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COMPARISON OF THE EFFECT OF PHENYLEPHRINE AND EPHEDRINE ON UMBILICAL ARTERIAL BLOOD GAS PARAMETERS IN ELECTIVE CAESAREAN SECTION UNDER LUMBAR SUBARACHNOID BLOCK

Anesthesiology

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ABSTRACT

Introduction: Potential side effects such as supraventricular tachycardia, tachyphylaxis, and most importantly, fetal acidosis render the use of ephedrine as a first line agent to treat hypotension in obstetric patient debatable. Phenylephrine, an alternative drug, has a reduced incidence of nausea and vomiting as well as decreased fetal acidosis, which gives it an advantage over the use of ephedrine.

Materials and methods: We conducted an observational study in 68 ASA II patients scheduled for lower segment caesarean section. Parturients who satisfied the inclusion criteria were randomly assigned into one of the two groups of 34 each- group P with parturients who were to receive phenylephrine boluses in 100 mcg increments and group E with parturients who were to receive ephedrine boluses in 6mg increments when they developed hypotension. Fetal umbilical arterial blood gas was analyzed and parameters were compared.

Results: On analyzing umbilical arterial blood values, a lower mean pH was found in group E (7.27± 0.09) when compared to group P (7.3± 0.04). Also a higher PCO_2 value (49± 7.4) was found in group E when compared to group P (43.9 ± 6.4). Other umbilical arterial blood gas values were comparable between both groups

KEYWORDS

1. INTRODUCTION

Extensive sympathetic blockade leading to the subsequent fall in systemic vascular resistance, the exaggerated neural blockade caused by the contraction of subarachnoid space as a result of the physiological changes of pregnancy, as well as the aortocaval compression caused by the fetoplacental unit are all factors contributing to the development hypotension in obstetric patients receiving subarachnoid block.[1]

Hypotension, especially if sustained and severe can have injurious effects on neonate, which include decline in uteroplacental flow, impaired fetal oxygenation with asphyxial stress, and fetal acidosis.[2] Subarachnoid block induced hypotension along with uteroplacental ischemia and intervillous hypoxemia, which may trigger chronic hypoxic fetoplacental vasoconstriction and can lead to fetoplacental hypertension & "cor placentale", where fetal cardiac function eventually becomes abnormal and the fetus suffers preterminal cardiac failure due to pressure overload and hypoxia .[3,4]

Use of ephedrine as the vasopressor in obstetric patients receiving subarachnoid block is supported by animal studies, which showed a better preservation of uteroplacental blood flow when ephedrine was used to increase maternal blood pressure.[5] It can increase nitric oxide expression in uterine arteries that enhances uterine blood flow.[6]

Drawbacks of ephedrine include a gradual onset and relatively long duration, which may make accurate titration of blood pressure difficult.[7] Ephedrine is associated with a dose-related propensity to depress fetal pH and base excess in recent studies.[2]

Phenylephrine is a pure α1 adrenergic agonist, which increases systemic vascular resistance and causes reflex bradycardia but it maintains cardiac output in healthy parturient.[8] When phenylephrine is used liberally to maintain maternal blood pressure and prevent symptoms, fetal acidosis has not been demonstrated.[9]

2. MATERIALS AND METHODS

The study was conducted among 68 parturients scheduled for elective cesarean delivery in Pushpagiri Medical College, Thiruvalla, after formal approval from institutional ethics committee.

INCLUSION CRITERIA

- Age 18 to 40 years willing for elective caesarean under subarachnoid blockade
- Parturients belonging to ASA II physical status, who develop hypotension following subarachnoid block (MAP decrease by 20% or more of the baseline value or became <60 mm Hg)

EXCLUSION CRITERIA

- Patient refusal
- Pregnancy hypertension, cardiovascular or cerebrovascular diseases
- Known fetal anomalies
- Preterm gestation/ multiple gestation
- Non reassuring fetal status
- Maternal height less than 145 CM
- Level of subarachnoid block higher than T4
- Patients with inadequate analgesia needing conversion to general anesthesia

Parturient belonging to ASA physical status II scheduled to undergo elective caesarean delivery under subarachnoid block were approached prior to study and written informed consent was obtained. Pre-anesthetic evaluation was done on the day before surgery. NPO status was achieved as per protocol – 6 hours for solids and 2 hours for clear fluids. All patients were premedicated with Tab. Ranitidine 150mg and Tab. Metoclopramide 10 mg on previous night and 2 hours before surgery. Intravenous access secured before the procedure.

Parturients who satisfied the inclusion criteria were randomly assigned into one of the two groups of 34 each:

Group P: with parturients receiving intravenous phenylephrine boluses in 100 mcg increments

Group E: with parturients receiving intravenous ephedrine boluses in 6mg increments.

Patients were shifted to the operation theatre in the morning of the surgery. Vital parameters were monitored using NIBP, continuous ECG and pulse oximetry. Oxygen was supplied via face-mask at 5 litres per minute. Intravenous lactated Ringer's solution infusion was started via the iv cannula. Baseline vital parameters were noted and MAP that is recorded first was taken as the baseline Patient was placed in left lateral position. Under strict aseptic precautions, lumbar subarachnoid block was administered in the left lateral position in the L2-L3 or L3-L4 intervertebral space after skin infiltration with 2ml 2% lignocaine. 2 ml 0.5 percentage hyperbaric bupivacaine was injected into the subarachnoid space using a 25 gauge Quincke- Babcock needle. The parturient was turned supine and a left lateral tilt was maintained using a 15 cm wedge placed under right hip and buttock. Highest level of block was noted. Changes in the maternal blood pressure and heart rate were monitored every 2 minutes till delivery of the baby. The parturient received the vasopressor solutions assigned to them whenever maternal mean arterial pressure (MAP) decreased by 20% of the baseline or more, or when MAP became <60 mm Hg. Oxytocin infusion was started after the delivery of the baby. Umbilical

arterial blood was drawn by attending pediatrician. Each sample was heparinized and sent to ABG (Arterial Blood Gas) analysis within 5 minutes of cord clamping. The results thus obtained were noted and were compared between the two drug groups for determination of acid-base status. APGAR scores were taken at 1 and 5 minutes.

Categorical and quantitative variables were expressed as frequency (percentage) and mean ± SD respectively. Independent t test was used to compare quantitative parameters between categories. Chi-square test was used to association between categorical variables. For all statistical interpretations, $p<0.05$ was considered the threshold for statistical significance. Statistical analysis was performed by using a statistical software package SPSS, version 2.0.

3. RESULTS

Collected data was compiled and subjected to statistical analysis using SPSS Software as described. To elucidate association and comparison between different parameters Unpaired T test was used. To compare distribution Chi- Square test was used. For all statistical evaluation, a probability value of less than 0.05 ($p <0.05$) was considered significant. The graphical representation, analysis and inference with respect to different study variables are as follows.

Table 1: Age Distribution

Age	Group E		Group P	
	Count	Percent	Count	Percent
21 – 25	5	14.7	9	26.5
26 – 30	15	44.1	10	29.4
31 – 35	10	29.4	11	32.4
36 – 39	4	11.8	4	11.8
Mean ± SD	30.1 ± 4.4		29.2 ± 5.2	

t = 0.73, p = 0.467

Table 2: Comparison of height based on group

Group	Mean	SD	N	t	P
Group E	158.0	4.5	34	0.21	0.838
Group P	158.3	6.0	34		

Table 3: Comparison of weight based on group

Group	Mean	SD	N	t	P
Group E	73.6	8.5	34	0.25	0.804
Group P	74.3	12.1	34		

There is no significant difference ($p>0.05$) between the group E and group P with respect to age, height or weight of the patients included in this study. Therefore, the two groups are relatively homogenous with respect to age, height and weight and hence comparable.

Table 4: Comparison of highest level block

Highest level of block	Group E		Group P		p#
	Count	Percent	Count	Percent	
T4	21	61.8	27	79.4	0.091
T6	13	38.2	7	20.6	

#Fisher's exact test:

The height of block is comparable among both groups with a p value >0.05

Table 5: Comparison of APGAR score

APGAR		Group E		Group P		X^2	P
		Count	Percent	Count	Percent		
At 1min	5	0	0.0	1	2.9	3.02	0.389
	7	1	2.9	0	0.0		
	8	0	0.0	1	2.9		
	9	33	97.1	32	94.1		
At 5 min	7	1	2.9	0	0.0	3.14	0.208
	9	31	91.2	34	100		
	10	2	5.9	0	0.0		

The difference in APGAR between the two groups was not found to be statistically significant at 1 minutes or five minutes.

Table 6: Comparison of umbilical arterial pH

Group	Mean	SD	N	t	P
Group E	7.27	0.09	34	2.24*	0.029
Group P	7.30	0.04	34		

*: - Significant at 0.05 level

Comparison of umbilical arterial pH showed that group E had lower umbilical pH when compared to group P (7.27± 0.09 vs 7.30± 0.04) which is statistically significant.

Table 7 : Comparison of umbilical arterial PCO_2

Group	Mean	SD	N	t	P
Group E	49.0	7.4	34	3.07**	0.003
Group P	43.9	6.4	34		

** :- significant at 0.01 level

Comparison of umbilical arterial PCO2 showed that group P had lower mean value of 43.9±6.4 when compared to group E with a mean value of 49± 7.4, which is statistically significant.

Table 8: Comparison of umbilical arterial PO_2

Group	Mean	SD	N	t	P
Group E	25.5	10.9	34	1.94	0.057
Group P	21.0	7.8	34		

Table 9: Comparison of umbilical arterial HCO_3

Group	Mean	SD	N	t	P
Group E	22.1	2.4	34	1.33	0.188
Group P	22.9	2.8	34		

Table 10: Comparison of umbilical arterial base excess (mmol/L)

Group	Mean	SD	N	t	P
Group E	-3.9	2.2	34	1.93	0.058
Group P	-2.9	2.0	34		

Umbilical arterial base excess, bicarbonate and PO2 were compared and difference between groups were found to be statistically insignificant.

3. DISCUSSION

Subarachnoid block is the preferred method for conducting uncomplicated caesarean delivery. It is technically simple and reliable, provides a rapid onset of dense lumbosacral and thoracic anesthesia with low doses of local anesthetic and opioid. However, the limited duration of anesthesia and limited ability to titrate extent of sensory blockade are its major disadvantages. Neonates of women with subarachnoid block induced hypotension were found to have significant acidosis. [10]

This study was an observational comparison study conducted in sixty-eight /68 patients, who were of the American Society of Anesthesiologists (ASA) classification - class II, admitted for elective aesarean section in Pushpagiri Institute of Medical Sciences and Research Centre. They were allocated into two equal groups of 34 each, randomly, according to the type of vasopressor used. Group P received a bolus of phenylephrine 100 mcg/ml increments and group E received boluses of ephedrine 6 mg/ml increments whenever maternal mean arterial pressure dropped by more than 20% of baseline or became less than 60 mm Hg. The mean arterial pressure (MAP) is a more important variable than systolic blood pressure as a determinant of organ perfusion. [11] Percentage decrease in placental perfusion is related to percentage reduction in maternal mean arterial pressure and not to absolute reduction in pressure.

Analysis of patient characteristics like age, block height, height and weight between the two groups revealed no statistically significant difference. This analysis confirmed that the two groups are comparable. The difference in APGAR scores between the two groups was not found to be statistically significant at 1 minute or 5 minutes. This was consistent with the result obtained by Lee et al in 2002. [12]

Neonates born to parturients who received ephedrine boluses for hypotension showed a decrease in umbilical arterial pH when compared to the phenylephrine group. This finding is consistent with other studies. [13] [14] A meta-analysis by Lin et al also supports similar findings.[15]

Ephedrine, being lipid soluble, readily crosses the placenta. Use of ephedrine was associated with greater umbilical arterial and venous plasma concentrations of lactate, glucose, epinephrine, and norepinephrine compared with phenylephrine, which perhaps reflects a direct fetal stimulation via β receptors that increases the oxygen demand- supply ratio of the fetus, thus prompting anaerobic metabolism resulting in acidosis.[14]

Neonates born to mothers of ephedrine group had higher CO_2 values. This may be due to elevated fetal CO_2 production, which may be due to the enhancement of fetal metabolism by ephedrine, as observed by Cooper et al.[16] According to a meta-analysis performed by Singh et al in 2019, ephedrine is placed at the lowest rank among five vasopressors on the basis of umbilical artery base excess which held true for pH and PCO_2 as well (probability rank order: norepinephrine > mephentermine > metaraminol > phenylephrine>ephedrine). Parturients receiving ephedrine had highest concentration of CO_2 in the umbilical artery.[17]

Umbilical artery base excess, PO_2 and HCO_3 were compared between the two groups and were not found statistically significant. In a study by Prakash et al, umbilical arterial base excess was significantly more negative in ephedrine group. [13]

4. CONCLUSION

Based on this clinical study comparing phenylephrine 100 mcg boluses and ephedrine 6 mg boluses, it was found that phenylephrine maintains umbilical arterial pH and PCO_2 values better than ephedrine. Thus phenylephrine is the better choice of vasopressor in subarachnoid block for obstetric anesthesia when compared to ephedrine with respect to umbilical arterial blood analysis.

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