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Q: Do I always need a central venous catheter to administer vasopressors?

A: Vasopressors are the cornerstone of treatment for shock, and a central venous (CV) catheter is generally preferred for their administration. The CV catheter carries risks, however, including procedural complications, infection, thrombosis, and hazards associated with its invasiveness. A growing number of studies are assessing the safety and feasibility of the peripheral intravenous (PIV) catheter for vasopressor administration, which may have a better risk profile than the CV catheter. Clinicians are obliged to assess, case by case, whether the PIV catheter can be used for vasopressor administration.

■ BACKGROUND

Vasopressors are used to restore blood pressure and tissue perfusion in 27% of patients admitted to intensive care units, and their use has been increasing over the past decade.¹ The CV catheter is the preferred mode for vasopressor administration because peripheral administration is associated with complications such as local extravasation and potential tissue damage.²⁻⁴ CV catheter insertion and maintenance also carry risks, however, which vary by the site of insertion. Complications include pneumothorax (1.5%–3.1% of patients), arterial puncture (6.3%–15%), hematoma (3.8%–4.4%), deep vein thrombosis (15%), and bloodstream infections.^{5,6} Further, the time required for CV catheter placement could delay delivery of vasopressors and, therefore, hemodynamic stabilization, leading to higher mortality.⁷

■ PERIPHERAL VASOPRESSOR ADMINISTRATION

Safety and risk

Studies assessing the safety and efficacy of peripheral administration have found relatively few instances of complications. For example:

- Among 202 patients with PIV catheters located in the forearm and antecubital fossa, 4% experienced extravasation events, all of which were managed conservatively⁸
- In a systematic review and meta-analysis of studies that included 1,835 patients, the total rate of complications with peripheral administration was 7%, of which 96% were minor⁹
- In a group of 310 patients, of whom more than 55% received peripheral administration, an adverse event of skin necrosis was reported in 1 patient (0.6%)¹⁰
- More recent studies have reported extravasation rates ranging from 0.6% to 3.4%¹¹⁻¹³; most adverse events, occurring in local and distal sites, were deemed nonfatal.

Only 1 randomized controlled trial has compared the complication rates of CV and PIV catheters regardless of the need for vasopressors.¹⁴ In this study, approximately 48% of patients in the PIV catheter group experienced major or minor complications vs 36% in the CV catheter group.¹⁴ The most frequent complication in the PIV catheter group was difficulty of insertion. The risks of infection and thrombus were similar in both groups. In addition, given that less than half of the PIV catheter group received vasopressors, all the reported complications might not have been related to peripheral vasopressor administration.¹⁴

More recently, Yerke et al¹⁵ reported that extravasation occurred in 5.5% of 635 patients who received peripheral

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TABLE 1
Adverse events with peripheral vasopressor administration

Study type	Number of patients	Vasopressors	Dose ^a	Duration	PIVC site	Events
Retrospective cohort ⁸	202	Norepinephrine (72%), phenylephrine (36%)	Median initial to maximum: norepinephrine 0.04–0.13, phenylephrine 25–95 µg/minute	Median 11.5 hours, maximum 19 hours	Forearm, antecubital fossa, hand	8 events (4%), all local extravasation
Randomized controlled trial ¹⁰	310 (155 early vasopressor, 155 standard treatment)	Norepinephrine (67.7%) and epinephrine (17.4%) in early vasopressor group	Median (IQR) maximum in early vasopressor group: norepinephrine 0.1 (0.05–0.18), epinephrine 0.41 (0.28–1.2)	NR	NR	6 events in early vasopressor group (3.8%): 1 skin necrosis, 5 acute limb or intestinal ischemia
Unblinded superiority trial ¹¹	1,563 (782 restrictive fluid, 781 liberal fluid)	NR	NR	9.6 hours in restrictive fluid group	NR	3 events in PIVC vasopressor group (n = 500), all 3 were site extravasation
Prospective cohort ¹³	64	Epinephrine (66%), norepinephrine (41%)	Median (IQR): norepinephrine 0.1 (0.01–0.48), epinephrine 0.12 (0.6–0.38)	Median (IQR) 19 hours (8.5–37)	Antecubital fossa, forearm, hand	2 events (2.9%), extravasation with local tissue swelling
Randomized controlled trial ¹⁴	263 (128 PIVC, 135 CVC)	Epinephrine, norepinephrine	< 2 mg/hour, if more, crossover to CVC	NR	NR	133 total events: 56 insertion difficulty, 20 erythema, 19 extravasation, 9 catheter infection
Prospective cohort ¹⁵	635	Norepinephrine	Median (IQR) maximum: 10 µg/minute (6–15)	Median (IQR) 5.8 hours (2–20)	Antecubital fossa	35 extravasation ^b events (5.5%)
Retrospective cohort ¹⁶	212 patients (39 PIVC, 155 PIVC followed by CVC, 18 CVC only)	Phenylephrine (41%), norepinephrine (38%)	Median (IQR) maximum in PIVC-only group: phenylephrine 0.17 (0.09–0.27), norepinephrine 0.99 (0.6–1.64)	Median (IQR) 10.5 hours (4.7–15.9) in PIVC-only group	NR	75 events (35%): 28 leakage, 25 tissue cannula, 19 extravasation, 2 erythema

^aDosing is given as µg/kg/minute except where noted.

^bOther complications were not reported in this study.

CVC = central venous catheter; IQR = interquartile range; NR = not reported; PIVC = peripheral intravenous catheter

vasopressor administration. Most extravasation events were reported to be infiltration grade 0 to 2, with the worst resulting in edema at the infiltration site with mild pain.¹⁵

Table 1 summarizes adverse events associated with peripheral vasopressor administration.^{8,10,11,13–16} Given case reports of catastrophic events such as compartment

syndrome and amputation,^{17,18} these complications should not be underestimated. Although such complications are rare, their consequences are significant.

Type and duration

Although most studies report the safety of peripheral norepinephrine administration, some also note the safety of peripheral phenylephrine administration.¹⁹⁻²¹ At least 1 study of peripheral epinephrine and dopamine administration suggests that peripheral strategies for these agents are safe.¹³ A comparative study of these different vasopressors is warranted to assess which vasopressors or inotropes can be administered peripherally.

Despite reports that support peripheral vascular administration of vasopressors, the safe duration for its use is unknown. A systematic review reported the time to onset of adverse events to be 55.9 hours.²² In a more recent report, extravasation occurred primarily in the first 24 hours.¹⁵ There is evidence to support a protocol allowing peripheral vasopressor administration for up to 24 to 48 hours.^{15,23,24} Given the mixed data, however, the safe duration of peripheral administration requires further investigation.

PROTOCOLS TO PREVENT COMPLICATIONS

Despite the reported safety and feasibility of peripheral administration of vasopressors, variations in setting and management across institutions are a consideration. Various protocols that emphasize certain practices have been implemented and reported:

- Guidance on size and location along with assessment of PIV catheters every 2 hours²⁵
- Preset sizes and locations of catheters, confirmation of catheter placement with ultrasonography, assessment of the catheter every 2 hours, and maximum norepinephrine dosage limited to 15 µg/min with a maximum duration up to 48 hours¹⁵
- In the event of extravasation, stopping the vasopressor infusion, aspiration of the residual vasopressor, and application of phentolamine to the site (in this protocol, none of the 2% of patients with extravasation had tissue injury).^{24,26}

While these protocols sound clinically reasonable, 1 study reported no associations between peripheral catheter diameters, dosage of vasopressors, patient age, and risk of extravasation.¹³ A wide range of norepinephrine concentrations, from 4 to 64 µg/mL, administered via PIV catheter has been described in the literature.²⁷ In a study supporting the safety of peripheral administration, most patients received 16 or 32 µg/mL of norepinephrine.⁸ In the absence of comparisons of different concentrations of norepinephrine,

a concentration in the range of 16 to 32 µg/mL may be a safer option than higher doses.

A protocol that defines the duration of peripheral administration, norepinephrine concentration, assessment frequency, and catheter type and size will minimize complications, delays in their identification, and confusion among staff.

BENEFITS OF PERIPHERAL ADMINISTRATION

The potential benefits of peripheral administration include earlier hemodynamic stabilization and avoidance of CV catheter placement.

In a post hoc analysis of a clinical trial on early septic shock, when compared with patients who received CV catheter administration, those in the peripheral administration group had a shorter median time to commencement of vasopressors (2.4 vs 4.9 hours) and antimicrobials (55 vs 71.5 minutes).²⁸ In a randomized controlled trial assessing early use of norepinephrine in septic shock resuscitation, the median time to CV catheter insertion from the diagnosis of septic shock was approximately 4 hours, whereas vasopressors were initiated via PIV or CV catheter within approximately 70 minutes.¹⁰ Early norepinephrine led to a significantly increased rate of shock control by 6 hours, implying that we should not delay starting norepinephrine until a CV catheter is placed. The authors suggested that rapid hemodynamic stabilization potentially benefits clinical outcomes.¹⁰

In addition to its potential clinical benefits, peripheral administration can help avoid unnecessary CV catheter insertion. In a study of 734 patients who received peripheral administration of vasoactive medication, only 13% needed CV catheter insertion.²⁵ Even when peripheral administration was limited to up to 24 hours in another study, approximately one-third of patients who received vasopressors did not require CV catheter placement.²³ A successful peripheral administration protocol could offer a significant patient-centric benefit of comfort by avoiding CV catheter-related complications.

The impact of safe vasopressor administration via PIV catheter can be significant in a resource-limited setting, although few studies have assessed its effect in such settings.^{13,29}

CURRENT PERCEPTIONS AND CONCERNS

The Surviving Sepsis Campaign guidelines suggest starting peripheral vasopressor administration to restore adequate mean arterial pressure until a CV catheter can be placed.³⁰ General acceptance of peripheral vasopressor administration is limited, however. A survey of

62 hospitals in Michigan reported that 36.5% supported PIV catheter use for vasopressors, 25% preferred CV catheter use only, and the remaining 36.5% preferred CV catheter use over peripheral administration.²⁴ Compared with rural institutions, urban hospitals tended to favor peripheral administration of vasopressors.²⁴ Low acceptance of peripheral vasopressor administration might reflect concerns about adverse events and lack of familiarity with the process.

We suggest a protocol-based approach to address these concerns. A recent before-and-after study using a nursing protocol for peripheral vasopressor administration showed a significant reduction in extravasation events, from 2.4% to 1.1%.³¹ The investigators protocolized the use of ultrasonography for peripheral placement, peripheral location, line assessment every 2 hours, and vasopressor infusion rates. A similar protocol that also included peripheral vasopressor administration for up to 48 hours was used in another study.¹⁵ Most studies of peripheral administration are conducted in the intensive care unit, where it is reasonable to implement peripheral vasopressor administration because the need for frequent assessment can be accommodated and clinicians are familiar with the medication.

Protocol-based approaches that include guidance on patient selection and location of placement of the PIV catheter, training on use of ultrasonography for placement of the PIV catheter, standardized assessment of

the peripheral site, and ready availability of antidotes can increase the safety of peripheral vasopressor administration.^{24,26} A large prospective study to confirm the duration of safe peripheral vasopressor administration is warranted, but the requirement for a vasopressor does not automatically translate to the need for a CV catheter.

■ TAKE-HOME POINTS

- Peripheral administration shortens the time to start vasopressors.
- PIV catheter use is associated with local adverse events such as tissue infiltration, which infrequently requires intervention but rarely leads to catastrophic adverse events such as compartment syndrome or amputation.
- Peripheral vasopressor administration requires close attention, especially during the first 24 hours.
- Most studies used protocols that allow peripheral administration of vasopressors for up to 24 to 48 hours.
- PIV catheter use can lessen the need for CV catheter placement, decreasing the risk of complications associated with the procedure and catheter maintenance.

■ DISCLOSURES

The authors report no relevant financial relationships which, in the context of their contributions, could be perceived as a potential conflict of interest.

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