International Journal of Anesthesia and Clinical Medicine
2025, Vol. 13, No. 2, pp. 70-75
https://doi.org/10.11648/j.ijacm.20251302.12

Research Article

Comparative Evaluation of the Effects of Ephedrine and Phenylephrine on Neonatal Umbilical Cord Blood Gases

Kolawole Israel Kayode[1], Oyedepo Olanrewaju Olubukola[1], Oparanozie Emmanuel Ikechukwu[2, *]

[1]Department of Anaesthesia, Unilorin Teaching Hospital Ilorin, Ilorin, Nigeria

[2]Department of Anaesthesia, Reddington Multispecialist Hospital VI, Lagos, Nigeria

Abstract

Background: Ephedrine has commonly been regarded as the vasopressor of choice for treatment of hypotension in obstetrics, but there are concerns it causes neonatal acidosis.While some authors have recommended phenylephrine because it has not been associated with neonatal acidosis, others have found no difference between the two. *Objective*: To compare umbilical cord blood gases in neonates of parturients who received ephedrine and phenylephrine for prevention of maternal hypotension following subarachnoid block for caesarean section. *Methods*: Sixty-two neonates whose mothers received either ephedrine (group E) or phenylephrine (group P) during elective caesarean section were randomized in this double blind study into two groups each of 31.Umbilical arterial blood sample was collected and analysed immediately following delivery using an ABGmachine. *Results*: The mean umbilical artery pH was 7.30 ±0.05 and 7.31 ±0.02 for groups E and P respectively (p value=0.097). The mean $PaCO_2$ (mmHg) was 44.44 ±4.01 and 46 ±3.95 for groups E and P respectively (p value=0.208). while the mean PaO_2 (mmHg) was 25.85 ±3.14 and 27.40 ±1.76 for groups E and P respectively (p value=0.075). The mean HCO_3^-(mmHg) between the groups were 22.53 ±1.76 and 22.18 ±1.21 for groups E and P respectively (p value=0.205). Also, the mean base excess in groups E and P were -3.72 ±0.90 and -3.05 ±1.1 respectively (p value=0.054). There was no difference in the Apgar scores and maternal haemodynamic parameters in both groups. *Conclusion*:There was no difference in the umbilical cord gases and Apgar scores of neonates whose mothers received either ephedrine or phenylephrine.

Keywords

Ephedrine, Phenylephrine, Umbilical Cord Blood Gases, Neonatal Acidosis

1. Introduction

Maternal hypotension following subarachnoid block for caesarean section is common occurring in up to 80% of pregnant patients and is implicated in foetal hypoxia and acidosis [1]. Prevention and prompt treatment of this hypotension is important to ensure good foeto-maternal outcomes. Methods that have been employed to prevent hypotension in obstetrics include uterine displacement, colloid or crystalloid pre-loading and co-loading [2-4] but these methods have been ineffective and associated with side effects hence prompt use of vasopressors remains important in avoiding maternal and neonatal adverse outcomes. [2]

Ephedrine and phenylephrine are the most commonly used

*Corresponding author: opansky2004@yahoo.com (Oparanozie Emmanuel Ikechukwu)

Received: 5 June 2025; **Accepted:** 23 June 2025; **Published:** 4 August 2025

vasopressors[5, 6]. Traditionally, ephedrine was the preferred choice but this has been challenged by some authors due to reports of increased incidence of foetal acidosis associated with maternal ephedrine administration [7-10] on which basis others recommended phenylephrine [8,11]. However, some authors have found no differences between the two. [12, 13] It is important in the intervention to deliver neonates that drugs that would lead to the best and optimal outcome of the newborn will be used. This will be particularly important in at risk newborn eg preterm, infants of preeclamptic mothers etc. Analysis of blood sample from foetal umbilical vessels gives an accurate and objective assessment of the metabolic state of the foetus at delivery [14-16]. Though a well researched topic, most studies were done in Europe and Asia with a paucity of studies in sub Saharan Africa.Moreso, Landau [9] proposed a genetic basis for ephedrine induced neonatal acidosis.Kinsella et al [2] noted that study protocols aimed at preventing hypotension rather than treating it when it occurred have been found to yield better neonatal outcomes with decreased incidence of acidosis than those in which hypotension was treated after it has occurred hence the choice of prophylactic administration protocol employed in this study.

This study sought to determine which of these two vasopressors had more effect on umbilical cord blood gases of neonates as a measure of ability to cause neonatal acidosis which is umbilical artery ph</=7.2 [14].

2. Methods

Ethical consent was obtained prior to commencement of study. The study was carried out at the University of Ilorin Teaching Hospital Ilorin Kwara State Nigeria. Sixty-two (62) neonates of consenting parturients who received either ephedrine or phenylephrine were randonmised into two groups of thirty one each. The parturients were scheduled for elective caesarean section under subarachnoid block and this randomization was doneby a research assistant who was not part of the researchers using computer generated sequence. The research assistant prepared the study drugs and handed them over to the researchers who administered them. The methodology was as per protocol. The study drugs were 5mg/ml and 50 µg/ml of ephedrine and phenylephrine bolus injections for groups E and P respectively, each contained in identical 5ml syringe to enable concealment. The research assistant also set up identical (to also enable concealment) 20ml infusions of ephedrine and phenylephrine in a syringe pump containing 4mg/ml and 50µg/ml of ephedrine and phenylephrine which was administered to groups E and P respectively. These were labeled as infusion drugs and the researcher and patients was blinded to the content. The infusion rates were equipotent as described by Saravan et al [17] (80:1). All consenting parturients above 18 years scheduled for elective Caesarean section at term under subarachnoid block were included. Exclusion criteria included patient's refusal, contraindications to subarachnoid block, high risk pregnancies (example multiple gestations, intrauterine growth retardation, hypertensive disesases of pregnancy).

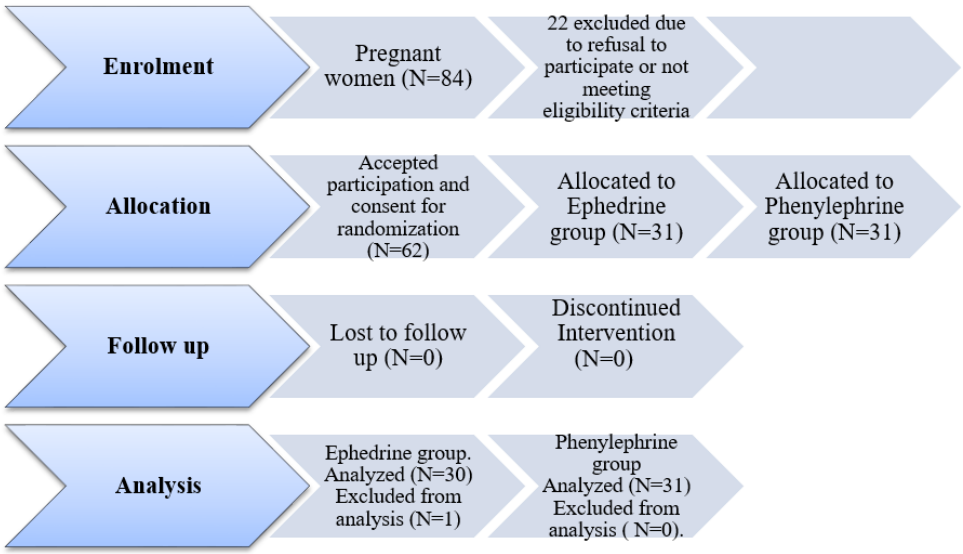

Figure 1. *Showing the patient flow chart. One neonate in the ephedrine group was excluded in the final analysis due to unanticipated difficulty with the surgery.*

Before spinal anaesthesia, all patients received about 15mls/kg normal saline as fast as possible. Thereafter,

subarachnoid block was performed in sitting position under aseptic condition using theL3/L4 or L4/L5 interspace by the researcher and injection of bupivacaine 12.5 mgand fentanyl 25 µg. Thereafter, patients were repositioned supine with a wedge under the right hip and head elevated with a pillow.The block height was of T6was considered appropriate. Immediately after performing the block, the researcher administered 1ml bolus of study drug and commenced the syringe pump infusion at 1ml/min in both groups,corresponding to 5mg ephedrine and 50 µg phenylephrine bolusesand 4mg/min ephedrine and 50 µg/min phenylephrine infusions for groups E and P respectively. The researcher was in charge of data collection and handed over the proforma to the research assistant to indicate the group at the end of the study. Hypotension (defined as a decrease in systolic arterial pressure >20% of baseline) was treated by further 1ml bolus of study drug administered by researcher. Once the blood pressure remained stable for more than 15 minutes or following development of reactive hypertension, vasopressor infusion was discontinued. Following delivery of the baby, umbilical artery sample was collected with a heparinized syringe from a double clamped cord segment and analysed using an already calibrated ABG machine. Apgar scores of the neonate were noted at first and fifth minute. Further management of the parturient was at the discretion of the attending anaesthetist. The primary outcome measure was umbilical artery pH. Secondary outcomes included HCO_3^-, base excess, $PaCO_2$ and $PaO_2$and apgar scores.

Data was analyzed using SPSS version 20. Continuos and ordinal variables were analysed with T-test and Mann-WhitneyU test respectively.A p-value of <0.05 was considered significant. From a previous study[1]we determined that a sample size of 62 patients will be sufficient to detect a difference of 0.2 in the mean umbilical cord blood pH using a power of 80% at 5% significance level.

3. Results

The patient flow information is shown in figure 1. One neonate in the ephedrine group was excluded in the final analysis due tounanticipated difficulty with the surgery.The remaining sixty one neonates did not require more than the usual routine neonatal resuscitation at birth.There was no significant difference in the maternal demographic data between the two groups (table 1) and overall haemodynamic control.

Table 1. *Maternal Demographic Data.*

Variables	Group E (n=30)	Group P(n=31)	P value
Age (years)	31.2 ±4.4	32.6 ±3.82	0.249
Weight (kg)	83.1 ±4.3	81.2 ±6.5	0.325
Height (m)	1.65 ±0.40	1.65 ±0.36	0.605
Gestational age (weeks)	38.3 ±1.4	38.7 ±1.3	0.515
*Parity	3 (0-5)	3 (0-5)	
Total study drug administered (phenylephrine equivalent)[a]	388.82±26.78	413.85±29.64	0.723
Incidence of hypotension	2(6.9%)	1(3.3%)	0.65

*Mean ±SD. * in median (range),* [a]According to equipotent infusion rate described by Savaranet a[17].

The mean birth weights (kg), Apgar score at one minute, and five minute Apgar score was similar in both groups. None of the neonates was admitted to the neonatal intensive care unit. The mean umbilical artery pH was 7.30±0.05 and 7.31±0.02 (p=0.097)respectively for groups E and P and the remaining details of the umbilical cord gases are shown in Table 2. None of the 61 neonates had true foetal acidosis (defined as umbilical pH < 7.2).

Table 2. *Neonatal outcomes.*

Variable	Group E (n=30)	Group P (n=31)	P value
Birth Weight	3.27±0.14	3.33±0.15	0.264
*One minute Apgar	7 (6-8)	7 (7-8)	0.764

Variable	Group E (n=30)	Group P (n=31)	P value
*5 minutes Apgar	9 (8-10)	9 (8-10)	0.665
NICU admission	0	0	
Umbilical artery PH	7.30 ±0.05	7.31 ±0.02	0.097
Umbilical artery $PaCO_2$	44.44 ±4.01	46 ±3.95	0.208
Umbilical artery PaO_2	25.85 ±3.14	27.40 ±1.76	0.075
Umbilical artery HCO_3^-	22.53 ±1.76	22.18 ±1.21	0.205
Umbilical artery Base Excess	-3.72 ±0.90	-3.05 ±1.1	0.054
Incidence of true foetal acidosis	0	0	

Mean ±SD,*median(range)

4. Discussion

This study showed that the umbilical artery pH, $PaCO_2$,PaO_2, HCO_3^-, base excess and Apgar scores of neonates of parturients who received ephedrine and phenylephrine were similar.

The mean umbilical artery pH in both groups in this study is comparable to the findings of Odagme et al [18] and Moslemi et al [1]. It however, differs with the results of Prakash et al [19] and Vakili et al [20] and this could be because they treated hypotension after it had occurred unlike a prophylactic approach that we employed thus leading to a high incidence of hypotension which causes neonatal acidosis. [13, 20-22] This is supported by Kinsella et al [2] who noted that study protocols aimed at preventing hypotension rather than treating it when it occurred have been found to yield better neonatal outcome with decreased incidence of acidosis than those in which hypotension was treated after it had occurred. A cord pH value less than 7.2 is defined as foetal acidosis. [14] A cord pH less than 7.0 when combined with other abnormal clinical findings, strongly correlates with adverse neonatal outcomes. [14]

This study also found out that patients in the ephedrine group had slightly lower umbilical artery pH, though there was no case of neonatal acidosis. This agrees with the findings of Simin et al. [22] Armstrong et al [16] had found out that neonates delivered by caesarean section had umbilical cord pH values compared to neonates delivered by spontaneous vaginal delivery and this study agrees with it. The mean $PaCO_2$ in this study agrees with the findings of Ngan et al [13], Higgins et al [21] and Abdalla et al. [23]However, the finding disagrees with that of Moslemi et al [1] who found that a high incidence of acidosis and that could account for this. The umbilical cord blood $PaCO_2$ correlates directly with pH with Kotaska et al [24] recommending it as the umbilical blood gas which correlated best with clinical outcome.

The values from this study of PaO_2were similar to the findings of Ngan et al [13], Higgins et al [21], and Simin et al [22]. PaO_2 ironically, is the least valuable parameter in evaluating foetal oxygenation and this is explained by the characteristicsof the foetal oxygen dissociation curve (Bohr effect) [25].

The index study found that there was no difference between the Apgar scores and this agrees with Odagme et al [18], Adigun et al [26], Higgins et al [21]. Although Sykes et al [27] had questioned the usefulness of Apgar scores citing itspoor correlation with umbilical cord gases,it has remained a reliable indicator of neonatal outcome following delivery [28] since first developed [29] providing acceptable and reproducible method for reporting on the status of the newborn. Most neonates will easily make transition from intra to extra uterine life with routine care with only 0.1% -0.3% requiring extensive resuscitation [30, 31] and this agrees with the index study. Of those that require resuscitation, Low Apgar scores at 5 minutes and beyond have been associated with poor neurologic outcome. [32] Notwithstanding the above usefulness, Apgar scores has its limitations. It is an expression of a neonate's physiologic state at a point in time and is affected by several factors which include choice of anaesthesia, gestational age at delivery, presence of congenital anomalies, trauma and inter-observer variations. [32] That is why analysis of blood sample from foetal umbilical vessels is believed to give much more accurate and objective assessment of the metabolic state of the foetus at delivery. [14] Neonates with poor Apgar scores at delivery despite adequate resuscitation may require admission to the neonatal intensive care unit (NICU), and may even be intubated if there is need for that. In this study, none of the neonates required such. Most neonates in this study did not require extensive resuscitation to make easy extra uterine transition and this agrees with available literature. [30, 31]

5. Conclusion

There was no difference in the umbilical cord blood gases and Apgar scores of neonates delivered by caesarean section in mothers who received either ephedrine or phenylephrine.

Prospective areas of future study. Since non labouring parturients were used in the study and neonates of ephedrine group had lower umbilical cord ph. The effect of this on at risk neonates (e.g foetal distress, preterm babies) may need to be evaluated.

Abbreviations

ABG	Arterial Blood Gas
HCO_3	Bicarbonate
PaO_2	Arterial Partial Pressure of Oxygen
PCO_2	Arterial Partial Pressure of Carbon-dioxide
SAB	Sub Arachnoid Block
SD	Standard Deviation
UA	Umbilical Artery
UV	Umbilical Vein

Author Contributions

Kolawole Israel Kayode: Conceptualization, Data curation, Formal Analysis, Supervision, Validation, Writing - original draft, Writing - review & editing

Oyedepo Olanrewaju Olubukola: Conceptualization, Data curation, Formal Analysis, Supervision, Validation, Writing - original draft Writing - review & editing

Oparanozie Emmanuel Ikechukwu: Conceptualization, Data curation, Formal Analysis, Funding acquisition, Supervision, Validation, Writing - original draft, Writing - review & editing

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Moslemi F, Rasooli S. Comparison of prophylactic infusion of phenylephrine with ephedrine for prevention of hypotension in elective cesarean section under spinal anesthesia. *Iran J Med Sci*. 2015; 40(1): 19-26.

[2] Kinsella SM, Carvalho B, Dyer RA, et al. International consensus statement on the management of hypotension with vasopressors during caesarean section under spinal anaesthesia. *Anaesthesia*. 2018; 73(1): 71-92. https://doi.org/10.1111/anae.14080

[3] Park G, Hauch M, Curlin F, Datta S, Bader A. The effects of varying volumes of crystalloid administration before cesarean delivery on maternal hemodynamics and colloid osmotic pressure. *Anesth Analg*. 1996; 83: 299-303. https://doi.org/10.1097/00000539-199608000-00017

[4] Dahlgren G, Granath F, Pregner K, Rosblad P, Wessel H, Irestedt L. Colloid vs. crystalloid preloading to prevent maternal hypotension during spinal anesthesia for elective cesarean section. *Acta Anaesthesiol Scand*. 2005; 49(8): 1200-1206.

[5] Nag D, Samaddar D, Chatterjee A, Kumar H, Dembla A. Vasopressors in obstetric anesthesia: A current perspective. *World J Clin Cases*. 2015; 3(1): 58-65. https://doi.org/10.12998/wjcc.v3.i1.58

[6] Brian BH. Adrenoceptor-activating and other sympathomimetic drugs. In: *Betram G Katzung (Ed.) Basic and Clinical Pharmacology 10th Edition, Singapore: McGraw Hill Education*.; 2007: 133-137.

[7] Lee A, Ngan KW, Gin T. A quantitative, systematic review of randomized controlled trials of ephedrine versus phenylephrine for the management of hypotension during spinal anesthesia for cesarean delivery. *Anaesth Analg*. 2002; 94: 920-926.

[8] American Society of Anesthesiologists Task Force on Obstetric Anesthesia.Practice guidelines for obstetric anesthesia: an updated report by the American Society of Anesthesiologist Task Force on Obstetric Anesthesia. *Anesthesiology*. 2007; 106: Anesthesiology 2007; 106: 843-63.

[9] Landau R, Shih-Kai L, Jean-Louis B, Richard MS, Ngan Kee W. The effect of maternal and fetal β2-adrenoceptor and nitric oxide synthase genotype on vasopressor requirement and fetal acid-base status during spinal anesthesia for cesarean delivery. *Anesth Analg*. 2011; 112(6): 1432-1437.

[10] Ngan-Kee W, Lee A. Multivariate analysis of factors associated with umbilical arterial pH and standard base excess after Caesarean section under spinal anaesthesia. *Anaesthesia*. 2003; 58(2): 125-130.

[11] Biddle C. To press or not to press, and if so, with what? A single question-focused meta-analysis of vasopressor choice during regional anesthesia in obstetrics. *AANA J*. 2013; 81: 261-264.

[12] Soltanifar S, Russell R. The National Institute for Health and Clinical Excellence (NICE) guidelines for caesarean section, 2011 update: implications for the anaesthetist. *Int J Obs Anesth*. 2012; 21: 264-272.

[13] Ngan KW, Khaw K, Lau T, Ng F, Chui K, Ng K. Randomised double-blinded comparison of phenylephrine vs ephedrine for maintaining blood pressure during spinal anaesthesia for non-elective Caesarean section. *Anaesthesia*. 2008; 63: 1319-1326.

[14] Saneh H, Mendez M, Srinivasan V. Cord Blood Gas. [Updated 2020 Jan 20]. In: *StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing*.; 2020: 1-6. https://www.ncbi.nlm.nih.gov/books/NBK545290/

[15] American C of O and G (ACOG) CON 348. Umbilical Cord Blood Gas and Acid-Base Analysis. *Obs Gynecol*. 2006; 108(5): 1319-1322.

[16] Armstrong L, Stenson BJ. Use of umbilical cord blood gas analysis in the assessment of the newborn. *Arch Dis Child Fetal Neonatal Ed*. 2007; 92(6): 430-434. https://doi.org/10.1136/adc.2006.099846

[17] Saravanan S, Kocarev M, Wilson R, Watkins E, Columb M, Lyons G. Equivalent dose of ephedrine and phenylephrine in the prevention of post-spinal hypotension in Caesarean section. *Br J Anaesth*. 2006; 96: 95-99.

[18] Odagme MT, Fyneface-Ogan S, Mato CN. Prophylactic infusions of phenylephrine and ephedrine during combined spinal epidural anaesthesia for caesarean section: A comparative study. *J Anesth Clin Res*. 2013; 4(9): 1-6. https://doi.org/10.4172/2155-6148.1000357

[19] Prakash S, Pramanik V, Chellani H, Salhan S, Gogia AR. Maternal and neonatal effects of bolus administration of ephedrine and phenylephrine during spinal anaesthesia for caesarean delivery : a randomised study. *Int J Obstet Anesth*. 2010; 19(1): 24-30. https://doi.org/10.1016/j.ijoa.2009.02.007

[20] Vakili H, Enayati H, Dashipour A. Comparing Intravenous Phenylephrine and Ephedrine for Hypotension During Spinal Anesthesia for Elective Cesarean Section: A Randomized Double-Blind Clinical Trial. *Iran Red Crescent Med J*. 2017; 19(10):e13978.https://doi.org/10.5812/ircmj.13978

[21] Higgins N, Fitzgerald P, van Dyk D, Dyer R, Rodriguez N, McCarthy R. The Effect of Prophylactic Phenylephrine and Ephedrine Infusions on Umbilical Artery Blood pH in Women With Preeclampsia Undergoing Cesarean Delivery With Spinal Anesthesia. *Anesth Analg*. 2018; 126(6): 1999-2006.

[22] Simin A, Zahra F, Pouya H, Reza T. Comparison the effect of ephedrine and phenylephrine in treatment of hypotension after spinal anesthesia during cesarean section. *Open J Obs Gynecol*. 2012; 02(03): 192-6.

[23] Abdalla E, Almaz M, Mohammed M, Wahba O. Ephedrine versus phenylephrine effects on fetal outcome and hemodynamics of pre-eclamptic mothers undergoing cesarean section under spinal anesthesia. *Ain-Shams J Anaesthesiol*. 2014; 7(2): 215.https://doi.org/10.4103/1687-7934.133444

[24] Kotaska K, Urinovska R, Klapkova E, Prusa R, Rob L, Binder T. Re-evaluation of cord blood arterial and venous reference ranges for pH, pO2, pCO2, according to spontaneous or cesarean delivery. *J Clin Lab Anal*. 2010; 24(5): 300-304. https://doi.org/10.1002/jcla.20405

[25] Thorp JA, Rushing RS. Umbilical cord blood gas analysis. *Obs Gynecol Clin North Am*. 1999; 26(4): 695-709.

[26] Adigun T, Amanor-Boadu, SD, Soyannwo O. Comparison of intravenous ephedrine with phenylephrine for the maintenance of arterial blood pressure during elective caesarean section under spinal anaesthesia. *Afr J Med Med Sci*. 2010; 39(1): 13-20.

[27] Sykes G, Molloy P, Johnson P, Gu W, Ashworth F, Stirrat G. Do APGAR scores indicate asphyxia? *Lancet*. 1982; 1: 494-496.

[28] Casey B, McIntire D, Levene K. The continuing value of the Apgar score for the assessment of newborn infant. *N Engl J Med*. 2001; 344: 467-471.

[29] Apgar V. A proposal for a new method of evaluation of the newborn infant. *Anesth Analg*. 2015; 120(5): 1056-1059. https://doi.org/10.1213/ANE.0b013e31829bdc5c

[30] Bjorland PA, Øymar K, Ersdal HL, Rettedal SI. Incidence of newborn resuscitative interventions at birth and short-term outcomes: A regional population-based study. *BMJ Paediatr Open*. 2019; 3(1): 13-16. https://doi.org/10.1136/bmjpo-2019-000592

[31] Fawke J, Wyllie J, Madar J, et al. Newborn resuscitation and support of transition of infants at birth 2021. *Ces Pediatr*. 2021; 76(7): 401-417. https://doi.org/10.1007/s10049-021-00894-w

[32] Pediatrics TAC of O and G and TAA of. The Apgar Score, Committee Opinion no 644 American college of Obstetrician and Gynecologists. *Obs Gynecol*. 2015; 4(126): 1-4.