

Epinephrine Versus Phenylephrine Use Before Intubation in Hypotensive Patient at Emergency Department

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ABSTRACT

This research aims to evaluate and compare the efficacy and safety of epinephrine and phenylephrine in the management of hypotension prior to intubation in the emergency department (ED). Epinephrine, a drug that mimics the sympathetic nervous system, and phenylephrine, which mainly affects alpha-1 receptors, have different pharmacological characteristics and may have different effects on blood flow. We performed an extensive review of the literature to find relevant research and examined available data to get a better understanding of the relative effectiveness, safety characteristics, and impact on blood flow of these two substances. Furthermore, we analyzed the frequencies of successful intubation and the resulting results in both groups. Bolus-dose phenylephrine (BDPE) has shown potential in increasing blood pressure in the emergency department (ED) without notable negative effects, indicating its viability as a substitute for epinephrine. Nevertheless, more prospective studies are necessary to validate its safety and efficacy. The use of push-dose vasopressors (PDP) must be carefully considered because of the risk of dosage mistakes and negative consequences. Improving results requires optimizing intubation safety by doing a thorough patient assessment and effectively managing comorbidities, such as metabolic acidosis. This research highlights the need of using evidence-based methods and personalized treatments to manage low blood pressure prior to intubation in the emergency department.

Keywords: *epinephrine, phenylephrine, hypotension, intubation, emergency department, bolus-dose phenylephrine, push-dose vasopressors, hemodynamic effects, patient outcomes.*

INTRODUCTION

This study aims to compare the use of epinephrine and phenylephrine in emergency medicine for managing hypotension before intubation. Epinephrine, a sympathomimetic agent, is commonly used due to its potent vasoconstrictive properties. However, its efficacy in raising blood pressure in hypotensive patients before intubation requires further investigation [1]. The review aims to provide insights into the comparative efficacy, safety profile, and hemodynamic effects of these two agents, guiding clinical decision-making and optimizing patient care. Postintubation hypotension is a life-threatening condition with higher mortality rates and longer intensive care stays. Common causes include drug-mediated vasodilation or positive pressure ventilation consequences. In the emergency department, managing hypotension is challenging and often requires vasopressors. Recently, bolus-dose phenylephrine has been used to treat hypotension during the peri-intubation period, but there is no evidence on its effectiveness in the ED during this period. This study aims to evaluate this practice pattern and efficacy. The use of epinephrine and phenylephrine before intubation in hypotensive patients in the emergency department is a complex decision [2]. Both drugs have distinct pharmacological profiles, with epinephrine acting on both alpha and beta adrenergic receptors, while phenylephrine primarily acts on alpha-1 receptors. This can lead to divergent hemodynamic responses, with epinephrine potentially causing tachycardia and increased oxygen consumption. The choice of vasopressor agent should also consider patient-specific factors like comorbidities and medication history. Comparative studies are essential for optimizing patient care [3].

The study compares the effectiveness of epinephrine and phenylephrine in raising blood pressure in hypotensive patients in the emergency department, assesses safety, examines hemodynamic effects, and compares intubation success rates and outcomes between the two groups.

METHOD AND MATERIAL

This study uses secondary qualitative research to compare epinephrine and phenylephrine use before intubation in hypotensive patients in the ED, analyzing existing data for new insights. The study will conduct a comprehensive literature search using electronic databases, reference lists, and systematic reviews to identify relevant studies related to epinephrine, phenylephrine, intubation, hypotension, and emergency departments.

Pharmacology Consideration

Bolus-dose phenylephrine (BDPE) is commonly used to treat hypotension in the operating room, prompting calls for its use in the Emergency Department (ED). However, there are few published data on the safety of BDPE use in the ED, with primary concerns including the potential to cause dangerous hypertension or reflex bradycardia. A structured chart review was conducted for all patients who received BDPE from preloaded syringes over 42 months. The study identified 181 cases of ED use, with 147 having complete pre/post vital signs. Five adverse events were identified, and no serious adverse events were found. Three patients developed systolic blood pressure > 180 mm Hg, while no patients had diastolic blood pressure > 110. Two patients developed bradycardia post-drug, but MAP improved despite bradycardia [4]. The study concluded that BDPE does not appear to cause reflex bradycardia or hypertension requiring intervention among hypotensive ED patients. The apparent safety of BDPE should be confirmed in prospective trials. Several studies from the anesthesia literature support the use of peripherally administered bolus doses of diluted vasopressors, or “bolus-dose vasopressors,” for transient hypotension. BDPE has several characteristics that make it ideal for use in the ED setting, such as its fast onset of action and ability to be administered peripherally [5]. Anesthesiologists use small doses of vasopressors like epinephrine, phenylephrine, and ephedrine to treat

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hypotension and maintain perfusion [6]. FDA-approved labeling includes indications, preparation, and dosing recommendations. These vasopressors are typically administered as continuous intravenous infusions outside the operating room setting.

While being hospitalized, it is crucial to take into account the risk of low blood pressure and its related consequences in order to ensure positive patient outcomes. There has been a significant surge in the use of push-dose vasopressors (PDP) in non-operating room settings as a means to counteract the detrimental consequences of low blood pressure. This study assesses the efficacy of PDP in its conventional perioperative context, as well as in emerging applications like as the emergency department and critical care unit. Articles assessing PDP demonstrate significant improvements in blood pressure across all medications, however they vary in terms of the occurrence of negative effects. Furthermore, most studies lack a direct comparison of PDP medications in terms of both safety and effectiveness. The agents used as peripheral vasoconstrictors, such as epinephrine, phenylephrine, norepinephrine, vasopressin, and ephedrine, differ in terms of their mechanism of action, commencement of effect, and duration of activity. The discrepancies in pharmacology, together with the existing literature, might result in variances in the desired pharmacodynamic profile (PDP) for different clinical situations. Numerous negative incidents linked to PDP have resulted from mistakes in dosage, emphasizing the need of educating individuals about the proper use of these substances. Further investigation is required to provide more clarity on the potential dangers and advantages of PDP in therapeutic settings, as well as to ascertain the really desired form of PDP [7]. Thorough deliberation is necessary while assessing the suitability of this way of administering vasopressors in different clinical situations.

Rapid sequence intubation (RSI) is crucial in emergency situations, but if not done correctly, it can lead to fatal consequences. Low systolic blood pressure during RSI increases the risk of cardiac arrest. Push-dose pressors (PDP) have been used in the operating room to control blood pressure, but their implementation in normal emergency care has not yet occurred. The emergency department faces challenges in providing secure administration, such as managing unknown patients, dealing with overcrowding, and relying on verbal instructions. PDP can introduce additional hazards to patient safety, including precise dosage computation, drug dilution, and step-by-step delivery of incremental push-doses. A quality improvement initiative in the emergency department included an RSI package with PDP mixing guidelines. The main nurse prepared and administered PDP according to the provided instructions, recording vital signs before and after surgery. Adverse effects such as extravasation and dysrhythmias were monitored during the 30-minute administration of PDP [8]. This study aimed to describe the current use of etomidate and other induction agents in patients with sepsis and compare adverse events between etomidate and ketamine in sepsis. The National Emergency Airway Registry (NEAR) data set was used to analyze the distribution of induction agents used in sepsis patients. The majority (71%) were intubated with etomidate as the initial induction agent. Etomidate was less frequently used in sepsis patients than nonsepsis patients, with ketamine being the most frequently used alternative. Postprocedure hypotension was higher between those intubated with ketamine versus etomidate (74% vs. 50%). Ketamine was associated with more postprocedural hypotension than etomidate. Future clinical trials are needed to determine the optimal induction agent in sepsis patients. With an estimated 1.7 million sepsis cases in the United States per year, optimizing intubation safety is important to improve sepsis outcomes [9].

DISCUSSION

A retrospective cohort study of 2518 emergency department patients who received vasopressors for peri-intubation hypotension found no significant difference in cardiovascular stability outcomes. The primary outcome was a composite of hypotension, bradycardia, and cardiac arrest within 2 hours following vasopressor initiation. Patients with a sepsis or septic shock diagnosis were more likely to receive PDPE before starting continuous infusion NE and more frequently experienced the composite outcome. The study suggests that selection of vasopressors should consider patient-specific factors and product availability, as cardiovascular instability following vasopressor initiation remains unaffected [10]. Push-dose vasopressors are widely used in emergency medicine, but there is limited data supporting their use. Anesthesiology studies focus on sedation and intubation-related hypotension, but these patient populations differ from those in the Emergency Department. The endorsement of PDPs is based on anecdotal or observational data, and deeper examinations are needed to determine their efficacy and safety. This study aimed to estimate preparation and administration times and errors with PD and CI epinephrine and phenylephrine when prepared by an ED/ICU pharmacist. The primary outcome was total preparation and administration time in seconds, while the secondary outcome was major preparation and administration errors. A total of 16 pharmacists participated, including nine ED and seven ICU pharmacists. PD had faster total preparation and administration time and administration time, but not preparation time. PD showed an approximate 70 s decrease in total preparation and administration time versus CI. PD had more major preparation and administration errors, and six PD preparations (18.8%, 6/32) had at least one major preparation and administration error. CI, on the other hand, had no major preparation and administration errors.

The simulation study found that ED/ICU pharmacists had faster median total preparation and administration times for PD epinephrine and phenylephrine versus CI, but PD also had more major preparation and administration errors. Dilutional errors during medication preparation were the cause of 83.3% (5/6) of the overdoses. Pharmacists in the ED/ICU setting have been associated with better patient outcomes and interventions made by pharmacists in this setting include coordinating medication administration, avoidance of medication errors, and preparing medications at the bedside [11]. Emergency medicine is crucial for successful airway management, with rapid-sequence intubation being the most common method. However, emergency physicians must also be able to manage critically ill patients with various physiologic challenges in the peri-intubation setting. First-pass success is crucial, especially in physiologically challenging airways, as multiple attempts increase adverse events. Difficult visualization and intubation occur in 6.6–12% of intubation attempts in critically ill patients. Severe complications occur in 24–28% of endotracheal intubation in critically ill patients, most commonly hypoxemia and hypotension. High-risk comorbid disease and preintubation factors, such as hypoxemia, hypotension, and severe acidosis, are at high risk for peri-intubation hemodynamic collapse and worse outcomes. The incidence of peri-intubation cardiac arrest is as high as 1 in 25 emergency airways in 1 series. Postintubation hypotension (PIH) is more common, occurring as frequently as 25% of emergency intubations, and is associated with increased mortality. Proper preparation and evaluation can help recognize and prevent preintubation risks for decompensation [12].

Intubation is a critical process in the emergency department, and it is essential to identify patients with pulmonary hypertension or right heart failure, avoid hypotension, and treat hypotension. Inappropriate mechanical ventilation settings can lead to high intrathoracic pressure,

and treating massive pulmonary embolism before induction and mechanical ventilation is crucial. In unstable patients, systemic thrombolytics should be administered before intubation. Intubation should be considered for patients with known right ventricle failure or pulmonary hypertension.

Severe hypoxemia can occur due to inadequate preoxygenation, failure to use noninvasive positive pressure ventilation (NIPPV), and failure to use proper PPE. Preintubation hypoxemia is associated with adverse events, and it is crucial to use airborne precautions during intubation and preoxygenation management [13].

Metabolic acidosis is a major challenge and risk for patient decompensation, and it is not corrected by mechanical ventilation. Diagnosis and treatment of the underlying cause are recommended, and patients with severe metabolic acidosis should avoid intubation if possible. The use of sodium bicarbonate is controversial, and it typically does not correct the underlying cause of the acidosis. If given, it should be delivered slowly and reserved for severe cases of metabolic acidemia with a pH < 7.20 [14]. Emergency medicine is crucial for successful airway management, with rapid-sequence intubation being the most common method. However, emergency physicians must also be able to manage critically ill patients with various physiologic challenges in the peri-intubation setting. First-pass success is crucial, especially in physiologically challenging airways, as multiple attempts increase adverse events. Difficult visualization and intubation occur in 6.6–12% of intubation attempts in critically ill patients. Severe complications occur in 24–28% of endotracheal intubation in critically ill patients, most commonly hypoxemia and hypotension. High-risk comorbid disease and preintubation factors, such as hypoxemia, hypotension, and severe acidosis, are at high risk for peri-intubation hemodynamic collapse and worse outcomes. The incidence of peri-intubation cardiac arrest is as high as 1 in 25 emergency airways in 1 series. Postintubation hypotension (PIH) is more common, occurring as frequently as 25% of emergency intubations, and is associated with increased mortality. Proper preparation and evaluation can help recognize and prevent preintubation risks for decompensation.

Intubation is a critical process in the emergency department, and it is essential to identify patients with pulmonary hypertension or right heart failure, avoid hypotension, and treat hypotension. Inappropriate mechanical ventilation settings can lead to high intrathoracic pressure, and treating massive pulmonary embolism before induction and mechanical ventilation is crucial. In unstable patients, systemic thrombolytics should be administered before intubation. Intubation should be considered for patients with known right ventricle failure or pulmonary hypertension. Severe hypoxemia can occur due to inadequate preoxygenation, failure to use noninvasive positive pressure ventilation (NIPPV), and failure to use proper PPE. Preintubation hypoxemia is associated with adverse events, and it is crucial to use airborne precautions during intubation and preoxygenation management. Metabolic acidosis is a major challenge and risk for patient decompensation, and it is not corrected by mechanical ventilation. Diagnosis and treatment of the underlying cause are recommended, and patients with severe metabolic acidosis should avoid intubation if possible. The use of sodium bicarbonate is controversial, and it typically does not correct the underlying cause of the acidosis. If given, it should be delivered slowly and reserved for severe cases of metabolic acidemia with a pH < 7.20 [15].

CONCLUSION

This study compares the use of epinehrine and phenylephrine in managing hypotension before intubation in the emergency

department. Despite epinehrine's efficacy, phenylephrine has shown promise in limited studies. Bolus-dose phenylephrine has shown efficacy without adverse events, but further trials are needed. Proper education and training for healthcare providers are crucial for dosage accuracy and potential adverse effects. Optimizing intubation safety and considering comorbidities is essential for improved patient outcomes.

Potential Conflicts of Interest: None

Competing Interest: None

Acceptance Date: 06-03-2024

REFERENCES

- Smischney NJ, Stoltenberg AD, Schroeder DR, et al. Noninvasive Cardiac Output Monitoring (NICOM) in the Critically Ill Patient Undergoing Endotracheal Intubation: A Prospective Observational Study. *J Intensive Care Med*, 2023;38(12):1108-1120.
- Price J, Moncur L, Lachowycz K, et al. *Predictors of post-intubation hypotension in trauma patients following prehospital emergency anaesthesia: a multi-centre observational study*. Scandinavian Journal of Trauma, Resuscitation and Emergency Medicine, 2023;31(1):26
- Kubena A, Weston S, Alvey H. Push-dose vasopressors in the Emergency Department: a narrative review. *Journal of Emergency and Critical Care Medicine*, 2022;6:22.
- Swenson K, Rankin S, Daconti L, et al. *Safety of bolus-dose phenylephrine for hypotensive emergency department patients*. The American journal of emergency medicine, 2018;36(10):1802-1806
- Holden, D. Ramich J, Timm E, et al. *Safety considerations and guideline-based safe use recommendations for "bolus-dose" vasopressors in the emergency department*. Annals of emergency medicine, 2018;71(1):83-92
- Mets B. *Should norepinephrine, rather than phenylephrine, be considered the primary vasopressor in anesthetic practice?.* Anesthesia & Analgesia, 2016;122(5):1707-1714
- McPherson KL, Kovacic Scherrer NL, Hays WB, et al., *A Review of Push-Dose Vasopressors in the Peri-operative and Critical Care Setting*. Journal of Pharmacy Practice, 2023;36(4):925-932
- Bakhsh A. and Alotaibi L. *Push-Dose Pressors During Peri-intubation Hypotension in the Emergency Department: A Case Series*. Clinical Practice and Cases in Emergency Medicine, 2021;5(4):390-393
- Mohr NM, Pape SG, Runde D, et al. *Etomidate use is associated with less hypotension than ketamine for emergency department sepsis intubations: a NEAR cohort study*. Academic Emergency Medicine, 2020;27(11):1140-1149.
- Schmitt, CJ, Mattson AE, Brown CS, et al. *The incidence of cardiovascular instability in patients receiving various vasopressor strategies for peri-intubation hypotension*. The American Journal of Emergency Medicine, 2023;65:104-108.
- Morley, H Seabury R, Parsels K, et al. *Preparation/administration of push-dose versus continuous infusion epinephrine and phenylephrine: A simulation*. The American Journal of Emergency Medicine, 2023;74:135-139.
- Karamchandani K, Wheelwright J, Yang AL, et al. *Emergency airway management outside the operating room: current evidence and management strategies*. Anesthesia & Analgesia, 2021;133(3):648-662.
- Lentz, S, Grossman A, Koyfman A, et al. *High-risk airway management in the emergency department: diseases and approaches, part II*. The Journal of Emergency Medicine, 2020;59(4):573-585.

14. Lentz, S, Grossman A, Koyfman A, et al. *High-risk airway management in the emergency department. Part I: diseases and approaches*. The Journal of emergency medicine, 2020;59(1):84-95.
15. Acquisto NM, Mosier JM, Bittner EA, et al. *Society of Critical Care Medicine Clinical practice guidelines for rapid sequence intubation in the critically ill adult patient*. Critical care medicine, 2023;51(10):1411-1430.