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Original Research Article

A prospective observational study involving three fixed infusion regimens of phenylephrine for hemodynamic support during spinal anaesthesia for caesarian delivery

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ABSTRACT

Background: Spinal anaesthesia used in caesarian section is associated with hypotension which can have maternal and fetal side effects. To determine the efficacy and ideal dosing of Phenylephrine in attenuating the hypotensive episodes during caesarean section under spinal anaesthesia.
Methods: 100 patients were allocated to four groups, placebo group (PE 0) and 3 fixed phenylephrine infusion regimens, phenylephrine 25 μg/min^{-1} (PE 25), phenylephrine 50 μg/min^{-1} (PE 50), and phenylephrine 75 μg/min^{-1} (PE 75). Blood pressure, heart rate were noted among primary variables and fetal parameters like umbilical blood pH and lactate were recorded as secondary parameters.
Results: There was a significant reduction in heart rate with increasing the infusion dosage of phenylephrine, with a mean of 86.8 beats/min at the end of procedure in placebo group and 69.4 beats/min in 75 μg group (p value <0.001). There was significant statistical difference among systolic blood pressure in the four groups after 7 min of the procedure and p-value of <0.05 with better attenuation of hypotension in infusion groups as compared to placebo. Similarly there was significant statistical difference in diastolic blood pressure among the four groups after 8 min of the procedure with p values <0.05.
Conclusions: Prophylactic phenylephrine infusions reduced the incidence and severity of maternal pre-delivery hypotension. Among the fixed rate phenylephrine infusion regimens investigated, infusion rates of 50 μg/min^{-1} were associated with greater maternal hemodynamic stability compared with 25 and 75 μg/min^{-1}, with minimal side effects and intervention.

Keywords: Caesarian section, Hypotension, Phenylephrine, Spinal anesthesia, Vasopressor

INTRODUCTION

Most of the patients undergoing caesarean delivery under spinal or epidural anaesthesia.[1] The sympathectomy resulting from the neuraxial blockade is exaggerated by the physiological changes of pregnancy and puerperium, leading to hypotension in as much as 55%-90% of the mothers receiving spinal anaesthesia for caesarean section.[2] Holmes et al, and Lee et al, indicated that the compression of the vena cava by gravid uterus impeded the venous return and caused hypotension.[3,4] Marx postulated that the subarachnoid block resulted in venous

pooling of blood in lower legs, leading to decreased venous return and reduced cardiac output.[5]

Systolic hypotension more than 20-30% of the baseline blood pressure can lead to maternal low perfusion pressure, manifested as nausea-vomiting, dizziness, low consciousness, utero-placental hypo-perfusion with fetal hypoxia and acidosis.[6] There are various measures to decrease the incidence and severity of hypotension which include left uterine displacement, intravenous fluid administration and the liberal use of vasopressors to prevent and treat hypotension. Phenylephrine is a selective α1 receptor agonist and β agonist action is only seen at much higher dose.[7] It is frequently used in obstetric anaesthesia to counteract the hypotension after Spinal Anaesthesia due to marked arterial vasoconstriction caused by its α1 agonist action.

The primary outcome of this study was to evaluate changes in heart rate and blood pressure post spinal block and the ideal dosing of the phenylephrine infusion which is best in attenuating episodes of hypotension and bradycardia, additional boluses of phenylephrine required and any episodes of hypertension with fixed dose infusions. The secondary outcomes were onset and level of block, APGAR score, fetal pH and fetal lactate levels.

METHODS

This prospective observational study was conducted in Gynecology and Obstetrics division of Department of Anaesthesiology and critical care of a tertiary care hospital and 100 pregnant women of American society of Anesthesiologists physical status I and II with singleton gestation at a gestational age of ≥36 weeks were included.

Pregnant patients who were in labor, with diabetes mellitus, hypertension or cardiac disease, obese with body mass index >45 $kg.m^{-2}$ or on drugs like monoamine oxidase inhibitors were excluded from the study.

After shifting the patient to operating room baseline arterial blood pressure and heart rate (HR) was measured in the supine position with left uterine displacement. Baseline systolic blood pressure (SBP) was determined by calculating mean of three consecutive SBP measurements taken 5 minutes apart when the patient was left undisturbed. Baseline SBP was used to determine the acceptable range of ±20% outside of which a physician intervention was indicated by study protocol.

Patients were allocated to a placebo group (PE 0) or 3 fixed phenylephrine infusion regimens: phenylephrine 25 $\mu g/min^{-1}$ (PE 25), phenylephrine 50 $\mu g/min^{-1}$ (PE 50), phenylephrine 75 μg/min-1 (PE 75). The infusions were given in identical 50mL syringes containing normal saline (PE 0), or phenylephrine at a concentration of 25, 50, 75 $\mu g/mL^{-1}$ by a physician involved in the study.

Standard noninvasive monitoring was applied, including pulse oximetry, electrocardiography, and noninvasive blood pressure. Spinal anaesthesia was performed in the sitting position at the L3-4 or L4-5 interspace using a 27-gauge Quinke's spinal needle with fentanyl 25 μg (0.5 ml) and 0.5% hyperbaric bupivacaine 2.5 mL (total volume 3 mL). Immediately after the injection of the intrathecal medication, infusion of study drug was started at 60 mL.h-1 in combination with a fluid co-load. Study drug infusion was connected to the most distal drug administration port and a pressurized 1 L bag of lactated Ringer solution was started, with the aim of administering at least 2 L before delivery of the baby. Patients were immediately laid supine with left uterine displacement. Noninvasive blood pressure readings were taken every minute for the first 10 minutes after spinal injection and 2.5 minutes thereafter. After delivery, 2.5 unit oxytocin was administered intravenously as a bolus followed by an infusion over the next 2 hours (10 units in 500 mL lactated Ringer solution).The study drug was infused until 10 minutes after delivery.

Physician interventions were triggered by a change in any of the following hemodynamic variables: a decrease in SBP >20% of baseline or SBP <90mmHg treated by administering a 100μg bolus of phenylephrine, an increase in the SBP to more than 20% of baseline treated by stopping the infusion. Infusions were restarted when the SBP decreased to below the upper limit of the target range (>20% above baseline). Glycopyrrolate 0.4 mg was administered for bradycardia defined as HR <50 beats/min.

The cephalad extent of the sensory block at 5, 10 and 20 minutes after placement of the spinal Anaesthesia was recorded using loss of pin prick sensation. Patients were asked to rate the severity of their nausea at 5, 10, and 15 minutes after spinal injection and at the end of the study using an 11-point verbal rating scale (0 = no nausea, 10 = worst possible nausea).They were asked to report nausea occurring at any other time. Intraoperative nausea or vomiting not related to hypotension will be treated with ondansetron 4 mg IV. Intraoperative nausea or vomiting occurring immediately before or after a 20% reduction in maternal SBP was recorded as hypotension- induced nausea or vomiting. Apgar scores at 1 and 5 minutes were recorded. Blood samples were collected from a double clamped segment of the umbilical cord for the measurement of umbilical vein blood gases.

Statistical analysis

Power of the study is 80%. Data was analyzed using SPSS software. Quantitative data was expressed using mean and standard deviation while qualitative data was expressed in frequency and percentage. Qualitative data was analyzed using chi-square test. Numeric measures will be compared using student t-test. All the results are discussed at 5% level of significance.

RESULTS

The mean age in our patients was 27.5±2.75 years, all the four groups were comparable in age and the difference was statistically insignificant with p-value of 0.871 (Table 1). The groups were also comparable with respect to BMI with the mean BMI of 26.86 kg/m^2 and a standard deviation of 2.77 (Table 1). Mean Gestation age in our patients was 38.3 with a standard deviation of 1.1 weeks, with no significant statistical difference among the groups (Table 1).

Table 1: Comparison of patient characteristics in study groups.

Patient characteristics	PE 0 (n=25)	PE 25 (n=25)	PE 50 (n=25)	PE 75 (n=25)	P-value
Age (years)	27.7±2.7	27.8±2.8	27.2±2.7	27.4±2.9	0.871
Body mass index (kg/m^{-2})	25.1±2.9	26.0±2.7	27.6±2.1	26.7±2.6	0.56
Gestational age (weeks)	38	38	38	39	0.737

Value expressed as mean±SD, ASA-PS: American society of anesthesiologist's physical status, SD: standard deviation

Table 2: Comparison of intra-operative variables in study groups.

Patient characteristics	PE 0 (n=25)	PE 25 (n=25)	PE 50 (n=25)	PE 75 (n=25)	P-value
Onset of block (min)	9.2±1.4	9.1±1.3	9.2±1.4	9.3±1.4	0.992
EBL (mL)	662±43.9	654±37.9	654±43.1	648±42.0	0.734
I.D time	5.06±0.79	5.14±0.83	5.12±0.84	5.08±0.78	0.989
U.D time	2.4±0.6	2.8±0.5	2.7±0.4	2.8±0.5	0.085
I.V. fluid infused (L)	2.43±0.17	2.49±0.05	2.49±0.05	2.49±0.05	0.849

Value expressed as mean±SD, ASA-PS: EBL-estimated blood loss, I.D Time- incision to delivery time, U.D time- uterine incision to delivery time

Table 3: Comparison of highest sensory level after spinal anesthesia in various study groups.

Highest sensory level	Study group				P Value
	PE 0 (n=25)	PE 25 (n=25)	PE 50 (n=25)	PE 75 (n=25)	
T4	15 (60%)	14 (56%)	10 (40%)	12 (48%)	0.873
T5	2 (8%)	2 (8%)	3 (12%)	3 (12%)	
T6	8 (32%)	9 (36%)	12 (48%)	10 (40%)	

Table 4: Means heart rate (in beats per minute) in various groups with standard deviation at different time intervals from the mean and the associated p-values.

Mean heart rate (Beats per minute)	Group PE 0 (n=25)		Group PE 25 (n=25)		Group PE 50 (n=25)		Group PE 75 (n=25)		P value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline	92	4.903	88.5	5.511	88.9	7.49	90.2	7.711	0.617
1 min	93.4	7.662	90.1	8.498	89	5.827	90	8.418	0.437
2 min	92.9	4.718	89.1	6.559	89.2	5.22	88.4	7.797	0.484
3 min	91	5.017	88.4	5.811	87.4	5.748	87.4	6.555	0.321
4 min	90.5	7.593	87.5	8.115	86.5	5.486	86	5.498	0.209
5 min	89	7.748	86.8	8.373	84.2	7.025	83.1	4.957	0.154
6 min	87.8	6.12	86	5.208	82.4	4.766	82.1	4.808	0.092
7 min	88	7.761	85.8	8.382	81.2	6.403	79.5	5.131	0.07
8 min	88.5	5.384	86.7	4.85	79.2	4.896	77.2	4.677	0.04*
9 min	88.3	4.51	86.4	4.888	78.1	5.123	76.1	6.185	0.03*
10 min	87.6	5.225	85.8	5.499	77.1	4.997	75.1	7.85	0.01*
12.5 min	88	8.362	86.2	8.102	76.2	6.082	74.5	8.082	0.007*
15 min	87.6	4.686	86	7.075	75.1	5.374	73.2	5.343	0.004*
17.5 min	87.2	7.081	85.3	4.828	74	5.205	70.9	6.768	<0.001*
20 min	87	5.221	85.1	6.923	73.8	7.67	70.4	7.29	<0.001*
End of surgery	86.8	7.636	84.4	6.611	73.4	6.975	69.4	5.819	<0.001*

*-statistically significant.

Table 5: Mean systolic blood pressure (in mmHg) in various groups with standard deviation at different time intervals from the mean and the associated p-values.

Mean SBP (mmHg)	GroupPE0 (n=25)		GroupPE25 (n=25)		Group PE 50 (n=25)		Group PE 75 (n=25)		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline	125.8	6.361	122.4	8.069	121.1	5.813	119.3	7.564	0.031
At 1 min	123.1	6.077	122	5.262	119.1	4.965	118.1	7.632	0.032
At 2 min	121.2	4.72	122.1	6.648	118.2	4.501	118.1	6.61	0.020
At 3 min	119.6	6.658	121	6.255	118	6.355	119	6.058	0.055
4 min	118.5	6.98	120.6	7.611	118.7	5.518	119.2	4.55	0.050
5 min	118.3	5.033	119.8	7.833	118.6	5.179	120.2	7.69	0.043
6 min	116.9	5.743	118.8	4.766	118.8	6.323	122.4	6.921	0.023
7 min	116.2	4.84	118.1	8.001	118.9	5.053	122.8	6.553	0.020
8 min	115.2	6.671	117.6	7.201	119	7.069	124.2	6.053	0.014
9 min	114.8	5.205	117.1	6.283	119.2	5.486	124.6	6.436	0.006
10 min	114.2	8.161	116.2	5.499	119.4	4.628	125.2	5.326	0.002
12.5 min	113.8	6.132	115.7	5.819	119.3	6.483	125.5	7.146	0.001
15 min	112.5	5.092	115.1	5.922	119.6	8.309	125.5	6.91	<0.001
17.5 min	110	7.458	114.2	4.864	120.2	5.595	126.2	7.294	<0.001
20 min	109.6	5.096	113.9	5.627	120.6	5.323	126.7	4.52	<0.001
End of surgery	108.9	5.127	113.5	6.674	120.8	6.741	127.1	6.86	<0.001

Table 6: Mean diastolic blood pressure (in mmHg) in various groups with standard deviation at different time intervals from the mean and the associated p-values.

Diastolic blood pressure (mmHg)	Group PE0 (n=25)		Group PE25 (n=25)		Group PE50 (n=25)		Group PE75 (n=25)		p-value
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline	75.5	7.205	71.2	6.01	69.7	5.408	72.6	7.915	0.033
1 min	74.2	5.336	74.6	7.29	67.2	8.431	68.2	6.952	0.019
2 min	73.8	6.315	73.1	5	67.5	6.456	67.6	6.764	0.014
3 min	72.4	8.489	71.8	7.22	68.2	5.973	68.2	4.734	0.084
4 min	70.5	7.801	70	6.994	68.1	4.507	68.6	7.445	0.081
5 min	70.1	6.294	70.5	5.251	68.5	7.719	69.5	7.344	0.071
6 min	69.7	7.857	69.1	4.858	68.4	7.698	69.6	4.55	0.067
7 min	69.2	4.709	68.3	6.162	68.4	7.366	69.6	7.575	0.058
8 min	68.7	5.753	67.4	5.667	68.5	4.788	69.8	4.846	0.005
9 min	68	6.883	66.4	4.852	68.7	6.118	69.4	5.379	0.043
10 min	67.2	8.37	67.2	5.546	68.6	5.898	70.3	5.691	0.031
12.5 min	66.1	7.813	66.1	6.803	68.8	6.225	72.4	6.66	0.024
15min	65.2	6.41	65.2	7.59	68.7	4.592	72.2	6.607	<0.001
17.5 min	62.7	8.311	62.7	5.796	68.5	8.437	71.5	7.653	<0.001
20 min	62.1	6.441	62.1	6.919	68.6	7.831	71.3	8.335	<0.001
End of surgery	61.6	6.1	59.2	7.248	68.6	8.126	71.2	7.482	<0.001

Table 7: Requirement of drugs in study groups intra-operatively.

Patient characteristics	PE 0 (n=25)	PE 25 (n=25)	PE 50 (n=25)	PE 75 (n=25)	P-value
No. of patients requiring rescue dose of PE (%)	23 (92%)	18 (72%)	7 (28%)	4 (16%)	<0.001*
No. of patients in which infusion was stopped	0 (0%)	0 (0%)	1 (4%)	18 (72%)	<0.001*
Mean amount of PE infused (µg)	0	440	854	1338	<0.001*
Mean total amount of PE in µg (infusion+bolus)	160	532	882	1358	<0.001*
Total no. of patients requiring glycopyrolate	0	0	0	4	
Total no. of doses of glycopyrrolate given	0	0	0	6	

Table 8: Comparison of fetal blood variables and Apgar score in different study groups.

Patient characteristics		PE 0 (n=25)	PE 25 (n=25)	PE 50 (n=25)	PE 75 (n=25)	P-value
Umbilical vein pH		7.34±0.06	7.35±0.04	7.33±0.03	7.33±0.05	0.231
Umbilical vein lactate		2.2±1.12	1.92±0.50	1.95±0.61	2.47±0.97	0.084
Apgar score at 1 min	7	6 (24%)	6 (24%)	3 (12%)	4 (16%)	0.78
	8	19 (76%)	19 (76%)	22 (88%)	21 (84%)	
Apgar score at 5 min	9	25	25	25	25	

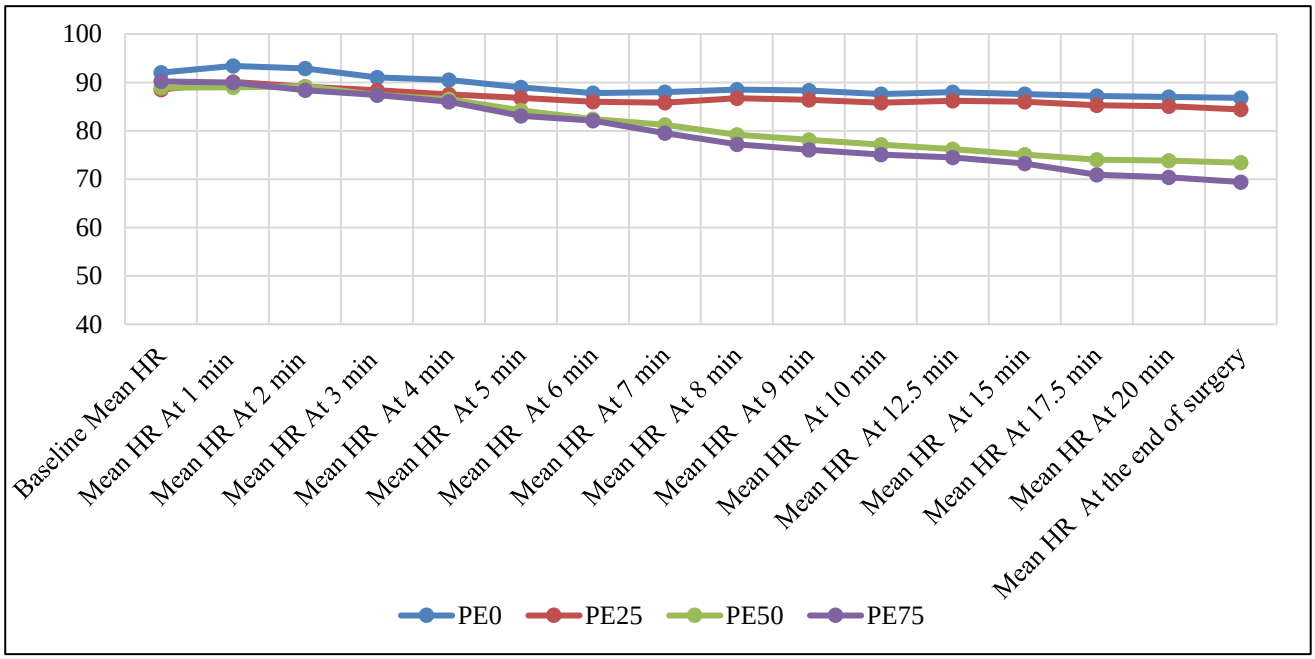

Figure 1: Comparison of mean heart rate (HR) in different groups at different study intervals.

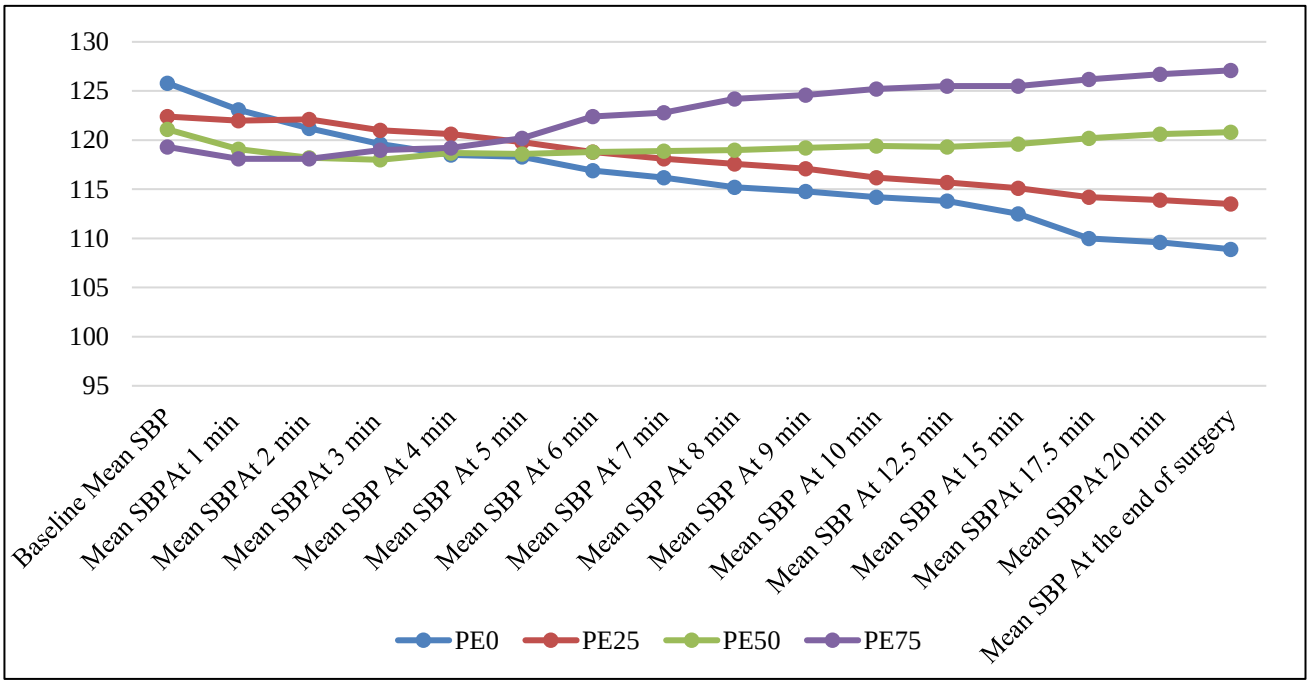

Figure 2: Comparison of mean systolic blood pressure (SBP) in different groups at different study intervals.

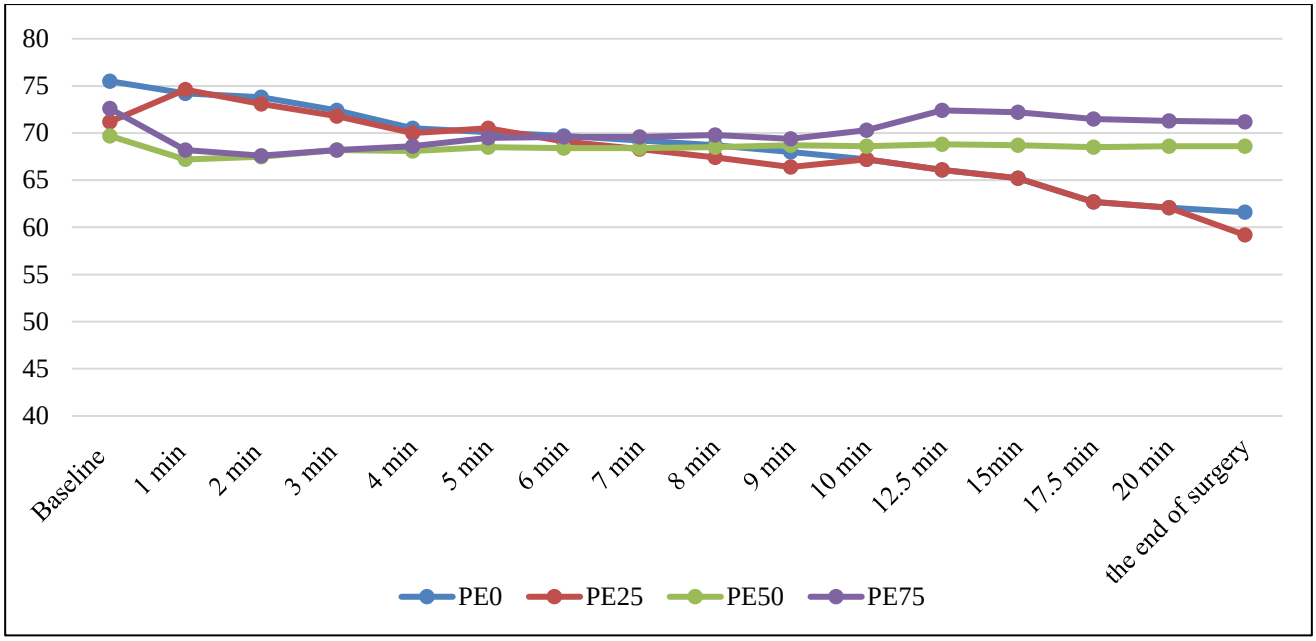

Figure 3: Comparison of mean diastolic blood pressure (DBP) in different groups at different study intervals.

The mean onset of block in this study group 9.20 minutes with SD of 1.37, the groups were comparable in terms of duration of onset of block and the difference among the groups was statistically insignificant with P value of 0.992 (Table 2). T4 was highest sensory level in 51% (n=51) patients T5 in 10% (n=10) and T6 in 39% (n=39) patients respectively (Table 3). The differences among the groups were statistically non-significant (P value 0.873). The estimated mean blood loss in our study was 654.5 ml with Standard Deviation of 41.2. The difference in blood loss among the different infusion groups was statistically insignificant with a p-value of 0.734 (Table 2). The average amount of fluid infused among the study groups was 2.47 litres with a Standard Deviation of 0.095. The groups were comparable and the difference was statistically insignificant with p-value of 0.849 (Figure 2).

The mean heart rate at different intervals in the four groups differed significantly with the mean heart rate highest in PE0 group and lowest in PE75 group. There was a significant reduction in heart rate with increasing the infusion dosage of phenylephrine, with a mean of 86.8/min at the end of procedure in placebo group and 69.4/min in 75µg group. The difference among the groups was statistically significant with a p-value of <0.001 (Table 4 and Figure 1).

The systolic blood pressure was constantly on higher side in patients who received phenylephrine infusion in contrast to those who did not receive phenylephrine infusion. There was no statistically significant difference between the four groups at the start of the procedure, the mean systolic blood pressure in the PE0 group was 125.8 mmHg, in the PE25 it was 122.4 mmHg, in the group PE50 it was 121.1mmHg and in the group PE75 it was 119.3 with p-value of 0.031. There was significant statistical difference among the four groups after 7 min of the procedure and p-value of <0.05 (Table 5, Figure 2).

The diastolic blood pressure was constantly on higher side in patients who received phenylephrine infusion in contrast to those who did not receive phenylephrine infusion. The readings were almost comparable between the four groups at the start of the procedure the mean diastolic blood pressure in the PE0 group was 75.5 mmHg, in the PE25 it was 71.2 mmHg, in the group PE50 it was 69.7 mmHg and in the group PE75 it was 72.6 with p-value of 0.033. There was significant statistical difference among the four groups after 8 min of the procedure with p values <0.05 (Table 6 and Figure 3).

Phenylephrine bolus of 100µg was given in study subjects who developed hypotension during the course of study, hypotension was defined as systolic BP of <80% of baseline. In this study, 92% (n=23) of patients who received saline only with no phenylephrine infusion (PE0) developed intra operative hypotension thereby requiring a phenylephrine bolus doses of 100µg, whereas the number dropped to 72 % (n=18) in group receiving 25µg infusion of phenylephrine (PE25). In the PE50 group 28% (n=7) patients required phenylephrine bolus doses whereas in the group PE75 only 16% patients required intervening phenylephrine bolus doses. The difference among the groups was statistically significant with p-value of <0.001 (Table 7).

Hypertension was defined as SBP of >120% of the baseline, and required stopping of the phenylephrine

infusion. In this study, none of the patients required stopping of infusion in zero phenylephrine (PE0) and 25 µg phenylephrine (PE25) groups. One patient required stoppage of infusion in 50 µg group (PE50) whereas in 75 µg (PE75) group infusion had to be stopped in 18 patients with an average of 1.7 times per patient where infusion needed to be stopped with total number of stoppage of infusions equal to 32. The difference among the groups was statistically significant with p value of <0.001 (Table 7).

The total amount of Phenylephrine infused in PE 0 Group was nil as the patients received normal saline infusions. In the PE25 group the mean amount of infused Phenylephrine was 440 µg per patient with minimum of 350 µg and maximum of 625 µg. In PE50 group it was 854 µg with a maximum and minimum of 1250 and 650 µg, and in PE 75 group total amount of phenylephrine infused was 1338 µg with a minimum of 1050 and maximum of 1725 µg. The difference among the groups was statistically significant as p <0.001 (Table 7).

The mean amount of total phenylephrine (bolus+ infusion) given in PE0 group was 160µg with a minimum of 0 µg and maximum of 400 µg. In the group PE25 the mean amount of total phenylephrine was 532 µg with a minimum of 400 µg and maximum of 700 µg, in PE50 group the total mean amount of phenylephrine was 882 µg with a minimum of 650 µg and maximum of 1350 µg, in the group PE75 the mean total amount of phenylephrine (bolus+infusion) was 1358 µg with a minimum of 1050 µg and maximum of 1725 µg. The difference among the groups was statistically significant as p value was <0.001 (Table 7).

Glycopyrrolate 0.4 mg was administered for bradycardia defined as HR <50 beats/min. In the group PE0, PE25 and PE50 none of the patients developed significant bradycardia (HR <50 beats/min) therefore did not require anticholinergics. In the group PE75, four (4) patients developed bradycardia and required net six (6) doses of glycopyrrolate (Table 7).

The mean fetal umbilical vein pH was 7.34 with a standard deviation of 0.05. The average fetal pH in PE0 group was 7.34 with a standard deviation of 0.06, whereas in PE 25 group it was 7.35 with a standard deviation of 0.04. The average fetal pH in PE50 group was 7.33 with a standard deviation of 0.03, whereas in PE 75 group it was 7.33 with a standard deviation of 0.05. The difference among the groups was statistically non-significant with p-value of 0.231 (Table 8).

The mean fetal umbilical vein lactate was 2.1±0.9 mmol/L. The average umbilical vein lactate in PE0 group was 2.2 with a standard deviation of 1.12, whereas in PE 25 group it was 1.92 with a standard deviation of 0.50. The average umbilical vein lactate in PE50 group was 1.95 with a standard deviation of 0.61, whereas in PE 75 group it was 2.47 with a standard deviation of 0.97. The difference among the groups was statistically non-significant with p-value of 0.084 (Table 8).

The APGAR score in the group PE 0 at 1 min was 8 in 76% (n=19) patients , 7 in 24% (n=6) in the group PE25 group the APGAR score at 1 minute was 7 in 24% (n=6) and 19 in 76% (n=19) patients. In the group PE 50 APGAR at 1 min was 7 in 12% (n=3) patients and 8 in 88% (n=22) patients. In PE75 group APGAR at 1 minute was 7 in 16% (n=4) and 8 in 84% (n=21) patients. The difference among the groups was statistically non-significant with p-value =0.78 (Table 8). The APGAR score at 5 minutes in all the patients was 9 in all the groups, there was no difference between the groups and was comparable.

DISCUSSION

Spinal anesthesia is commonly used for cesarean delivery because it avoids the risks of general anesthesia related to difficult intubation and aspiration of gastric contents. It is frequently associated with hypotension, which can have detrimental effects on the mother and neonate, including nausea, vomiting, and dizziness in the mother, as well as decreased utero-placental blood flow resulting in impaired fetal oxygenation and fetal acidosis. Various intravenous vasopressors have been tried for prevention and treatment of this hypotension.

In this study, author used fixed dose infusions of phenylephrine in three groups and compared with one who received normal saline as placebo. All the patients were monitored for onset and level of block, heart rate, blood pressure, amount of phenylephrine used, number of bolus doses given, number of times infusion stopped, APGAR score, fetal pH and fetal lactate levels and were analyzed statistically.

All the four groups were comparable with respect to age, BMI, gestational age, onset of block, estimated blood loss, incision to delivery time, uterine incision to delivery time and amount of fluid infused.

There was no statistically significant difference between the groups with respect to level of the sensory block; T4 was the highest sensory block in 51% of the patients followed by T5 and T6. The results were similar to Sayyid SM et al.[8]

The mean heart rate at different intervals in the four groups differed significantly with the mean heart rate highest in PE0 group and lowest in PE75 group. The HR in PE50 group was well controlled. The results were in concordance with Allen et al, who observed that higher phenylephrine infusion rates were associated with lower heart rates.[9]

The systolic and diastolic blood pressures were constantly higher throughout the procedure and at the end of the procedure in the patients receiving phenylephrine,

the higher concentrations of phenylephrine was associated with higher systolic and diastolic blood pressures. The pressures were appropriate in PE50 group with less episodes of hypotension in terms of lesser number of phenylephrine boluses needed and lesser episodes of hypertension in terms of lesser episodes of stopping of phenylephrine infusion. Our results were in concordance with Allen et al, and Doherty et al.[9,10]

The requirement of phenylephrine bolus doses (thereby hypotensive episodes) was highest in the group PE0 with 92% of patients requiring a phenylephrine bolus dose of 100µg, whereas the number dropped to 72% in group receiving 25µg infusion of phenylephrine and 28% in 50µg and 16% in 75µg group. Similar results were obtained by Sayyid SM et al, and Doherty et al.[8,10]

None of the patients required stopping of infusion in zero phenylephrine and 25 µg phenylephrine groups. One patient (4%) required stoppage of infusion in 50µg group whereas in 75 µg group infusion had to be stopped in 18 patients (72%), with total number of 33 at an average 1.7 times per patient (average 1.7 times per patient where infusion needed to be stopped), the difference among the groups was significant statistically(p=value <0.001). Similar results were obtained by Sayyid SM et al, and Allen et al, and Stewart et al.[8,9,11]

The PE0 group received the least amount of total phenylephrine (160 µg), in the group PE25 the mean amount of total phenylephrine was 532 µg, in PE50 group the total mean amount of phenylephrine was 882 µg and in the group PE75 the mean total amount of phenylephrine was 1358 µg. The difference among the groups was statistically significant as p value was <0.001. This was in concordance with Allen et al, and Stewart et al.[9,12]

In the group PE0, PE25 and PE50 none of the patients developed significant bradycardia (HR <50 beats/min) therefore did not require anticholinergics. In the group PE75, four (4) patients developed bradycardia and required net six (6) doses of glycopyrrolate. The results were similar to Allen et al, where Glycopyrrolate was administered to 1 patient in the control group, 3 patients in group PE 25, 2 patients in group PE 75, and 7 patients in group PE 100.[9]

There was no statistically significant difference between the four groups with respect to APGAR score, fetal umbilical vein pH, and fetal umbilical vein lactate. The results were in concordance with Allen et al, who observed that the pH in PE 0 group was 7.34 (7.30-7.36), in the PE25 group it was 7.35 (7.33-7.37), whereas pH in the group PE50 7.33 (7.32-7.35) and in group PE75 it was 7.33 (7.31-7.36) and in PE100 group pH was 7.33 (7.30-7.35) with a non-significant p value of 0.22.[9] Stewart et al, also had similar results with pH in the group PE25 as 7.36±0.02 , in the group PE50 it was 7.35±0.03 and in the group PE100 it was 7.35±0.03 with a non-significant p- value.[12] Sayyid SM et al, had similar results and observed that neonatal outcomes were not different between the 2 groups with phenylephrine group having UV pH 7.3±0.1 and in saline infusion group the mean UV pH was 7.3±0.0, with a non-significant p-value (p=0.60).[8] Similar results were obtained by Stewart et al.[12]

In conclusion, the regimen of prophylactic variable rate phenylephrine infusion initially started at 50 $\mu g/kg^{-1}/min^{-1}$ combined with a crystalloid solution co-load of at least 2 liters and rescue phenylephrine boluses in parturients undergoing cesarean delivery with spinal fentanyl 25 µg (0.5 ml) and 0.5% hyperbaric bupivacaine (2.5 ml) is more reliable than crystalloid co-load and rescue phenylephrine boluses or infusion rates of 25 or 75 mcg/min.

It is associated with fewer physician interventions, less hypotension and nausea/vomiting, minimal incidence of hypertension, as well as greater hemodynamic stability, all of which lead to increased maternal comfort. Authors did not see any adverse effects on the fetus in our study as indicated by Apgar scores and umbilical venous gases and lactate. Further work investigating more flexible regimens would be of interest and might result in the complete elimination of hypotension.

This study confirmed the clinical impression that starting a prophylactic infusion of phenylephrine immediately after the induction of spinal anesthesia for cesarean delivery would be effective at reducing the incidence, frequency, and severity of hypotension. It is noteworthy that in the PE group, despite the administration of a large total dose of phenylephrine, the fetal acid-base status and clinical condition of infants were excellent and similar in all the study groups.

Limitations of the study with large doses of phenylephrine, hypertension and maternal bradycardia can occur, reactive hypertension can be a problem and is a concern with the use of prophylactic phenylephrine infusions. Present study findings may not be applicable to clinical situations in which IV fluids are not co-administered or an alternative volume of crystalloid or colloid is administered. The simple fixed rate infusion regimen used in this study was stopped when maternal SBP exceeded the set limits and lacked titration.

CONCLUSION

Doppler sonography is an indispensable tool in In conclusion prophylactic phenylephrine infusions reduced the incidence and severity of maternal pre-delivery hypotension. Among the fixed rate phenylephrine infusion regimens investigated, infusion rates of 50 µg/min were associated with greater maternal hemodynamic stability compared with 25 and 75 µg/min, with minimal side effects and intervention.

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