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Perfusion index as a predictor of hypotension following subarachnoid block in parturients with non-severe pre-eclampsia undergoing lower segment cesarean section

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***Abstract*---**Background and Aims: Perfusion index, which assesses perfusion dynamics is used as a non-invasive method in spinal anesthesia cases to detect the occurrence of hypotension. A Perfusion Index value after which hypotension is common can be assessed. Methods: In this prospective double-blind observational study, 100 parturients were included. Baseline Perfusion Index was recorded and spinal anesthesia was carried out with Injection bupivacaine 0.5% (hyperbaric), 10 mg at L3 - L4 / L2 - L3 intervertebral space. Fall in Systolic Blood Pressure < 20 % of baseline was defined as

hypotension. Chi-Square test and independent sample t-test was used for the statistical analysis. Spearman's rank correlation coefficient was applied to assess the correlation between baseline PI and hypotension. The receiver operating characteristic (ROC) curve was mapped for PI and the occurrence of hypotension. Results: The occurrence of hypotension in parturients with PI < 4.25 was 40.9% compared to 94.6% in parturients with PI > 4.25. There was a remarkable association between baseline PI > 4.25, the number of episodes of hypotension 53/100 (p-value < 0.0001) and the total dose of phenylephrine used 53/100 (p-value 0.02). The sensitivity and specificity of baseline PI of 4.25 to predict hypotension was 74.5% and 89.7% respectively. Conclusion: Baseline perfusion index value > 4.25 is associated with a higher incidence of hypotension following spinal anesthesia in elective LSCS.

***Keywords*---**hypotension, non-severe pre-eclampsia, perfusion index, pregnancy, spinal anesthesia, cesarean section.

Introduction

In non-severe preeclampsia parturients, the vascular epithelium is damaged by a process involving placental derived proteins, leading to an imbalance between pro and anti-angiogenic growth factors.[1, 2] Spinal anesthesia is now the technique of choice for cesarean section.[3] If recognized and treated promptly, maternal hypotension may not be associated with maternal or neonatal morbidity.[4] The risk of hypotension and associated emetic symptoms correlate directly with the level of segmental sympathetic blockade.[5] Spinal anesthesia induced hypotension can be treated safely. There is no evidence that neonatal outcomes are compromised. Risks associated with general anesthesia, such as hypertensive crisis, cerebrovascular accident and difficult intubation scenario are leading causes of morbidity and mortality. No specific monitor has been proven to impact maternal or fetal outcomes in the setting of non severe pre-eclampsia.[6] The ratio of pulsatile blood flow to non-pulsatile blood flow in the peripheral vascular tissue is defined as the perfusion index (PI).[7] Measuring PI value is simple by using a non - invasive pulse oximeter. Hence, now being used to assess the development of spinal anesthesia induced hypotension.[8, 9, 10] We hypothesized that PI can anticipate spinal anesthesia induced hypotension and a PI cut - off value after which hypotension is more common, can be predicted.

Methods

This Prospective double-blind observational study was carried out from August 2017 to November 2017. Institutional Ethics Committee permission www.ctri.nic.in. CTRI/2018/12/ 016702 was obtained for conductance of the study. Informed written consent of every participant in the study was obtained. The study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice. The study involved 100 parturients between 20 and 35 years of age with non-severe preeclampsia posted for elective and emergency lower segment cesarean section with ASA grade of II & III. Parturients with

complicated obstetric history, cardiovascular or cerebrovascular disease, impending eclampsia and eclampsia, more than 750ml intraoperative blood loss, requiring > 10 units oxytocin or other additional uterotonic drugs and those with contraindications to spinal anesthesia were eliminated from the study.

Standard monitoring with electrocardiography, pulse oximetry (SpO_2) and automated Noninvasive blood pressure (NIBP) was done. Baseline values and intraoperative assessment was carried out. The perfusion index was calculated in the supine position with the pulse oximeter probe (Masimo Radical 7®; Masimo Corp., Irvine, CA, USA) by placing it over left index finger uniformly. An anesthesiologist who was not a part of our study measured the baseline vital values and PI in the supine position. Left upper limb was used for peripheral venous assess uniformly. All participants were given injection ranitidine 50 mg I.V, injection metoclopramide 10 mg I.V, 500 ml Ringer lactate over 20 min beforemmnnn. The baseline values of heart rate (HR), pulse oximetry (SPO2), systolic blood pressure (SBP), diastolic blood pressure (DBP), perfusion index (PI) were recorded. With patient in left lateral position, spinal anesthesia was given by an anesthesiologist not included in the study. Quincke's 25-gauge spinal needle was inserted at L3-L4 or L2-L3 intervertebral space. 10 mg of injection bupivacaine 0.5% (hyperbaric) was injected into the subarachnoid space. The parturient was made to lie in supine position with a 15^0 left lateral tilt to avoid aortocaval compression. Oxygen face mask was connected to the parturient and a delivery rate of 4L/min was set.

Ringer's lactate was infused at the rate of 100ml/ 10min. Level of analgesia and level of block was assessed after 5 min of administering spinal anaesthesia. Parturients with absent sensory block at T6 level were exempted from the study and managed as per the institutional protocol. The maximum cephalad spread of spinal drug was examined at 20 min following the SAB. Hemodynamic parameters such as HR, SP02, SBP, DBP, MAP and PI were recorded every 2 min up to 20 min and then followed by 5-minute interval till the completion of surgery.
Hypotension was defined as SBP < 20 % from baseline. Injection Phenylephrine 50 microgram, IV bolus and 100 ml of Ringer lactate were used to treat hypotension. Hypotension in the first 60 min following SAB was recognized as spinal anesthesia induced hypotension. Injection atropine 0.6 mg IV bolus was used to treat bradycardia which was defined as HR < 55 beats /min. After the delivery of the baby, the Apgar score at 1st and 5th min was recorded. Uterotonic, injection oxytocin - 10 unit was administered as a separate infusion at a rate of 200 mU / min was administered to the parturient. The duration of surgery and 1.V fluids transfused were noted. Patients with non - contracted uterus were exempted from the study. Any adverse effects if occurred was recorded.

Statistical Methods and Analysis

The correlation coefficient was calculated for baseline PI values and the magnitude of fall in systolic blood pressure was found to be 0.583. To achieve similar results at the power of 80% and assuming an alpha error of 0.05, keeping the confidence interval at 95%, a minimum of 100 participants were needed. Discrete and continuous data were analyzed for normal distribution using the Shapiro–Wilk test. Independent sample *t*-test applied for continuous data which

showed normal distribution. A Chi-square test was applied to assess statistical significance for discrete and categorical data. Figures represent categorical and discrete data, graphs represent continuous data. For correlation between baseline PI with other parameters, Spearman's rank correlation coefficient was used. A Receiver Operating Characteristic (ROC) curve was procured for baseline PI Comparision with the hypotension episodes of 100 parturients. Evaluation of data was done using SPSS (Statistical Package for Social Sciences) version 21. (IBM SPSS Statistics for Windows, version 21.0, IBM Corp., Armonk, NY, USA). $P < 0.05$ was considered statistically significant.

Results

A total of 100 parturients were enrolled for the study and all 100 were included in the study. There were no dropouts. The ROC curve revealed 4.25 as a more appropriate cut-off value of PI with 74.5% sensitivity and 89.7 % specificity. The area under the ROC curve (AUC) was 0.871. The demographic parameters such as age, weight and height and duration of surgery are as shown in Table 1.

Table 1
Demographic Parameters

Parameter		Mean ± Standard Deviation
Age (year)		23.91 ± 3.45
Height (centimeter)		154.56 ± 4.89
Weight (kilogram)		73.13 ± 11.84
Duration of Surgery (minute)		57.8 ± 4.5
		Count
Gravida	1	58
	2	31
	3	10
	4	1
Para	0	58
	1	2
	2	29
	3	10
	4	1

The demographic parameters such as age (year), height (centimetre), weight (kilogram), duration of surgery (minute) and obstetric score of the study participants are depicted in Table 1. Values are expressed as mean ± SD.

Table 2
Area under the Curve - Test Result Variable(s) - PI baseline

Area	Std. Error [a]	P value	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
0.871	0.047	0.000	0.778	0.963

The test result variable(s): PI baseline has at least one tie between the positive actual state group and the negative actual state group. Statistics may be biased.
a. Under the nonparametric assumption
b. Null hypothesis: true area = 0.5
PI: Perfusion Index.

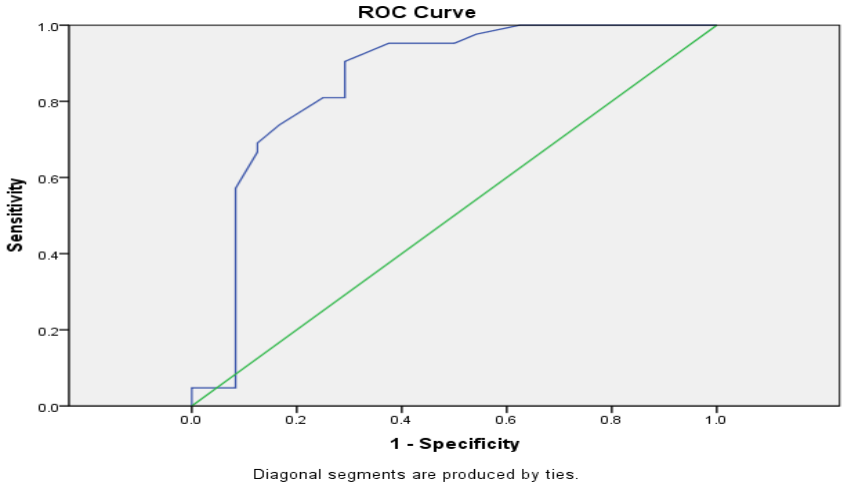


Figure 1. ROC Curve

Table 3
Incidence, Number of Episodes of Hypotension, Inj. Phenylephrine use, Total Blood Loss and Intravenous Fluids used in individuals with PI < 4.25 and PI > 4.25

		PI*		
		<4.25	>4.25	p
Hypo-tension	No	26(59.1%)	3(5.4%)	<0.0001
	Yes	18(40.9%)	53(94.6%)	
(No. of Episodes of hypotension)	00	26(59.1%)	3(5.4%)	<0.0001
	1.00	12(27.3%)	17(30.4%)	

		PI*		
		<4.25	>4.25	p
Hypo-tension	No	26(59.1%)	3(5.4%)	<0.0001
Dose of Inj. Phenylephrine (microgram)	2.00	6(13.6%)	36(64.3%)	
	50.00	11(64.7%)	17(32.1%)	0.02
	100.00	6(35.3%)	36(67.9%)	
Total blood loss (mL)†		330.68(93.52%)	338.39(76.87%)	0.6
Total IV‡ fluids (mL)		1397.73(170.4%)	1517.86(180%)	0.001

The incidence of hypotension in individuals with PI < 4.25 was 40.9% (18/44) compared to 94.6% (53/56) in individuals with PI > 4.25. This was clinically and statistically significant ($P < 0.0001$).

* Perfusion Index, † millilitre, ‡ Intra Venous fluid

%: Percent, p: p value.

Concerning systolic blood pressure (SBP) and diastolic blood pressure (DBP), the difference between the two groups (PI < 4.25, PI > 4.25) was statistically noteworthy for the first 10 min. Most remarkable differentiation in SBP was noted at the baseline, 2nd min, 4th min with values being lower in Group with PI > 4.25 than in Group with PI < 4.25, remarkable differentiation in DBP was most significant at 4th min. The DBP was also low in Group with PI > 4.25 than in Group with PI < 4.25. The incidence of hypotension in Group with PI < 4.25 was 40.9% (18/44) compared to 94.6% (53/56) (Table-3). Remarkable both clinically and statistically ($P < 0.001$). In Group with PI < 4.25, 12 patients had one episode and 6 patients had 2 episodes of hypotension. In Group with PI > 4.25, 17 patients had one episode and 36 patients had two episodes of hypotension (Table 3).

Fifty nine percent of patients in Group with PI < 4.25 had no hypotension. Whereas three percent of patients in Group with PI > 4.25 had no episodes of hypotension. With respect to spearman's rho correlation, there was significant association with hypotension (correlation coefficient of 0.588 with p value < 0.001), number of episodes of hypotension (correlation coefficient of 0.616 with p value < 0.001) with changes in PI value. 17 parturients (11 and 6 requiring 50 and 100 microgram respectively) in Group with PI < 4.25 required phenylephrine usage compared to 53 parturients (17 and 36 requiring 50 and 100 microgram respectively) in group with PI > 4.25 with significant p value of 0.02. There was significant difference in the total amount of IV fluids required in both groups (Mean 1,397.73 ± 170.48 ml in PI < 4.25. Mean 1,517.86 ± 180.01 in PI > 4.25) with $P < 0.001$. Total amount of blood loss in group with PI < 4.25 was 330.68 ± 93.52 ml (Mean) and in group with PI > 4.25 was 338.39 ± 76.87 (Mean). Insignificant difference were observed with respect to respiratory rate, SpO2 and Apgar score.

Discussion

Our hypothesis was that the baseline PI predicts the development of hypotension in parturients with non-severe pre-eclampsia receiving subarachnoid block and we also studied for a PI cut-off value that correlated the best with occurrence of hypotension. Our study favours the hypothesis and observed that PI > 4.25 correlated with occurrence of significant hypotension. Phenylephrine usage was more in parturients with baseline PI > 4.25. Differentiation amongst non severe preeclamptic parturients undergoing cesarean section as to who develops hypotension following subarachnoid block was possible with the help of ROC curve, which provided a new baseline PI cut off value of 4.25. Increase in basal metabolic rate in pregnancy demands increase in total blood volume, cardiac output and reduction in systemic vascular resistance. Resultant vasodilation increases the perfusion index value. Spinal anaesthesia further decreases systemic vascular resistance, exacerbating hypotension.

Hypotension is defined as fall in baseline MAP of 20% [11] The incidence of hypotension can be as high as 70-80% when pharmacological prophylaxis is not used. A Cochrane review terminated that none of the technique alone was effective in eliminating hypotension and advised that future analysis be directed towards the investigation of combinations of interventions.[12] Presently, a definitive monitoring system which anticipates hypotension is not available. Studies are being undertaken to assess the correlation between PI and its efficacy in predicting hypotension following spinal anesthesia especially in cesarean section. Non Invasive Blood Pressure (NIBP) does not measure beat to beat variation in perfusion dynamics. Further research is required to elucidate strategies to optimize hemodynamics and uteroplacental perfusion among non severe preeclamptic parturients during spinal anesthesia for cesarean delivery.

Factors affecting vascular resistance affects the PI value.[13] The PI rapidly and constantly indicates perfusion status of the monitoring site. Potential Future Applications of Perfusion Index are as an indicator of the circulatory function of reimplanted body segment such as fingers or hands, restoration of peripheral perfusion after cardiopulmonary bypass, estimation of volume status in trauma patients Mowafi and co-workers[14] studied the efficacy of perfusion index as an indicator for intravascular injection of epinephrine-containing epidural test dose in propofol-anesthetized adults and concluded that PI is a reliable alternative to conventional hemodynamic criteria for detection of hypotension. Ginosar and colleagues[15] observed that higher PI value during epidural anesthesia correlated with sympathectomy. Study performed by Yokose and co-workers[16] showed that PI did not predict hypotension in parturients undergoing LSCS following SAB. This disparity was observed due to difference in conductance of study.

In our study, the ROC curve revealed 4.25 as a more appropriate cut-off value of PI with 74.5% sensitivity and 89.7 % specificity. The area under the ROC curve (AUC) was 0.871. In a study by Toyama and others,[17] related to perfusion index derived from a pulse oximeter predicting the incidence of hypotension during spinal anesthesia for Cesarean delivery, demonstrated that higher baseline PI was related to profound hypotension and that baseline PI would predict the occurrence of spinal anesthesia induced hypotension during Cesarean delivery. In

their study, the PI value of 3.5 best predicted the hypotension. Factors affecting PI value attribute to limitations in the study. OT temperature and patients temperature was not monitored. Perfusion Index (PI) helps in anticipating hypotension in non-severe pre-eclamptic parturients undergoing cesarean section under SAB. High risk of developing hypotension following SAB was observed in parturients with baseline PI > 4.25 in comparison with parturients with baseline PI ≤ 4.25.

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