The Use of Bolus-Dose Vasopressors in the Emergency Department

Sabrina Weigand, MD; J. Nate Hedrick, PharmD; William J. Brady, MD

While bolus-dose vasopressors are commonly used in critical care medicine and anesthesiology to treat patients with hypoperfusion, its application in emergency medicine is minimal with little penetration into daily care.

The use of bolus-dose vasopressors in anesthesiology and other areas of critical care medicine is well known. This common medical intervention, however, is not often employed in emergency medicine (EM). Bolus-dose vasopressors are defined as the administration of small bolus doses of vasopressor agents, such as epinephrine or phenylephrine, to patients with compromised perfusion who continue to have a pulse (ie, these patients are not in cardiac arrest). This intervention is considered as a temporizing measure for transient hypotension or as a bridge to more definitive therapy.

Clinical Application

Bolus-dose vasopressive therapy is also referred to as push-dose pressor (PDP) therapy—a term coined by Weingart.[1-3] Theoretically, any vasopressor could be used in a mini-dose, bolus fashion, though in current clinical practice, anesthesiologists primarily employ ephedrine, epinephrine, and phenylephrine. Two of these agents are likely more appropriate for the ED, including epinephrine and phenylephrine. Both of these agents have a short half-life and therefore an abbreviated period of effect. In addition, dosing and related administration of epinephrine and phenylephrine is relatively straightforward. Moreover, most emergency physicians and nurses are quite familiar with both agents.

With respect to ephedrine, due to its longer half-life, complex dosing regimen, and associated higher-incidence of cardiovascular (CV) complications, its use is likely not appropriate in the ED as a bolus-dose vasopressor.

Epinephrine and Phenylephrine

Epinephrine is a potent sympathomimetic agent with alpha- and beta-receptor activity. In addition to its vasopressor effects, epinephrine is also an inotropic and chro-

Dr Weigand is a senior resident, department of emergency medicine, University of Virginia School of Medicine, Charlottesville. **Dr Hedrick** is a clinical pharmacist, emergency department, University of Virginia Health System, Charlottesville. **Dr Brady** is a professor of emergency medicine, department of emergency medicine, University of Virginia School of Medicine, Charlottesville.

Authors' Disclosure Statement: The authors report no actual or potential conflict of interest in relation to this article.

DOI: 10.12788/emed.2018.0085

notropic agent, increasing cardiac output, heart rate (HR), and systemic vascular resistance, which can markedly improve perfusion. Epinephrine also can be given to patients with hypoperfusion and/or shock due to low-cardiac output with or without vasodilation, lacking significant tachycardia.

Phenylephrine is a pure alpha agonist and therefore does not appreciably affect cardiac output and HR, but does significantly increase systemic vascular resistance and thus systemic perfusion. Phenylephrine can be used to treat patients with hypoperfusion and/or shock states due to vasodilation with coexistent, significant tachycardia.

Preparation and Administration

The preparation and dosing of push-dose epinephrine and phenylephrine are not particularly complex. Many clinicians recommend the pre-mixed, manufacturer-prepared agents for PDP therapy. These premixed formulations not only facilitate administration, but also reduce the chance of a preparation error that can result in incorrect dosing.[3-5] If pre-mixed formulations are not available, clinicians can readily prepare epinephrine and phenylephrine for PDP use.

Push-Dose Epinephrine. Clinicians can prepare epinephrine for push-dose administration as follows:[1-3]

- Obtain 1 mL of epinephrine 1:10,000 (ie, 0.1 mg/mL or 100 mcg/mL);
- Obtain a 10 mL syringe of normal saline and remove 1 mL;
- Inject the 1 mL of epinephrine 1:10,000 (100 mcg/mL) into this syringe containing 9 mL of normal saline; and
- Result: 10 mL of epinephrine (10 mcg/mL), with each 1 mL of this solution containing 10 mcg of epinephrine.

Administration of push-dose epinephrine (10 mcg/mL) produces effect within 1 minute of use with a duration of approximately 5 to 10 minutes. Dosing at this concentration ranges from 0.5 to 2.0 mL every 2 to 5 minutes, delivering 5 to 20 mcg.[1-3]

Push-Dose Phenylephrine. To prepare phenylephrine for push-dose administration, clinicians may use the following approach:[1-3]

- Obtain 1 mL of phenylephrine (10 mg/mL concentration);
- Inject this 1 mL of phenylephrine (10 mg/mL) into a 100 mL bag of normal saline; and
- Result: 100 mL of phenylephrine (100 mcg/mL), with each 1 mL of this solution containing 100 mcg of phenylephrine.

Administration of push-dose phenylephrine (100 mcg/mL) produces effect within 1 minute of use with a duration of approximately 10 to 20 minutes. Dosing at this concentration ranges from 0.5 to 2.0 mL every 2 to 5 minutes, delivering 50 to 200 mcg.[1-3]

Alternative Push-Dose Preparations for Phenylephrine. Two other methods of preparing phenylephrine for bolus-dose administration include the following: (1) the addition of phenylephrine 20 mg to a bag of 250 cc of normal saline, resulting in an 80 mcg/mL concentration; and/or (2) phenylephrine (20 mg) is commercially available for continuous infusion in a 250 mL bag of normal saline, yielding the same concentration of 80 mcg/mL; in either case, medication can be drawn up and administered. Dosing at this concentration ranges from 0.5 to 2.5 mL every 2 to 5 minutes, delivering 40 to 200 mcg. Lastly, phenylephrine is also commercially available in pre-made mixtures, specifically manufactured for bolus-dose therapy.

Indications

Both epinephrine and phenylephrine can be considered in the management of significant transient or sustained hypoperfusion. Although the definition of significant hypotension is complex, Brunauer et al[6] have suggested that a mean arterial pressure (MAP) of approximately 35 mm Hg is associated with a significant risk of CV

collapse. Of course, a MAP of 40 to 50 mm Hg is also very concerning clinically, with significant risk of deterioration and CV collapse.

Procedural events, such as conscious sedation or rapid sequence intubation (RSI), can produce significant hypotension; PDP can rapidly correct hypotension. In other clinical scenarios in which sustained hypotension is likely and not transient (eg, sepsis with shock), PDP can be used as a bridge to definitive care (eg, volume replacement, continuous vasopressor infusion). It is important to note, however, that PDP administration must occur in conjunction with or after the patient has received other appropriate therapies such as a normal saline bolus and continuous vasopressor infusions. Push-dose pressors are not a replacement for these proven interventions, but rather are an important augmentation to these therapies.

Emergency Medicine Literature

As previously noted, the literature base describing and supporting the clinical use of PDP in EM is extremely limited. The few articles that comprise this literature base address significant hypotension in periendotracheal intubation intervention, post-return of spontaneous circulation (ROSC) management, and shock management with preload augmentation.[7-9] In addition, there are several articles in the literature that address safety concerns surrounding the use of PDP in the ED.[4,5]

Panchal et al[10] investigated the use of phenylephrine in hypotensive patients undergoing RSI-assisted endotracheal intubation. The authors performed a 1-year retrospective review of hypotensive patients managed with endotracheal intubation for a range of clinical conditions that required clinical care intervention. In this study, 20 of the 119 patients received phenylephrine in the peri-intubation period. A range of clinical conditions requiring critical care intervention were encountered; in addition, almost three-quarters of these patients were receiving at least one other vasopressor infusion. Further differences were seen in the timing of PDP administration. In those patients receiving bolus-dose phenylephrine, blood pressure (BP) improved without change in HR. Panchal et al[10] concluded that while push-dose phenylephrine improved hemodynamic status, there was significant variation among clinicians regarding dosing, timing of use, and overall clinical situation The significant variation in PDP management in this study was noted to be a potential source of medical error, thus increasing the chance of adverse clinical event.

Push-dose pressor therapy can be employed for significant hypotension while more definitive therapy is being readied and applied. For instance, patients with significant hypotension requiring continuous vasopressor infusion can be managed with PDP while appropriate venous access is established, intravenous fluids are administered, and medications are prepared. The immediate period after resuscitation from cardiac arrest can be complicated by shock of many types. In fact, hypotension following ROSC in the cardiac arrest patient is not uncommon and has been identified as a risk issue associated with poor outcome. Prompt treatment of this altered perfusion may improve outcome. Gottlieb[8] described three patients with ROSC after cardiac arrest. All three patients experienced significant, sustained hypotension with systolic blood pressure reading in the 50 to 60 mm Hg range; bolus-dose epinephrine was administered with significant improvement in the hemodynamic status while central venous access was established.

In a related clinical scenario, Schwartz et al[9] considered the impact of PDP on central venous line (CVL) placement with continuous vasopressor infusion. In this ED study, although patients experienced an increase in BP, this impact was transient with approximately half of these individuals ultimately requiring CVL. In addition,

serious adverse effect was noted more commonly in the phenylephrine-treated patients with "reactive" hypertension and ventricular tachycardia occurring in study patients.

Patient-Safety Considerations

In addition to the limited literature base supporting PDP use in the ED, another major significant issue focuses on safety concerns and adverse effects. Extremely limited data is available describing adverse events related to ED-administered PDP. Extrapolating from other EM and critical care administrations of peripheral epinephrine, both local and systemic adverse effects have been reported.[11,12] The range of adverse events noted in these studies are considerable, including local skin and soft-tissue injury (necrosis), end-organ tissue ischemia (eg, digits, tip of nose), acute hypertension, cardiac ischemic events, and left ventricular (LV) dysfunction.[11,12]

When comparing peripheral infusion with central infusion, the risk of extravasation with resultant local tissue injury is markedly greater with peripheral vasopressor administration. In a systematic review of this issue, Loubani and Green[11] noted that such local adverse events were much more commonly associated with peripheral administration.

In another report of vasopressor use in the ED, Kanwar et al[12] described apparent confusion with epinephrine dosing and route of administration, resulting in very significant, systemic CV maladies, including severe elevations in BP, acute LV dysfunction, and chest pain associated with ST segment elevation.

It must be stressed that the publications by Loubani and Green[11] and Kanwar et al[12] described peripheral vasopressor administration: neither study included PDP therapy. Therefore, as previously noted, the aforementioned statements are extrapolated from when applied to PDP strategy.

Acquisto et al[4] describe several errors in medication administration of PDP in the ED and other critical care areas of the hospital. In this report, all treating physicians were present at the patients' bedside, either administering the medication or directly supervising its use. Agents involved included epinephrine and phenylephrine, delivered at exceedingly high doses. In their study, the authors noted several issues which they believe contributed to medication errors, including heterogeneity of pathology treated in these patients, apparent "earlier-than-appropriate" use of vasopressors (ie, prior to giving an appropriate fluid bolus), and medication preparation at the bedside by clinicians who may not possess the experience and training to mix these agents.

From a patient-safety perspective, Holden et al[5] noted the potential for dosing error with significant adverse medical consequence related to PDP, as well as several contributing issues. First, they highlight the lack of a solid literature base to support administration of PDP in the ED and the development of decision-making guidelines for use in the ED. They also observed an inconsistency in approach to patient selection, medication choice, agent preparation, dosing, and other therapies. As seen in the Acquisto et al[4] report, the patient-care scenarios are high risk and quite dynamic.

Conclusion

Bolus-dose vasopressor therapy is a potentially very useful treatment in the ED and other emergency/critical care settings. However, despite its benefits in treating patients in shock or with hypoperfusion, PDP is not widely used in EM due to the lack of studies, reviews, and guidelines in the literature to support its use in the ED. Such a literature base is required to provide an appropriate, safe means of patient selection, medication choice, dosing, and administration. Continued educational and research efforts are needed to more fully explore the use of PDP therapy in the ED.

When used correctly and appropriately, PDP has promise to be an important aid in the management of shock in the ED. Although bolus-dose therapy is appropriate for select clinical scenarios involving significant shock states which have the potential for progression to complete CV collapse without timely therapy, it is an adjunct to, not a replacement for commonly employed and medically indicated therapies such as crystalloid bolus or continuous vasopressor infusions.

References

1. Weingart S. EMCrit podcast 6—push-dose pressors. EMCrit RACC Web site. July 2009. https://emcrit.org/racc/bolus-dose-pressors. Accessed March 12, 2018.
2. Weingart S. EMCrit podcast 205—push-dose pressors update. EMCrit RACC Web site. August 2017. https://emcrit.org/racc/push-dose-pressor-update/. March 12, 2018.
3. Weingart S. Push-dose pressors for immediate blood pressure control. *Clin Exp Emerg Med*. 2015;2(2):131-132. doi:10.15441/ceem.15.010.
4. Acquisto NM, Bodkin RP, Johnstone C. Medication errors with push dose pressors in the emergency department and intensive care units. *Am J Emerg Med*. 2017;35(12):1964-1965. doi:10.1016/j.ajem.2017.06.013.
5. Holden D, Ramich J, Timm E, Pauze D, Lesar T. Safety considerations and guideline-based safe use recommendations for "bolus-dose" vasopressors in the emergency department. *Ann Emerg Med*. 2018;71(1):83-92. doi:10.1016/j.annemergmed.2017.04.021.
6. Brunauer A, Koköfer A, Bataar O, Gradwohl-Matis I, Dankl D, Dünser MW. The arterial blood pressure associated with terminal cardiovascular collapse in critically ill patients: a retrospective cohort study. *Crit Care*. 2014;18(6):719. doi:10.1186/s13054-014-0719-2.
7. Panchal AR, Satyanarayan A, Bahadir JD, Hays D, Mosier J. Efficacy of bolus-dose phenylephrine for peri-intubation hypotension. *J Emerg Med*. 2015;49(4):488-494. doi:10.1016/j.jemermed.2015.04.033.
8. Gottlieb M. Bolus dose of epinephrine for refractory post-arrest hypotension. *Can J Emerg Med*. 2017;409:1-5. doi:10.1017/cem.2016.409.
9. Schwartz MB, Ferreira JA, Aaronson PM. The impact of push-dose phenylephrine use on subsequent preload expansion in the ED setting. *Am J Emerg Med*. 2016;34(12):2419-2422. doi:10.1016/j.ajem.2016.09.041.
10. Panchal AR, Satyanarayan A, Bahadir JD, Hays D, Mosier J. Efficacy of bolus-dose phenylephrine for peri-intubation hypotension. *J Emerg Med*. 2015;49(4):488-494. doi:10.1016/j.jemermed.2015.04.033.
11. Loubani OM, Green RS. A systematic review of extravasation and local tissue injury from administration of vasopressors through peripheral intravenous catheters and central venous catheters. *J Crit Care*. 2015;30:653.e9-e17.
12. Kanwar M, Irvin CB, Frank JJ, et al. Confusion about epinephrine dosing leading to iatrogenic overdose: A life-threatening problem with a potential solution. *Ann Emerg Med*. 2010;55:341-344.