Incidence and Risk Factors of Hypotension and Bradycardia after Spinal Anesthesia for Cesarean Section

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Background: *Hypotension or bradycardia after spinal anesthesia for cesarean section remain common and are serious complications. The current study evaluated factors associated to the incidences of hypotension or bradycardia in this context.*

Material and Method: *A prospective cross sectional study from November 1, 2004 to July 31, 2005 was conducted on 722 parturients undergoing cesarean section under spinal anesthesia. T-test and Chi-square test were used in univariate analysis to compare continuous data and categorical data respectively. Multivariate logistic regression was performed on the variables hypotension (systolic pressure decrease > 30% of baseline value) and bradycardia (heart rate < 60 bpm) p-value < 0.05 was considered significant.*

Results: *Incidence of hypotension and bradycardia were 52.6% and 2.5%. The probability of hypotension increased with estimated blood loss 500-1000 mL (odds ratio [OR] = 1.86; 95% CI 1.30-2.67, p = 0.001), estimated blood loss > 1000 mL (OR = 5.31; 95% CI 1.47-19.19, p = 0.011), and analgesia level > T_4 (OR = 1.94; 95% CI 1.18-3.19, p = 0.009). Hypotension occurred despite left uterine displacement (OR = 1.56; 95% CI 1.11-2.19, p = 0.01). Risk factors associated with bradycardia were adding intrathecal morphine 0.2 mg (0.2 mL) (OR = 4.61; 95% CI 1.31-16.19, p = 0.017) to local anesthetics.*

Conclusion: *The present results indicated that the incidence of hypotension after spinal anesthesia for cesarean section increased with amount of estimated blood loss > 500 mL and analgesic level > T_4. Adding intrathecal morphine 0.2 mg (0.2 mL) to local anesthetics increased incidence of bradycardia.*

Keywords: *Spinal anesthesia, Cesarean section, Hypotension, Bradycardia, Complication, Adverse events*

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The most common serious problem associated with spinal anesthesia remains the rapid onset of profound hypotension[1,2]. The clinical importance of this side effect was shown in a study by Sanborn et al who proved that hypotensive episodes detected by an automated record keeping system clearly correlate with mortality[3]. In previous studies, the incidence of hypotension after subarachonoid administration of 0.5% bupivacaine varied from 55% to 64%[4-8]. Many studies have been conducted concerning prophylaxis and therapy of hypotension after neuraxial anesthesia. The incidence of hypotension after spinal anesthesia for cesarean section in the authors' institution was 60%[8]. Prediction of hypotension after neuraxial anesthesia, however, has been addressed by only a few authors[1,2,9]. The present study was conducted to identify factors associated with hypotension and/or bradycardia after spinal anesthesia for cesarean section, which is one of most common surgical procedures.

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Material and Method

The present study was approved by the institutional ethic committee of the Faculty of Medicine, Chulalongkorn University as part of the Thai Anesthesia Incidents Study (THAI Study) of anesthetic adverse

outcomes[10,11]. From November 1, 2004 until July 31, 2005, the authors prospectively studied patients consenting to spinal anesthesia for cesarean section at King Chulalongkorn Memorial Hospital, a 1500-bed university hospital. Attending anesthesiologists and anesthesia residents recorded data of the patients on the structured data collection form. Patient care was delivered in the usual fashion and was not altered in any way by the investigators. Research data were collected in parallel with clinical data. Before surgery, the authors collected data regarding age, height and weight. The authors also recorded any preoperative history of hypertension, diabetes mellitus, and cardiovascular diseases. The ASA physical status was assigned according to the classfication of the American Society of Anesthesiologists. Variables related to technique and conduct of spinal anesthesia included the preoperative drugs, spinal drug and dosage, site of spinal puncture, patient position during performance of the spinal block, left uterine displacement, use of anticholinergic agents or vasopressors and adjusting position for adequate analgesia.

Blood pressure was measured at baseline, every 1 minute since conduction of spinal anesthesia until delivery and at least every 5 min, hemoglobin oxygen saturation (SpO_2) and electrocardiogram were continuously monitored after delivery. The following data were collected at baseline and every 15 min during anesthesia: systolic, diastolic blood pressures, heart rate, SpO_2, and anesthetic level (determined by pinprick). The intra-operative IV sedative medication, prehydration fluid, intra-operative fluid volume administered, and estimated blood loss were also recorded. This data was used for subsequent statistical analysis.

Side effects of spinal anesthesia included hypotension (defined as decreased blood pressure $\geq$ 30%), bradycardia (defined as heart rate < 60 beats/min), nausea and vomiting. The time whenever side effects occurred was also noted.

Statistical analysis was performed by using the statistics program SPSS version 11.5. The dichotomous variables "relevant hypotension" and "relevant bradycardia" after spinal anesthesia (yes/no) was used as a target criterion. Firstly, variables were checked with univariate analysis for associations with hypotension and/or bradycardia. Categorical variables were assessed for a significant association by using either x^2 statistics or Fisher's exact test. Continuous variables were assessed by t-test. Secondly, logistic regression was used to investigate independent factors with a significant association to hypotension and/or bradycardia within a multivariate model. A forward stepwise algorithm was used. At each step, independent variables not yet included in the equation were tested for possible inclusion. The variable with the significant contribution ($p < 0.05$) to improving the model was included. Variables already included in the logistic regression equation were tested for exclusion_based on the probability of a log likelihood test ratio. The analysis ended when no further variables for inclusion or exclusion were available with $p < 0.05$ considered as statistically significant.

Results

Seven hundred and twenty-two parturients undergoing cesarean section under spinal anesthesia were recruited during the study period. Preanesthetic evaluation revealed history of hypertension in 12 patients (1.7%), anemia in 11 patients (1.5%) and respiratory disease in five patients (0.7%). Peak anesthetic level at 30 min after conduction of spinal anesthesia $\geq T_4$ and $\geq T_6$ dermatome segment occurred in 584 patients (80.9%), and 709 patients (98.2%) respectively. Hypotension, bradycardia, and hypotension together with bradycardia occurred in 380 patients (52.6%), 18 patients (2.5%) and 15 patients (2.1%) respectively. Three hundred and eighteen patients (44.0%), 53 patients (7.3%), and nine patients (1.2%) experienced one, two and three episodes of hypotension respectively. Average (standard deviation) onset of the first episode of hypotension was 7.84 min (7.241) (minimum 1 min and maximum at 50 min). Average dose of IV ephedrine administered for treatment of hypotension was 11.86 (7.189) mg. Among 18 patients who developed bradycardia, average onset of bradycardia was 7.33 (4.073) min (minimum 3 min and maximum 15 min). Demographic and baseline characteristics of parturients receiving spinal anesthesia are shown in Table 1. Details of spinal anesthetic technique, blood loss and adverse effects (univariate analysis are shown in Table 2, 3).

Discussion

Pregnancy brings about profound alterations in maternal hemodynamics[12]. The central hemodynamic profile of the pregnant woman is further altered by position changes, compounded in late pregnancy by the effects of the gravid uterus on the vena caval and aortic blood flow in the supine position[13]. The present study confirms the authors' recent study that hypotension after spinal anesthesia occurred more frequently than other operation[14].

Table 1. Demographic and baseline characteristic of patients undergoing cesarean section (univariate analysis)

Variables	Hypotension (n = 722)				Bradycardia (n = 722)			
	n	Yes (n = 380)	No (n = 342)	p-value	n	Yes (n = 18)	No (n = 704)	p-value
Age (yr)	721	31.3 (6.11)	30.3 (6.54)	0.030	721	30.8 (6.31)	30.8 (6.34)	0.990
Weight (kg)	718	69.1 (10.55)	67.6 (10.15)	0.054	718	66.9 (6.99)	68.5 (10.46)	0.528
Height (cm)	718	156.3 (5.80)	157.0 (7.22)	0.172	718	156.2 (5.66)	156.6 (6.54)	0.777
BMI (kg/m^2)								
≥ 30	190	107 (30.2%)	83 (25.9%)	0.250	190	3 (16.7%)	187 (26.6%)	0.421
≥ 35	30	17 (4.8%)	13(4.1%)	0.781	30	0 (0.0%)	30 (4.3%)	0.457
ASA PS	720			0.480	720			0.796
I	623	326 (85.8%)	297 (87.4%)	0.310	623	17 (94.4%)	606 (86.3%)	0.600
II	91	49 (12.9%)	42 (12.4%)		91	1 (5.6%)	90 (12.8%)	
III	6	5 (1.3%)	1 (0.3%)		6	0 (0.0%)	6 (0.8%)	
Emergency	369	185 (48.7%)	184 (53.8%)	0.194	369	7 (38.9%)	362 (51.4%)	0.417
History								
Hypertension	12	5 (1.3%)	7 (2.0%)	0.634	12	1 (5.6%)	11 (1.6%)	0.263
IHD	2	2 (0.5%)	0 (0.0%)	0.501	2	0 (0.0%)	2 (0.3%)	1.000
Anemia	11	4 (1.1%)	7 (2.0%)	0.433	11	0 (0.0%)	11 (1.6%)	1.000
Respiratory	5	5 (1.3%)	0 (0.0%)	0.063	5	0 (0.0%)	5 (0.7%)	1.000

Value shown as mean (SD) and frequency (%)

Table 2. Details of spinal anesthetic technique and clinical characteristic of parturients (univariate analysis)

Variables	Hypotension				Bradycardia			
	n	Yes (n = 380)	No (n = 342)	p-value	n	Yes (n = 18)	No (n = 704)	p-value
Aanl $5 \geq T_4$	722	149 (39.2%)	89 (26.0%)	<0.001	722	8 (44.4%)	230 (32.7%)	0.426
$15 \geq T_4$	722	323 (85.0%)	261 (76.3%)	0.004	722	15 (83.3%)	569 (80.8%)	1.000
$30 \geq T_4$	722	345 (90.8%)	275 (80.4%)	<0.001	722	15 (83.3%)	605 (85.9%)	0.731
Prehydration fluid	722			0.170	722			0.022
< 500		55 (14.5%)	60 (17.5%)			1 (5.6%)	114 (16.2%)	
500-1000		324 (85.3%)	278 (81.3%)			16 (88.9%)	586 (83.2%)	
> 1000		1 (0.3%)	4 (1.2%)			1 (5.6%)	4 (0.6%)	
Total fluid administration	711			0.007	711			0.977
< 500		0 (0.0%)	1 (0.3%)			0 (0.0%)	1 (0.1%)	
500-1000		19 (5.1%)	26 (7.6%)			1 (5.6%)	44 (6.3%)	
1000-1500		130 (35.0%)	152 (44.7%)			8 (44.4%)	274 (39.5%)	
> 1500		222 (59.8%)	161 (47.4%)			9 (50.0%)	374 (54.0%)	
Side effect								
Nausea	722	61 (16.1%)	16 (4.7%)	<0.001	722	3 (16.7%)	74 (10.5%)	0.427
Vomiting	722	29 (7.6%)	9 (2.6%)	0.005	722	2 (11.1%)	36 (5.1%)	0.244
Shivering	722	49 (12.9%)	63 (18.4%)	0.052	722	1 (5.6%)	111 (15.8%)	0.335
Fainting	722	6 (1.6%)	0 (0.0%)	0.032	722	0 (0.0%)	6 (0.9%)	1.000

Value shown as frequency (%)

The anesthetic management in this observational study was not randomized and several factors were simultaneously analyzed. Such an approach was chosen for the following reasons, it enables the analysis of factors which are difficult to control (e.g. spread of block), it avoids the bias resulting by separately analyzing each variable[15], and it enables the simultaneous analysis of factors characterized by a large variability,

Table 3. Factors associated with hypotension, bradycardia (multivariate analysis)

Variables	Odds ratio	95% confidence Intervals	p-value
Hypotension			
Estimated blood loss			
500-1000 mL	1.86	1.30-2.67	0.011
> 1000 mL	5.31	1.47-19.19	0.001
Left uterine displacement	1.56	1.11-2.19	0.010
Analgesia level $\geq T_4$	1.94	1.18-3.19	0.009
Bradycardia			
Intrathecal morphine	4.61	1.31-16.19	0.017

which could not safely be accomplished with a randomized study (e.g. pregnant patients might receive a high dose of local anesthetic). The authors' data were prospective with respect to data collection. Prospective data should be more reliable than retrospective[16] because the variables that were thought to be prognostic to the complications were collected with the greatest possible accuracy and the definitions of complications were similar among different anesthesiologists.

Although hypotension is clearly defined as "subnormal arterial blood pressure", the definition of subnormal arterial blood pressure remains controversial. However, previous studies support the authors' criteria of 30% decrease in systolic blood pressure as the definition of hypotension[1,2]. The authors also defined common acceptable heart rate of less than 60 as clinical bradycardia. The incidence of hypotension and bradycardia in the present study was 52.6% and 2.5% respectively, which are similar to those in previous reports[4,8,14]. The possible explanations of different incidence rate to some reports[17,18,19,20] are: 1) different definitions of primary outcomes; 2) different clinical settings; and 3) different methods of data collection.

The following variables were identified with univariate analysis as having an association with a higher incidence of hypotension: age, adjusted position for adequate analgesia, use of intrathecal morphine, uterine displacement, estimated blood loss > 500 mL, analgesia level > T_4, and total amount of fluid administration. However, the results of stepwise logistic regression analysis revealed that the amount of estimated blood loss and left uterine displacement were significantly associated with hypotension. Estimated blood loss > 1000 mL showed strong association (OR 5.31) with hypotension while estimated blood loss 500-1000 mL had OR 1.86. However, estimation of blood loss by attending anesthesiologists or anesthesia residents was not accurate and may be over-estimated. Performing of left uterine displacement showed 1.5 fold increased risk for hypotension. In the present study, left uterine displacement was done in 273 out of 722 (37.8%) of all cesarean sections, 168 out of 380 (44.2%) of hypotension cases, and 105 out of 342 (31.7%) of non-hypotensive cases. This may represent the low compliance to practice guideline in term of left uterine displacement procedure in our institution. The possible explanation of higher proportion of left uterine displacement in hypotensive group was left uterine displacement was performed after the hypotensive episode had occurred in some patients. In 1976, Clark et al showed that the combination of fluid and uterine displacement did not eliminate hypotension[21]. One major flaw in the Clark et al study was the failure to include a group that had uterine displacement alone. Further study as a randomized controlled trial may be required to investigate the hypotension preventive effect of left uterine displacement.

The maximum block height $\geq T_4$ was associated with increased risk of hypotension (OR 1.94). The effect of sensory block height is believed to result from blockade of the sympathetic nervous system. When the sympathetic block level is less than T_4, compensatory vasoconstriction in the upper extremities moderates the blood pressure drop[22]. At a higher level of spinal anesthesia, however, this compensatory mechanism is blocked, as are the cardioaccelerator fibers. Furthermore, higher sensory levels of anesthesia correlated with relatively greater decreases in systolic blood pressure[2]. However, there was small variation of block height in pregnant patients in the present study.

There was significant correlation between the incidence of hypotension and the incidence of nausea ($p < 0.001$), vomiting ($p = 0.005$), and fainting ($p = 0.032$) in univariate but not in multivariate analysis. The incidence of bradycardia alone did not correlate with the incidence from any other side effects. The present study showed that nausea and vomiting occurred commonly during anesthesia (10.7% and 5.3% respectively). These results are consistent with historical reports[2,23,24]. The etiology of nausea during spinal anesthesia is unknown. Some authors have suggested that unopposed vagal activity that occurs when sympathetic nerves are blocked during spinal anesthesia, is the cause. Supporting this theory is the observation that atropine was more effective in relieving nausea during spinal

anesthesia than was elevation of the blood pressure with vasopressors[25]. Other authors have speculated that cerebral hypoxia is the primary cause of nausea during spinal anesthesia[23,26]. Decrease in blood pressure ultimately reduces cerebral blood flow to the extent that cerebral hypoxia occurs and causes nausea[26].

The incidence of bradycardia (2.5%) and bradycardia together with hypotension (2.1%) were low and many have prevented the authors from detecting the influence of other factors on the probability of bradycardia. The maximum onset of bradycardia in the present study was shorter than maximum onset of hypotension (15 min vs. 50 min). In univariate analysis, adding intrathecal morphine with local anesthetic and amount of prehydration fluid before initiation of spinal anesthesia were associated with occurrence of hypotension. From logistic regression model, adding intrathecal morphine was associated with bradycardia (OR 4.61). There were two possible explanations: 1) direct effect of intrathecal morphine; 2) increasing volume of local anesthetic with intrathecal morphine 0.2 mg (0.2 mL). Further study may be required to investigate effect of neuraxial opioids on incidence of bradycardia.

In summary, the present results indicated that the incidence of hypotension may increase with estimated blood loss > 500 mL and analgesic level $\geq T_4$. Adding intrathecal morphine was associated with bradycardia.

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อุบัติการณ์และปัจจัยเกี่ยวข้องกับภาวะความดันเลือดต่ำและหัวใจเต้นช้าในหญิงที่รับการฉีดยาชาเข้าช่องไขสันหลังสำหรับการผ่าตัดคลอด

วรรณา สมบูรณ์วิบูลย์, อรนุช เกี่ยวข้อง, สมรัตน์ จารุลักษณานันท์, อรุณชัย นรเศรษฐกมล

***ภูมิหลัง**: ภาวะความดันเลือดต่ำ, หัวใจเต้นช้าหลังจากการได้ยาระงับความรู้สึกโดยฉีดยาชาเข้าช่องไขสันหลังสำหรับการผ่าตัดคลอดเด็กทางหน้าท้องเป็นปัญหาที่พบบ่อยและอาจเกิดอันตราย*

***วัตถุประสงค์**: เพื่อหาปัจจัยที่เกี่ยวข้องกับภาวะความดันเลือดต่ำ, หัวใจเต้นช้าในผู้ป่วยกลุ่มนี้*

***วัสดุและวิธีการ**: การศึกษาแบบตัดขวางเก็บข้อมูลไปข้างหน้าระหว่างพฤศจิกายน พ.ศ. 2547 - กรกฎาคม พ.ศ. 2548 ในหญิง 722 ราย ที่ได้รับการฉีดยาชาเข้าช่องไขสันหลังสำหรับการผ่าตัดคลอด วิเคราะห์แบบ univariate โดยใช้ t-test และ Chi-square test วิเคราะห์แบบ multivariate logistic regression ของภาวะความดันเลือดต่ำ (ความดันซิสโตลิกลดลง $\geq$ 30 % ของค่าเริ่มต้น) และหัวใจเต้นช้า (< 60 ครั้ง/นาที) โดยค่า $p < 0.05$ ถือว่ามีนัยสำคัญทางสถิติ*

***ผลการศึกษา**: อุบัติการณ์เกิดภาวะความดันเลือดต่ำ และหัวใจเต้นช้าเท่ากับ 52.6% และ 2.5% ตามลำดับ โดยปริมาณเลือดที่เสียระหว่างผ่าตัด 500-1,000 มล. (OR = 1.86; 95% CI 1.30-2.67, p = 0.001), > 1,000 มล. (OR = 5.31; 95% CI 1.47-19.19, p = 0.011) และระดับความชา $\geq T_4$ (OR = 1.94; 95% CI 1.11-2.19, p = 0.009) ความดันเลือดต่ำยังคงเกิดขึ้นทั้งที่ยังมีการผลักมดลูกไปด้านซ้าย (OR = 1.56; p = 0.01) ปัจจัยเกี่ยวข้องกับการเกิดภาวะหัวใจเต้นช้าได้แก่ การผสมมอร์ฟีน 0.2 มก. (0.2 มล.) เข้ากับยาชาในการฉีดยาชาเข้าช่องไขสันหลัง (OR = 4.61; 95% CI 1.31-16.19, p = 0.017)*

***สรุป**: ปริมาณเลือดที่เสียระหว่างผ่าตัดคลอดเด็กทางหน้าท้อง > 500 มล. และระดับการชา $\geq T_4$ เป็นปัจจัยเสี่ยงต่อการเกิดภาวะความดันเลือดต่ำ การผสมมอร์ฟีน 0.2 มก. (0.2 มล.) ในยาชาสำหรับฉีดเข้าช่องไขสันหลังเป็นปัจจัยเกี่ยวข้องกับภาวะหัวใจเต้นช้า*