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Push dose vasopressor

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Objective

Discuss the safety consideration of push-dose vasopressors

Pre-assessment question

What is the final concentration of push dose epinephrine?

A. 1 mcg/mL
B. 10 mcg/mL
C. 100 mcg/mL

Patient case

CC/HPI: RM is a 65 year old female with past medical history of hypertension. She presented to the emergency department with chief complaint of altered mental status. Her daughter reported that she may have accidentally taken an extra hydralazine tablet this morning.

Vitals: Temp 37C HR 112 BP: 75/48 RR: 20

BMP, CBC and blood sugar all within normal limit

Introduction

Intermittent administration of small doses of vasopressor such as epinephrine and phenylephrine has been reported in anesthesia literature[1-2]

This practice is commonly referred to as bolus-dose vasopressor, Neo-stick, Phenyl-stick etc.

Updated phenylephrine labeling for bolus dosage[3]

- Direction: 40 - 100 mcg every 1-2 minutes prn (not to exceed 200 mcg)

1. Doherty A. Anesth Analg. 2012;115(6):1343-50.
2. Mohta M. Anaesth Intensive Care. 2015;43(1):74-80.
3. Éclat Pharmaceuticals. Vasculep prescribing information. Accessed September 20, 2017.

Pharmacology and dosing of common push-dose vasopressors

	Epinephrine	**Phenylephrine**	**Ephedrine**
Target receptors	α, β1, β2	α	α, β1
Onset (minutes)	Rapid	Rapid	Rapid
Duration (minutes)	5-10	10-20	60
Recommended dosing per dose	5-20 µg	40-200 µg	5-10 mg
Patient selection	Low cardiac output, anaphylaxis	Tachycardia, vasodilation	Usually used in the operation room due to long duration of action

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Clinical considerations

- Indication: Urgent reversal of hypotension
- Temporary measure to limit inadequate perfusion of vital organs
- Does not replace appropriate resuscitation effort such as fluid bolus and vasopressor infusion

Possible scenarios

Before, during and after intubation

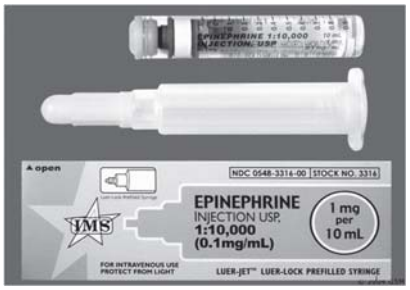
- 20-46% patient experienced hypotension [1-2]
- Post-intubation hypotension was associated with increased in-hospital mortality [1-2]

Post cardiac arrest with return of spontaneous circulation [3]

Traumatic brain injury

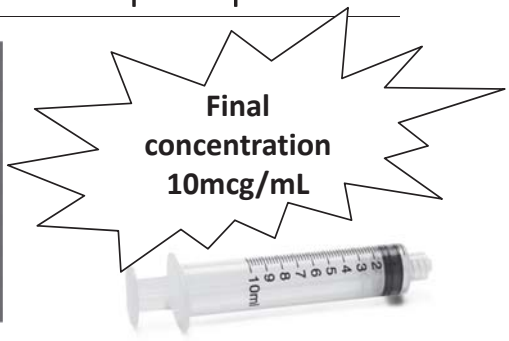
1. Smischney NJ. Med Sci Monit. 2016;22:346-55.
2. Green RS. J Crit Care. 2015;30(5):1055-60.
3. Sundgreen. Stroke. 2001;32(1):128-32.

Mixing instruction for push dose epinephrine



1 mL epinephrine (100mcg/mL)

9 mL 0.9% Sodium Chloride



10 mL syringe

Dosage: 0.5–2 mL (5–20 mcg) slow IV push every 1–5 minutes.

Commercially available phenylephrine syringe

Mixing instruction for push dose phenylephrine

Final concentration ~100 mcg/mL*

1 mL phenylephrine (10mg/mL)

100 mL 0.9% sodium chloride IVPB

*up to 10% overfill for IVPB

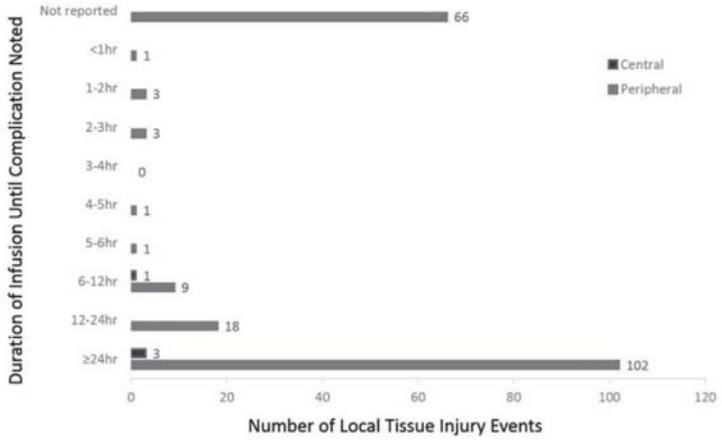
Dosage: 0.5–2 mL (50–200 mcg) slow IV push every 1–5 minutes

Safety risks

- Complex multi-step process that involves dose calculation, drug dilution and incremental push-dose administration
- Name confusion: “Neo-stick” vs Neostigmine
- Dosage administration error of push-dose vasopressor has been reported[1-2]
- Adverse effects reported: Cardiogenic shock with severe left ventricular dysfunction, chest pain with ST-elevation

1. Kanwar M. Ann Emerg Med. 2010;55(4):341-4.
2. Campbell RL. J Allergy Clin Immunol Pract. 2015;3(1):76-80.

Risk of extravasation



Analysis of 325 separate local tissue injury and extravasation events associated with vasopressor infusion

Loubani OM. J Crit Care. 2015;30(3):653.e9-17.

Location of local tissue injury

Location	Local tissue injury % (n = 204)	Extravasation % (n=114)
Distal	85.3	34.2
Saphenous vein	56.9	13.2
Hand	7.4	12.3
Forearm	8.3	5.3
leg	5.9	0.9
Proximal	9.8	11.4
Antecubital fossa	8.8	11.4
Neck	0.5	0
Not reported	4.9	54.4

*Each subject can have multiple sites of local tissue injury

Loubani OM. J Crit Care. 2015;30(3):653.e9-17.

Risk of extravasation

- Risk of local tissue injury / extravasation associated with administration of vasopressor is higher with **peripheral access** than central access
- Most extravasation event occurred after infusion of **> 6 hours**
- If possible, try to infuse push dose vasopressor via **proximal** intravenous access instead of distal access

Loubani OM. J Crit Care. 2015;30(3):653.e9-17.

Monitoring

- Must be monitored by licensed independent practitioner at bedside
- Measure heart rate and blood pressure at least every 5 minutes while administering and titrating
- Follow up with the establishment of vasopressor infusion

Holden D. Ann Emerg Med. 2017;

Post-assessment question

What is the final concentration of push dose epinephrine?

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C. 100 mcg/mL

Patient case

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Result:

- *Emergency room department pharmacist prepared push dose phenylephrine*
- *Patient received 100mcg phenylephrine and blood pressure improved*
- *Fluid bolus and norepinephrine infusion is promptly set up and administered by nurse*

References

1. Doherty A, Ohashi Y, Downey K, Carvalho JC. Phenylephrine infusion versus bolus regimens during cesarean delivery under spinal anesthesia: a double-blind randomized clinical trial to assess hemodynamic changes. Anesth Analg. 2012;115(6):1343-50.
2. Mohta M, Harisinghani P, Sethi AK, Agarwal D. Effect of different phenylephrine bolus doses for treatment of hypotension during spinal anaesthesia in patients undergoing elective caesarean section. Anaesth Intensive Care. 2015;43(1):74-80.
3. Éclat Pharmaceuticals. Vasculep prescribing information. Éclat Pharmaceuticals , Chesterfield, MO. Available at https://www.accessdata.fda.gov/drugsatfda_docs/label/2014/204300lbl.pdf. Accessed September 20, 2017.
4. Smischney NJ, Demirci O, Diedrich DA, et al. Incidence of and Risk Factors For Post-Intubation Hypotension in the Critically Ill. Med Sci Monit. 2016;22:346-55.
5. Green RS, Turgeon AF, Mcintyre LA, et al. Postintubation hypotension in intensive care unit patients: A multicenter cohort study. J Crit Care. 2015;30(5):1055-60.
6. Sundgreen C, Larsen FS, Herzog TM, Knudsen GM, Boesgaard S, Aldershvile J. Autoregulation of cerebral blood flow in patients resuscitated from cardiac arrest. Stroke. 2001;32(1):128-32.
7. 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(3):653.e9-17.
8. Weingart S. Push-dose pressors for immediate blood pressure control. Clin Exp Emerg Med. 2015;2(2):131-132.
9. 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. 2017.
10. Kanwar M, Irvin CB, Frank JJ, Weber K, Rosman H. Confusion about epinephrine dosing leading to iatrogenic overdose: a life-threatening problem with a potential solution. Ann Emerg Med. 2010;55(4):341-4.
11. Campbell RL, Bellolio MF, Knutson BD, et al. Epinephrine in anaphylaxis: higher risk of cardiovascular complications and overdose after administration of intravenous bolus epinephrine compared with intramuscular epinephrine. J Allergy Clin Immunol Pract. 2015;3(1):76-80.

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