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Safe use of bolus-dose vasopressors necessitates communication and coordination between caregivers. Bolus-dose vasopressor use differs in the operating room and ED. In the operating room, a (usually) more controlled environment than the ED, anesthesiologists prepare or obtain the medication, make the decision to give the vasopressor, administer the dose, and monitor effects. In the ED, these tasks are likely to be performed by multiple individuals who are less familiar with the practice and have additional tasks to attend to, presenting risks for miscommunication, confusion, and error. As such, organizations should implement systematic safety measures for bolus-dose vasopressors appropriate for the identified potential risks and specific characteristics of the institution and ED.

A summary of recommended practices developed by the authors for safe use of bolus-dose vasopressors according to current medication use guidelines is listed in Figure 3.

CONCLUSION

Despite the apparent common use of bolus-dose vasopressors in the ED setting, no data are available to demonstrate outcome or safety benefits over other patient management strategies. Use of bolus-dose vasopressors in the ED presents a number of safety challenges generally not present in the operating room, where use of these vasopressors is more commonplace. As with all medications, a comprehensive systems-based approach should be used to assess risks and benefits of bolus-dose vasopressors in the ED. The clinical, pharmaceutical, operational, and safety concerns discussed within this article must be considered and addressed by each organization choosing to allow use of bolus-dose vasopressors in the ED. Many of the safety considerations and related concerns with bolus-dose vasopressors can be addressed through application of widely available and accepted safe medication practices.

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b. If they are stored within an ADC, the product name appearing on selection lists should indicate the organization's term for the product ("push" or "bolus" dose vasopressor) rather than only the drug name and concentration to differentiate them from other epinephrine and phenylephrine products stored in the ADC.
   i. Given the nature of situations in which these drugs are most likely to be used, orders may be verbal and the drug will be obtained from the ADC on override (no pharmacist verification); staff should be educated to look for the indication within the product name when making a selection from the ADC.
      (a). We recommend that the ADC display a verification message screen to verify that a bolus-dose vasopressor drug has been selected.

8. Organizations should provide clear, concise, and readily available drug information to support the safe use of bolus-dose vasopressors. An example from drug information resource is provided in Figure 3.[19,20,22]
9. The administration of and response to bolus-dose vasopressors should be clearly documented in the patient's medical record.
10. Staff is to be encouraged to report any adverse events, close calls, or hazardous conditions associated with the use of IV bolus-dose vasopressors, and the information obtained should be used for continuous quality improvement.

IV, Intravenous; *ADC*, automated dispensing cabinet.

Figure 3. Continued.

burden on the pharmacy to continuously reprepare syringes to ensure in-date supply for only occasional use.

Intravenous bolus vasopressor syringes may also be purchased from an outside pharmacy (sterile products compounders). Despite an increase in per-unit cost, purchasing ready-to-use bolus-dose vasopressor syringes from appropriately certified and licensed commercial compounders limits internal work, may reduce risks associated with manually compounding syringes, and typically provides longer beyond-use dates (such as 90 days) because of completion of stability and sterility testing by the outside vendor. In response to quality problems with pharmacy compounders, the Drug Quality and Security Act of 2013 allowed the FDA greater control to regulate these outsourcing pharmacies.[50,51] However, it is the individual organization's responsibility to ensure that any outsourced compounded stocks purchased comply with state and federal regulations and US Pharmacopeia Chapter 797 guidelines.

An alternative to the stocking of ready-to-use syringes is the preparation and stocking of kits containing appropriate instructions, drugs, diluents, syringes, and labels needed to prepare the bolus-dose vasopressor products (eg, all placed in a single labeled ziplock bag). In general, use of such kits reduces the risk of drug product selection, calculation, compounding, and labeling confusion compared with a practitioner's collecting all the components on demand at preparation. Similar kits for preparation of vasopressor infusions should be considered to reduce treatment delays and as a safety strategy whether or not the organization chooses to use bolus-dose vasopressors.

ADDITIONAL OPERATIONAL AND SAFETY CONSIDERATIONS

For obvious reasons, any ad hoc preparation of medications, including intravenous bolus-dose vasopressors in urgent situations, is less than optimal from a safety standpoint. Human error is a factor whenever a product is manually compounded or manipulated, and therefore steps must be taken to prevent errors. Many of the available descriptions and methods for the preparation and use of bolus-dose vasopressors include components that are addressed in (or conflict with) the Institute for Safe Medication Practices safe practices recommendations, and organizations should evaluate and address such issues.[26,29] An additional added risk of bolus-dose vasopressors is the absence of the control and safety features provided by modern intravenous pumps used when these drugs are given as infusions.

The many uses of epinephrine, variable doses, multiple routes, multiple available forms, outdated naming convention (eg, 1:10,000 instead of 0.1 mg/mL) are known sources of errors and confusion.[52] Fortunately, the use of these "dose ratio" concentration designations is finally being phased out.[53] Adding a new and unfamiliar use of epinephrine such as use as a bolus-dose vasopressor is likely to increase the potential for error. Organizational assessment of epinephrine bolus-dose vasopressor use must consider the risks within the overall context of the environment of care, all epinephrine product uses, available dosage forms, preparation or compounding practices, storage method and location, access, and staff knowledge.

1. Organizations should systematically evaluate the use of bolus-dose vasopressors in the ED. This evaluation should include stakeholders from all potentially affected areas within and outside of the ED.
2. If IV bolus-dose vasopressors are to be used, the organization should officially approve, with guidance and approval of ED leadership, the use and method of use of bolus-dose vasopressors in the ED.[19,20,22]
   a. Consensus must occur in regard to who can order and administer bolus-dose vasopressors, and under what circumstances. Organizational policy should be written and communicated reflecting this consensus. This includes both physicians and other licensed independent practitioners, as well as nursing staff or any other individuals who may administer these medications.
   b. In general, situations in which bolus-dose vasopressors will be used require direct prescriber involvement. Dangerous situations could evolve if prescribers of bolus-dose vasopressors are not immediately present for rapid decisionmaking and communication. We recommend that bolus-dose vasopressors be administered only by appropriate licensed independent practitioners or by a nurse (or other appropriate staff) under the direction of a licensed independent practitioner at the bedside.
   c. The organization should establish a common name for the practice to reduce confusion (eg, push dose, bolus dose).
      i. Note the use of the name "Neo-sticks" or "phenyl sticks" is not recommended because of potential for confusion with neostigmine and other drugs.
3. Education of prescribers, nursing staff, pharmacy staff, and others as appropriate should be provided.[19,20,22]
   a. All stakeholders, including nursing, physicians, and pharmacy, should participate in the development of learning modules.
   b. Key components of education should include indications for use, role of practitioners, compounding instructions (if appropriate) or product selection, administration, monitoring, and institution-specific policies and procedures. Education should occur with orientation of new staff on an appropriate regular basis to reinforce safety measures.
   c. Staff knowledge of prescribing, preparing, and administering IV bolus-dose vasopressors should be assessed initially and at regular intervals as appropriate for the organization.
4. Standardize concentrations, syringe size, and labeling of bolus-dose vasopressor syringes to be used in an ED.[19,20,22]
   a. Standardize bolus-dose vasopressor syringes across the organization wherever bolus-dose vasopressors may be used (eg, EDs, operating room, procedural areas).
5. Organizations should consider providing pharmacy-prepared or purchased stocks of standard-concentration, bolus-dose vasopressor, ready-to-use syringes in the ED. These stock syringes may be prepared by the organization's pharmacy, or alternatively purchased from an appropriately certified compounder.[19,20,22,30]
6. If ad hoc nonpharmacy preparation of bolus-dose vasopressor syringes is to be allowed, clear and easy-to-find step-by-step preparation and use instructions should be provided (Figure 1).[17]
   a. Organizations should consider providing the components needed for ad hoc preparation of bolus vasopressor syringes as kits containing the appropriate instructions, drugs, diluents, syringes, and labels needed to prepare the products.
      i. Any ad hoc preparation should follow appropriate guidelines for aseptic IV drug preparation.
      ii. Appropriately label prepared vasopressor syringe(s) after preparation (do not prelabel). (Whenever possible, organizations should provide labels that include appropriate prompts for complete information and a barcode for scanning before administration.)
7. Bolus-dose vasopressor syringes, kits, or components should be stored in such a way that they are secure but easily accessible during emergency situations. Safeguards must be taken to ensure that the correct product is selected when needed.[21,26]
   a. If they are stored in a refrigerator or cabinet, provide a clearly labeled area, bin, or box to separate and differentiate them from other medications that may look similar.

Figure 3. Practices for safe use of bolus-dose vasopressors according to current medication use guidelines.

EPINEPHrine 10 mcg/mL Syringe Preparation:

1. Draw up 9 mL of normal saline into a 10 mL syringe (DO NOT use 10ml IV line "flush" syringes)
2. Into this syringe, draw up 1 mL of EPINEPHrine 0.1 mg/mL (1 mg/10ml) from a cardiac syringe
3. Label syringe

Phenylephrine 100 mcg/mL Syringe Preparation:

1. Draw up 1 mL of phenylephrine from a 10 mg/mL vial into a 3 mL syringe
2. Inject this into a 100 mL bag of normal saline. Label bag; safely discard when finished
3. Draw up 10 mL into a 10 mL syringe
4. Label syringe
5.

ePHEDrine 5 mg/mL Syringe Preparation:

1. Draw up 9 mL of normal saline into a 10 mL syringe (DO NOT use 10ml IV line "flush" syringes)
2. Into this syringe, draw up 1 mL of ePHEDrine from a 50 mg/mL vial
3. Label syringe

Figure 2. Instructions for ad hoc preparation of bolus-dose vasopressors (adapted from Weingart[6] and Cocchio[9]).

entire syringeful is accidentally administered. The risk of administering an entire syringeful (instead of administering it incrementally in titrated aliquots) should be considered a significant one with bolus-dose vasopressors and needs to be a major focus of staff education and training. An additional factor to consider is that the risk from extravasation injury likely increases as the concentration of the solution increases. We recommend use of the lowest appropriate concentration of solutions to reduce safety risks at the expense of requiring additional syringes when patients require higher or repeated doses.

Without appropriate commercially available dosage forms, institutions will have to determine how to safely prepare or provide bolus-dose vasopressors for the foreseeable future. Recommendations for bolus-dose vasopressor syringe preparation are provided in a number of resources.[6-10] Figure 2 contains examples of recommended instructions on how to prepare epinephrine, ephedrine, and phenylephrine for bolus-dose administration using commonly available vials and diluents. In his EMCrit blog, Weingart[6] includes video demonstrations of how ED practitioners can prepare dilutions of epinephrine and phenylephrine syringes. Some resources advocate the use of cards containing preparation and administration recommendations to facilitate communication.[6] All references stress the importance of correct syringe preparation.

The recent Institute for Safe Medication Practices safe practices guidelines for adult intravenous push medications and other publications recommend pharmacy-based preparation of intravenous medications whenever possible.[26,47] Unfortunately, timely provision of pharmacy-prepared vasopressor syringes on demand is not feasible in many organizations because they do not have in-ED pharmacists, and few have 24-hour ED pharmacist presence. The alternative to on-demand preparation is the routine stocking of pharmacy-prepared syringes in the ED. However, this is also generally not practical because of the limited shelf life stability and sterility of pharmacy preprepared syringes in light of current professional standards compliance.[48] The US Pharmacopeia serves as the enforceable standards-setting organization for preparation and storage of medications. Its standards in regard to sterile medication compounding (known as US Pharmacopeia Chapter 797) is based on ensuring stability and sterility up to the "beyond-use date" for a medication product. A beyond-use date is the date after which a compounded preparation should not be used according to stability and sterility data. In the absence of such data, the US Pharmacopeia offers standards for determining an appropriate beyond-use date according to the risk of contamination and storage conditions. Beyond-use dating often is limited to 1 hour after preparation.[49] Prolonged beyond-use dating suitable for the stocking of an internally prepared sterile product can also be established by testing and documenting stability (initial lot) and sterility (each lot). This process is expensive and would usually not be cost-effective for bolus-dose vasopressor syringes because of the cost of testing, short shelf life, and infrequent use. As such, providing a pharmacy-prepared supply of ready-to-use bolus-dose vasopressor syringes may put a considerable

The choice of vasopressor agent is determined by the patient's clinical situation. Although ephedrine is a popular vasopressor agent among anesthesiologists, because of its extended duration, epinephrine and phenylephrine appear to be more commonly used in the ED. The pharmacologic profiles of common vasopressors are shown in the Table. Generally epinephrine, which has inotropic and vasopressor activity, may be preferred over the pure vasopressor phenylephrine if a patient could benefit from an increase in pulse rate and cardiac output. However, because of epinephrine's b- and a-adrenergic activity, patients may experience tachycardia after administration, making it a suboptimal choice for use in those with significant tachycardia or tachyarrhythmia. Phenylephrine has no direct chronotropic or inotropic effect on the heart and therefore may be a better option for use in such patients. In addition, it may even be able to decrease pulse rate through an increase in parasympathetic tone. These differences in pharmacology lead to requests for availability of more than one drug for use as a bolus-dose vasopressor in the ED, adding complexity and a potential for confusion and error as safety concerns.

Commonly recommended individual doses of bolus-dose vasopressors are listed in the Table. The FDA-approved bolus-dose range of phenylephrine for hypotension during anesthesia is 40 to 100 mg intravenously repeated every 1 to 2 minutes, up to a total of 200 mg.[5] Recommended vasopressor dose, frequency, and rate of administration (per minute), as well as redosing frequency, therefore provide dose delivery similar to that used when the same drug is given at recommended doses as a continuous infusion.

There are no commercially available, FDA-approved, ready-to-use dosage forms or concentrations of epinephrine or phenylephrine suitable for bolus-dose vasopressor or infusion use. Thus, in all cases appropriate dosage form preparation requires product manipulation before use (dilution and transfer to a suitable bag or syringe), a major safety concern. The phenylephrine prescribing information for the only currently available brand of phenylephrine injectable includes information about diluting and administering phenylephrine by syringe for bolus dosing during anesthesia.[5] In a new drug application approval letter for phenylephrine in 2012,[45] the FDA requested that a previous new drug application applicant (West-Ward Pharmaceuticals, Eatontown, NJ) develop an appropriate ready-to-use concentration of phenylephrine suitable for bolus dosing. However, this requirement was absent from the new drug application approval for the only currently available brand of phenylephrine (Vazculep; Eclat Pharmaceutical, Chesterfield, MO).[46]

Commonly recommended bolus-dose vasopressor drug concentrations vary (Table), but generally provide a concentration appropriate to deliver a dose in a volume of 0.5 to 2 mL. The intravenous bolus vasopressor concentrations commonly recommended in online resources (such as phenylephrine 100 mg/mL) are usually based on simplicity of preparation for practitioners using readily available vials and solution containers. For example, the commonly recommended solution of phenylephrine at 100 mg/mL is prepared by adding a 10-mg vial of phenylephrine to a 100-mL normal saline solution "minibag" and then drawing it into 10-mL syringes for administration (the FDA-approved Vazculep prescribing information recommends the same). Bolus-dose epinephrine is usually made by diluting 1 mL of epinephrine at 0.1 mg/mL in 10 mL of saline solution.

The usual recommendation is to prepare a syringe with 10 mL of diluted vasopressor solution. When syringes with drug concentrations given in the Table are used, the highest volume that should usually be pushed at one time is 2 mL. As such, the 10-mL syringe will contain multiple (5 or more) "usual" individual doses of bolus-dose vasopressor to allow multiple doses to be administered according to patient response. Using more concentrated solutions potentially increases the risk of overdose if the syringe plunger is pushed too quickly or if an

Table. Pharmacology and dosing of common bolus-dose vasopressors.

Pharmacology	Epinephrine	Phenylephrine	Ephedrine
Pharmacologic effect	Inotrope and vasopressor	Vasopressor	Inotrope
Target receptor	b1, b2, a	Pure a	b1 (indirect a)
Onset, min	1	1	1
Duration, min	5–10	10–20	60
Desired concentration/mL	10 mg	40–100 mg	5 mg
Recommended dosing/2–5 min	5–20 mg	40–200 mg	5–10 mg
Rate, mL/min	0.5–2	0.5–2	0.5–2
Patient selection	Low cardiac output associated with shock; anaphylaxis	Tachycardia and low mean arterial pressure predominately caused by vasodilation	Not recommended in the ED because of extended duration
Adverse events	Tachycardia, rebound hypertension	Rebound hypertension, bradycardia	Tachycardia

PHARMACOLOGIC OR PHARMACEUTICAL CONSIDERATIONS AND SAFETY CONCERNS

Traditionally, hemodynamic support with vasopressors in the ED involves administration by continuous infusion with titration of infusion rates. Vasopressors are typically administered from an intravenous bag or syringe controlled by an infusion pump. Disadvantages of vasopressor infusions include delays because of the need for preparation and "pump setting," and drug waste when vasopressor support is needed for only a short period. Bolus-dose vasopressors have been advocated as an alternative strategy to infusions to overcome these issues.[6-10] Bolus-dose vasopressors are similarly used in a titratable fashion, with incremental dosing by manual, intermittent, slow intravenous push from a syringe, repeated as needed according to patient response and condition. The commonly recommended method of administering bolus-dose vasopressors is to give an appropriate dose intravenously, manually "pushed" by syringe over 30 to 60 seconds. The necessity of repeating or increasing the dose is based on patient response and can occur every 1 to 5 minutes (Figure 1).

ED ONLY ADULT PUSH DOSE PRESSOR IV Administration Guidelines	
Form Provided	Phenylephrine 40mcg/ml 10ml syringes (ED only)
Starting Dose	**Titration / Incremental Dose**
40-80mcg (1-2ml) slow IV push	Repeat dose per direction of LIP every 1-5min as needed Increase dose per direction of LIP to 40-200mcg based on response
Important Information	• Syringe provides dose to be given incrementally (eg 1-2ml (40-80mcg) with additional doses, or dose increase based on response every 1-5 minutes • **MUST BE GIVEN BY LIP, OR MAY BE GIVEN BY RN PER DIRECTION OF LIP PRESENT AT BEDSIDE.** • Extravasation risk- use CVL or large vein when available • Used as temporizing measure for hypotension. • Phenylephrine has solely α-adrenergic activity and therefore has no effect on the heart. Use when patient is tachycardic. May cause reflex increase in parasympathetic tone and therefore cause a decrease in heart rate.
Minimum Monitoring	• ED use only • Monitor HR and BP at least every 5min while administering / titrating, and if appropriate, q5min x3 after administration.

ED ONLY ADULT PUSH DOSE PRESSOR IV Administration Guidelines	
Form Provided	Epinephrine 10mcg/ml 10ml syringes (ED Only)
Starting Dose	**Titration / Incremental Dose**
5-20mcg (0.5-1ml) slow IV push	Repeat dose per direction of LIP every 1-5minutes as needed. Increase dose per direction of LIP to 10-20mcg based on response
Important Information	• Syringe provides dose to be given incrementally (eg 0.5-1ml (5-10mcg) with additional doses, or dose increase based on response every 1-5 minutes • **MUST BE GIVEN BY LIP, OR MAY BE GIVEN BY RN PER DIRECTION OF LIP PRESENT AT BEDSIDE.** • Extravasation risk- use CVL or large vein when available • Used as temporizing measure for hypotension. • Epinephrine has both α- and β-adrenergic activity – may cause tachycardia in addition vasoconstriction. Consider phenylephrine in significant tachycardia or any tachyarrhythmia.
Minimum Monitoring	• ED use only • Monitor HR and BP at least every 5min while administering / titrating, and if appropriate, q5min x3 after administration.

Figure 1. Example of bolus-dose vasopressor drug information resource. LIP, Licensed independent practitioner; CVL, central venous line.

There is, however, a paucity of research for emergency airway management that encompasses and discusses the triad of bolus-dose vasopressors, peri-intubation hypotension, and ED patients.

Patients with traumatic brain injury represent a distinct population that may benefit from the rapid use of vasopressors. When cerebral blood flow is compromised, harmful and potentially permanent secondary brain injury may result. Hypotension may be a contributing factor to these patients' morbidity, disability, and death. Therefore, rapidly maintaining perfusion throughout the brain is a vital component of traumatic brain injury management. There has been a multitude of research demonstrating the correlation between hypotension and increased mortality in patients with traumatic brain injury. In a landmark 1993 article, Chestnut et al[40] analyzed the relationship between hypotension and hypoxia and their secondary effects on patients with major traumatic brain injury. They found that patients with a major traumatic brain injury and hypotension had a 150% increase in mortality. In 2 publications analyzing data from the Excellence in Out-of-Hospital Injury Care Study, Spaite et al[41,42] examined the relationship between patients with major traumatic brain injuries and the effects of out-of-hospital hypotension and hypoxia and its relationship with mortality and whether a systolic blood pressure cutoff of 90 mm Hg as defining hypotension is clinically relevant in relation to mortality. They found that out-of-hospital hypotension and hypoxia were associated with increased mortality. In addition, they found that a linear association exists between blood pressure and mortality, with each 10% increase in blood pressure between 40 and 119 mm Hg leading to a decrease in the odds of death of 18%. Their findings are in favor of the potential need for "aggressive prevention and treatment of hypotension and hypoxia. ."[42] Manley et al[43] also found hypotension to be associated with increased mortality after traumatic brain injury (Glasgow Coma Scale score < 12). The duration of hypotension may be only short lived (< 10 minutes). They found that repeated episodes of hypotension also increased the odds of death. By rapidly increasing mean arterial pressure and thus cerebral perfusion pressure, bolus-dose vasopressors may help to prevent secondary brain injury. Much more research is needed on this important topic.

Optimal blood pressure management is also important for patients with return of spontaneous circulation. Identifying the underlying cause, maintaining proper temperature control, and ensuring oxygen delivery are just a few examples of treatment goals for return of spontaneous circulation. Another principal goal is the maintenance of end-organ perfusion, which is often impaired after return of spontaneous circulation. For example, during the initial period after cardiac arrest, cerebral autoregulation may be impaired.[44] Therefore, it is recommended that blood pressure management remain one of the crucial components for management of return of spontaneous circulation; however, the role of bolus-dose vasopressors in this situation remains undefined.

The place of bolus-dose vasopressors is clearly not established. Panchal et al[16] described bolus-dose phenylephrine use for peri-intubation hypotension. This was a retrospective chart review of intubated hypotensive patients in which phenylephrine was used. Although bolus-dose phenylephrine demonstrated an increase in systolic blood pressure, the authors recommended further studies to understand the best use for phenylephrine for postintubation hypotension. Another retrospective analysis investigated the number of patients treated with bolus-dose vasopressors who subsequently required continuous vasopressor infusions in relation to proper preload expansion before bolus-dose vasopressor use.[17] They found that only 34% of patients were given a proper fluid challenge before bolus-dose vasopressor administration. Furthermore, they found that patients who were not adequately fluid challenged required more doses of bolus-dose phenylephrine and were more likely to need a continuous vasopressor infusion within 30 minutes of administration of bolus-dose phenylephrine. Their findings suggest that prescribers may circumvent standard resuscitation practices of fluid administration in favor of using bolus-dose vasopressors. These 2 articles constitute virtually the entirety of the literature on this topic. As a result, the dose, method of administration, and agent of choice remain a topic of discussion and expert opinion.

We acknowledge that the use of vasopressors (bolus-dose or continuous infusion) does not treat the underlying cause of hypotension. For example, a hypotensive trauma patient with active internal bleeding needs blood products and an interventional surgical procedure. Elevating the blood pressure with bolus-dose vasopressors in this patient population does not correct the underlying cause of blood loss and hypotension. In similar hypotensive patients with profound fluid loss from vomiting or diarrhea, burns, or profound sepsis, the real need is for fluid replacement to increase the patient's blood pressure. In these instances, a bolus-dose vasopressor does not treat the vast underlying fluid deficit. It does, however, offer the potential of temporarily aiding in the perfusion of critical organs such as the heart, brain, and kidneys. Bolus-dose pressures are a temporizing or bridging measure until definitive care can be initiated, such as fluid or blood product replacement or the potential initiation of vasopressors as a continuous infusion.

risk for errors.[27,28] Errors in preparation, drug selection, and administration have been frequently reported with epinephrine, which is commonly used as a bolus-dose vasopressor.[23-25] Much of the currently available information on ED bolus-dose vasopressor use addresses the implementation and use by individual practitioners[6-10] rather than through a more systematic, safety-based organizational approach.[29] Such systems-based safety practices support safer care of patients by individual practitioners of all levels of experience when they perform risky tasks. In their safe practice guidelines for adult intravenous push medications, the Institute for Safe Medication Practices specifically identifies the following as a risk factor for errors: "lack of administrative policies/protocols/guideline development for intravenous injections, so the expectation for safe practices is undefined and left solely to each individual's and/or department's preferences."[26] During the past 2 decades, general and specific safe medication practice guidelines have been developed, disseminated, and widely implemented[22,26,30-33] and should be systematically applied to the use of bolus-dose vasopressors in the ED.

This article summarizes clinical, pharmacologic, pharmaceutical, operational, and safety-related considerations with the use of bolus-dose vasopressors in the ED. The intent is not to advocate for or against use of bolus-dose vasopressors in the ED, but rather to provide organizations with information to consider when determining whether use of bolus-dose vasopressors is appropriate in their ED, and, if used, how this therapy might be most safely implemented in accordance with current safe medication practice guidelines.[22,30]

MATERIALS AND METHODS

With PubMed, Web of Science, Cochrane Database, Google, and Google Scholar, the medical literature was searched for published articles pertaining to these key words: "push-dose pressors," "bolus-dose pressors," "Neosticks" and "phenylsticks." Similarly, Google was used to search for FOAM sites. References related to the topic included in relevant documents and articles were also reviewed. A similar search process was used to identify relevant publications and guidelines related to medication safety in general and medication safety in the ED. Because the article was not intended to be a systematic review and because of the rapidly changing and dynamic nature of the FOAM literature, article inclusion was based on our consensus and discretion.

Clinical, operational, pharmaceutical, and safety considerations of storing, obtaining, preparing, administering, and monitoring bolus-dose vasopressors in the ED were identified through process mapping and evaluation of the identified process steps by an emergency physician, ED nurse, and clinical pharmacist.[29,34]

Guidelines and recommendations for safe medication practices were identified and reviewed for items relevant to the mapped process of using bolus-dose vasopressors in the ED.[21,22,26,30]

Specific recommendations for safe use were then developed and delineated by consensus of all authors after application of the identified relevant general safe medication practices to the process of bolus-dose vasopressor use in the ED.

We identified 2 retrospective observational studies and 3 descriptive reviews of the use of bolus-dose vasopressors in the ED setting.[14-18] More than 100 FOAM-related citations were identified; this number appears to be expanding weekly to monthly. Out of the hundreds of relevant medication safety citations and FOAM-related citations, references encompassing identified process steps were selected as representative of the larger literature.[19-22,26,29-33]

CLINICAL CONSIDERATIONS

In the ED, indications for bolus-dose vasopressors center around optimizing hemodynamics for clinical conditions in which hypotension may result in poor outcomes. Bolus-dose vasopressors have been suggested as a treatment for any patient when rapid intervention is needed to support blood pressure before vasopressor infusion and other interventions can be started. This temporary measure may limit the duration of hypotension while potentially limiting inadequate perfusion of vital organs. Clinical examples in which inadequate blood pressure may result in adverse outcomes include patients with major traumatic brain injury, post–cardiac arrest patients with return of spontaneous circulation, and patients needing emergency airway care. It is possible that these patients will have improved outcomes when hypotension is limited, reversed, or expeditiously treated.

Airway management represents a high-risk period for the critically ill patient, with multiple challenges and potential complications. Rapid optimization of blood pressure before, during, and after intubation remains a crucial component because hypotension during this period represents a reversible pitfall during emergency airway care. Postintubation hypotension is a well-described complication of airway management, may occur in up to 25% of patients,[16,35-39] and may lead to significant complications, including cardiovascular collapse and death. Therefore, rapidly optimizing blood pressure during this important period remains a staple of airway management.

Safety Considerations and Guideline-Based Safe Use Recommendations for "Bolus-Dose" Vasopressors in the Emergency Department

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The use of intermittently administered doses of vasopressors to correct hypotension in the emergency department (ED), commonly referred to as bolus-dose pressors, push-dose pressors, Neo-sticks, or phenyl sticks, has been widely advocated outside of the traditional printed medical literature. No outcomes data of this practice exist to demonstrate benefits over traditional continuous infusion of vasopressors. Use of bolus-dose vasopressors in the ED setting raises a number of patient safety concerns, and misuse and errors in the preparation and administration of bolus-dose vasopressors may result in patient harm. A systems-based approach should be implemented to maximize safety and patient benefits if bolus-dose vasopressors are used. This article discusses the wide range of issues to consider when evaluating the role of bolus-dose vasopressors in the ED and provides recommendations based on current safe medication practices guidelines. [Ann Emerg Med. 2017;- :1-10.]

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SEE EDITORIAL, P. XXX.

INTRODUCTION

Intermittent administration of small doses of vasopressors such as epinephrine, phenylephrine, and ephedrine to treat hypotension and maintain adequate perfusion has been a long-standing evidence-based practice of anesthesiologists.[1-4] Both older and recently revised Food and Drug Administration (FDA)–approved labeling of phenylephrine injection includes an indication for use, preparation, and dosing recommendations for use as a bolus for hypotension during anesthesia.[5] This common practice is variably referred to as bolus-dose pressors, push-dose pressors, Neo-sticks, or phenyl sticks; this article will refer to them as bolus-dose vasopressors. Outside of the operating room setting, vasopressors for hemodynamic management are typically administered as continuous intravenous infusions.

Extending the use of bolus-dose vasopressors, usually epinephrine and phenylephrine, to emergency departments (EDs) has been advocated as a practical strategy to urgently manage hemodynamically unstable patients. Reflecting the shift from traditional literature and professional dialogue to Web-based information resources, much of the information available in regard to the use of bolus-dose vasopressors in the ED is found on the Internet in blogs and free open access medical education (FOAM) resources, as opposed to traditional peer-reviewed medical literature.[6-10] Additionally, bolus-dose vasopressor use is taught at emergency medicine national educational conferences.[11,12] There are even commercially available bolus-dose vasopressor applications for mobile electronic devices that provide dosing and preparation instructions.[13] Despite the apparent widespread use (our observation based on browsing the Web), we were able to find only 2 retrospective observational studies and 3 discussion articles of the practice in the traditional emergency medicine literature.[14-18]

The ED environment presents unique challenges in ensuring patient safety: treatment of unfamiliar patients, necessity for emergency care, crowding, reliance on verbal orders, dispensing and administering medications without verification by a pharmacist, and understaffing.[19] The use of bolus-dose vasopressors in the ED adds additional patient safety risks, and the complex multistep process of using bolus-dose vasopressors involves well-known problem-prone practices.[19-22] Risks include the need for dose calculation, drug dilution, and incremental push-dose administration, which are all areas in which errors are common and potentially fatal.[23-25]

In addition, intravenous bolus medications present considerable safety risk in general and are the subject of recently published safe practice guidelines.[26] Furthermore, most drugs are typically prepared by pharmacists and administered by nurses in the ED; thus, physicians are less experienced in performing these tasks, which increases the