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Original Research

PHENYLEPHRINE FOR THE MANAGEMENT OF HYPOTENSION DURING SPINAL ANESTHESIA FOR CESAREAN SECTION DELIVERY

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ABSTRACT

Objectives: *To evaluate the efficacy of intravenous phenylephrine for the control of spinal anesthesia induced intra- operative hypotension in C- section and its side effects.*

Methods: *A cross-sectional descriptive study was conducted on 322 women with indications of spinal anesthesia for C- section received IV phenylephrine (50-100 µg) titrated to maintain maternal systolic BP at near-baseline values.*

Results: *The mean SBP was ≤ 95% of the baseline from 2 to 10 minutes after the spinal anesthesia induction, then gradually stabilized until the end of surgery. In which, mean SBP <80% and <70% of the baseline at 3rd and 4th minute were 34.16% and 36.33%; 10.86% and 11.80%, respectively. Heart rate decreased > 10 beats per minute (bpm) by the 6th minute till the end of surgery, 4.04% of patients had bradycardia (<55 bpm). The average IV dose of phenylephrine was 95,96 ± 36,16µg. Total crystalloid solutions loading volume at the moment of and just after spinal anesthesia ("co-/post-loading") was 1222.89 ± 141.67ml. 7,76% of patients had vomiting. The average one - minute and five - minutes APGAR score were 8.35 ± 0.24 and 8.99 ± 0.07, respectively.*

Conclusion: *Phenylephrine for managing hypotension during spinal anesthesia for cesarean section was a safe and effective strategy of choice.*

Key words: *phenylephrine, hypotension, C- section*

I. BACKGROUND

Nowadays, there are many anesthesia types for C- section delivery; however, spinal anesthesia was most widely recommended due to reducing the risk of aspiration pneumonia [1], and minimum fetal effects; the mother also remained awake to witness the birth of her child.

Moreover, spinal anesthesia was relatively simple, fast and achieved good muscle relaxation to ensure the surgical manipulations economically and safely.

Despite conveniences, spinal anesthesia in C-section delivery also had many possible risks, such as hypotension and bradycardia. Hypotension affects not only the mother but also placenta circulation and the fetus. [2]. Nowadays many mesures were used to overcome the inconveniences of spinal anesthesia during C- section delivery, such as anesthesia drugs to be reduced in dosage, combined in usage; changing the type of IV solutions; timing and rate of IV solutions infusion; vasoconstrictor drugs use such as ephedrin, phenylephrine and achieved many positive results [2,3]. Ephedrin has been a vasopressor of choice for years, and this drug stimulated both alpha and beta sympathomimetic receptors, causing vasoconstriction that increased blood pressure. However, it also increased maternal heart rate and caused fetal acidosis, especially with high dose use [2,4].

Phenylephrine was a selective α1-adrenergic receptor agonist that caused vasoconstriction that increased blood pressure (similar to ephedrine) but had few adverse effects on maternal heart rate,

reduced the risk of fetal acidosis. Phenylephrine is better at preventing hypotension than ephedrine due to its faster duration of action.

Many methods for preventing hypotension during spinal anesthesia for cesarean delivery have been investigated worldwide, such as Ngan Kee (2005) studied the efficacy of combining simultaneous rapid crystalloid infusion (cohydration) with a high - dose phenylephrine infusion [3].

However, in Vietnam, research on the efficacy of phenylephrine in preventing hypotension in spinal anesthesia was limited, and its use in clinical practice was not common. Therefore, we carried out this study to evaluate the efficacy of phenylephrine for the treatment or prevention of spinal anesthesia-induced maternal hypotension during C- section delivery; and evaluate fetal and maternal effects of Phenylephrine during Spinal Anesthesia for C- section delivery

II. MATERIALS AND METHODS

2.1. Subjects

Inclusion criteria: Women with indications for C- section delivery, aged 20-45, meeting ASA I, II criteria and with pregnancy at 38-41 weeks gestation. Maternal informed consent was obtained.

Exclusion criteria: contraindications to spinal anesthesia: severe fetal distress, uterine rupture, umbilical cord prolapse, acute pulmonary oedema risk, eclampsia, HELP syndrome

Study location and time: at the obstetric surgery room, Department of Anesthesia and Resuscitation A, Hue Central Hospital. Time: from 02/2020 to 09/2020.

2.2. Methods

Cross- sectional descriptive study design with convenient sample size (n = 322).

Preparation of facilities: similar to those for conventional C- section delivery

Antihypotensive drugs: Phenylephrine AGUETTANT 50 µg/ml, 10ml pre-fill seringue

Prepared the patient: Received the patient for C-section delivery, established the intravenous access, monitored the pulse and blood pressure, performed an obstetric examination, and indicated routine spinal anesthesia.

Conducting research:

- The L2–3 level was the puncture site for spinal anesthesia, Levobupivacaine (0.5%) 9mg.

- Use IV phenylephrine when:

+ if SBP < 95% of baseline SBP, only rapid crystalloid fluid infusion.

+ if 95% ≤ SBP ≤ 80% of baseline SBP, heart rate > 70 l/min: rapid crystalloid fluid infusion and IV phenylephrine 50 µg, repeated the dose if SBP did not show improvement.

+ if baseline SBP < 80% SBP ≤ 70% baseline SBP, heart rate > 70 bpm: rapid crystalloid fluid infusion and IV phenylephrine 100µg.

+ If SBP decreased and bradycardia: IV ephedrine 3 - 6 mg/ Atropin 0,5mg.

Data collection:

According to study design: After spinal anesthesia, SBP, pulse, SpO2 and clinical symptoms (nausea, vomiting ...) were monitored and recorded at baseline, every 1 minute for 10 minutes, then every 5 minutes until the end of surgery.

Hypotension definition: 20% decrease from the baseline SBP.

Bradycardia : < 60 bpm.

Sensory testing by Pin - Prick

Motor blockage evaluated by Bromage scale

Assessing surgical analgesia degree according to Abouleizh Ezzat scale: divided into 4 degrees: good, fair, average and poor.

Data processing using SPSS 16.0 software

III. RESULTS

3.1. General characteristics of the study subjects

Table 1: Age, weight, height

	N	Min	Max	Mean	SD
Age	322	20	42	29,30	5,08
Weight	322	45	100	63,27	7,31
Height	322	140	168	155,92	4,83

The mean age, weight and height of pregnant women were 29,30 ±5,08, 63,27± 7,31 and 155,92 ± 4,83 cm, respectively.

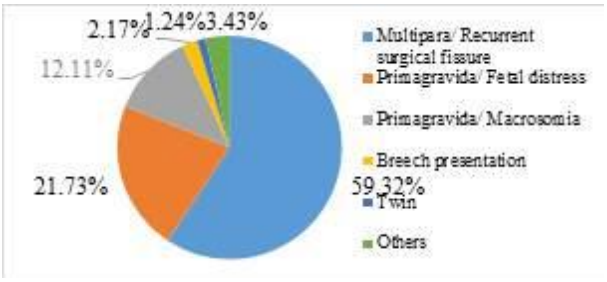

Figure 1: The indications of C – section delivery

The indications of C- section delivery were repeated C – section (59,32%), fetal distress (21,73%).

3.2. The characteristics of spinal anesthesia and surgery

Table 2: Assessment of surgical analgesia degree according to Abouleizh Ezzat scale

N = 322	**Degree**	**n**	**%**
Surgical analgesia degree, according to Abouleizh	Good Fair Average/ poor	276 46 0	85,71 14,29 0

85,71% of patients achieved a good analgesia degree.

Table 3: Motor blockage evaluated by Bromage scale

N = 322	**M_0**	**M_1**		**M_2**		**M_3**	
	n	**n**	**%**	**N**	**%**	**N**	**%**
After 3 minutes	0	257	79,81	65	20,19	0	0
After 5 minutes	0	8	2,48	212	65,83	102	31,69
After 8 minutes	0	0	0	37	11,49	285	88,51

After 08 minutes, 88,51% of patients achieved M3 level: unable to bend the knees and feet.

Table 4: The important phases during the surgery

	Min	**Max**	**mean**	**SD**
Induction–to–skin incision interval	3 m	5 m	4,41 m	0,51 m
Induction–to–fetal extraction interval	6 m	9 m	7,98 m	0,82 m
Total operation interval	30 m	60 m	44,27 m	5,80 m

Since anesthesia induction, it took 4.41±0.51 minutes and 7.98±0.82 minutes for the patient to be eligible for skin incision and fetal extraction, respectively.

3.3. Hemodynamics monitoring and management since spinal anesthesia starting

Table 5: % of patients needed phenylephrine

N=322	**Types**	**n**	**%**
Hypotension occurring date since anesthesia induction	< 5 m ≥ 5 m	251 71	78,0 22,0
Phenylephrine dose	50 µg. IV 100 µg. IV 150 µg. IV 200 µg. IV	94 167 57 4	29,19 51,86 17,70 1,25
Phenylephedrine dose	03mg. IV 06 mg. IV	2/ 322 4/ 322	0,62 1,23
Atropine dose	0,5mg. IV	7/322	2,17

Most women dropped their blood pressure early within 5 minutes of anesthesia. 81.05% of patients required a dose of less than 100 g of Phenylephrine.

Table 6: The mean values of the parameters.

	Min	**Max**	$\overline{X}$	**SD**
Phenyle-phrine dose	50 µg	200 µg	95,96 **µg**	36,16 **µg**
Crystalloid fluid	800 ml	1800 ml	1222,89 ml	141,67 ml
SpO_2	95%	100%	98,79%	2,86%
Mean blood pressure	41	94		

The average IV dose of phenylephrine was 96,96 ± 36,16µg. Total crystalloid solutions loading volume at the moment and just after spinal anesthesia ("co-/post-loading") was 1222.89 ± 141.67ml.

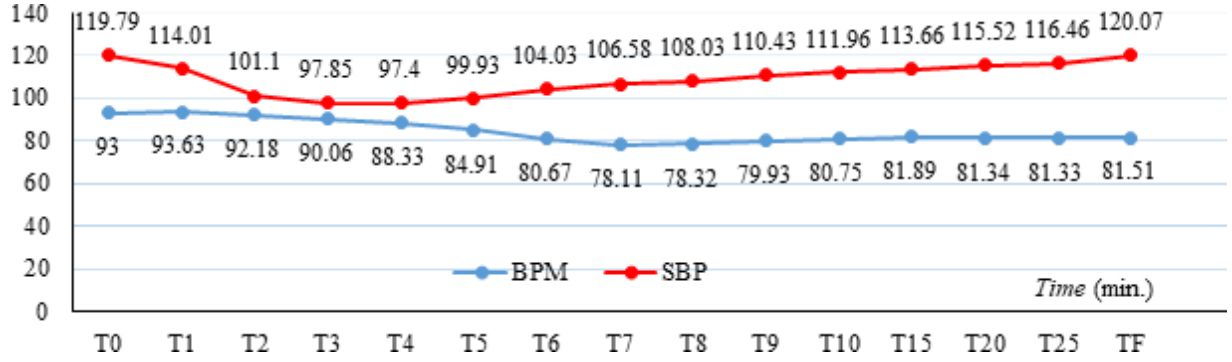

Figure 2: Changes in pulse and blood pressure during and after anesthesia

Heart rate decreased > 10 beats per minute (bpm) by the 6th minute until the end of the surgery, 4.04% of patients had bradycardia (<55 bpm). SBP decreased slightly after spinal anesthesia starting but remained above 90 mmHg.

Table 7: SBP at every minute in comparison to baseline SBP (mmHg) during spinal anesthesia (n=322)

	Min	**Max**	$\bar{X}$ ± **SD**	**% of decrease from baseline SBP**	**Decrease of more than 20% from baseline SBP**	**Decrease of more than 30% from baseline SBP**	**P**
T_0	99	142	119,79 ± 8,56				
T_1	70	150	114,01 ± 12,45	- 4,16	16 (4,97%)	5 (1,55%)	
T_2	60	139	101,49 ± 15,69	- 14,94	90 (27,95%)	36 (11,18%)	**.000**
T_3	61	140	97,85 ± 13,10	- 17,65	110 (34,16%)	35 (10,86%)	**.000**
T_4	66	138	97,40 ± 12,12	- 18,02	117 (36,33%)	38 (11,8%)	**.000**
T_5	68	143	99,93 ± 12,14	- 15,91	81 (25,15%)	30 (9,31%)	**.000**
T_6	70	145	104,03 ± 11,46	- 12,48	51 (15,83%)	13 (4,03%)	**.000**
T_7	65	140	106,58 ± 12,0	- 12,42	40 (12,42%)	12 (3,72%)	**.000**
T_8	70	150	108,03 ± 11,12	- 10,37	27 (8,38%)	8 (2,48%)	
T_9	76	140	110,43 ± 9,97	- 8,57	19 (5,90%)	0	
T_{10}	87	140	111,96 ± 9,61	- 7,15	10 (3,11%)	0	
T_{15}	91	145	113,66 ± 8,68	- 4,45	3 (0,93%)	0	
T_{20}	91	145	115,52 ± 8,03	- 2,90	2 (0,62%)	0	
T_{25}	89	145	116,46 ± 8,03	- 2,12	2 (0,62%)	0	

	Min	Max	$\bar{X}$ ± SD	% of decrease from baseline SBP	Decrease of more than 20% from baseline SBP	Decrease of more than 30% from baseline SBP	P
T_{kt}	97	150	120,70 ± 7,17	1,41			

After spinal anesthesia, SBP was recorded every 1 minute for the first 10 minutes, then every 5 minutes till the end of the surgery, and compared to baseline SBP, pair-matching P (P).

SBP decreased significantly from 2 to 7 minutes since spinal anesthesia induction.

3.4. Maternal and fetal effects of spinal anesthesia

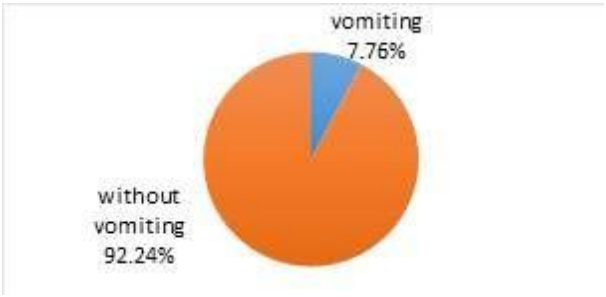

Figure 3: Vomiting rate under spinal anesthesia

7,76 % of patients had vomiting under spinal anesthesia.

Table 8: 1- minute and 5 – minute Apgar score

	Min	Max	$\bar{X}$	SD
1- Minute APGAR	8	9	8,35	0,24
5- minute APGAR	8	10	8,99	0,07

All neonates had good Apgar scores under spinal anesthesia.

IV. DISCUSSION

4.1. General characteristics of the study subjects

The subjects were 322 healthy pregnant women who met the study's inclusion criteria with informed consent. The characteristics of their mean age, weight and height were similar to the results of the other studies nationwide, such as Nguyễn Hữu Tuấn's [1], Sầm Thị Quy's [6].

As far as the indications of C-section delivery were concerned, repeated C–sections occupied 59,32%. This was higher than the result of Nguyễn Hữu Tuấn's study (43,3%).

4.2. The characteristics of motor blockage and analgesia degree since spinal anesthesia induction

Regarding motor blockage evaluated by Bromage scale, after 5 minutes, % of patients achieved M2 and M3 were 65,83 and 31,69, respectively; after 08 minutes, % of patients achieved M3 level and M2 level were 88,51 and 11,49, respectively.

About surgical analgesia degree, according to Abouleizh Ezzat scale, % of patients who achieved a good degree and a fair degree were 85,71% and 14,29%, respectively.

Thus the efficacy of spinal anesthesia in our study was to provide enough analgesia and muscle relaxation to facilitate maximum operation.

4.3. Duration of the surgical phases

Since anesthesia induction, it took 4.41 ± 0.51 minutes (equivalent to the result of Nguyen Huu Tuan's study, which was 3,97 ± 0,85 minutes) for the patient to be eligible for skin incision; 7.98±0.82 minutes for the patient to be eligible for fetal extraction. Therefore, this duration was enough to facilitate the operation, with 85,71 % of patients who achieved complete motor blockage (M3 level) after 08 minutes since spinal anesthesia induction.

The total operation duration was 44,27 ± 5,80 minutes, longer than that of Nguyễn Hữu Tuấn's study (30,00 ± 7,66 minutes). Perhaps 52,92 % of patients with repeated C – sections in our study, higher than the result of Nguyễn Hữu Tuấn's study (43,3%).

4.4. Hemodynamics changes and management since spinal anesthesia induction

From table 7: baseline SBP (T_0) was 119,78 ± 8,56 mmHg. The mean SBP was ≤ 95% of the baseline from 2 to 10 minutes since the spinal anesthesia induction, then gradually stabilized till the end of surgery. In which, mean SBP <80% and <70% of the baseline at 3rd and 4th minute were 34.16% and 36.33%, 10.86% and 11.80%, respectively**.** % of SBP decrease from baseline SBP at 3rd, 4th and 5th minute were 17,65%; 18,02% and 15,91%, respectively. The mean heart rate decreased slightly. It decreased > 10 beats per minute (bpm) by the 6th minute till the end of surgery and decreased deeply >15 bpm at the 7th minute (15,08%). 4.04% of patients had bradycardia (<55 bpm).

The average IV dose of phenylephrine was 95,96 ± 36,16µg, minimum dose 50µg and a maximum dose 200µg, in which 100µg dose to be used mostly 167/322 (51,86%). In Nguyễn Hữu Tuấn'study, phenylephrine mean dose was 101,67 ± 33,43µg (min 50 mcg và max 150mcg). In Cooper. D et al.'study, phenylephrin infusion rate was 67 µg/min (phenylephrin dose used from 670 - 1000µg/ patient).

In this study, 7 cases (2,17%) with bradycardia ≤ 55 bpm after phenylephrine use increased SBP to allowable thresholds required atropine 0,5mg IV. There were 6 cases (1,85%) with mean SBP <80% associated with bradycardia ≤ 55 bpm and phenylephrin ≥ 100 µg use before, we added more 3-6 mg ephedrin to increase SBP and pulse to return to the normal ranges. According to Ngan Kee, W. D., bradycardia was recorded in 13 patients (12%). In our study, mean SBP <80% of the baseline and mean SBP <70% of the baseline occupied 36,33% and 11,8% of patients, respectively (table 7). According to Nguyễn Hữu Tuấn'study, mean SBP <80% of the baseline occupied 56,7%, mean SBP <70% of the baseline occupied 16,6% of patients [1]. According to Cooper, mean SBP <80% of the baseline occupied 48% of patients in group with IV phenylephrine [2]. According to Sầm Thị Quy's study, mean SBP <80% of the baseline only occupied 20% of patients [6]. In Siddik-Sayyid, S. M. et al.'s study, hypotension rate occupied 20% of patients in the group with IV phenylephrine 0,75µg/kg/min compared to 90% in the group without phenylephrine [7].

IV fluid infusion: co-/pre-loading at the moment and before spinal anesthesia was the way to compensate for the circulatory load to prevent and support hypotension. Total crystalloid solutions loading volume at the moment of and just after spinal anesthesia ("co-/post-loading") was 1222.89 ± 141.67ml. In Nguyễn Hữu Tuấn's study, the co-/pre-loading volume was 1135 ± 153 ml. In Sầm Thị Quy's study, it was 1083,3 ± 102,8ml.

4.5. Respiratory changes

Mean SpO2 values was 98,79± 2,86%. No cases of respiratory distress, similar to the results of other author's studies.

4.6. Adverse effects on pregnant women

7,76 % of patients had vomiting under spinal anesthesia, similar to the results of Sam Thi Quy's study.

4.7. 1- minute and 5 – minute Apgar score

In our study, 1- minute and 5 – minute Apgar score were 8,35 ± 0,24 and 8,99 ± 0,07, respectively. No cases with APGAR score < 7 (asphyxia). These results were similar to those from studies of Sầm Thị Quy [6], Cooper [2] and Sabyasachi [8]. Therefore, Levobupivacain used for spinal anaesthesia and phenylephrine used in our study did not badly affect APGAR score.

Ngan Kee (2009) and other recent clinical studies have demonstrated that ephedrine was associated with a greater propensity toward fetal acidosis than phenylephrine [9].

Ngan Kee (2009), whose study on 90 pregnant women divided into 2 groups, P Group (100µg Phenylephrine use) and E Group (8mg Ephedrine use). Umbilical venous pH from P group and E group were 7,34 and 7,31, respectively. Umbilical arterial pH from P group and E group were 7,33 and 7,25, respectively, with p < 0,01 [9].

V. CONCLUSION

Phenylephrine for managing hypotension during spinal anesthesia for cesarean section delivery was a safe and effective strategy of choice.

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