



# Phenylephrine Effectiveness in Handling Hypotensive Issues During Spinal Anesthesia Conductance for Cesarean Section Deliveries

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## Abstract

**Background:** Hypotension is frequent clinical challenge during spinal mode of anesthetic induction for cesarean delivery. Requiring an effective and prompt management mode since it has unfavorable clinical outcomes such as hemodynamic cardiovascular instability issues besides reduced uteroplacental perfusion.

**Aim:** Investigating the impact and effectiveness of different prophylactic dosages of Phenylephrine on hypotensive issues during spinal anesthesia for cesarean section deliveries.

**Methodology:** A prospective, randomized, clinical research study involved 184 cases That are classified as American Society of Anesthesiologists physical status I and II with term singleton pregnancies scheduled for elective cesarean section under spinal anesthesia randomized to receive 0.9% saline 2mL (Control Group) or phenylephrine 1.0ug/kg (PHE1 research Group), 1.5ug/kg (PHE1.5 research Group), or 2.0ug/kg (PHE2 research Group) immediately after induction of spinal anesthesia.

**Results:** The adverse effects of prophylactic bolus of Phenylephrine among the research groups control, Phenylephrine 1,1.5,2 in which there was statistically significant difference as regards hypotension, rescue Phenylephrine, lowest SBP, highest SBP, early highest SBP, mean SBP, occurrence of hypertension (p values=<0.001, <0.001,0.002, <0.001, <0.001, <0.001 consecutively) there was no statistical significant difference as regards nausea and bradycardia (p values=0.929, 0.823 consecutively).

**Conclusions:** The research findings obtained denote and imply that a prophylactic Phenylephrine 1.5ug/kg bolus followed by additional boluses when necessary could be an alternative management protocol to decrease the frequency of hypotensive issues occurrence during spinal anesthetic mode for cesarean deliveries.

**Keywords:** Cesarean section; Phenylephrine; Spinal hypotension

## Introduction

Spinal anesthesia mode for cesarean deliveries could prevent critical maternal complications linked and correlated to general mode of anesthetic practice [1]. Hypotension is frequent clinical challenge during spinal mode of anesthetic induction for cesarean delivery. Requiring an effective and prompt management mode since it has unfavorable clinical outcomes such as maternal nausea, vomiting, dizziness, and hemodynamic cardiovascular instability issues besides reduced uteroplacental perfusion causing fetal bradycardia, acidosis, and hypoxic issues. Reduced cardiac output is an issue of concern in obstetric anesthesia practice [2]. Phenylephrine as an alpha agonist is a vasopressor of choice for avoidance and management of spinal anesthesia triggered

hypotension. Prior research groups of investigators have shown that Phenylephrine is an agent correlated to baroreceptor-mediated bradycardia and therefore causes a consecutive decrease in cardiac output having an incidence of around 30%, in physiologically healthy maternal and fetal status, those changes occurring from Phenylephrine are considered of trivial impact on the other hand heart rate and cardiac output conservation is of critical value in high-risk clinical scenarios e.g. maternal cardiac illnesses, placental inadequate vascular performance issues, and fetal distress challenges and concerns [3,4].

Phenylephrine being used for management of hypotensive issues have been revealed and displayed by various research groups of

investigators to enhance the fetal acid base physiological balance, by raising fetal pH and decreasing PCO<sub>2</sub> in comparison and contrast to other agents such as ephedrine [5]. Investigators in previous research studies have shown among their findings that prophylactic infusion using rescue Phenylephrine boluses is an efficient mode for maternal maintenance of hemodynamic physiologic stability, and furthermore could reduce physician interventions in comparison to rescue boluses alone [5]. The optimum protocol for Phenylephrine administration haven't been elucidated by researchers as it was shown by prior research groups of investigators in prior studies that continuous infusion protocols of Phenylephrine which are frequently implemented in obstetric anesthetic practice is linked and correlated to very low statistically estimated incidence of hypotension and decreased nausea and vomiting clinical incidence [6]. On the other hand, even though infusion in a continuous manner is an efficient and convenient in nature, it necessitates appropriately

trained personnel with necessary tools such as infusion pump [7]. A prior research study have compared and contrasted Phenylephrine bolus and infusion management protocols, and revealed among their research study findings that blood pressure is superiorly sustained using boluses, particularly within the initial 6 min after spinal anesthesia conductance [8]. It is statically estimated from prior research groups that the hypotension clinical after spinal anesthesia is around 32.5 percent in cases that were administered Phenylephrine as a prophylactic bolus in comparison to 85 percent among a research group that was administered Phenylephrine as a therapeutic dosage only after occurrence of hypotension [9].

### Aim of the work

Investigating the impact and effectiveness of different prophylactic dosages of Phenylephrine on hypotensive issues during spinal anesthesia for cesarean section deliveries (Tables 1-5).

**Table 1:** research study subjects basic and demographic characteristics.

	Control group	PHE1 group	PHE1.5 group	PHE2 group	Test value	P-value	Sig.
Age (years)	31.88± 4.65	33.42± 5.26	30.85 ± 4.93	32.73 ± 4.28	2.464	0.064	NS
Height (cm)	164.32±9.27	161.52 ±11.84	162.45 ±10.54	166.34 ±9.42	1.967	0.121	NS
Weight (kg)	65.84 ± 7.32	67.92 ± 6.83	64.54 ± 8.67	66.45 ± 7.39	1.575	0.197	NS
BMI (kg/m <sup>2</sup> )	24.38 ± 3.27	26.03 ± 4.21	24.46 ± 5.32	24.02 ± 4.89	1.817	0.146	NS
Systolic BP (mmHg)	116.87 ± 6.45	118.23 ± 5.87	119.47 ± 6.24	117.65 ± 5.46	1.525	0.21	NS
Heart rate (beats/min)	81.82 ± 13.65	83.54 ± 14.32	82.65 ± 12.65	80.36 ± 11.27	0.496	0.686	NS
Estimated blood loss (mL)	650.13 ± 115.3	715.86 ± 130.5	684.69 ±115.96	690.87±130.64	2.22	0.087	NS
Fluid until delivery (mL)	875.37 ±115.3	850.69 ±125.98	915.36 ±125.33	883.84±136.45	2.066	0.106	NS

•: Data were presented as mean and standard deviations and compared between groups using One Way ANOVA

**Table 2:** Adverse effects of prophylactic bolus of Phenylephrine.

	Control group	Phe1 group	Phe1.5 group	Phe2 group	Test value	P-value	Sig.
Hypotension	34 (73.9%)	32 (69.6%)	16 (34.8%) a,b	22 (47.8%)a,b	19.108*	<0.001	HS
Rescue Phenylephrine (mg)	150 (0 – 300)	200 (0 – 300)	0 (0 - 200) a,b	100 (0 – 200)a,b	4.421	<0.001	HS
Lowest SBP (mmHg)	82.15 ±15.27	85.32 ± 12.32	93.45 ± 12.43a	87.54 ±14.52	5.342	0.002	HS
Highest SBP (mmHg)	118.35±10.87	121.14±12.91	128.85±11.57 a,b	132.64 ± 15.24 a,b	12.444	<0.001	HS
Early highest SBP (mmHg)	116.25 ± 10.63	127.18±12.32a	129.71 ± 10.29a	132.84 ± 12.41a	18.239	<0.001	HS
Mean SBP (mmHg)	105.58 ± 12.26	111.21 ± 12.52	117.34 ± 11.43a	117.67 ± 14.52a	9.353	<0.001	HS
Nausea	7 (15.2%)	8 (17.4%)	8 (17.4%)	6 (13.0%)	0.45	0.929	NS
Bradycardia	4 (8.7%)	4 (8.7%)	2 (4.3%)	3 (6.5%)	0.91	0.823	NS
Hypertension	3 (6.5%)	3 (6.5%)	8 (17.4%)	16 (34.8%) a,b	18.002	<0.001	HS

\*: Data were presented as number and percentages and compared using Chi-square test.

•: Data were presented as means and standard deviations and compared using One Way ANOVA followed by post hoc using LSD test; ≠: Data were presented as medians with inter-quartile ranges and compared using Kruskal-Wallis test followed by post hoc using Mann-Whitney test (°: Significant from Control; °: Significant from PHE1; °: Significant from PHE1.5).

P < 0.05: Significant; P < 0.01: Highly significant.

**Table 3:** Changes in the systolic blood pressure (mmHg) during the time of measurement in the four groups.

SBP (mmHg)	Control group	PHE1 group	PHE1.5 group	PHE2 group	Test	P-value	Sig.
Baseline	118.35 ± 11.27	119.41±12.2	120.64±9.95	119.42±12.48	0.304	0.823	NS
1	110.45 ± 12.32	120.53±13.25a	118.32±11.51a	117.94±13.53a	5.519	0.001	HS
2	107.86 ± 10.35	118.67±11.28a	120.45± 12.03a	120.32±11.56a	13.055	0	HS
3	106.68 ± 11.36	112.32±13.29	118.87± 12.04a	115.45±13.57a	7.68	0	HS
4	105.47 ± 12.67	110.24± 13.63	116.63± 14.35a	116.63± 13.88a	7.277	0	HS
5	106.58 ± 10.98	109.32±11.91	115.24± 11.66a	115.47±12.19a	6.573	0	HS
6	107.32 ± 12.36	108.84±13.29	110.23±11.04	113.71±13.57	2.157	0.095	NS
7	105.15 ± 11.54	109.32±12.47	109.68±10.22	115.32±12.75a	5.775	0.001	HS
8	103.36 ± 14.36	107.34±13.29	108.61± 12.04	110.57±15.57	2.215	0.088	NS
9	103.86 ± 12.64	108.68±13.57	109.14±11.32	110.76±13.85	2.446	0.066	NS
10	104.46 ± 10.69	105.62± 12.62	110.68± 15.37	112.48± 14.9	2.514	0.06	NS
11	107.54 ± 14.32	108.14±15.25	112.63±13.53	113.91±15.53	2.169	0.093	NS
12	107.21 ± 15.65	107.53±16.58	110.31±14.33	113.01±16.86	1.343	0.262	NS
13	109.69 ± 12.69	105.14±13.62	111.85±11.37	110.54±13.9	2.338	0.075	NS
14	110.63 ± 10.65	106.64±11.58	112.14± 14.33	109.08±11.86	1.709	0.167	NS
15	106.31 ± 15.32	105.69±16.25	112.63±14.65	110.69±16.53	2.12	0.099	NS

Data were presented as means and standard deviations and compared using One Way ANOVA followed by post hoc analysis using LSD test: a: Significant difference from control group; b: Significant difference from PHE1, c: significant difference from PHE1.5.

**Table 4:** Number of boluses used in each period among the four research groups.

Time/minute	Control group	PHE1 group	PHE1.5 group	PHE2 group
1 - 3 min	17	7	2	4
4 - 6 min	37	19	8	9
7 - 9 min	30	26	11	11
10 - 12 min	22	12	3	4
13 - 15 min	10	8	2	3
16 - 18 min	3	2	0	2
Total no.	119	74	26	33
Median (IQR)	19.5 (10 - 30)	10 (7 - 19)	2.5 (2 - 8)	4 (3-9)
X <sup>2</sup> /P-value	8.348 / 0.039 (S)			

Data were presented as number of boluses used in each period and compared using median and inter-quartile range with Kruskal-Wallis test

**Table 5:** Comparison between the four studied groups regarding neonatal outcome.

	Control group	PHE1 group	PHE1.5 group	PHE2 group	Test	P-value	Sig.
Apgar score 1 min	8 (8 - 9)	8 (8 - 8)	7 (7 - 9)	8 (8 - 9)	1.254	0.315	NS
Apgar score 5 min	9 (8 - 9)	9 (8 - 9)	9 (8 - 9)	8 (8 - 9)	1.654	0.253	NS
UV pH	7.35± 0.03	7.36 ± 0.04	7.36 ± 0.03	7.35 ± 0.03	1.426	0.237	NS
UV PCO2 (mmHg)	43.9 ± 2.65	44.6 ± 4.39	42.95±5.85	44.3 ± 4.69	1.15	0.331	NS
UA pH	7.33 ± 0.03	7.33± 0.02	7.32 ± 0.03	7.33 ± 0.04	1.211	0.307	NS
UA PCO2 (mmHg)	51.6 ± 4.35	49.5 ± 5.28	49.6 ± 5.89	50.65 ± 4.66	1.745	0.159	NS
7	105.15 ± 11.54	109.32±12.47	109.68±10.22	115.32±12.75a	5.775	0.001	HS

8	103.36 ± 14.36	107.34±13.29	108.61± 12.04	110.57±15.57	2.215	0.088	NS
9	103.86 ± 12.64	108.68±13.57	109.14±11.32	110.76±13.85	2.446	0.066	NS
10	104.46 ±10.69	105.62± 12.62	110.68± 15.37	112.48± 14.9	2.514	0.06	NS
11	107.54 ± 14.32	108.14±15.25	112.63±13.53	113.91±15.53	2.169	0.093	NS
12	107.21 ± 15.65	107.53±16.58	110.31±14.33	113.01±16.86	1.343	0.262	NS
13	109.69 ± 12.69	105.14±13.62	111.85±11.37	110.54±13.9	2.338	0.075	NS
14	110.63 ± 10.65	106.64±11.58	112.14± 14.33	109.08±11.86	1.709	0.167	NS
15	106.31 ± 15.32	105.69±16.25	112.63±14.65	110.69±16.53	2.12	0.099	NS

### Methodology

A randomized (using computer-generated random allocation) double blinded clinical; research trial conducted from January 2017 till January 2019, after approval of local ethical committee on the current research study and written informed consent was taken from all participant, conducted at Mohamed Saleh Bashrahil Hospital in Holy Makka, Saudi Arabia. Current clinical research study involved 184 cases that are classified as American Society of Anesthesiologists physical status I and II with term singleton pregnancies scheduled for elective cesarean section under spinal anesthesia randomized to 4 groups; receive 0.9% saline 2mL (Control Group) or Phenylephrine 1.0ug/kg (PHE1 research Group), 1.5ug/kg (PHE1.5 research Group), or 2.0ug/kg (PHE2 research Group) immediately after induction of spinal anesthesia. Maternal blood pressure and heart rate were recorded at 1min intervals until delivery. Hypotension, defined as systolic blood pressure <80% of baseline, was treated with rescue doses of Phenylephrine 100ug at 1min intervals until hypotension resolved. The incidence of nausea, vomiting, bradycardia, and hypertension, as well as Apgar scores and umbilical blood gases (GEM premier 3500, USA) were recorded. Exclusive research criteria involved the following pre-existing or pregnancy-induced hypertension, cardiac or respiratory disease, cerebrovascular disease, fetal anomalies or contraindications to spinal anesthesia. Cases among Control research Group were administered 0.9% saline 2mL, while cases among Phenylephrine

research groups 1, 1.5, and 2 were administered Phenylephrine 1.0, 1.5, and 2.0ug/kg, consecutively, diluted in 2ml of saline .Before the induction of anesthesia, an 18gauge intravenous cannula was inserted. Typical monitoring devices was attached, involving non-invasive blood pressure, electrocardiogram, three lead ECG (Carestation monitor B650, GE healthcare, Helsinki, Finland), blood pressure and heart rate were measured at 1min intervals. Cases have been positioned in the left lateral decubitus position for the spinal procedure. After skin decontamination and injection of cutaneous local anesthetic, a 27G needle (Polymed spinal needle with Quincke type point, Brussels, Belgium) was inserted at the L3-4 or L4-5 interspace and the dura mater was punctured, After verifying free flow of cerebrospinal fluid, a mixture of 0.5% hyperbaric bupivacaine 11mg and fentanyl 15ug was administered over 10s.

### Primary Research Outcome

Have been determination of the incidence of hypotension, defined as systolic blood pressure (SBP) <80% of baseline. Hypotension was managed using rescue doses of Phenylephrine 100ug every 1min till hypotension was resolved. The total rescue dosage of Phenylephrine that has been administered to each patient was recorded. Cases that have been experiencing bradycardia in conjunction to hypotension were administered atropine 0.5mg Apgar scores at 1 and 5min, estimated blood loss, and fluid administration till time of delivery were recorded (Figures 1-3).

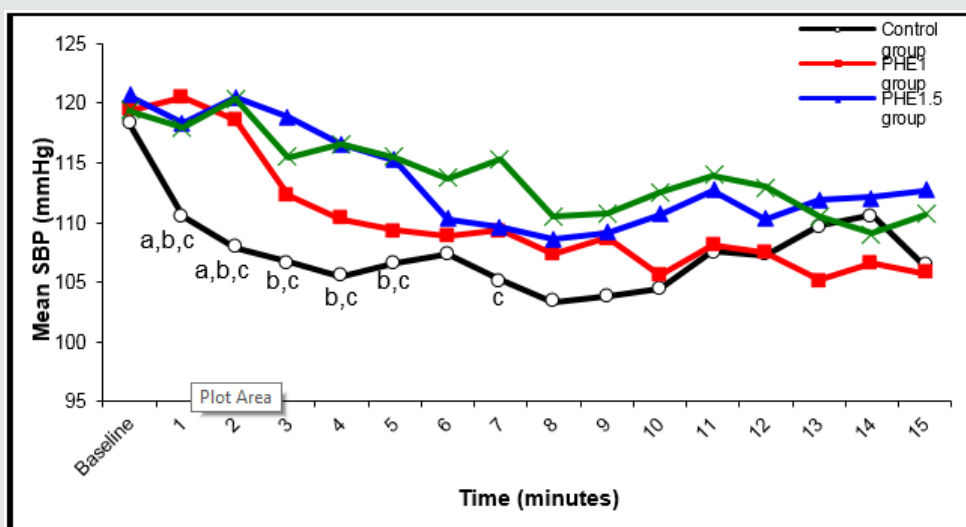


Figure 1: Changes in systolic blood pressure in the four studied groups during time. <sup>a</sup>P <0.05 compared with the PHE1 group; <sup>b</sup>P <0.05 compared with the PHE1.5 group and <sup>c</sup>P <0.05 compared with the PHE2 group.

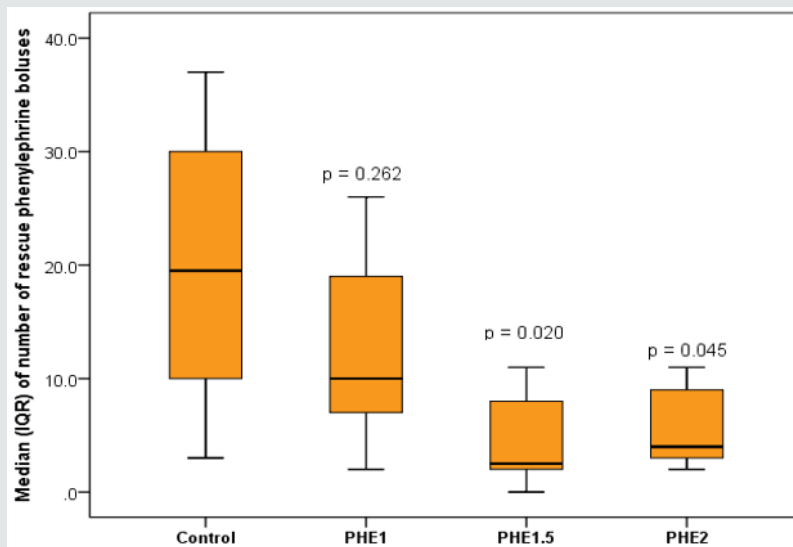


Figure 2: Median (IQR) of number of rescue Phenylephrine boluses among the four research groups.

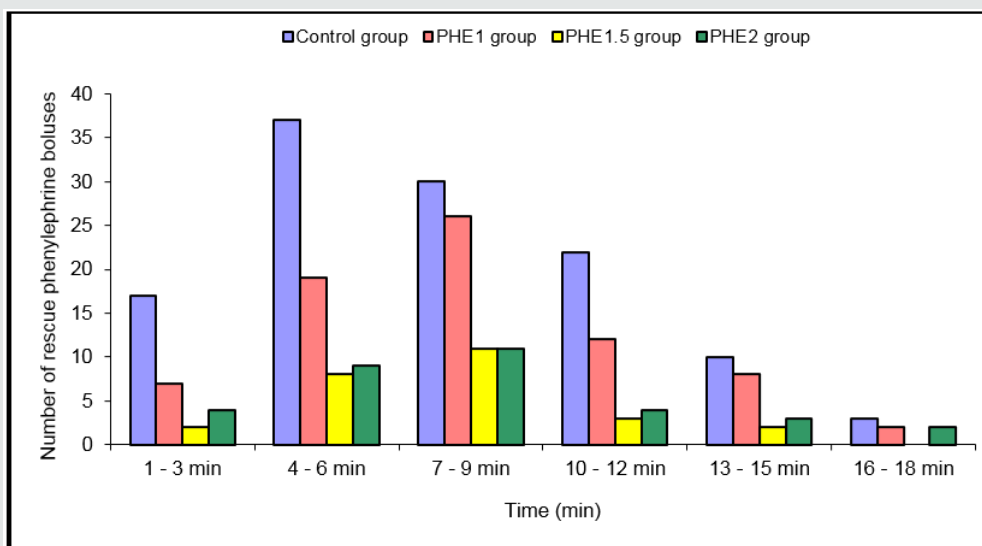


Figure 3: Display the number of rescue boluses that were administered over time among the four research groups.

### Statistical Analysis

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The distribution of quantitative data was tested by Kolmogorov-Smirnov test of normality. So, the quantitative data were presented as means, standard deviations and ranges when parametric and compared between groups using One Way ANOVA followed by post hoc analysis using LSD test while non-parametric were presented as medians with inter-quartile ranges (IQR) and compared between groups using Kruskal-Wallis test followed by post hoc analysis using Mann-Whitney test. Also, qualitative variables were presented as numbers and percentages and compared between groups using Chi-square test. The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant at the level of < 0.05.

### Discussion

Administration of a Phenylephrine infusion can reduce the incidence and severity of hypotension and nausea during spinal anesthesia for cesarean delivery. However, good hemodynamic control may not be attained if the drug is administered as a prophylactic fixed rate infusion. A variable rate infusion adjusted based on changes in arterial blood pressure and heart rate may better maintain baseline blood pressure [10]. Over time, methods have changed for managing blood pressure (BP) changes during spinal anesthesia for cesarean delivery. Phenylephrine is now the preferred vasopressor for treating hypotension, but how it should be used is still debated. One method is the use of a prophylactic infusion after the block is placed [11]. A prior research study similar to the current study in approach and methodology have revealed and displayed among its findings that prophylactic administration


of Phenylephrine boluses 1.5 and 2ug/kg decreased the incidence of hypotension during conductance of spinal anesthetic mode for cesarean deliveries [1,3]. Furthermore it was shown by a prior research team of investigators the total additional dosages used for managing hypotensive issues in spinal anesthetic techniques in cesarean section of Phenylephrine agent was small among the investigated cases [2,5]. Another research team of investigators have shown among their study findings that the large Phenylephrine dosage of 2ug/kg is correlated and linked to higher rates of hypertension. Interestingly according to Phenylephrine dosages best suiting managing and preventing hypotensive attacks during spinal anesthesia conducted for cesarean delivery is administering a prophylactic Phenylephrine bolus of 1.5ug/kg [5,8]. A previous group of investigators have compared three dissimilar dosage protocols: continuous infusion (0.15ug/kg/min) versus prophylactic bolus (50ug) versus therapeutic bolus (50ug) it was revealed and displayed that the incidences of hypotension have been 17.5%, 32.5% and 85%, consecutively. Even though the best results have been observed among the continuous infusion research group, a 50ug prophylactic dosages was also efficient in preventing hypotensive attacks during spinal anesthesia for cesarean sections [4,7].

## Conclusion and Recommendation for Future Research

The research findings obtained denote and imply that a prophylactic Phenylephrine 1.5ug/kg bolus followed by additional boluses when necessary could be an alternative management protocol to decrease the frequency of hypotensive issues occurrence during spinal anesthetic mode for cesarean deliveries. Future research efforts are recommended to consider racial and ethnic differences in conjunction to BMI differences.

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