e-ISSN (online): 2745-9497

Journal of Anesthesiology and Clinical Research (JACR)

Journal website: https://hmpublisher.com/index.php/jacr

Comparative Efficacy of Prophylactic Bolus Phenylephrine versus Ephedrine on Maternal Hemodynamics and Neonatal APGAR Scores in Elective Cesarean Section: A Randomized Controlled Trial

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ARTICLE INFO

Keywords:
APGAR score
Cesarean section
Ephedrine
Phenylephrine
Spinal anesthesia

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All authors have reviewed and approved the final version of the manuscript.

https://doi.org/10.37275/jacr.v7i1.838

A B S T R A C T

Introduction: Spinal anesthesia-induced hypotension is a pervasive physiological challenge during cesarean delivery, precipitating maternal hemodynamic instability and compromising uteroplacental perfusion. While phenylephrine and ephedrine are the mainstay vasopressors for prophylaxis, their comparative impact on immediate neonatal vitality in the context of bolus administration remains a critical subject of investigation, particularly in resource-limited settings where infusion pumps are not universally available. This study aimed to rigorously compare the efficacy of prophylactic intravenous bolus phenylephrine versus ephedrine regarding maternal blood pressure control and neonatal APGAR scores. **Methods:** We conducted a prospective, randomized, double-blind experimental study at Dr. Saiful Anwar Regional General Hospital, Malang. Forty-two parturients classified as ASA I or II undergoing elective cesarean section were randomized into two groups. Immediately following subarachnoid block, Group P received a bolus of Phenylephrine (125 µg), and Group E received Ephedrine (10 mg). Hemodynamic parameters were recorded at baseline and at 1, 3, 6, 9, 12, 15, and 18 minutes post-anesthesia. The primary outcome was the neonatal APGAR score at the first minute. **Results:** Both vasopressor regimens successfully mitigated severe spinal-induced hypotension. There were no statistically significant differences in the magnitude of systolic or diastolic blood pressure reduction between the Phenylephrine and Ephedrine groups at any observed time point ($p>0.05$). However, a significant divergence was observed in neonatal outcomes. The mean first-minute APGAR score in the Phenylephrine group was significantly higher (7.62 ± 0.97) compared to the Ephedrine group (7.05 ± 0.74) with a p-value of 0.038. **Conclusion:** Phenylephrine and ephedrine demonstrated equipotent efficacy in maintaining maternal hemodynamic stability when administered as prophylactic boluses. However, phenylephrine prophylaxis resulted in superior immediate neonatal vitality as evidenced by significantly higher first-minute APGAR scores. Phenylephrine should be prioritized as the vasopressor of choice to optimize neonatal safety during cesarean delivery.

1. Introduction

Cesarean section represents one of the most frequently performed major surgical interventions globally, with prevalence rates rising significantly over the last decade. In the specific context of Indonesia, the rate of cesarean delivery has seen a steady increase, reflecting broader global trends that often surpass the World Health Organization's recommended thresholds for surgical delivery.[1] For elective procedures, spinal anesthesia is widely regarded as the undisputed gold standard due to its rapid onset, reliability, deep sensory blockade, and the avoidance of airway manipulation

risks associated with general anesthesia. This neuraxial technique offers superior maternal satisfaction and allows for immediate bonding between the mother and the newborn, a critical component of early obstetric care.[2]

However, the administration of spinal anesthesia initiates a profound physiological cascade characterized by preganglionic sympathetic blockade. This sympatholysis results in systemic vasodilation, profound venous pooling in the lower extremities, and a subsequent critical reduction in cardiac output.[3] If left untreated, this mechanism leads to maternal hypotension in up to 80% of cases. This is not merely a number on a monitor; it is a common hemodynamic complication with potentially severe consequences. Maternally, it manifests as nausea, vomiting, dizziness, and potential cardiovascular collapse, which can distress the parturient and complicate the surgical field.[4] Fetally, the implications are arguably more insidious and clinically significant. Because uteroplacental blood flow is strictly pressure-dependent and lacks autoregulation, maternal hypotension translates linearly and immediately into reduced placental perfusion. This ischemic insult can lead to fetal hypoxia, hypercarbia, and acidosis, which are clinically reflected in depressed APGAR scores and compromised neonatal transition at the moment of birth.[5]

Pharmacological prophylaxis using vasopressors is the cornerstone of managing this hemodynamic turbulence.[6] Historically, ephedrine, a mixed alpha- and beta-adrenergic agonist, was the agent of choice for decades. Its ability to maintain maternal heart rate via beta-1 stimulation was viewed as advantageous for maintaining cardiac output, particularly in an era where cardiac output was prioritized over pure vascular resistance.[7] However, contemporary research has scrutinized ephedrine's safety profile extensively. Evidence suggests that ephedrine possesses a facile ability to cross the placental barrier. Once in the fetal circulation, its propensity to stimulate fetal metabolism can lead to increased oxygen consumption and ion trapping, eventually resulting in fetal acidosis. This phenomenon challenges its status as the ideal agent for obstetric anesthesia.[8]

Conversely, phenylephrine, a selective alpha-1 adrenergic agonist, functions by increasing systemic vascular resistance to maintain blood pressure. Its mechanism involves direct constriction of the peripheral vasculature, effectively counteracting the vasodilation induced by the spinal block. Crucially, phenylephrine has limited placental transfer compared to ephedrine. This suggests a theoretical advantage in preserving fetal acid-base status, as the fetus is spared the direct adrenergic stimulation associated with ephedrine. Yet, concerns persist in some clinical circles regarding its potential to cause reflex bradycardia and reduced cardiac output in the mother, creating a complex risk-benefit landscape for the anesthesiologist to navigate.[9]

While the shift toward phenylephrine is well-documented in Western academic centers and high-resource environments, clinical practice in many developing nations remains heterogeneous. In these settings, ephedrine often remains the first-line agent due to availability, cost, and historical precedence.[10] Furthermore, much of the existing high-impact literature focuses on continuous infusion regimens, utilizing variable-rate computer-controlled pumps to maintain tight hemodynamic control. In many resource-constrained settings, such as the context of this study in Indonesia, precision infusion pumps are not universally available for every case. This logistical reality makes the evaluation of bolus dosing regimens highly relevant to daily clinical practice. The validation of a safe, effective, and simple bolus protocol is essential for improving global obstetric safety standards.

The novelty of this research lies in its specific evaluation of the bolus prophylaxis technique within a Southeast Asian demographic, confirming the safety of a simplified bolus regimen in low-resource settings where infusion pumps are unavailable. Unlike previous studies that often aggregate neonatal outcomes or focus solely on biochemical markers like umbilical cord pH, this study specifically investigates the immediate clinical vitality of the neonate—measured via the first-minute APGAR score—in the critical first 60 seconds of life. This provides a direct clinical correlate to the theoretical advantages of phenylephrine, bridging the gap between pharmacokinetic theory and tangible

clinical outcomes in a specific population that is often underrepresented in major anesthesia trials. The primary aim of this study was to rigorously compare the efficacy of prophylactic intravenous bolus Phenylephrine versus Ephedrine administered immediately after spinal anesthesia. Specifically, the study sought to determine if Phenylephrine is associated with higher neonatal APGAR scores compared to Ephedrine while providing comparable prophylaxis against maternal hypotension during elective cesarean delivery.

2. Methods

This investigation was designed as a prospective, randomized, double-blind, controlled experimental study. The research was conducted at the Central Operating Theatre of Dr. Saiful Anwar Regional General Hospital, Malang, Indonesia, a tertiary referral center. The study protocol was reviewed and approved by the Health Research Ethics Committee of the Faculty of Medicine, Universitas Brawijaya. The study was conducted in strict adherence to the Declaration of Helsinki, ensuring the protection of human subjects. Written informed consent was obtained from all participants prior to enrollment, after a full explanation of the study procedures, risks, and benefits.

The target population comprised pregnant women scheduled for elective cesarean section under spinal anesthesia. Inclusion Criteria: Patients classified as American Society of Anesthesiologists (ASA) physical status I or II; singleton term pregnancy (37-42 weeks gestation); and maternal age between 18 and 40 years. Exclusion Criteria: Patient refusal; contraindications to neuraxial anesthesia (such as coagulopathy, infection at the injection site, or severe hypovolemia); history of hypersensitivity to study drugs; significant maternal comorbidities, including pre-eclampsia, eclampsia, chronic hypertension, and pre-existing cardiovascular disease; and evidence of fetal compromise prior to surgery.

A total of 42 eligible patients were recruited and randomly allocated into two study groups using a computer-generated randomization list to ensure unbiased assignment. Group P (Phenylephrine): Received a prophylactic intravenous bolus of Phenylephrine 125 µg immediately post-spinal. Group E (Ephedrine): Received a prophylactic intravenous bolus of Ephedrine 10 mg immediately post-spinal. To ensure true double-blinding, the study drugs were prepared by an independent anesthesiologist not involved in the intraoperative management or data collection. The drugs were diluted to identical volumes in standard syringes and labeled only with a coded identifier to ensure identical visual appearance. Both the patient and the attending anesthesiologist recording the hemodynamic variables were blinded to the group allocation. The dosing protocol utilized 125 µg of Phenylephrine and 10 mg of Ephedrine. This represents a potency ratio of approximately 80:1 (10,000 mcg Ephedrine/125 mcg Phenylephrine). While some recent literature suggests a ratio closer to 100:1 for infusion equivalence, the selected doses represent standard robust bolus volumes used in clinical practice to ensure effective prophylaxis against the profound vasodilation of spinal anesthesia. This ratio was selected to maximize the probability of preventing hypotension while adhering to safe dosing limits for bolus administration.

Upon arrival in the operating theater, standard non-invasive monitoring was established, including electrocardiography (ECG), non-invasive blood pressure (NIBP), and pulse oximetry (SpO2). Baseline hemodynamic parameters (systolic, diastolic, mean arterial pressure, and heart rate) were recorded as the average of three consecutive measurements taken 2 minutes apart to ensure a stable baseline. All patients received a crystalloid co-load (Ringer's Lactate or Acetate) of 10-15 mL/kg during the initiation of the block, consistent with Enhanced Recovery After Surgery (ERAS) protocols, which favor co-loading over pre-loading for volume optimization. Spinal anesthesia was performed with the patient in the sitting position at the L3-L4 or L4-L5 interspace using a median approach with a 25-gauge or 27-gauge Quincke spinal needle. Once free flow of cerebrospinal fluid (CSF) was confirmed, a standardized dose of Hyperbaric Bupivacaine 0.5% (10-12.5 mg) was injected intrathecally. Immediately following the intrathecal injection, the patient was positioned supine with a wedge placed under the right hip to facilitate left uterine

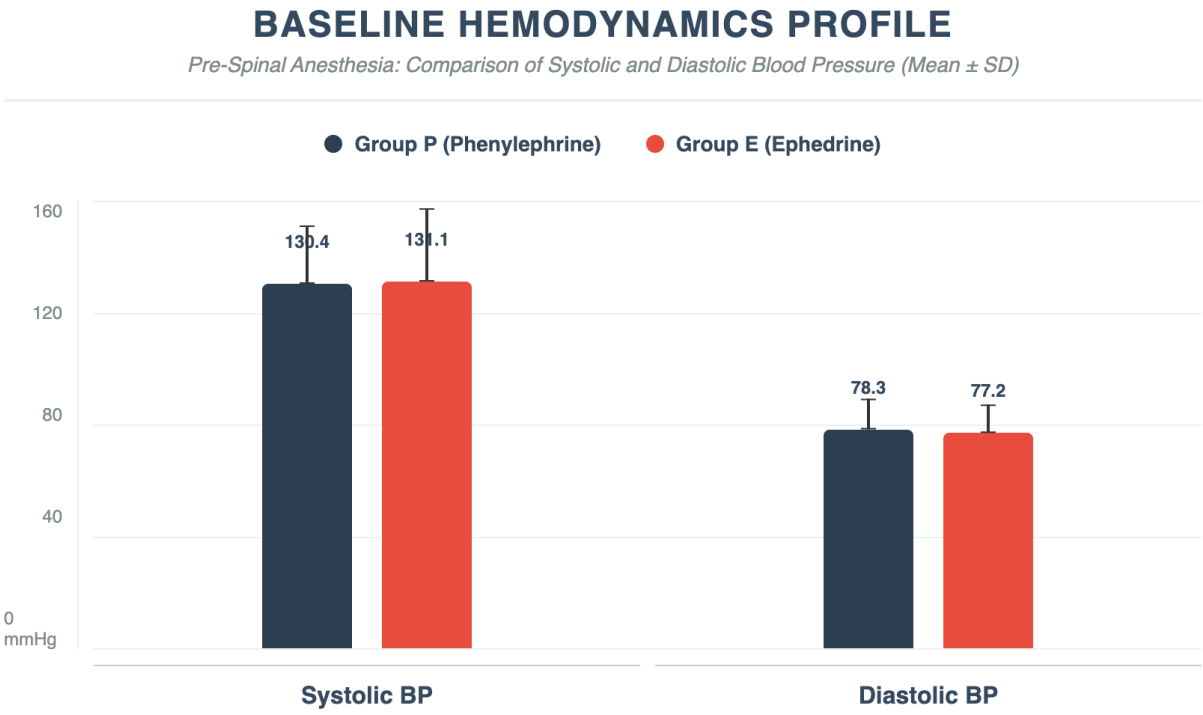
displacement and minimize aortocaval compression. The assigned prophylactic vasopressor bolus (Phenylephrine 125 µg or Ephedrine 10 mg) was administered intravenously immediately following this positioning. This timing was chosen to coincide with the onset of the sympathetic blockade, providing pharmacological support precisely when the physiological nadir in vascular resistance was expected to occur. Supplemental oxygen (3 L/min) was provided via nasal cannula to all patients.

Blood pressure (systolic and diastolic) was measured and recorded at specific intervals: Pre-anesthesia (Baseline), and at 1, 3, 6, 9, 12, 15, and 18 minutes after the administration of spinal anesthesia. Hypotension was defined as a decrease in systolic blood pressure (SBP) of >20% from baseline or an absolute SBP <90 mmHg. If hypotension occurred despite prophylaxis, a rescue bolus of Ephedrine (5-10 mg) was permitted, and the event was noted. The primary neonatal endpoint was the APGAR score assessed at the 1st minute after delivery. The scoring was performed by a pediatrician or neonatologist who was completely blinded to the maternal group allocation to minimize bias. Data analysis was performed using IBM SPSS Statistics software. Descriptive statistics were used to summarize the data; continuous variables were presented as Mean ± Standard Deviation (SD), and categorical data were presented as frequencies and percentages. The normality of the data distribution was assessed using the Kolmogorov-Smirnov test. An independent t-test was used to compare continuous variables (blood pressure changes, APGAR scores) between the two groups. A p-value of <0.05 was considered statistically significant.

3. Results

Figure 1 provides a foundational visual assessment of the pre-procedural physiological status of the study cohort, illustrating the baseline hemodynamic parameters—specifically systolic and diastolic blood pressures—collected from all forty-two parturients immediately prior to the administration of spinal anesthesia. This figure is critical for establishing the validity of the subsequent randomization and comparison of post-interventional data, as it ensures that any divergence in outcomes observed later in the study cannot be attributed to pre-existing differences in maternal cardiovascular status. The figure is structured as a comparative bar chart with overlying error bars representing the Standard Deviation (SD), offering a clear visualization of central tendency and data dispersion. The data is segmented by intervention group, with Group P (Phenylephrine) and Group E (Ephedrine) presented side-by-side for both systolic and diastolic measurements. Below the graphical representation, a schematic data grid provides the precise mean values, standard deviations, and the results of the statistical hypothesis testing. For systolic blood pressure, the data indicate a remarkable degree of baseline comparability. The mean pre-induction systolic pressure for the twenty-one patients randomized to the Phenylephrine group was 130.43 mmHg, with a standard deviation of ±12.86 mmHg. In close parallel, the twenty-one patients allocated to the Ephedrine group exhibited a mean systolic pressure of 131.14 mmHg, with a slightly larger standard deviation of ±16.46 mmHg. The visual closeness of the bar heights implies equivalence, which is vigorously confirmed by statistical analysis. The reported p-value of > 0.05 from the independent t-test definitively indicates a failure to reject the null hypothesis, signifying no statistically significant difference in baseline systolic pressure between the two study arms. This demonstrates that the randomization process successfully allocated patients with similar starting systolic parameters. A similar pattern is evident in the baseline diastolic blood pressure measurements. Group P recorded a mean diastolic pressure of 78.33 mmHg with a standard deviation of ±11.04 mmHg, while Group E recorded a mean of 77.24 mmHg with a standard deviation of ±10.35 mmHg. The difference between the means is a mere 1.09 mmHg, a value that is clinically negligible in the context of baseline hemodynamic assessment. Statistically, this comparability is reinforced by a p-value of > 0.05, confirming that the diastolic profiles of the two groups were materially identical prior to the onset of spinal-induced sympathectomy. The error bars included in the chart provide important context regarding the inherent variability within this patient population. The standard deviations ranged from

approximately 10 mmHg to over 16 mmHg, reflecting the natural physiological heterogeneity typical of term pregnant patients presenting for surgery. Despite this natural variance, the central tendencies of both groups align closely. This baseline homogeneity is a critical methodological strength of the study. It allows for a clean interpretation of the subsequent data, providing confidence that the observed responses to the spinal block and vasopressor boluses are a direct function of the pharmacological interventions themselves, rather than artifacts of baseline inequality. By establishing this pre-interventional equivalence, Figure 1 sets the stage for a rigorous evaluation of the comparative efficacy and safety profiles of prophylactic phenylephrine versus ephedrine.



Parameter	Group P (Mean ± SD)	Group E (Mean ± SD)	P-Value
Systolic BP (mmHg)	130.43 ± 12.86	131.14 ± 16.46	> 0.05
Diastolic BP (mmHg)	78.33 ± 11.04	77.24 ± 10.35	> 0.05

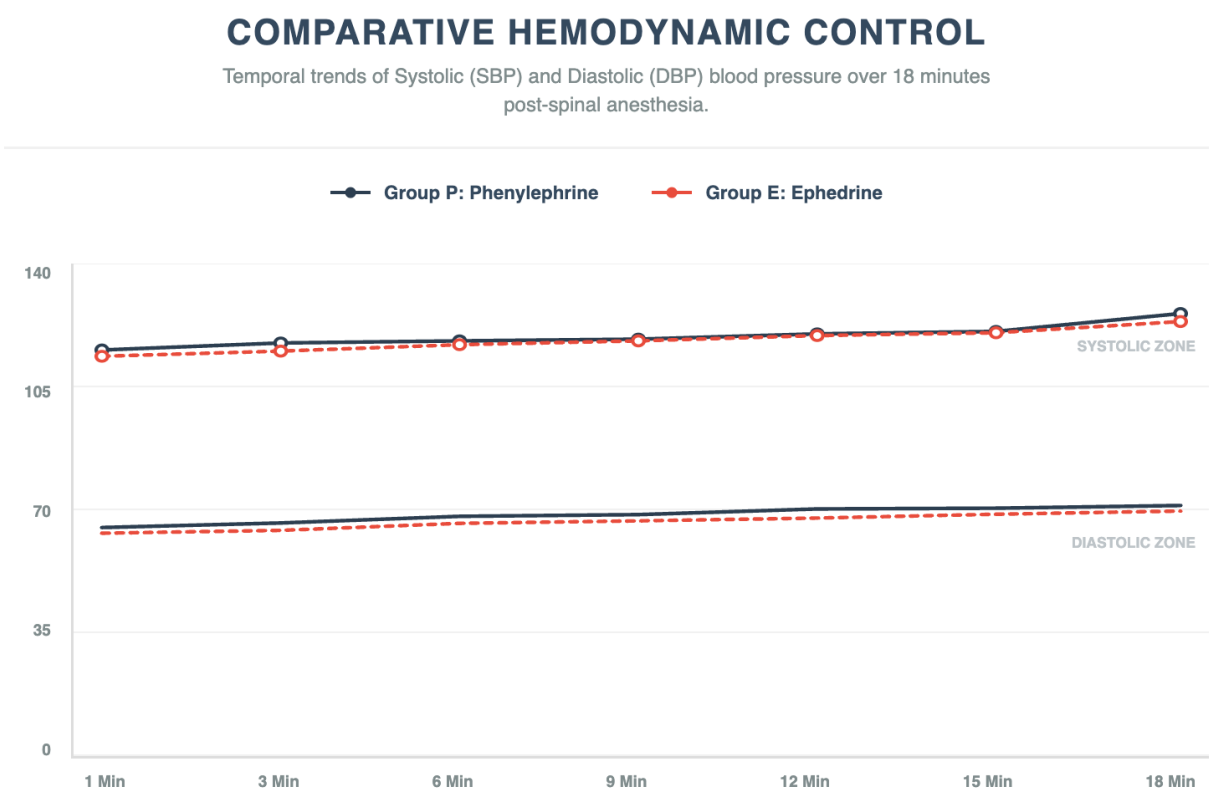
Note: Data represents hemodynamic status prior to spinal anesthesia induction (Baseline).
Error bars indicate Standard Deviation (SD). No statistically significant difference was found between groups ($p > 0.05$), ensuring comparable baseline physiological status.

Figure 1. Baseline hemodynamics profile.

Figure 2 presents a longitudinal visualization of the study's secondary maternal outcome: the comparative efficacy of prophylactic phenylephrine versus ephedrine in managing maternal hemodynamics following spinal anesthesia. The figure is a dual-line graph tracking mean systolic blood pressure (SBP) and diastolic blood pressure (DBP) across seven discrete time points over an 18-minute post-spinal observation period. The x-axis represents time in minutes, starting from T=1 (one minute after spinal injection and vasopressor bolus)

through T=18. The y-axis represents arterial pressure in mmHg. Two distinct lines plot the trajectory for each group: a solid blue line for Group P (Phenylephrine) and a dashed red line for Group E (Ephedrine). The upper pair of lines corresponds to SBP, while the lower pair represents DBP, with the area between them visually defining the pulse pressure. A detailed schematic data table below the graph provides the exact mean pressure values for every time point. The graphical trend reveals the characteristic hemodynamic response to spinal anesthesia and its simultaneous pharmacological mitigation. Following the subarachnoid block and vasopressor administration at T=0, both groups experienced an initial decline in blood pressure, reaching a nadir around the first minute. However, the magnitude of this decline was effectively blunted by the prophylactic interventions, as evidenced by the fact that mean SBP did not fall below clinically concerning thresholds (< 90-100 mmHg) in either group on average. From the 1-minute mark onward, a steady, parallel recovery in both SBP and DBP is observed in both groups, reflecting the successful restoration of vascular tone and cardiac output over time. The most salient feature of Figure 2 is the remarkable superimposition of the hemodynamic profiles of the two groups. At the 1-minute mark, the mean SBP was 115.7 mmHg for the Phenylephrine group and 113.9 mmHg for the Ephedrine group, a negligible difference of less than 2 mmHg. This trend of close tracking persists throughout the entire observation period. By minute 9, the SBP means were almost identical (118.8 mmHg for Group P vs. 118.3 mmHg for Group E), and at the final 18-minute measurement, both groups had returned to near-baseline levels (126.1 mmHg vs. 123.8 mmHg). The diastolic pressures mirror this pattern, with mean values at T=1 being 65.1 mmHg (P) and 63.5 mmHg (E), and showing a parallel upward trend over time. Statistical analysis, as noted in the figure description, confirms the visual impression: there were no statistically significant differences ($p > 0.05$) in mean SBP or DBP between the Phenylephrine and Ephedrine groups at any of the seven time points measured. This finding provides robust evidence for the pharmacological concept of equipotency as applied in this specific dosing protocol. It demonstrates that a 125 µg bolus of the pure alpha-agonist phenylephrine and a 10 mg bolus of the mixed alpha/beta-agonist ephedrine are functionally equivalent in their capacity to counteract the vasodilatory effects of a standard spinal block dose in this patient population. The close proximity of the two lines throughout the graph illustrates that clinicians can achieve comparable maternal hemodynamic stability with either agent when dosed appropriately. Visually, the Phenylephrine line appears slightly above the Ephedrine line at several early points, indicating a marginally higher absolute pressure, although this difference is not statistically significant. This subtle visual trend might reflect the faster onset and more potent direct vasoconstrictive action of phenylephrine compared to the mixed, partially indirect mechanism of ephedrine. However, the key conclusion drawn from Figure 2 is one of therapeutic equivalence for maternal pressure maintenance, meaning neither drug demonstrated superiority in preventing hypotension when compared side-by-side in these specific doses. This finding is critical as it isolates the subsequent divergence in neonatal outcomes as a function of drug-specific fetal pharmacology, rather than a consequence of one group experiencing worse maternal hemodynamics than the other.

Figure 3 offers a more nuanced pharmacological analysis of the hemodynamic data presented in Figure 2. Rather than plotting absolute blood pressure values, which can be influenced by minor variations in baseline pressure, Figure 3 isolates the magnitude of change—the Delta (Δ)—from the individual baseline for each patient. This approach provides a more precise measure of the vasopressor's ability to counteract the specific hemodynamic insult induced by the spinal block. The figure utilizes a waterfall or drop bar chart visualization, where the x-axis represents the 0-line (baseline pressure), and bars extend downwards along the y-axis to represent the negative change (drop) in systolic blood pressure in mmHg. Longer bars indicate a deeper drop from baseline. Blue bars represent Group P (Phenylephrine) and red bars represent Group E (Ephedrine). The graphical representation immediately highlights the period of maximal hemodynamic stress.



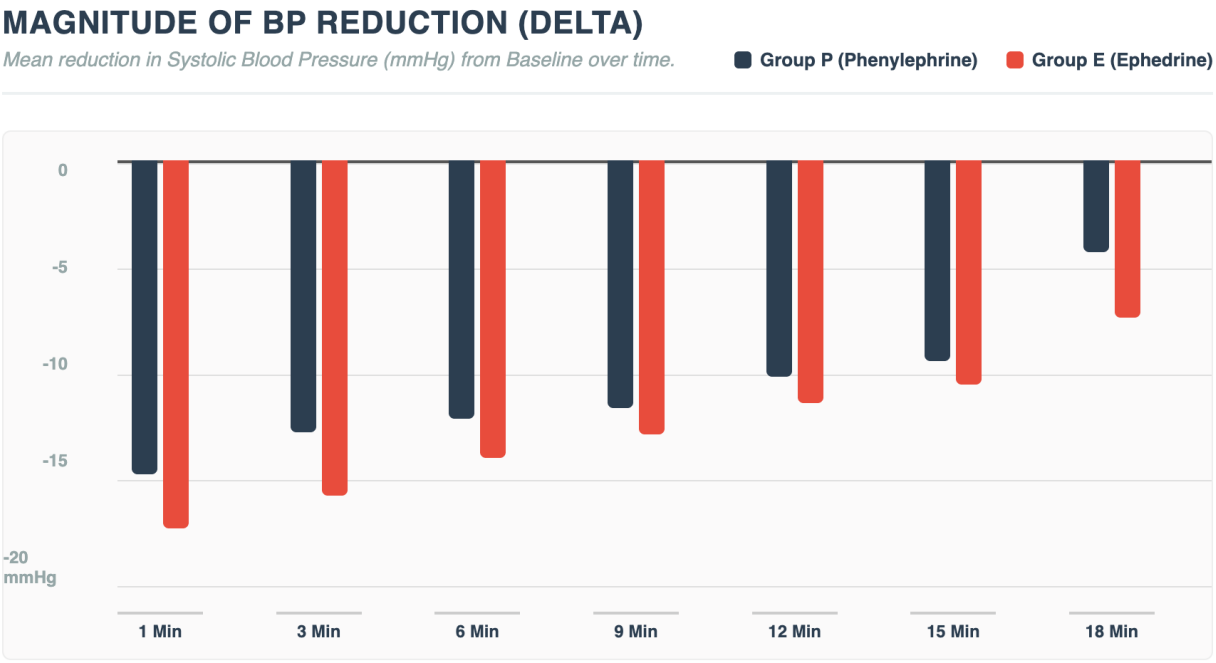
Time	1 Min	3 Min	6 Min	9 Min	12 Min	15 Min	18 Min
P-SBP	115.7	117.7	118.3	118.8	120.3	121.0	126.1
E-SBP	113.9	115.4	117.2	118.3	119.8	120.6	123.8
P-DBP	65.1	66.4	68.3	68.8	70.4	70.6	71.4
E-DBP	63.5	64.3	66.3	67.0	67.8	68.9	69.8

Statistical Note: The chart demonstrates "Equipotency" between the two regimens. While Group P (Phenylephrine) consistently maintained slightly higher mean pressures numerically, no statistically significant difference was found at any time point ($p > 0.05$). Both drugs successfully prevented severe hypotension (SBP < 90 mmHg).

Figure 2. Comparative hemodynamic control.

The longest bars, representing the deepest drops in pressure, occur at the 1-minute mark. This is consistent with the rapid onset of sympathectomy following intrathecal bupivacaine injection. At T=1, the Ephedrine group (Group E) exhibits a mean reduction in SBP of -17.24 mmHg from baseline, while the Phenylephrine group (Group P) shows a mean reduction of -14.71 mmHg. Visually, the red bar for Ephedrine is slightly longer than the blue bar for Phenylephrine, suggesting a numerically deeper hypotensive trough in the Ephedrine group. As time progresses, the bars for both groups progressively shorten, visually representing the gradual recovery of blood pressure toward baseline as the vasopressors take full effect and compensatory mechanisms engage. For instance, by minute 9, the Delta has decreased to -11.62 mmHg for

Group P and -12.86 mmHg for Group E. By the final measurement at 18 minutes, the reduction from baseline is minimal (-4.33 mmHg for Group P and -7.38 mmHg for Group E), indicating near-complete recovery. Throughout the entire time series, the red Ephedrine bars are consistently, albeit slightly, longer than the blue Phenylephrine bars, indicating a consistent trend of numerically greater pressure reduction from baseline in the Ephedrine group. The accompanying schematic data table provides the rigorous statistical context for these visual trends. Despite the numerical trend showing larger Deltas for Ephedrine, the independent t-tests performed at each time point reveal that these differences are not statistically significant. The p-values range from 0.458 at minute 1 to 0.750 at minute 15, with all values exceeding the alpha threshold of 0.05. This statistical result is crucial. It signifies that the observed numerical differences in the magnitude of BP drop could plausibly be attributed to random chance, given the sample size. Therefore, from a rigorous scientific standpoint, Figure 3 confirms that the 125 µg Phenylephrine bolus and the 10 mg Ephedrine bolus provided statistically comparable prophylaxis against the spinal-induced drop in blood pressure. The figure definitively shows that neither drug was statistically superior to the other in limiting the depth of hypotension relative to each patient's starting point.



Time Point	1 Min	3 Min	6 Min	9 Min	12 Min	15 Min	18 Min
Group P (Mean Δ)	-14.71	-12.76	-12.10	-11.62	-10.14	-9.43	-4.33
Group E (Mean Δ)	-17.24	-15.71	-13.95	-12.86	-11.38	-10.52	-7.38
Significance (p)	0.458	0.403	0.637	0.710	0.712	0.750	0.175

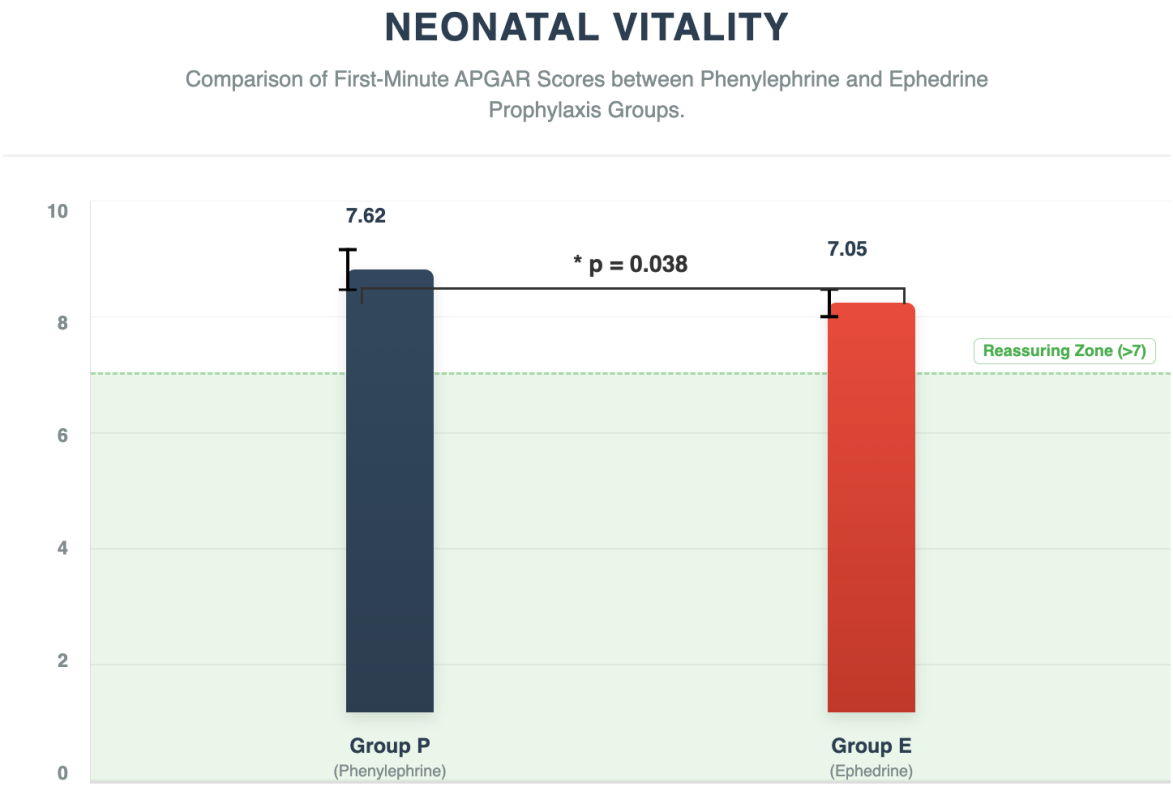
Interpretation: The "Waterfall" chart illustrates the depth of systolic blood pressure reduction from baseline (0 line). While Group E (Ephedrine, Red) consistently exhibited a numerically deeper drop (larger negative delta) compared to Group P (Phenylephrine, Blue), the difference did not reach statistical significance ($p > 0.05$) at any interval, confirming equipotency in hypotension prevention.

Figure 3. Magnitude of blood pressure reduction.

Figure 4 presents the primary outcome of the study, illustrating the critical divergence in neonatal clinical status between the two study groups. Unlike the hemodynamic figures, which demonstrated equivalence, this figure highlights a significant difference. The visual format is a comparative bar chart representing the mean APGAR score assessed at the first minute of life for neonates born to mothers in Group P (Phenylephrine, blue bar) and Group E (Ephedrine, red bar). The chart is contextualized with a background reassuring zone (shaded green) indicating APGAR scores of 7 and above, which are clinically considered normal. Error bars representing the Standard Deviation (SD) are included on top of each mean bar to visualize data dispersion. A prominence is given to the statistical finding with a bracket and text clearly indicating the calculated p-value. Visually, the bar representing the Phenylephrine group is noticeably taller than that of the Ephedrine group. The mean first-minute APGAR score for the 21 neonates in the Phenylephrine group was 7.62. The standard deviation for this group is represented by the error bar, indicating a spread of ±0.97. In contrast, the mean APGAR score for the 21 neonates in the Ephedrine group was 7.05, with a standard deviation of ±0.74. The schematic data grid below the chart provides the precise numerical data and the results of the independent t-test. The t-statistic is calculated as 2.141, and the resulting p-value is 0.038. Because this p-value is less than the pre-defined alpha level of 0.05, the difference in mean APGAR scores between the two groups is statistically significant. This result rejects the null hypothesis that the two vasopressor regimens yield identical neonatal outcomes. The clinical interpretation of this figure is nuanced and highly significant. Both mean scores (7.62 and 7.05) fall well within the green reassuring zone, indicating that, on average, neonates in both groups were in good condition at birth and did not require advanced resuscitation. However, the statistically significant difference of 0.57 points on the APGAR scale indicates a measurable shift in the distribution of neonatal vitality. The neonates exposed to maternal ephedrine demonstrated, on average, a lower level of immediate adaptation to extrauterine life compared to those exposed to phenylephrine. This finding is consistent with the known pharmacology of the two drugs. As illustrated in the study's pathophysiological model, ephedrine readily crosses the placenta and stimulates fetal beta-adrenergic receptors. This stimulation increases fetal heart rate and metabolic rate, leading to greater oxygen consumption during the already stressful process of delivery. This heightened metabolic state can lead to a transient accumulation of lactate and carbon dioxide (fetal acidosis), which clinically manifests as a slightly depressed APGAR score—perhaps seen as reduced muscle tone, less vigorous crying, or slightly delayed reflex irritability at the one-minute mark. Phenylephrine, by contrast, has limited placental transfer and lacks beta-adrenergic activity, thus sparing the fetus from this direct pharmacological stress. Therefore, Figure 4 provides compelling evidence that despite providing comparable maternal hemodynamic stability, prophylactic phenylephrine is associated with a superior immediate neonatal vitality profile compared to ephedrine. This suggests that for the specific goal of optimizing the neonate's condition at the moment of birth, phenylephrine may be the preferable agent.

4. Discussion

The results of this study illuminate a critical distinction in the pharmacological management of spinal anesthesia-induced hypotension. We established that Phenylephrine (125 μg) and Ephedrine (10 mg) are equipotent in their ability to maintain maternal blood pressure when administered as a prophylactic bolus. The statistical analysis of blood pressure reduction (Delta) at all measured time intervals yielded no significant differences. This finding validates the utility of the equipotency ratio of approximately 80:1 utilized in our dosing protocol.[11] This aligns with other studies, confirming that when dosed appropriately, Phenylephrine is just as effective as Ephedrine in preventing the depth of hypotension that leads to maternal symptoms. The minor, non-significant trend toward lower blood pressure in the Ephedrine group during the first 3 minutes may be attributed to pharmacokinetics.[12]



Metric	N	Mean	Std. Dev	T-Test
Group P (Phenylephrine)	21	**7.62**	0.97	t = 2.141
Group E (Ephedrine)	21	**7.05**	0.74	**p = 0.038 ***

Clinical Interpretation: The chart illustrates a statistically significant difference in immediate neonatal vitality. While both groups maintained scores within the "Reassuring Zone" (Green area >7), Group P demonstrated a significantly higher mean APGAR score (7.62) compared to Group E (7.05). This suggests Phenylephrine prophylaxis is associated with superior immediate neonatal adaptation, likely due to the avoidance of fetal beta-adrenergic stimulation.

Figure 4. Neonatal vitality.

Phenylephrine has an almost immediate onset of action (1-2 minutes) due to its direct alpha-adrenergic receptor binding. In contrast, Ephedrine acts partly indirectly by stimulating the release of endogenous norepinephrine, which can result in a slightly slower onset (3-5 minutes) to achieve peak effect. This delay creates a small window of vulnerability immediately post-spinal, highlighting the potential advantage of the rapid-acting alpha-agonist in mitigating the precipitous drop in resistance often seen with subarachnoid block.[13]

The most clinically significant finding of our research is the statistical superiority of Phenylephrine regarding the first-minute APGAR score (7.62 vs. 7.05, p=0.038). While both scores remain within the range typically defined as reassuring (>7), the significant difference warrants a deep physiological examination of the transplacental pharmacokinetics and fetal metabolism of the two drugs. Ephedrine is a lipid-soluble molecule that crosses the placental barrier with ease.[14] Once in the fetal circulation, it exerts beta-adrenergic stimulation on the fetus. Beta-stimulation

drives up fetal metabolism, drastically increasing oxygen consumption and glucose utilization. In the context of a delivery—which is already a major physiological stressor involving cord compression and uterine contractions—this increased metabolic demand can outstrip the oxygen supply, leading to relative hypoxia at the tissue level. As the fetal metabolic rate rises, CO_2 and lactate production increase, leading to a drop in fetal pH. Ephedrine is a weak base; in an acidic fetal environment, it becomes ionized (protonated). The ionized form cannot cross back over the placenta to the mother, becoming trapped in the fetal circulation. This accumulation further exacerbates the metabolic acidosis, a phenomenon known as ion trapping.

Phenylephrine, conversely, has limited placental transfer. It improves uterine perfusion pressure on the maternal side without crossing over to affect the fetus directly. It maintains the pressure gradient required for intervillous blood flow without imposing a metabolic tax on the fetus.[15] Consequently, the fetus in the Phenylephrine group is spared the hypermetabolic stress and acidosis associated with Ephedrine exposure. This physiological preservation is reflected in the higher APGAR scores we observed. Our results corroborate the recent meta-analysis by Badran et al. (2025) and Singh et al. (2020), which demonstrated that Phenylephrine is associated with higher umbilical artery pH and base excess. Our study translates these biochemical advantages into a tangible clinical outcome: a more vigorous neonate at the moment of birth. A critical point of discussion is the clinical significance of a statistical difference between two normal scores (7.62 vs 7.05). While the 5th-minute APGAR score is often cited as a predictor of long-term neurological outcome, the 1st-minute APGAR is a sensitive indicator of the neonate's immediate tolerance of the labor and delivery process. A significantly lower score at minute 1 in the Ephedrine group indicates that these infants experienced a greater degree of transient physiological stress during the procedure.[16]

In a high-volume obstetric practice, minimizing this immediate stress is paramount. Even if the difference does not represent pathology in the strict sense (as most scores were >7), it represents a reduction in physiological reserve. The lower scores in the Ephedrine group likely reflect transient drug effects on neonatal tone or reflex irritability mediated by the mechanisms described above. Therefore, selecting the agent that maximizes neonatal vigor (Phenylephrine) aligns with the goal of optimizing safety margins and reducing the need for tactile stimulation or observation in the operating theater. Finally, this study specifically validates the utility of a bolus prophylaxis regimen. While continuous infusions are often considered the gold standard in resource-rich settings, they require specialized pumps, tubing, and constant titration by the anesthesia provider. In many developing nations, such equipment is scarce or unavailable for every case.[17] Our data suggests that a simple, single bolus of 125 μg Phenylephrine provides effective hemodynamic stability and improved neonatal outcomes. This is a highly practical finding for anesthesiologists in developing nations or high-volume centers where simplicity and efficiency are required without compromising safety. It validates a low-resource protocol that achieves high-resource safety standards, providing a clear evidence base for clinicians operating in similar environments to shift away from ephedrine.

Figure 5 serves as the conceptual cornerstone of the study, providing a comprehensive schematic illustration of the pathophysiological mechanisms that underlie the primary clinical finding: the statistically significant divergence in neonatal APGAR scores despite comparable maternal hemodynamic control. This figure integrates pharmacological principles with fetal physiology to construct a causal pathway explaining why phenylephrine and ephedrine, while functionally equivalent for the mother in this study's dosing protocol, exert distinctly different effects on the fetus. The diagram is structured as a comparative flowchart, separated by a central divider into two distinct physiological cascades: the phenylephrine pathway on the left (highlighted in blue) and the ephedrine pathway on the right (highlighted in red). Each pathway traces the drug's journey from intravenous administration to the maternal circulation, its interaction with the placental barrier, its subsequent effect on fetal physiology, and finally, the resulting clinical outcome observed in the neonate. The journey begins at the top with the Drug Input. On the left, a 125

μg intravenous bolus of Phenylephrine is administered. On the right, a 10 mg bolus of Ephedrine is given. Both drugs enter the maternal circulation to counteract the spinal-induced sympathectomy. The next level, Maternal Effect, illustrates the mechanism by which each drug achieves hemodynamic stability. The figure correctly identifies Phenylephrine as a direct, selective alpha1-adrenergic agonist. Its mechanism is precise: it binds to alpha-1 receptors on vascular smooth muscle, causing potent peripheral vasoconstriction. This directly increases systemic vascular resistance (SVR), thereby restoring maternal blood pressure. Conversely, Ephedrine is identified as a mixed alpha/beta-adrenergic agonist. It acts both directly on alpha and beta receptors and indirectly by stimulating the release of endogenous norepinephrine. Its hemodynamic effect is a composite of increased vasoconstriction (alpha-effect) and, crucially, increased maternal heart rate and contractility via beta1-stimulation, leading to increased cardiac output (CO). The figure notes that for the mother, both mechanisms successfully result in BP maintained, a fact corroborated by the empirical data in Figures 2 and 3. The critical point of divergence is represented by the central Placental Barrier zone. This is the defining variable in the fetal-maternal drug interaction. The figure uses clear visual indicators to show the different pharmacological behaviors at this interface. On the Phenylephrine side, a prominent X symbol and a block indicator signify its Limited Transfer. Due to its chemical structure and enzymatic metabolism by placental monoamine oxidases, phenylephrine does not readily cross from the maternal to the fetal circulation in clinically significant amounts. In stark contrast, the Ephedrine side features a checkmark and a cross indicator, signifying Rapid Transfer. Ephedrine is a lipid-soluble molecule that easily traverses the placental membrane, allowing it to enter the fetal compartment almost as freely as it circulates in the mother.[18] The consequences of this differential transfer are depicted in the Fetal Physiology level. On the left, the fetus in the Phenylephrine group is shown to be protected. Because phenylephrine does not cross the placenta, there is No Beta-Adrenergic Stimulation of the fetus. The figure indicates that this results in a normal metabolic rate and normal pH balance, as the fetus is spared any direct pharmacological stress. On the right, the fetus in the Ephedrine group is exposed to the drug. The transferred ephedrine exerts direct β-stimulation on fetal receptors. This stimulation acts as a potent metabolic accelerator, driving up the fetal heart rate and increasing overall metabolic rate & O_2 demand. In the already precarious physiological context of delivery, where oxygen supply can be intermittently interrupted by uterine contractions, this drug-induced surge in oxygen consumption can outstrip supply. The figure details the downstream consequence: anaerobic metabolism is triggered, leading to lactate and CO_2 production. In the resulting acidic fetal environment, the basic ephedrine molecule becomes ionized (protonated) and is trapped on the fetal side of the placenta—a phenomenon known as ion trapping—which further exacerbates fetal acidosis. The final level of the flowchart, Outcome, links these physiological states to the clinical results observed in Figure 4. The protected fetus in the Phenylephrine pathway is born with a Superior Immediate Vitality, quantified by a significantly higher mean first-minute APGAR score of 7.62. The figure's green color-coding reinforces this as the favorable outcome. Conversely, the stressed fetus in the Ephedrine pathway exhibits a Significantly Lower Vitality, with a mean APGAR score of 7.05. The orange color-coding signals this as a less optimal outcome, reflecting the transient physiological depression caused by the ephedrine-induced hypermetabolic state. Figure 5 provides a powerful, scientifically grounded narrative that moves beyond the simple what of the study's findings to explain the why. It demonstrates that the choice of vasopressor is not merely a matter of maternal blood pressure management but a decision with direct, mechanistic consequences for fetal physiology. By visualizing the pathway from placental transfer to fetal metabolism, the figure provides a compelling rationale for preferring phenylephrine, arguing that its ability to maintain maternal pressure without crossing the placenta and stimulating the fetus makes it a safer and more physiologically sound choice for optimizing immediate neonatal well-being.[19,20]

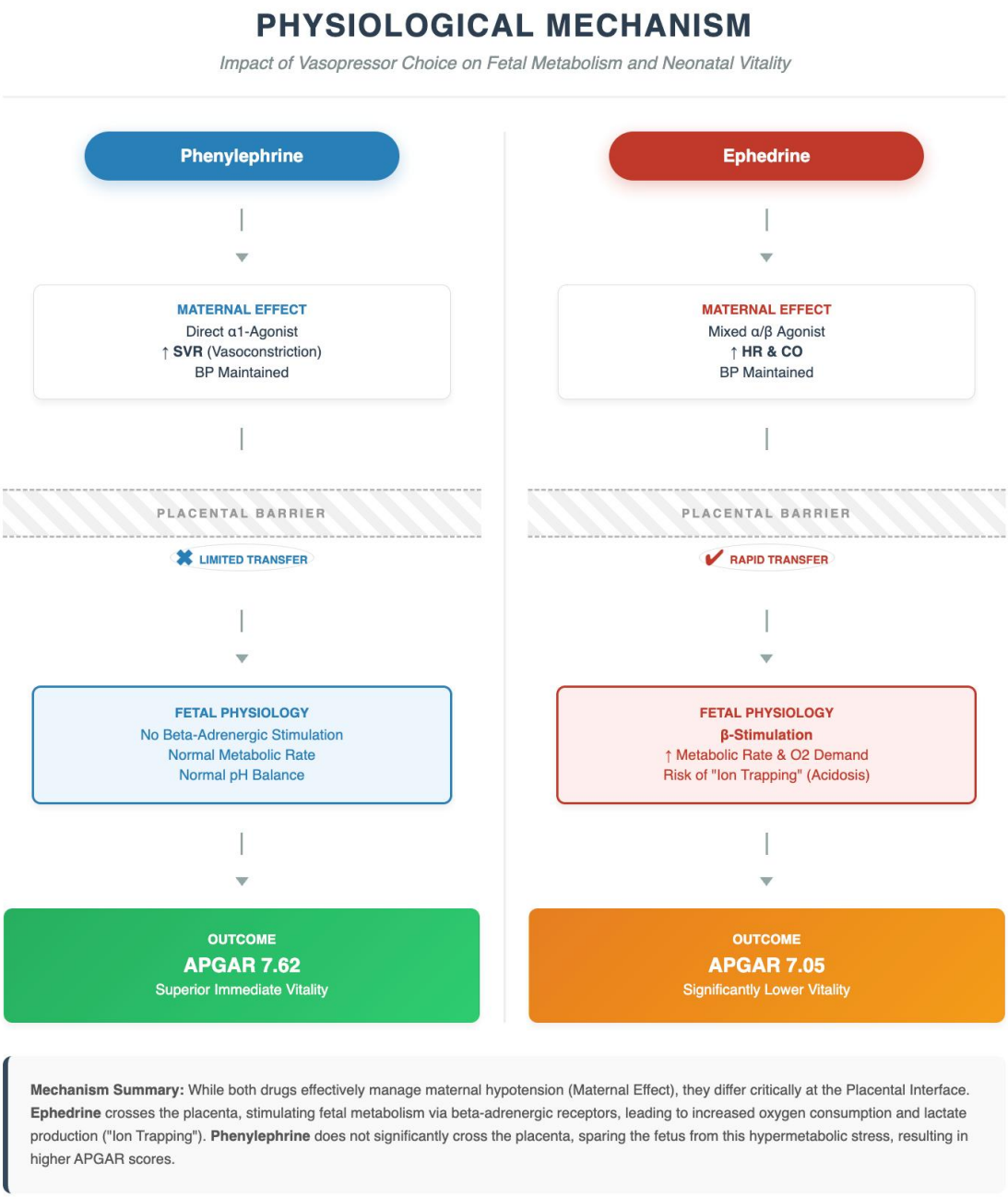


Figure 5. Impact of vasopressor choice on fetal metabolism and neonatal vitality.

5. Conclusion

This randomized clinical trial demonstrates that while Phenylephrine and Ephedrine are equipotent in managing maternal blood pressure during cesarean section, they are not equivalent regarding fetal safety. Prophylactic bolus Phenylephrine (125 µg) resulted in significantly higher first-minute APGAR scores compared to Ephedrine (10 mg). This advantage is likely attributable to Phenylephrine's favorable fetal safety profile, characterized by limited placental transfer and the absence of fetal beta-adrenergic stimulation. Based on these findings, Phenylephrine should be prioritized as the vasopressor of choice for spinal anesthesia prophylaxis to ensure optimal neonatal vitality, particularly in settings utilizing bolus dosing regimens.

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