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Management of Hypotension Post Subarachnoid Block in C Section Patients: What's the Difference between Ephedrine Vs Phenylephrine?

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Author's contribution

The sole author designed, analysed, interpreted and prepared the manuscript.

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Review Article

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ABSTRACT

Aims: The present review is aimed at revisiting the caesarean delivery under spinal anesthesia, comparing the application of two different vasopressors namely ephedrine and phenylephrine. For understanding beneficiary along with unwanted hypotensive effect between the two drugs.
Discussion: Elective cesarean sections are so commonly performed under spinal anesthesia. Unfortunately, this procedure often leads to hypotension, which may adversely jeopardize maternal and fetal outcomes. Immediate post spinal anesthesia hypotension is basically elucidated as reduction of normal blood pressure, estimated 80–90% below its baseline value. Various strategies have been implemented to reduce the incidence of spinal anesthesia-induced hypotension, including the immediate administration of vasopressors such as phenylephrine and or ephedrine, aimed for preventing and treating hypotension. Clinically, both phenylephrine and ephedrine were proven effective in protecting normal maternal hemodynamic balance by counteract the unwanted

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effect of hypotension both to the maternal and the newborn. Newborns benefited more from the application of phenylephrine in elective cesarean delivery, compared to those who receive ephedrine, but unfortunately not in unscheduled emergency cesarean delivery or in vulnerable parturient with pre-eclampsia. More in depth clinical study should be conducted to obtain more conclusive results, especially regarding the most effective prevention and predictive method, its active surveillance during critical anesthesiology procedure throughout cesarean sectio and recovery from hypotension chronologically.

Keywords: Hemodynamic; vasopressors; management; elective cesarean delivery; Ephedra; C9H13NO2; intravenous.

1. INTRODUCTION

"Hypotension, or settled low blood pressure, is a common side effect of spinal anesthesia" (Ghidini, et al., 2023). "This gap of sudden drop in blood pressure can occur during spinal anesthesia due to the rapid onset of sympatholysis, which causes peripheral vasodilation and reduced venous return. This leads to a drop in systemic vascular resistance and cardiac output, often accompanied by a decreased cardiac preload" (Ghidini, et al., 2023; Knigin, et al., 2020). Factors like the dose of the anesthetic, patient position, and pregnancy can influence the severity and speed of this sudden drop in blood pressure Intraoperative hypotension immediately after spinal anesthesia conducted for Caesarean section is associated with maternal morbidity and mortality (Zwane, et al., 2018; Lin et al., 2022) and also to the neonatal outcomes (Knigin, et al., 2020). Even though it can pose dangerous risks both for the maternal and neonatal but actually it is manageable (Park & Choi, 2024).

Hypotension actually is a recurrent side effect of spinal anesthesia, occurring silently and immediately, in the range of incidence varies in divergent studies, from 7.4% to 74.1% of cases (Šklebar, et al., 2019). Several factors, including maternal characteristics (Santoso, et al., 2024) and anesthetic techniques (Bhat, et al., 2024), can affect the risk of occurring hypotension. Basically, it occurs due to a decrease in systemic vascular resistance and/or cardiac output, often exacerbated by the supine position during procedures like cesarean sections (Patel & Ninanve, 2024). "The physiological changes that occur during pregnancy necessitate modifications to anesthesia and analgesia procedures to provide safe and efficient care for the expectant patient" (Patel & Ninave, 2024). While mild hypotension may be managed with volume expansion, e.g., infusion of fluids to increase effective blood volume (Chooi, et al., 2017); but on the other hand severe or expeditiously worsening condition mandate aggressive treatment with vasopressors like phenylephrine or ephedrine, and in extreme cases, epinephrine (Biricik, et al., 2020). The aim of this review is to compare the effectivity of ephedrine versus norepinephrine in treating anesthesia-induced hypotension in c- sectio patients.

2. EPHEDRINE

Ephedra or Ma huang species of plants are widely used for their medicinal properties. Ma-huang had variable effects on blood pressure and increased heart rate in healthy, normotensive adults (White, et al., 1997). Polysaccharides are macromolecular components in Ephedra plants. At present time, the foremost polysaccharides secluded from Ephedra are polysaccharides A, B, C, D, and E, and hyperbranched acidic polysaccharides (ESP-B4) (Tang, et al., 2023). The main functioning constituent in the Ephedra species is ephedrine (González-Juárez, et al., 2020). Ephedrine is a phenethylamine alkaloid. which, as naturally occurring ephedrine alkaloids, possesses two chiral center carbon atoms and has four stereoisomers, (1R,2S)–(−)–ephedrine, (1S,2R)–(+)–ephedrine, (1S,2S)–(+)–pseudoephedrine, and (1R,2R)–(−)–pseudoephedrine (Segawa, et al., 2021). Chemically, it's a substituted amphetamine derivative with a hydroxyl group (-OH) and an amino group, making it similar to epinephrine and methamphetamine.

"Ephedrine, a stereoisomer to the widely-known pseudoephedrine, is a sympathomimetic amine with unique effects due to its indirect mechanism than other sympathomimetic agents like pseudoephedrine and phenylephrine" (Mandal, et al., 2024). "Ephedrine, a synthetic noncatecholamine agonist at α, β1, and β2 receptors, acts as both a direct and indirect sympathomimetic" (Statler, et al., 2023). Its

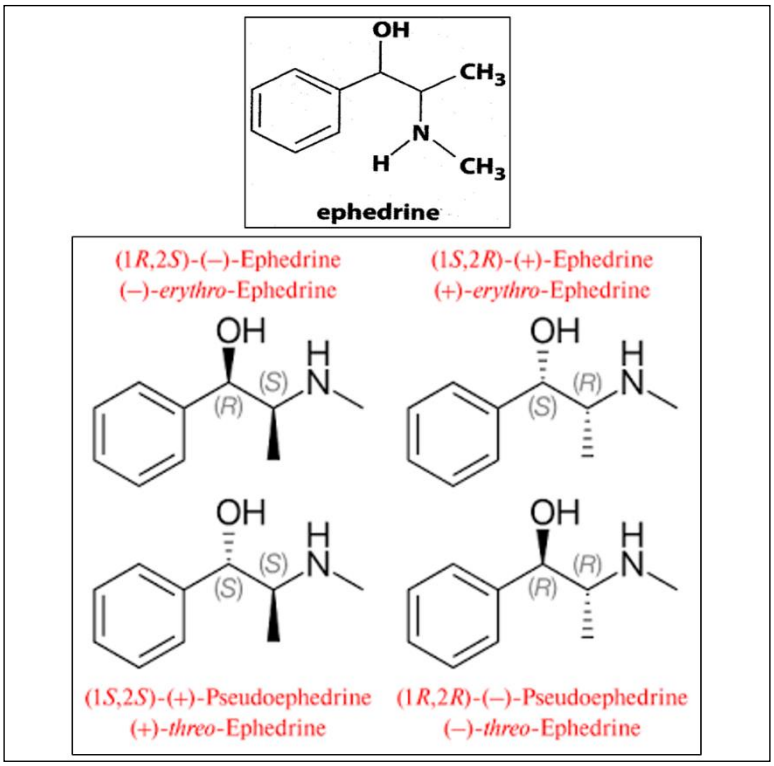

Fig. 1. Chemical structure of Ephedrine and its four stereoisomers

primary method of action is secondarily accomplished by disrupting neuronal traffic of norepinephrine reuptake and displacing more norepinephrine from storage vesicles in the nerve cells (National Center for Biotechnology Information, 2025). "This mode of action permits norepinephrine to dwell sufficiently and extendedly in the synapse cleft region to bind postsynaptic alpha and beta receptors. This prolonged interaction is crucial for norepinephrine ability to effectively modulate various brain functions like arousal, attention, and mood" (Maity, et al., 2022).

"Ephedrine's indirect mechanism results in heart's activated chronotropic effect, marked by sustained or even increased heart rate" (Kitaura, et al., 2019) as "a consequences of the norepinephrine's ability to bind alpha and beta receptors" (Gordan, et al., 2015), whereas more direct sympathomimetic like phenylephrine results in reflex bradycardia, in higher doses, it can trigger dangerous and extreme reflex bradycardia or even asystole (Horowitz, et al., 2023).

Intravenous ephedrine administration leads to several hemodynamics changes (Wang, et al., 2025) which consists of

1. increases in heart rate which sometime can also cause or worsen tachycardia (Abe, et al., 2023), as in case of propofol anesthesia which actually augments the pressor responses to i.v. ephedrine (Kanaya, et al., 2002),
2. increases in systolic and diastolic blood pressure (Ali Elnabtity & Selim, 2018). Prophylactic ephedrine significantly attenuated the decrease in blood pressure and heart rate during induction of anesthesia with fentanyl and propofol (Shin, et al., 2002).
3. Mean arterial pressure (Ali Elnabtity & Selim, 2018) and cardiac output (Mon et al., 2017). A study conducted by Uemura et al which aimed to determine whether aging would reduce the pressor effect of ephedrine on hypotension during general anesthesia. Those researchers found out that "the administration of ephedrine significantly increased MAP and CO; however, no significant correlation with age was observed in patients aged > 45 years. These findings suggest that ephedrine is effective for the correction of hypotension during general anesthesia, even in elderly patients" (Uemura, et al., 2023), and

4. coronary artery blood flow (Ishikawa, et al., 2011). Ishikawa et al., reported co-administration of ephedrine prevents reductions in cardiac output and systemic oxygen delivery secondary to lung compression maneuvers during one-lung ventilation, without reducing arterial oxygenation

"Ephedrine is recommended to treat hypotension during general or regional anesthesia procedure" (Statler, et al., 2023). Worthy to note that the indirect effect is most profound on arterial blood pressure (Ali Elnabtity & Selim, 2018; Shin, et al., 2002), while on the other hand the direct vasoconstriction action roles on vessels, especially more on the venous system, just as in the case of their vasoconstrictive action on the nasal mucosa, ephedrine (and also pseudoephedrine) are highly efficient amines for relief of nasal congestion (Laccourreye, et al., 2015). And in systemic context, therefore, the administration of ephedrine is effective in elevating central venous pressure when the patient is challenged with fluids (El-Mekawy, et al., 2012).

Clinically, stimulation of α-1 adrenergic smooth muscle receptors within vasculature wall results in an increase in systemic vascular resistance (Trammel & Sapra, 2023) with the consequences of elevation in blood pressure, either systolic or both with diastolic (Magder, 2018). Stimulation of β-1 receptors (Alhayek & Preuss, 2023) by norepinephrine and ephedrine directly elevates cardiac chronotropic and inotropic (lin, et al., 2022). eventually, β-2 adrenergic receptor stimulation in the lungs outturn in bronchodilation (Abosamak & Shahin, 2023) with ephedrine administration, which widens the airways and eases breathing, though it is not as pronounced as its cardiovascular effects (Statler, et al., 2023).

3. PHENYLEPHRINE

"Phenylephrine is a small-molecule compound of organic substance with the molecular formula C9H13NO2 and a molecular weight of 167.205 g/mol. It is a highly hydrophilic compound, with an experimental log P of -0.3. Phenylephrine's chemical structure is that of a substituted phenethylamine, specifically (R)-β,3-dihydroxy-N-methylphenethylamine. It is closely related to epinephrine, differing only by the absence of one hydroxyl group on the phenyl ring. Phenylephrine is a chiral compound, and the (R)-stereoisomer is the form used in medications. The molecule contains an aromatic ring, a hydroxyl group (-OH), and an amine group (-NH2)" (National Center for Biotechnology Information, 2025).

Phenylephrine incipiently performs as a relatively selective α-1 adrenergic receptor agonist (Richards, et al., 2023) and displays negligible beta-adrenergic activity (Torp, et al., 2001) or inotropic effect (Varma, et al., 2003) and therefore does not increase contractility (Kalmar, et al., 2018). "Alpha-1 agonists are a group of medications applied in the stewardship of many diseases, including hypotension as in the case of post-spinal hypotension in pre-eclamptic patients undergoing caesarean section" (Mohta et al., 2023), hypoperfusion (Meng, et al., 2024), circulatory shock (Hollenberg, 2011), septic shock (Hawn, et al., 2021; Bonfiglio, et al., 1990), cardiac arrest (Cope, et al., 1997), pulmonary arrest (Joyce, et al., 1983) and also other lower acuity conditions such happen in accommodative system of the eyes (Esteve-Taboada, et al., 2016).

Consequently, "the medication is an optimal choice for raising mean arterial pressure" (Etania, et al., 2025) by inducing vasoconstriction in both veins and arteries (Højlund, 2024) and enhancing cardiac preload (Kalmar, et al., 2018, Valks, et al., 2002) without exerting significant effects on cardiac myocytes (Valks, et al., 2003). "The US Food and Drug Administration (FDA) has approved intravenous phenylephrine hydrochloride to elevate blood pressure in adults experiencing clinically significant hypotension, primarily attributed to vasodilation, in situations such as septic shock or anesthesia" (The US Food and Drug Administration (FDA) (2025).

"Phenylephrine HCl is also an over-the-counter (OTC) medication in ophthalmic formulations to facilitate mydriasis and vasoconstriction of conjunctival blood vessels. Furthermore, this medication is administered intranasally to treat uncomplicated nasal congestion and is an OTC additive to topical hemorrhoid medications". (Richards, et al., 2023)

4. WHICH ONE IS PREFERRABLE FOR C SECTIO?

In the past 20 years, many studies have differentiated the effect of phenylephrine with ephedrine to prevent or treat hypotension in elective or emergency cesarean delivery and parturient with pre-eclampsia (Etania et al., 2025;

Park & Choi, 2024; Santoso, et al., 2024; Ghidini, et al., 2023; Xu, et al., 2018). These studies generally indicate that both drugs are effective in preventing or treating hypotension, but they have different characteristics and potential benefits or drawbacks.

During those past decade, phenylephrine, a primarily alpha-adrenergic agonist, has been the preferred vasopressor for cesarean sections (Park, et al., 2024). Phenylephrine, a potent selective α-1 adrenergic agonist with minimal to no β-agonist activity (Richards, et al., 2023). “the use of phenylephrine is recommended and an optimal choice for raising mean arterial pressure by inducing vasoconstriction in both veins and arteries and enhancing cardiac preload without exerting significant effects on cardiac myocytes. The US Food and Drug Administration (FDA) has approved intravenous phenylephrine hydrochloride to elevate blood pressure in adults experiencing clinically significant hypotension, primarily attributed to vasodilation, in situations such as septic shock or anesthesia” (US FDA, 2012). Phenylephrine has earned popularity and preference owing to its advantages over ephedrine, particularly in preventing and treating spinal hypotension during anesthesia.

While both drugs can raise blood pressure, phenylephrine is favored for its more targeted vasoconstrictive action (Højlund, 2024) and reduced impact on beta-adrenergic receptors (Torp, et al., 2001), which can lead to fewer side effects (Xu, et al., 2018). “In managing maternal hypotension during spinal anesthesia for cesarean delivery, both phenylephrine and ephedrine are used, but they have different effects on neonates. Phenylephrine, a pure alpha-adrenergic agonist, is associated with higher umbilical artery pH values, potentially indicating less fetal acidosis, but it may also cause maternal bradycardia” (Cooper, et al., 2002). Ephedrine, a mixed alpha- and beta-adrenergic agonist, can cause fetal tachycardia and acidosis due to its placental crossing and stimulation of fetal beta-adrenergic receptors (Landau, et al., 2011).

“Closed noninvasive monitoring during cesarean section (C-section) can help prevent hypotension” (Vasile, et al., 2023; Illies, et al., 2012) and actually have the potential to revolutionize patient monitoring (Fortin, et al., 2021). “Technique such as continuous, non-invasive blood pressure monitoring systems” (Fortin, et al., 2021), like the CNAP device, are more effective at detecting rapid blood pressure changes and hypotension compared to traditional intermittent methods (Yamada, et al., 2018). This allows for timely intervention with vasopressors and fluids, potentially preventing or mitigating hypotensive episodes immediately and prevent a more catastrophe condition.

In addition to the pharmacological characteristics of the two vasopressors discussed previously, there is also the potential for interactions with other drugs that are also commonly used in parturients, for example oxytocin and methergine which are commonly used post-delivery to control bleeding (Wormer, et al., 2024), but oxytocin is recommended as the first-line treatment, according to the World Health Organization (WHO) (WHO, 2012) and the “American College of Obstetricians and Gynecologists (ACOG). Methergine is a second-line option used if bleeding continues after oxytocin” (Blumenfeld, et al., 2015). The combined effects of oxytocin and phenylephrine or ephedrine can interact significantly, with both ephedrine and epinephrine potentially increasing the risk of hypertension and severe headaches when used with oxytocin, requiring close monitoring of blood pressure (Statler, 2023). While phenylephrine can actually counteract oxytocin-induced hypotension, ephedrine and epinephrine pose a significant risk of increasing blood pressure and are contraindicated with oxytocin in certain contexts.

5. CONCLUSION

Ephedrine and phenylephrine, while crucial for managing hypotension during cesarean sections, have limitations that include potential side effects on both the mother and the fetus, and the need for careful titration to avoid complications. These limitations stem from the drugs' mechanisms of action and the unique physiological considerations of pregnancy. More advanced study, clinically or biomedically, should be encouraged in order to draw more indisputable results, especially in the context of the most effective prevention and predictive method, its active surveillance during critical anesthesiology procedure throughout cesarean sectio and recovery from hypotension chronologically.

CONSENT AND ETHICAL APPROVAL

It is not applicable.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that no generative AI technologies such as large language models (chatgpt, copilot, etc) and text-to-image generators have been used during writing or editing of this manuscript.

COMPETING INTERESTS

Author has declared that no competing interests exist.

REFERENCES

Abe, S., Suzuki, K., Hamamura, M., Tamanoi, T., Takahashi, K., Wakamatsu, K., Yoshida, K., Kawaai, H., & Yamazaki, S. (2023). Ventricular tachycardia following ephedrine during dexmedetomidine dental procedural sedation. *Anesthesia Progress, 70*(4), 184–190. https://doi.org/10.2344/anpr-70-03-04

Abosamak, N. E. R., & Shahin, M. H. (2023). Beta2 receptor agonists and antagonists. [Updated 2023 Jul 3]. In *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK559069/

Alhayek, S., & Preuss, C. V. (2023). Beta 1 receptors. [Updated 2023 Aug 14]. In *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532904/

Ali Elnabtity, A. M., & Selim, M. F. (2018). Norepinephrine versus ephedrine to maintain arterial blood pressure during spinal anesthesia for cesarean delivery: A prospective double-blinded trial. *Anesthesia, Essays and Researches, 12*(1), 92–97. https://doi.org/10.4103/aer.AER_204_17

Bhat, A. D., Singh, P. M., & Palanisamy, A. (2024). Neuraxial anesthesia-induced hypotension during Caesarean section. *BJA Education, 24*(4), 113–120. https://doi.org/10.1016/j.bjae.2024.01.003

Biricik, E., Karacaer, F., Ünal, İ., Sucu, M., & Ünlügenç, H. (2020). O efeito de epinefrina, norepinefrina e fenilefrina no tratamento da hipotensão pós-raquianestesia: Estudo clínico comparativo [The effect of epinephrine for the treatment of spinal-hypotension: Comparison with norepinephrine and phenylephrine, clinical trial]. *Brazilian Journal of Anesthesiology (Elsevier), 70*(5), 500–507. https://doi.org/10.1016/j.bjan.2020.04.017

Blumenfeld, Y. J., El-Sayed, Y. Y., Nelson, L. M., & Bateman, B. T. (2015). Second-line uterotonics and the risk of hemorrhage-related morbidity. *American Journal of Obstetrics and Gynecology, 212*(5), 642.e1–642.e6427. https://doi.org/10.1016/j.ajog.2015.01.008

Bonfiglio, M. F., Dasta, J. F., Gregory, J. S., Townsend, M. C., Reilley, T. E., & Flancbaum, L. (1990). High-dose phenylephrine infusion in the hemodynamic support of septic shock. *DICP: The Annals of Pharmacotherapy, 24*(10), 936–939. https://doi.org/10.1177/106002809002401005

Chooi, C., Cox, J. J., Lumb, R. S., Middleton, P., Chemali, M., Emmett, R. S., Simmons, S. W., & Cyna, A. M. (2017). Techniques for preventing hypotension during spinal anesthesia for caesarean section. *The Cochrane Database of Systematic Reviews, 8*(8), CD002251. https://doi.org/10.1002/14651858.CD002251.pub3

Cooper, D. W., Carpenter, M., Mowbray, P., Desira, W. R., Ryall, D. M., & Kokri, M. S. (2002). Fetal and maternal effects of phenylephrine and ephedrine during spinal anesthesia for cesarean delivery. *Anesthesiology, 97*(6), 1582–1590. https://doi.org/10.1097/00000542-200212000-00034

Cope, J. T., Mauney, M. C., Banks, D., Binns, O. A., Moore, C. L., Rentz, J. J., Shockey, K. S., King, R. C., Kron, I. L., & Tribble, C. G. (1997). Intravenous phenylephrine preconditioning of cardiac grafts from non-heart-beating donors. *The Annals of Thoracic Surgery, 63*(6), 1664–1668. https://doi.org/10.1016/s0003-4975(97)00092-1

El-Mekawy, N. M. (2012). Comparative study between ephedrine infusion vs. CO/post loading of fluids for prevention of hypotension in emergency cesarean section under spinal anesthesia. *Egyptian Journal of Anaesthesia, 28*(3), 193–198. https://doi.org/10.1016/j.egja.2012.02.009

Esteve-Taboada, J. J., Del Águila-Carrasco, A. J., Bernal-Molina, P., Ferrer-Blasco, T.,

López-Gil, N., & Montés-Micó, R. (2016). Effect of phenylephrine on the accommodative system. *Journal of Ophthalmology, 2016*, 7968918. https://doi.org/10.1155/2016/7968918

Etania, C., Hanafie, A., & Lubis, A. P. (2025). Prophylactic effectiveness of phenylephrine 100 mcg and ephedrine 10 mg on the incidence of spinal anesthesia induced hypotension in patients undergoing cesarean section. *Indonesian Journal of Anesthesiology and Reanimation, 7*(2), 85–92. https://doi.org/10.20473/ijar.V7I22025.85-92

Fortin, J., Rogge, D. E., Fellner, C., Flotzinger, D., Grond, J., Lerche, K., & Saugel, B. (2021). A novel art of continuous noninvasive blood pressure measurement. *Nature Communications, 12*(1), 1387. https://doi.org/10.1038/s41467-021-21271-8

Ghidini, A., Vanasche, K., Cacace, A., Cacace, M., Fumagalli, S., & Locatelli, A. (2023). Side effects from epidural analgesia in laboring women and risk of cesarean delivery. *AJOG Global Reports, 4*(1), 100297. https://doi.org/10.1016/j.xagr.2023.100297

González-Juárez, D. E., Escobedo-Moratilla, A., Flores, J., Hidalgo-Figueroa, S., Martínez-Tagüeña, N., Morales-Jiménez, J., Muñiz-Ramírez, A., Pastor-Palacios, G., Pérez-Miranda, S., Ramírez-Hernández, A., Trujillo, J., & Bautista, E. (2020). A review of the *Ephedra* genus: Distribution, ecology, ethnobotany, phytochemistry and pharmacological properties. *Molecules (Basel, Switzerland), 25*(14), 3283. https://doi.org/10.3390/molecules25143283

Gordan, R., Gwathmey, J. K., & Xie, L. H. (2015). Autonomic and endocrine control of cardiovascular function. *World Journal of Cardiology, 7*(4), 204–214. https://doi.org/10.4330/wjc.v7.i4.204

Hawn, J. M., Bauer, S. R., Yerke, J., Li, M., Wang, X., Reddy, A. J., Mireles-Cabodevila, E., & Sacha, G. L. (2021). Effect of phenylephrine push before continuous infusion norepinephrine in patients with septic shock. *Chest, 159*(5), 1875–1883. https://doi.org/10.1016/j.chest.2020.11.051

Højlund, J., Cihoric, M., & Foss, N. B. (2024). Vasoconstriction with phenylephrine increases cardiac output in preload dependent patients. *Journal of Clinical Monitoring and Computing, 38*(5), 997–1002. https://doi.org/10.1007/s10877-024-01186-7

Hollenberg, S. M. (2011). Vasoactive drugs in circulatory shock. *American Journal of Respiratory and Critical Care Medicine, 183*(7), 847–855. https://doi.org/10.1164/rccm.201006-0972CI

Horowitz, A. J., Frey, D., Denault, D., & Smith, T. (2023). Sympathomimetics. In *StatPearls* [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan–. Available from: https://www.ncbi.nlm.nih.gov/books/NBK546597/

Ilies, C., Kiskalt, H., Siedenhans, D., Meybohm, P., Steinfath, M., et al. (2012). Detection of hypotension during Caesarean section with continuous non-invasive arterial pressure device or intermittent oscillometric arterial pressure measurement. *British Journal of Anaesthesia, 109*(3), 413–419.

Ishikawa, S., Makino, F., & Kobinata, S. (2011). Co-administration of ephedrine prevents reductions in cardiac output and systemic oxygen delivery secondary to lung compression maneuvers during one-lung ventilation, without reducing arterial oxygenation. *Journal of Anesthesia, 25*, 163–169.

Joyce, S. M., Barsan, W. G., & Doan, L. A. (1983). Use of phenylephrine in resuscitation from asphyxial arrest. *Annals of Emergency Medicine, 12*(7), 418–421. https://doi.org/10.1016/s0196-0644(83)80335-7

Kalmar, A. F., Allaert, S., Pletinckx, P., Maes, J. W., Heerman, J., Vos, J. J., Struys, M. M. R. F., & Scheeren, T. W. L. (2018). Phenylephrine increases cardiac output by raising cardiac preload in patients with anesthesia induced hypotension. *Journal of Clinical Monitoring and Computing, 32*(6), 969–976. https://doi.org/10.1007/s10877-018-0126-3

Kanaya, N., Satoh, H., Seki, S., Nakayama, M., & Namiki, A. (2002). Propofol anesthesia enhances the pressor response to intravenous ephedrine. *Anesthesia and Analgesia, 94*(5). https://doi.org/10.1097/00000539-200205000-00029

Kitaura, A., Houri, K., & Nakao, S. (2019). Ephedrine-induced increases in blood pressure and heart rate due to suspected cardiac sympathetic denervation

supersensitivity in a patient with Parkinson's disease under spinal anesthesia. *The American Journal of Case Reports, 20*, 1104–1107. https://doi.org/10.12659/AJCR.916188

Knigin, D., Avidan, A., & Weiniger, C. F. (2020). The effect of spinal hypotension and anesthesia-to-delivery time interval on neonatal outcomes in planned cesarean delivery. *American Journal of Obstetrics and Gynecology, 223*(5), 747.e1–747.e13. https://doi.org/10.1016/j.ajog.2020.08.005

Laccourreye, O., Werner, A., Giroud, J. P., Couloigner, V., Bonfils, P., & Bondon-Guitton, E. (2015). Benefits, limits and danger of ephedrine and pseudoephedrine as nasal decongestants. *European Annals of Otorhinolaryngology, Head and Neck Diseases, 132*(1), 31–34. https://doi.org/10.1016/j.anorl.2014.11.001

Landau, R., Liu, S. K., Blouin, J. L., Smiley, R. M., & Ngan Kee, W. D. (2011). The effect of maternal and fetal β_2-adrenoceptor and nitric oxide synthase genotype on vasopressor requirement and fetal acid-base status during spinal anesthesia for cesarean delivery. *Anesthesia and Analgesia, 112*(6), 1432–1437. https://doi.org/10.1213/ANE.0b013e3182179424

Lin, T.-Y., Mai, Q. N., Zhang, H., Wilson, E., Chien, H.-C., Yee, S. W., Giacomini, K. M., Olgin, J. E., & Irannejad, R. (2022). Cardiac contraction and relaxation are regulated by beta 1 adrenergic receptor-generated cAMP pools at distinct membrane locations.

Magder, S. (2018). The meaning of blood pressure. *Critical Care, 22*, 257. https://doi.org/10.1186/s13054-018-2171-1

Maity, S., Abbaspour, R., Nahabedian, D., & Connor, S. A. (2022). Norepinephrine, beyond the synapse: Coordinating epigenetic codes for memory. *International Journal of Molecular Sciences, 23*(17), 9916. https://doi.org/10.3390/ijms23179916

Mandal, P., Singh, A., Sharma, K., Jain, P., Manisha, Chaudhary, M., & Chinmayee, P. (2024). Ephedrine and pseudoephedrine: A comprehensive review of their pharmacology and clinical applications. *Journal of Chemical Health Risks, 14*(1), 1447–1455.

Meng, L., Sun, Y., Zhao, X., Meng, D. M., Liu, Z., Adams, D. C., McDonagh, D. L., & Rasmussen, M. (2024). Effects of phenylephrine on systemic and cerebral circulations in humans: A systematic review with mechanistic explanations. *Anaesthesia, 79*(1), 71–85. https://doi.org/10.1111/anae.16172

Mohta, M., Kumari, S., Malhotra, R. K., Tyagi, A., & Agarwal, R. (2023). Calculation of effective dose of phenylephrine bolus for treatment of post-spinal hypotension in pre-eclamptic patients undergoing caesarean section – a non-randomised controlled trial. *International Journal of Obstetric Anesthesia, 56*, 103929. https://doi.org/10.1016/j.ijoa.2023.103929

Mon, W., Stewart, A., Fernando, R., Ashpole, K., El-Wahab, N., MacDonald, S., Tamilselvan, P., Columb, M., & Liu, Y. M. (2017). Cardiac output changes with phenylephrine and ephedrine infusions during spinal anesthesia for cesarean section: A randomized, double-blind trial. *Journal of Clinical Anesthesia, 37*, 43–48. https://doi.org/10.1016/j.jclinane.2016.11.001

National Center for Biotechnology Information. (2025). PubChem Compound Summary for CID 6041, Phenylephrine. Retrieved August 21, 2025, from https://pubchem.ncbi.nlm.nih.gov/compound/Phenylephrine

National Center for Biotechnology Information. (2025). PubChem Compound Summary for CID 9294, Ephedrine. Retrieved August 20, 2025, from https://pubchem.ncbi.nlm.nih.gov/compound/Ephedrine

Park, H. S., & Choi, W. J. (2024). Use of vasopressors to manage spinal anesthesia-induced hypotension during cesarean delivery. *Anesthesia and Pain Medicine, 19*(2), 85–93. https://doi.org/10.17085/apm.24037

Patel, S., & Ninave, S. (2024). Postspinal anesthesia hypotension in caesarean delivery: A narrative review. *Cureus, 16*(4), e59232. https://doi.org/10.7759/cureus.59232

Richards, E., Lopez, M. J., & Maani, C. V. (2023). Phenylephrine. In *StatPearls* [Internet]. StatPearls Publishing. Available from https://www.ncbi.nlm.nih.gov/books/NBK534801/

Santoso, T. B., Widodo, W., Istiqomah, N., & Purwaningsih, H. (2024). The relationship between maternal characteristics and intraoperative hypotension during

cesarean section using spinal anesthesia. *Journal of Maternal-Fetal & Neonatal Medicine, 37*(1), 1–10.

Segawa, H., Okada, Y., Yamamuro, T., Kuwayama, K., Tsujikawa, K., Kanamori, T., & Iwata, Y. T. (2021). Stereoselective analysis of ephedrine and its stereoisomers as impurities and/or by-products in seized methamphetamine by supercritical fluid chromatography/tandem mass spectrometry. *Forensic Science International, 318*, 110591. https://doi.org/10.1016/j.forsciint.2020.110591

Shin, C. H., Kim, S. S., Kim, D. S., Ryu, S. J., Jang, T. H., Kim, S. H., & Kim, K. H. (2002). The effect of ephedrine on blood pressure and heart rate during induction with propofol and fentanyl in hysterectomy patients. *Korean Journal of Anesthesiology, 43*(1), 33–37.

Šklebar, I., Bujas, T., & Habek, D. (2019). Spinal anesthesia-induced hypotension in obstetrics: prevention and therapy. *Acta Clinica Croatica, 58*(Suppl 1), 90–95. https://doi.org/10.20471/acc.2019.58.s1.13

Statler, A. K., Maani, C. V., & Kohli, A. (2023). Ephedrine. In *StatPearls* [Internet]. StatPearls Publishing. Available from https://www.ncbi.nlm.nih.gov/books/NBK547661/

Tang, S., Ren, J., Kong, L., Yan, G., Liu, C., Han, Y., Sun, H., & Wang, X.-J. (2023). *Ephedrae herba*: A review of its phytochemistry, pharmacology, clinical application, and alkaloid toxicity. *Molecules, 28*(2), 663. https://doi.org/10.3390/molecules28020663

The US Food and Drug Administration (FDA). (2025). *Phenylephrine Hydrochloride in 0.9% Sodium Chloride Injection*. https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/216830s000lbl.pdf

Torp, K. D., Tschakovsky, M. E., Halliwill, J. R., Minson, C. T., & Joyner, M. J. (2001). Beta-receptor agonist activity of phenylephrine in the human forearm. *Journal of Applied Physiology (Bethesda, Md. : 1985), 90*(5), 1855–1859. https://doi.org/10.1152/jappl.2001.90.5.1855

Trammel, J. E., & Sapra, A. (2023). Physiology, systemic vascular resistance. In *StatPearls* [Internet]. StatPearls Publishing. Available from https://www.ncbi.nlm.nih.gov/books/NBK556075/

Uemura, Y., Kinoshita, M., & Sakai, Y. (2023). Hemodynamic impact of ephedrine on hypotension during general anesthesia: A prospective cohort study on middle-aged and older patients. *BMC Anesthesiology, 23*, 283. https://doi.org/10.1186/s12871-023-02244-4

US FDA. (2012). *Phenylephrine Hydrochloride. Reference ID: 3235127*. https://www.accessdata.fda.gov/drugsatfda_docs/label/2012/203826s000lbl.pdf

Valks, D. M., Cook, S. A., Pham, F. H., Morrison, P. R., Clerk, A., & Sugden, P. H. (2002). Phenylephrine promotes phosphorylation of Bad in cardiac myocytes through the extracellular signal-regulated kinases 1/2 and protein kinase A. *Journal of Molecular and Cellular Cardiology, 34*(7), 749–763. https://doi.org/10.1006/jmcc.2002.2014

Varma, D., Rindt, H., Chemtob, S., & Mulay, S. (2003). Mechanism of the negative inotropic effects of α_1-adrenoceptor agonists on mouse myocardium. *Canadian Journal of Physiology and Pharmacology, 81*, 783–789. https://doi.org/10.1139/y03-071

Vasile, F., La Via, L., Murabito, P., Tigano, S., Merola, F., Nicosia, T., De Masi, G., Bruni, A., Garofalo, E., & Sanfilippo, F. (2023). Non-invasive monitoring during Caesarean delivery: Prevalence of hypotension and impact on the newborn. *Journal of Clinical Medicine, 12*(23), 7295. https://doi.org/10.3390/jcm12237295

Wang, S., Yu, L., Fang, J., & Jiang, Y. (2025). Effects of different doses of ephedrine spinal anesthesia on hemodynamics and adverse reactions in patients undergoing transurethral resection of the prostate. *BMC Urology, 25*(1), 186. https://doi.org/10.1186/s12894-025-01880-x

White, L. M., Gardner, S. F., Gurley, B. J., Marx, M. A., Wang, P. L., & Estes, M. (1997). Pharmacokinetics and cardiovascular effects of ma-huang (*Ephedra sinica*) in normotensive adults. *Journal of Clinical Pharmacology, 37*(2), 116–122. https://doi.org/10.1002/j.1552-4604.1997.tb04769.x

World Health Organization. (2012). *WHO recommendations for the prevention and treatment of postpartum haemorrhage*.

Wormer, K. C., Jamil, R. T., & Bryant, S. B. (2024). Postpartum hemorrhage. In

StatPearls [Internet]. StatPearls Publishing. Available from https://www.ncbi.nlm.nih.gov/books/NBK499988/

Xu, C., Liu, S., Huang, Y., Guo, X., Xiao, H., & Qi, D. (2018). Phenylephrine vs ephedrine in cesarean delivery under spinal anesthesia: A systematic literature review and meta-analysis. *International Journal of Surgery (London, England), 60*, 48–59. https://doi.org/10.1016/j.ijsu.2018.10.039

Yamada, T., Vacas, S., Gricourt, Y., & Cannesson, M. (2018). Improving perioperative outcomes through minimally invasive and non-invasive hemodynamic monitoring techniques. *Frontiers in Medicine, 5*, 144. https://doi.org/10.3389/fmed.2018.00144

Zwane, S., Bishop, D., & Rodseth, R. (2018). Hypotension during spinal anesthesia for Caesarean section in a resource-limited setting: Towards a consensus definition. *Southern African Journal of Anaesthesia and Analgesia, 25*(1), 1–5. https://doi.org/10.1080/22201181.2018.1550872

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