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Research Article

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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 prophylacticdosages 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 2 mL (Control Group) or phenylephrine1.0 ug/kg (PHE1 research Group), 1.5 ug/kg (PHE1.5 research Group), or 2.0 ug/kg (PHE2 research Group) immediately after induction of spinal anesthesia.*

Results: *The adverse effects of prophylactic bolus ofPhenylephrine 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, <0.001consecutively) there was no statistical significant difference as regards nausea and bradycardia (p values=0.929, 0.823consecutively).*

Conclusions: *The research findings obtained denote and imply that a prophylactic Phenylephrine 1.5 ug/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].

Hypotensionis 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 isa 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 hypotensiveissues 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_2 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 manneris 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.

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 2 mL (Control Group) or Phenylephrine 1.0 ug/kg (PHE1 research Group), 1.5 ug/kg (PHE1.5 research Group), or 2.0 ug/kg (PHE2 research Group) immediately after induction of spinal anesthesia. Maternal blood pressure and heart rate were recorded at 1-min intervals until delivery. Hypotension, definedas systolic blood pressure <80% of baseline, was treated with rescue doses of Phenylephrine 100 ug at 1-min intervals untilhypotension resolved. The incidence of nausea, vomiting, bradycardia, and hypertension, as well as Apgar scores and umbilical bloodgases (GEM premier 3500, USA) were recorded.Exclusive research criteria involved the following pre-existingor pregnancy-induced hypertension, cardiac or respiratory disease, cerebrovascular disease, fetal anomaliesor contraindications to spinal anesthesia.

Cases among Control research Group were administered 0.9% saline2 mL, while cases among Phenylephrine research groups 1, 1.5, and2 were administered Phenylephrine 1.0, 1.5, and 2.0ug/kg, consecutively; diluted in 2 mL of saline.Before the induction of anesthesia, an 18-gauge 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 weremeasured at 1-min intervals. Cases have been positioned in the left lateral decubitus position for the spinal procedure. After skin decontamination and injection of cutaneous local anesthetic, a27G needle (Polymed spinal needle with Quincke type point, Brussels, Belgium) was inserted atthe L3–4 or L4–5 interspace and the dura mater was punctured, after verifyingfree flow of cerebrospinal fluid, a mixture of 0.5% hyperbaric bupivacaine 11 mg and fentanyl 15ug was administered over 10s.

Primary research outcome

Have been determination of theincidence of hypotension, defined as systolic blood pressure (SBP) <80% of baseline. Hypotension was managed using rescue doses of Phenylephrine 100 ug every 1 mintill hypotensionwas resolved. The total rescue dosage of Phenylephrine that has been administered to each patient ware recorded. Cases that have been experiencing bradycardia inconjunction tohypotension were administeredatropine 0.5 mg. Apgar scores at 1 and 5 min, estimatedblood loss, and fluid administration till time of delivery were recorded.

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 Kruskall-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.

Results

Table 1 reveals and displays the basic and demographic research characteristics of the research groups control, Phenylephrine 1, 1.5, 2 in which there was no statistical significant difference between the research groups as regards age, height, weight, BMI, systolic BP, heart rate, estimated blood loss, fluid until delivery (p values =0.064, 0.121, 0.197, 0.146, 0.210, 0.686, 0.087, 0.106 consecutively).

Table 2 reveals and displays 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, <0.001) there was no statistical significant difference as regards nausea and bradycardia (p values=0.929, 0.823 consecutively).

Table 3 and figure 1 reveals and displays Changes in the systolic blood pressure (mmHg) during the time of measurement in the four groups in which there was no statistical significant difference at baseline, 6, 8 till 15 minutes (p value= 0.823, 0.095, 0.088, 0.066, 0.060,0.093, 0.262, 0.075, 0.167, 0.099 consecutively) whereas there was statistical significant difference as regards 1 till 5 min,7 min readings (p values= 0.001, 0.000, 0.000, 0.000, 0.000, 0.001 consecutively).

Table 4 and figures 2,3 reveals and displays that there is statistical significant difference as regards the number of boluses in each period between the four research groups (p value= 0.039).

Table 5: Reveals and displays the comparative statistical analysis as regards the neonatal outcome in which there was no statistical significant difference between the four research groups (p values =0.315, 0.253, 0.237, 0.331, 0.307, 0.159 consecutively).

Table 1: Research study subjects basic and demographic characteristics

	Control group No. = 46	PHE1 group No. = 46	PHE1.5 group No. = 46	PHE2 group No. = 46	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/m2)	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	0.210	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	2.220	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 No. = 46	PHE1 group No. = 46	PHE1.5 group No. = 46	PHE2 group No. = 46	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 (µg)	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 ± 12.43[a]	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 ± 10.29[a]	132.84 ± 12.41[a]	18.239	<0.001	HS
Mean SBP (mmHg)	105.58 ± 12.26	111.21 ± 12.52	117.34 ± 11.43[a]	117.67 ± 14.52[a]	9.353	<0.001	HS
Nausea	7 (15.2%)	8 (17.4%)	8 (17.4%)	6 (13.0%)	0.450	0.929	NS
Bradycardia	4 (8.7%)	4 (8.7%)	2 (4.3%)	3 (6.5%)	0.910	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 Kruskall-Wallis test followed by post hoc using Mann-Whitney test ([a]: Significant from Control; [b]: Significant from PHE1; [c]: 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) Time (minutes)	Control group No. = 46	PHE1 group No. = 46	PHE1.5 group No. = 46	PHE2 group No. = 46	Test value	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±13.25[a]	118.32±11.51[a]	117.94±13.53[a]	5.519	0.001	HS
2	107.86 ± 10.35	118.67±11.28[a]	120.45± 12.03[a]	120.32±11.56[a]	13.055	0.000	HS
3	106.68 ±11.36	112.32±13.29	118.87± 12.04[a]	115.45±13.57[a]	7.680	0.000	HS
4	105.47 ±12.67	110.24± 13.63	116.63± 14.35[a]	116.63± 13.88[a]	7.277	0.000	HS
5	106.58 ± 10.98	109.32±11.91	115.24± 11.66[a]	115.47±12.19[a]	6.573	0.000	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	0.060	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	2.120	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.

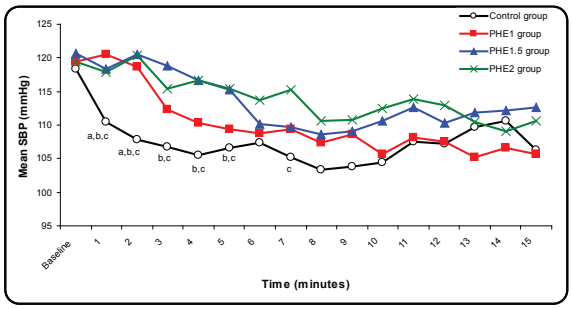

Figure 1: Changes in systolic blood pressure in the four studied groups during time.[a]P <0.05 compared with the PHE1 group;[b]P <0.05 compared with the PHE1.5 groupand [c]P <0.05 compared with the PHE2 group

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

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

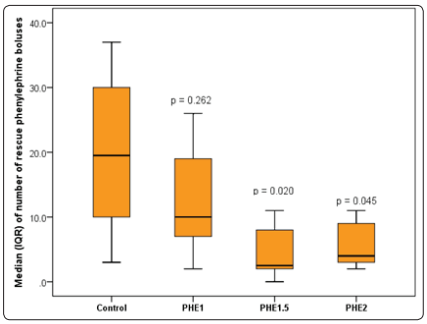

Figure 2: Median (IQR) of number of rescue Phenylephrine boluses among the four research groups

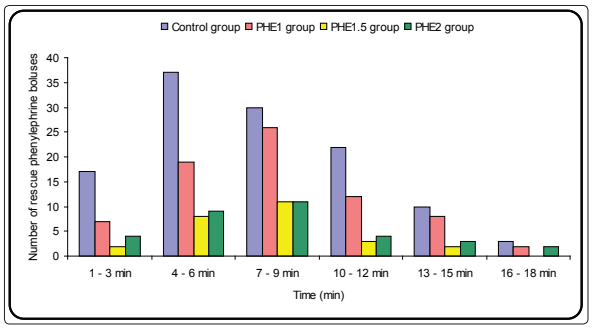

Figure 3: Display the number of rescue boluses that were administered over time among the four research groups

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

	Control group No. = 46	PHE1 group No. = 46	PHE1.5 group No. = 46	PHE2 group No. = 46	Test value	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 PCO_2 (mmHg)	43.9 ± 2.65	44.6 ±4.39	42.95±5.85	44.3 ± 4.69	1.150	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 PCO_2 (mmHg)	51.6 ± 4.35	49.5 ± 5.28	49.6 ±5.89	50.65 ± 4.66	1.745	0.159	NS

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 vasopressorfor treating hypotension, but how it should beused 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 anesthesic 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 aprophylactic 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, a50ug prophylactic dosages was also efficient in preventing hypotensive attacks during spinal anesthesia for cesarean sections [4,7].

Conclusions and recommendations for future research

The research findings obtained denote and implythat a prophylactic Phenylephrine 1.5 ug/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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