# Intrathecal Fentanyl for Prevention of Shivering in Cesarean section

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**Objectives:** The aim of this randomized double-blind study was to investigate whether 20  $\mu$ g of intrathecally administered fentanyl would influence the incidence and severity of shivering in patients undergoing cesarean section.

*Material and Method:* Sixty healthy patients scheduled for cesarean section under spinal anesthesia using 2.2 ml of 0.5% hyperbaric bupivacaine with 0.2 ml of morphine 0.2 mg, were randomly allocated to receive an additional 0.4 ml of fentanyl 20 mg intrathecally (Group F) or normal saline 0.4 ml (Group S).

**Results:** The incidence of shivering three hours after spinal anesthesia was 6 of 30 patients, 20% in Group F and 15 of 30 patients, 50% in Group S. The difference was statistically significant (p < 0.05). Almost all of the shivering patients started in their first hour after spinal anesthesia (5 patients in Group F and 13 patients in Group S). None in Group F but 4 patients in Group S started shivering before their babies were delivered. The shivering score was also significantly lower in Group F (p < 0.05). Treatment for shivering was requested in 16% and 26% of the shivering patients in Group F and Group S, respectively. There was no difference in the incidence of pharmacologic side effects. The core temperature did not differ significantly between the groups during 3 hours after spinal anesthesia.

**Conclusion:** The addition of 20  $\mu$ g fentanyl in 2.2 ml of 0.5% hyperbaric bupivacaine with 0.2 ml of morphine 0.2 mg intrathecally can reduce the incidence and severity of intraoperative and postoperative shivering after spinal anesthesia for patients who were receiving cesarean section without increasing other side effects.

Keywords: Intrathecal opioid, Postoperative, Shivering, Fentanyl, Cesarean section.

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Shivering associated with spinal anesthesia in patients undergoing cesarean section is one of the common problems, occurring in up to 45-85%<sup>(1)</sup>. Shivering is very uncomfortable for the patients and may interfere with the monitoring of electrocardiogram, blood pressure, and oxygen saturation. It also increases oxygen consumption, lactic acidosis, and carbon dioxide production; thus, it may cause distress to parturient who have a low cardiac pulmonary reserve and high metabolism<sup>(2-5)</sup>. Although intravenous meperidine, tramadol is widely used to treat shivering after spinal anesthesia, it may have adverse effects on the baby that parturients received it before delivery of the baby<sup>(6,7)</sup>.

A small dosage of fentanyl (10-40  $\mu$ g) administered directly into the cerebrospinal fluid has been found to be very effective in minimizing discomfort during and after cesarean section without increasing serious adverse effects<sup>(8-12)</sup>. Chow et al. have suggested that intrathecal fentanyl could decrease both the incident and severity of shivering during spinal anesthesia for transurethral resection of prostate<sup>(13)</sup>. Chu et al. reported that intrathecal fentanyl 12.5 and 15  $\mu$ g added in bupivacaine decreased the incidence of shivering in cesarean section<sup>(14)</sup>.

The present prospective, double-blind, and randomized study was performed to determine whether

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fentanyl 20  $\mu$ g, added to bupivacaine and morphine spinal mixture, decreases the incidence and severity of shivering during spinal anesthesia for cesarean section. The safety of added intrathecal fentanyl was also studied.

#### **Material and Method**

After receiving approval of the ethics committee of the hospital and written informed consent of every subject was obtained, 60 ASA physical status I parturients at full-term gestation presenting for elective cesarean section were recruited in the present study. Parturients with contraindication to spinal anesthesia, allergy to the local anesthetics or fentanyl or morphine were excluded.

#### Protocol

Subjects were randomly divided into two groups by random drawing of sealed envelopes. In order to facilitate blinding, test solutions were prepared by an anesthetic nurse who was not involved in the present study. Neither the anesthesiologist nor the parturient herself was aware of the drugs. The ambient temperature of operating room was maintained at 23°C and no active patient warming was used. Large-bore IV assess was secured and normal saline 10 ml/kg was administered. An oral temperature, pulse oximetry, blood pressure cuff, and electrocardiogram were placed for baseline measurements.

Spinal anesthesia was performed under standard technique at L3-4 with 27 G Quincke needle in the left lateral position. All patients received 2.2 ml of 0.5% hyperbaric bupivacaine combined with 0.2 ml of morphine 0.2 mg intrathecally, in addition to 0.4 ml of unknown adjuvant, constituting a total volume of 2.8 ml. The patients allocated to the study group had 0.4 ml of fentanyl 20  $\mu$ g (Group F) while the control group had normal saline 0.4 ml (Group S) added to the mixture. On completion of the spinal injection, the patient was placed in the supine position.

#### Measurements

Sensory analgesia was evaluated by pinprick at intervals of 1 min, until the baby was delivered for at lease 15 min after spinal anesthesia, every 5 min until the completion of surgery and then at 1 h, 2 h and 3 h after spinal anesthesia. Heart rate and arterial oxygen saturation were monitored continuously; noninvasive arterial blood pressure was recorded at 1 min intervals until delivery, at 5 min interval until the end of surgery, and thereafter at 15 min interval for 3 h after spinal anesthesia; oral temperature was measured at 1 h, 2 h and 3 h after spinal injection.

Formal assessment of the patients was conducted before the baby was delivered, 1 h, 2 h and 3 h after the spinal injection. Pain was recorded on a 0-10 cm visual analogue scale (VAS). Shivering, pain, nausea/ vomiting, pruritus and sedation were assessed on a modified four point rating score with treatment as shown in Table 1. Severe pain was treated with nalbuphine 5 mg IV. Severe shivering was treated with tramadol 0.5 mg/kg IV. Vomiting was treated with metoclopramide 10 mg IV. Severe pruritus was treated with nalbuphine 2.5 mg IV.

Episodes of perioperative side effects such as hypotension (SBP < 30 % from baseline or < 80 mmHg), bradycardia (HR < 60 bpm), oxygen desaturation (SpO<sub>2</sub><92%) respiratory depression (RR<12 bpm)

scale	Shivering	Pain-VAS	Nausea & vomiting	Pruritus	Sedation
0	None	0	None	None	Fully awake
1	Muscular activity in only one muscle group	1-3	Nausea	Mild	Somnolent, response to call
2	Muscular activity in more than one muscle group but not generalized shivering	4-6	Retching	Moderate	Somnolent, response to tactile stimuli
3	Shivering involving whole body, need treatment with tramadol 0.5 mg/kg	> 6, need treatment with nalbuphine 5 mg	Vomiting, need treatment with metoclopramide 10 mg	Severe, need treatment with nalbuphine 2.5 mg	Deep sedation, response to painful stimuli

Table 1. Recorded parameters as four-point rating score

VAS = visual analogue scale

and hypothermia (temperature < 35 C) were recorded. Hypotension was treated with bolus of fluid, left uterine displacement and incremental dose of ephedrine 6 mg IV. Bradycardia was treated with atropine 0.6 mg IV. Oxygen desaturation was treated with oxygen mask 6 L/min. Respiratory depression was treated with incremental dose of naloxone 0.04 mg IV.

#### Data Analysis

Group size was determined by power analysis with  $\alpha = 0.05$  and  $\beta = 0.1$  to detect 30% reduction in the intraoperative and postoperative shivering in Group F. It was estimated that a minimum of 30 subjects would be necessary for each group. All statistical analysis was performed with SPSS version 11.0. Data were expressed as mean±SD and number (percent). Categorical scales were compared by Independent-Sample t-test. Ordinal scales were compared by Mann-Whitney U-test. Nominal scales were compared by  $x^2$  tests. For all determinations, a p value of < 0.05 was considered significant.

#### Results

A total of 60 parturients were recruited into the present study. There was no difference between groups with regard to demographic data, NPO time, duration of surgery, perioperative IV fluid or Apgar scores of the baby (Table 2).

The total incidence and severity of shivering after spinal anesthesia are shown in Table 3. Group F had significantly less shivering than Group S (6 of 30 patients, 20% in Group F and 15 of 30 patients, 50% in Group S, p < 0.05). Almost all shivering patients started shivering in the first hour after spinal anesthesia

#### Table 2. Patient parameters

	Group F (n $=$ 30)	Group S (n $=$ 30)	p value
Age (y)	30.4 <u>+</u> 5.3	31.7 <u>+</u> 5.7	0.374
Weight (kg)	69.3 <u>+</u> 11.4	67.0 <u>+</u> 8.8	0.393
Height (cm)	157.4 <u>+</u> 5.9	156.9 <u>+</u> 5.4	0.743
NPO time (hr)	12.2 <u>+</u> 3.5	13.2 <u>+</u> 3.8	0.301
Duration of surgery (min)	53.5 <u>+</u> 13.1	51.7 <u>+</u> 13.9	0.610
Perioperative IV fluid (ml)	1590 <u>+</u> 275	1645 <u>+</u> 226	0.441
Apgar scores at			
5 min	8.8 <u>+</u> 0.5	8.7 <u>+</u> 1.1	0.788
10 min	10+0.0	10+0	1.0

Values are mean+SD

No statistical difference between the groups by unpaired t - test

Table 3.	Incidence	and	severity	of	shivering
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Shivering	Group F ( $n = 30$ )	Group S ( $n = 30$ )	p value
Incidence, n (%)			
The total incidence	6 (20%)	15 (50%)*	0.029
In the first hour	5 (13.3%)	13 (43.3%)*	0.047
In the second hour	3 (10%)	9 (30 %)	0.104
In the third hour	2 (6.7%)	7 (2.3%)	0.145
Severity (a, b, c)			
In the first hour	4, 0, 1	3, 6, 4*	0.013
In the second hour	3, 0, 0	3, 5, 1*	0.015
In the third hour	2, 0, 0	4, 3, 0*	0.022

a Values are mild shivering: muscular activity in only one muscle group

b Values are moderate shivering: muscular activity in more than one muscle group but not generalized shivering

c Values are severe shivering: shivering involving whole body, need treatment with tramadol 0.5 mg/kg

\* P <0.05 considered significant

(5 patients in Group F and 13 patients in Group S). None in Group F but 4 patients in Group S started shivering before the babies were delivered. One patient in Group F and 2 patients in Group S started shivering in the second hour. None started shivering in the third hour. None in Group F but 4 patients in Group S had continuous shivering throughout the three hours after spinal anesthesia. Two patients in Group F and 8 patients in Group S had continuous shivering for two hours after spinal anesthesia.

The severity of shivering in Group F was significantly lower than in Group S throughout the period of three hours after spinal anesthesia (p < 0.05). In the first hour, there was 1 patient in Group F and 4 patients in Group S who experienced severe shivering and required treatment with intravenous tramadol. Among those who shivered severely, 1 patient in Group S still had severe shivering after 0.5 mg/kg tramadol IV, 2 patients in Group S did not respond well with tramadol but decreased the severity of shivering to a mild level and 1 patient in each group stopped shivering with tramadol and did not have a relapse of shivering again.

The records of core temperature after spinal anesthesia are shown in Table 4. There was no difference in the temperature between the two groups regarding their baseline temperature, temperature at 1 h, 2 h and 3 h after spinal anesthesia. Applying the general linear model of comparison within-subjects factors, the mean core temperature of Group F at the first and the second hour were significantly lower than the baseline temperature, while in the mean core temperature of Group S at all time (the first, the second and the third hour) were significantly lower than the baseline temperature (p < 0.05). During the three hours after spinal anesthesia, none developed hypothermia (oral temperature  $< 35^{\circ}$ C).

Time to highest sensory level and the highest sensory level showed no difference between the groups. Regression of sensory blocks at the first, the second and the third hour after spinal anesthesia were significantly delayed in Group F compared to Group S (p < 0.05) (Table 5). During the operation all patients in Group F had completed intraoperative analgesia (painfree), whereas 22 patients (73.3%) in group S did so (p < 0.05). In the postoperative period (in the second hour and the third hour after spinal anesthesia) all patients in Group F still had no pain, whereas 24 patients (80%) at 2 h and 23 patients (76.7%) at 3 h in Group S did so (p < 0.05). The VAS pain score was also lower in Group F compared to Group S at all three hours after spinal anesthesia (p < 0.05). There were 3 patients in Group S who needed nalbuphine 5 mg IV because their pain scores were higher than 6 at the time before the baby delivery. The other 2 patients in Group S required the anti-pain medicine at the 3 h.

During the operation, there was no difference in the incidence of hypotension between the two groups. Eleven patients (36.7%) in Group F and 15 patients (50%) in Group S had hypotension that required treatment with 6-18 mg of ephedrine. During the three hours after spinal anesthesia, there was no difference in the incidence and severity of nausea and vomiting. Metoclopramine was administered to treat vomiting of 3 patients in each group (Table 6). None developed bradycardia, respiratory depression (RR < 12 bpm), SpO2 < 92%, pruritus or sedation.

#### Discussion

So far the mechanism of shivering under spinal anesthesia is not fully understood. Possible contributing factors that decrease the core temperature such as: (1) sympathetic blockage which results in peripheral vasodilatation, increased cutaneous blood

Temperature	Group F ( $n = 30$ )	Group S ( $n = 30$ )	p value
T0 (baseline temperature)	36.68 <u>+</u> 0.37	36.63 <u>+</u> 0.37	0.553
T1 (temperature at the first hour)	$35.89 \pm 0.62$	35.78 <u>+</u> 0.52	0.446
T2 (temperature at the second hour)	35.91+0.57	35.85+0.58	0.656
T3 (temperature at the third hour)	36.26 <u>+</u> 0.66	$36.04 \pm 0.77$	0.227
p value <sup>+</sup>	<0.001	<0.001	

**Table 4.** The mean skin temperature (°C) at the baseline before spinal anesthesia (T0), the first (T1), the second<br/>(T2), and the third (T3) hour after intrathecal injection

Values are mean  $\pm$  SD

General Linear Model comparing within-subjects factors (T0, T1, T2 and T3)

#### Table 5. Sensory blockage

	Group F ( $n = 30$ )	Group S $(n = 30)$	p value
Time to highest sensory level (min)	5.3 <u>+</u> 0.1 (3-10)	5.8 <u>+</u> 0.1 (4-9)	0.354
The highest sensory level (thoracic level)	4.0 <u>+</u> 0.7 (3-6)	4.1 <u>+</u> 0.8 (3-6)	0.746
Number of segment regression (level) at			
The first hour	0.0 <u>+</u> 0.2 (0-1)	0.2 <u>+</u> 0.3 (0-1)	0.154
The second hour	1.5 <u>+</u> 0.9 (0-3)	2.9 <u>+</u> 2.2 (0-9)*	0.009
The third hour	4.3 <u>+</u> 1.7 (0-7)	6.1 <u>+</u> 2.4 (3-12)*	0.004
The most severe pain (VAS pain score) in			
The first hour	0 (0)	1.1±2.3 (0-8)*	0.011
The second hour	0 (0)	1.1 <u>+</u> 2.2 (0-6)*	0.017
The third hour	0 (0)	$0.7\pm1.5~(0-8)^*$	0.011

Values are mean  $\pm$  SD (range)

\* p < 0.05 considered significant

#### Table 6. Other side effects

Side effects	Group S ( $n = 30$ )	Group F ( $n = 30$ )	p value
Hypotension, n (%)	11 (36.7%)	15 (50%) <sup>a</sup>	0.192
Nausea/vomiting (a, b, c)			
In the first hour	0, 0, 2	2, 1, 2	0.317
In the second hour	0, 0, 3	0, 0, 3	0.552
In the third hour	1, 0, 1	1, 0, 1	1.000
Pruritus (d, e, f)			
In the first hour	5, 1, 0	2, 1, 0	0.300
In the second hour	10, 3, 0	10, 1, 0	0.494
In the third hour	10, 2, 0	18, 1, 1	0.064
Sedation (g, h, i)	· ·	, ,	
In the first hour	0, 0, 0	0, 0, 0	1.000
In the second hour	0, 1, 0	1, 0, 0	0.317
In the third hour	3, 0, 0	3, 0, 0	1.000

a Values are nausea, b Values are retching, c Values are vomiting need treatment with metoclopramide 10 mg

d Values mild pruritus, e Values are moderate pruritus, f Values are severe pruritus need treatment with nalbuphine 2.5 mg g Values are somnolent, response to call, h Values are somnolent, response to tactile stimuli, i Values are deep sedation, response to painful stimuli

flow, and subsequently increased heat loss via the  $skin^{(15)}$ ; (2) a cold operating room, or the rapid infusion of crystalloid solutions at room temperature<sup>(16)</sup>; (3) decrease the vasoconstriction and shivering thresholds, possibly by increasing the temperature of the lower part of the body<sup>(17)</sup>; or (4) the direct effects of cold anesthetic solutions upon thermosensitive structures within the spinal cord<sup>(18)</sup>.

In the present study almost all shivering patients started shivering in the first hour after spinal anesthesia (5 of 6 patients, 83.3% in Group F and 13 of 15 patients, 86.7% in Group S). The core temperature at the first hour dropped significantly from the baseline temperature in both groups. These data suggest that the heat loss was extreme during the operation. Moreover, post-anesthetic shivering is associated with consequences that could be potentially harmful to the parturient and her baby, including increased oxygen consumption, carbon dioxide production, circulating catecholamines, cardiac output, and lactic acidosis<sup>(2-5)</sup>. Attempts to treat post-anesthetic shivering have included a range of intravenous drugs (meperidine, tramadol), radiant heaters, increased ambient temperatures, active warming blankets, warm local anesthetic solution or warm intravenous fluids<sup>(6,7,19,20)</sup>. Addition of various opioids (meperidine, fentanyl) extradurally also reduces the incidence of shivering in parturients who underwent cesarean section under epidural anes-thesia<sup>(21,22)</sup>.

The present study was designed to standardize these possible confounding factors while reflecting the usual practice in our institution. Operating room temperature was constantly held at 23°C, intravenous fluids and all drugs were administered at room temperature and a double layer blanket was used for all parturients to cover the upper part of the body during the operation and the whole part of body after the operation.

Chow et al and Chu et al have found that intrathecal fentanyl could decrease both the incidence and severity of shivering during spinal anesthesia<sup>(13,14)</sup>. The present study not only formally evaluated the effects of intrathecal fentanyl on both the incidence and severity of shivering in the period after spinal anesthesia but also deeply explored in the period before the baby is delivered, in the first hour, the second and the third hour after spinal anesthesia. The present results suggest that intrathecal fentanyl could prevent the shivering by decreasing the severity of shivering throughout three hours after spinal anesthesia and decrease the incidence of shivering in the first hour including in the time before the baby is delivered. The decreasing of intravenous drug requirement for antishivering at the time before the baby is delivered could be reduing harmful to the baby.

Fentanyl is a highly ionized, lipophilic µreceptor agonist. When it is administered spinally, the unionized component is rapidly transferred into the spinal cord. Rapid systemic absorption also occurs as fentanyl dissociates from binding sites within the spinal cord. Intrathecally administered fentanyl has its analgesic action both in the spinal cord and systemic<sup>(23)</sup>. The reduction of shivering in the present study may be attributable to the effect of fentanyl that was added into the subarachnoid space on thermoregulator and could affect afferent thermal inputs at the spinal cord<sup>(24)</sup>. Because of its lipophilicity, little fentanyl reaches the brain via the cerebrospinal route and is unlikely to impair the thermoregulation control of hypothalamus<sup>(25,26)</sup>. The disadvantage of the reduction of shivering effect is increasing the risk of hypothermia because low core temperature can not initiate autonomic protective response<sup>(23)</sup>. None in the present study developed hypothermia. The result of the present study shows that the mean core temperature of the patients in Group F was lower than baseline for only two hours after spinal anesthesia and the core temperature gained

up to equal the baseline temperature at the third hour, while the mean core temperature of the patients in Group S was lower than baseline temperature for three hours after the spinal anesthesia. So the effect of fentanyl on thermoregulator by decreasing the body temperature may not be harmful and not too long.

For the treatment of shivering, patients responded to tramadol (0.5 mg/kg) 75 % in Group S and 100% in Group F. The efficiency in the treatment of shivering with tramadol is similar to other reports (80-87%)<sup>(6)</sup>. Addition of intrathecal fentanyl to hyperbaric bupivacaine in parturients undergoing cesarean section improved quality of anesthesia without producing significant side effects<sup>(8,9)</sup>. In the present study, all patients who received intrathecal fentanyl did not experience any pain (VAS = 0) for three hours after spinal anesthesia. This compared to 22 patients (73.3%) in the first hour, 23 patients (83.3%) in the second hour and 24 patients (89%) in the third hour after spinal anesthesia in Group S who had no pain. The authors found that there was no statistically significant difference in the onset and the highest level between the groups. The number of segments regressed at the second hour and the third hour in Group F was less than in Group S. This indicated that the duration of surgical anesthesia was prolonged with administered intrathecal fentanyl.

Belzarena et al investigated on a dose per kilogram body weight basis was 80 kg, which approximated to examining the effects of the following doses of 20, 40 and 60 µg intrathecal fentanyl and found that intraoperative respiratory depression and increased sedation were observed in those who received 40 µg or more<sup>(9)</sup>. Because the use of two central neuraxial opioids (fentanyl and morphine) in the present study may associate with respiratory depression, the delayed onset of respiratory center is within 2 hours for intrathecal fentanyl and 6-12 h for intrathecal morphine, so the authors observed respiratory rate and oxygen saturation about 3 hours after spinal anesthesia and we found no patient experienced respiratory depression (RR < 12 bpm, SpO2 < 92 %) during the three hours after spinal anesthesia. Hunt et at reported that it was significant increase of the incidence of nausea in only the group that received  $6.25 \ \mu g$  fentanyl but Dahlgren et al reported that the addition of intrathecal fentanyl 60 µg for cesarean section reduced the need for intraoperative antiemetic medication<sup>(10,11)</sup>. In the present study the incidence and severity of nausea / vomiting, sedation did not increase in Group F. Itching is another frequent complication of subarachnoid and epidural opioid administration. In several studies there was no increased incidence of itching in the low doses of intrathecal fentanyl (<  $50 \ \mu g$ )<sup>(10-12)</sup>. In the present study the incidence of itching had no statistically significant difference in throughout the three hours after spinal anesthesia between the groups.

In conclusion, the present study reveals a beneficial effect of adding fentanyl into bupivacainemorphine in spinal anesthesia for cesarean section. There is significance in preventing intraoperative and postoperative shivering in recovery without increasing the side effects.

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## การผสม fentanyl ร่วมไปกับการฉีดยาชาเข้าช่องไขสันหลัง เพื่อป้องกันอาการสั่นในการผ่าตัด คลอดทางหน้าท้อง

### อัญชลี เตซะนิเวศน์, อรลักษณ์ รอดอนันต์, วสินี เตซาวัฒนวิศาล, ธีรพล สมศิริ

**วัตถุประสงค**์: เพื่อศึกษาว่าการผสม fentanyl ร่วมไปกับการฉีดยาชาเข้าซ่องไขสันหลัง ในการผ่าตัดคลอดทางหน้าท้อง สามารถป้องกันอาการสั่นในระหว่างการผ่าตัดและหลังผ่าตัดหรือไม่ และมีผลข้างเคียงอะไร

**วัสดุและวิธีการ**: ผู้ป่วยที่มารับการผ่าตัด คลอดทางหน้าท้องและฉีดยาซาเข้าซ่องไขสันหลังโดยใช้ 0.5% bupivacaine 4 มล. ผสม มอร์ฟีน 0.2 มก. (0.2 มล.) จำนวน 60 ราย ผู้ป่วยทุกรายไม่มีข้อห้ามในการฉีดยาซา เข้าซ่องไขสันหลัง และไม่เคยมีประวัติแพ้ fentanyl, ยาซา หรือมอร์ฟีน ผู้ป่วยได้รับการอธิบายถึงการศึกษา และได้รับการยินยอมเป็น ลายลักษณ์อักษร ผู้ป่วยถูกแบ่งเป็น 2 กลุ่มโดยการสุ่มตัวอย่าง ได้แก่ กลุ่ม F จะได้รับ fentanyl 10 ไมโครกรัม (0.2 มล.) และกลุ่ม S จะได้รับ normal saline 0.4 มล. ร่วมไปทางช่องไขสันหลัง โดยวิสัญญีพยาบาลจะเป็นผู้ผสมยาให้ และวิสัญญีแพทย์ผู้ซึ่งไม่ทราบว่าผู้ป่วยอยู่ในกลุ่มใด จะเป็นผู้ที่ฉีดยา เข้าซ่องไขสันหลัง

**ผลการศึกษา**: จำนวนผู้ป่วยทั้งหม<sup>ื</sup>ดที่มีอาการสั่นภายหลังการฉีดยาซาเข้าซ่องไขสันหลัง 3 ซม. ใน กลุ่ม F น้อยกว่า ในกลุ่ม S อย่างมีนัยสำคัญทางสถิติ คือ 6 รายในกลุ่ม F (ร้อยละ 20) และ 15 รายในกลุ่ม S (ร้อยละ 50) โดยผู้ป่วย ส่วนใหญ่ในทั้งสองกลุ่มเริ่มมีอาการสั่นในชั่วโมงแรกหลังการฉีดยาซาเข้าซ่องไขสันหลัง (5 รายในกลุ่ม F และ 13 ราย ในกลุ่ม S) ซึ่งในจำนวนดังกล่าวนี้พบผู้ป่วยจำนวน 4 รายในกลุ่ม S ที่อาการสั่นเกิดก่อนการคลอดของทารก และยังพบความรุนแรงของอาการสั่นในกลุ่ม F น้อยกว่าในกลุ่ม S อย่างมีนัยสำคัญทางสถิติ โดยพบอาการสั่น รุนแรงมากต้องการยารักษาร้อยละ 16 ของผู้ป่วยที่มีอาการสั่นทั้งหมดในกลุ่ม F และ ร้อยละ 26 ของผู้ป่วย ที่มีอาการสั่นทั้งหมดในกลุ่ม S ไม่พบความแตกต่างของอาการข้างเคียงในทั้งสองกลุ่ม และไม่พบความแตกต่าง ของอุณหภูมิเฉลี่ยในทั้งสองกลุ่มตลอด 3 ชั่งโมงภายหลังการฉีดยาซาเข้าซ่องไขสันหลัง

**สรุป**: การให้ fentanyl ร่วมไปกับการฉีดยาซาเข้าซ่องไขสันหลัง ในการผ่าตัดคลอดทางหน้าท้อง ช่วยป้องกันอาการ สั่นในช่วงระหว่างการผ่าตัดและช่วยลดความรุนแรงของอาการสั่นได้นาน 2 ชั่วโมงหลังการผ่าตัด