid administration, and bleeding were observed between the both groups (p>0.05).

TABLE 10. Length of operation, fluid administration, and bleeding (mean ± SD) during spinal anesthesis on the ondansetron and the phetidine groups.

| Variables | Ondansetron | Pethidine | p |
|---|---|---|---|
| Duration of surgery (minute) | 66.88 ± 14.389 | 66.56 ± 11.631 | 0.91 |
| Amount of fluid administration (mL) | 1447.92 + 260.923 | 1418.75 + 267.101 | 0.59 |
| Volume of b leeding (mL) | 500.00 ± 115.316 | 455.43 ± 112.659 | 0.06 |

## DISCUSSION

Ondansetron is a 5-$HT_3$ antagonist that it is indicated to prevent nausea and vomiting.[17] In addition, ondansetron is useful for prevention of shivering in patients undergoing spinal anesthesia, regional anesthesia and pain medicine.[16] In this study we reported the efficacy of intravenous bolus of ondansetron 8 mg in comparison to intravenous bolus of pethidine 0.4 mg/kg BW for prevention of POS in pregnant patients undergoing a cesarean section with spinal anesthesia. The incidence of POS was observed in 15 minutes time intervals during 120 minutes. The results showed that the incidence of POS between groups of ondan-setron and pethidine was not significantly different (p> 0.05) (TABLE 3). Moreover, the severity of POS in both groups were laso not significantly different (p>0.05) (TABLE 4). The severity of POS varied from

degree 1 to degree 4. Pethidine 25 mg intravenouly was given to patients who suffering from POS at degree 3 and 4.

Normally, the incidence of POS was observed at 45, 60 and 75 minutes time intervals, although at 15, 90 and 120 mintues time interval, the incidence of POS was also observed (TABLE 4). It is reported that the incidence of POS occurs noramlly at 0.5 to 1 hour after patients undergoing spinal anesthesia. During temperature measurement, the axillary temperature decreases significantly in the minute 15 until the minute 75, while the tympanic temperature decreases significanlty in the minute 15 untul the minute 90. The axillary and tympanic temperatures are generally tounght to be the most accurate for checking a body temperature. The decrease of axillary and tympanic temperatures reflecting the decrease of the body temperature or hypotermia leads to the POS as a compensation of the body to increase heat production. Kelsaka[16] and Powel and Buggy[20] reported that patients who underwent spinal or epidural anesthesia can not maintain the central temperature due to impaired peripheral vasoconstriction. In addition, the patients who underwent spinal anesthesia produce relatively little heat due to only small part of the muscles that contract i.e. just part of the blocked chepalad.

Among 48 patients who underwent the cesarean section with spinal anesthesia in the ondansetron group, only two patients (4.2%) suffer POS indicating that its effectiveness in reducing of POS is 95.8%. While in pethidine group, among 48 patients who underwent the cesarean section, six patients (12.5%) suffer POS indicating that its effectiveness is 87.5%. The effectiveness of ondansetron in reducing of POS has been reported by some authors varying from 84 to 92%[16,20,21] while the effectiveness of pethidine varied from 84 to 90%.[14,21,22]

The side effects of drugs including nausea and vomiting were observed in this study. The incidence of nausea on ondansetron group (4.2%) was significantly lower than pethidine group (16.7%) ($p<0.05$). Moreover, the incidence of vomiting was just observed on pethidine group (4.2%) although it was not significantly difference compare to ondansetron group ($p>0.05$). This study was in accordance with the previous studies indicating that the side effects of nausea and vomiting were lower on the ondansetron group compare to pethidine group.[16] The higher incidence of nausea and vomiting on pethidine group was caused by its stimuli effect directly on the vomiting center in the chemoreceptor trigger zone. In contrast, ondansetron is an antagonist of 5-$HT_3$ that it is indicated to prevent nausea and vomiting.[17] The results of this study support the previous study indicating that ondansetron can reduce both POS and PONV.[17,18]

The disadvantage of ondansetron to prevent POS has been indicated. Ondansetron is related to the incidence of heart rhythm disorders such as arrythmias. The incidence of arrhytmias due to ondansetron has been reported in the previous studies although it is relatively rare. Moreover, ondansetron has a wide dosage range with the maximum doses of 100 mg/day therefore ondansetrone is relatively safe. The side effect of arrhytmias due to ondansetron is normally suffered patients who a history of QT prolongation or QT syndrome with electrolyte disturbances and severe hepatic function. Therefore, Food and Drug Administration (FDA) USA is not recommended ondansetron for these patients.[16,23,24]

The history of misoprostol administration of patients did not influence the incidence of POS ($p>0.05$). Among eight patients who experienced POS, only one patients who had a hostory of misoprostol administration. Misoprostol is reported to have side effect of

shivering that it is accociated with dose and time administration. The side effect of shivering appears after 2-6 hours misoprostol administration in high dose.[16,25,26]

## CONCLUSION

In conclusion, the efficacy of ondansetron 8 mg intravenous bolus is comparable to pethidine 0.4 mg/kgBW intravenous bolus for prevention of shivering in pregnant patients after spinal anesthesia. In addition, the incidence of nausea after ondansetron administration is significantly lower than after pethidine administration.

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