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ORIGINAL RESEARCH

Safety of Peripheral Intravenous Administration of Vasoactive Medication

Jose Cardenas-Garcia, MD[1]*, Karen F. Schaub, BS[1], Yuly G. Belchikov, PharmD[2], Mangala Narasimhan, DO[1], Seth J. Koenig, MD[1], Paul H. Mayo, MD[1]

[1]Division of Pulmonary, Critical Care and Sleep Medicine, Hofstra North Shore–Long Island Jewish School of Medicine, Hempstead, New York; [2]Clinical Pharmacy Services, Department of Pharmacy, Westchester Medical Center, Valhalla, New York.

BACKGROUND: Central venous access is commonly performed to administer vasoactive medication. The administration of vasoactive medication via peripheral intravenous access is a potential method of reducing the need for central venous access. The aim of this study was to evaluate the safety of vasoactive medication administered through peripheral intravenous access.

METHODS: Over a 20-month period starting in September 2012, we monitored the use of vasoactive medication via peripheral intravenous access in an 18-bed medical intensive care unit. Norepinephrine, dopamine, and phenylephrine were all approved for use through peripheral intravenous access.

RESULTS: A total of 734 patients (age 72 ± 15 years, male/female 398/336, SAPS II score 75 ± 15) received vasoactive medication via peripheral intravenous access 783 times. Vasoactive medication used was norepinephrine (n = 506), dopamine (n = 101), and phenylephrine (n = 176). The duration of vasoactive medication via peripheral intravenous access was 49 ± 22 hours. Extravasation of the peripheral intravenous access during administration of vasoactive medication occurred in 19 patients (2%) without any tissue injury following treatment, with local phentolamine injection and application of local nitroglycerin paste. There were 95 patients (13%) receiving vasoactive medication through peripheral intravenous access who eventually required central intravenous access.

CONCLUSIONS: Administration of norepinephrine, dopamine, or phenylephrine by peripheral intravenous access was feasible and safe in this single-center medical intensive care unit. Extravasation from the peripheral intravenous line was uncommon, and phentolamine with nitroglycerin paste were effective in preventing local ischemic injury. Clinicians should not regard the use of vasoactive medication is an automatic indication for central venous access. *Journal of Hospital Medicine* 2015;000:000–000. © 2015 Society of Hospital Medicine

Vasoactive medications (VMs) are often required to improve hemodynamic function in patients with shock. They are usually given through central venous catheter (CVC) access, primarily out of concern that extravasation of peripheral intravenous (PIV) access may result in local tissue injury due to the vasoconstrictive effect of the VM. However, insertion of CVC is associated with a variety of mechanical complications and risk of central line–associated bacteremia. To examine the feasibility and safety of using VM via PIV access, we report on the administration of VM in the form of norepinephrine, dopamine, and phenylephrine via PIV access, with the rationale that this would be a method of reducing the need of CVC use. Our hypotheses are that VM via PIV access is both feasible and safe.

*Address for correspondence and reprint requests: Jose Cardenas-Garcia, MD, Department of Medicine, Division of Pulmonary, Critical Care and Sleep Medicine, Hofstra–North Shore LIJ School of Medicine, 410 Lakeville Rd, Suite 107, New Hyde Park, NY 11042; E-mail: jdecardenasg@gmail.com

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MATERIAL AND METHODS

Study Design

This was a single-arm, consecutive-patient study conducted from September 2012 to June 2014. The study site was an 18-bed medical intensive care unit (MICU) staffed by full-time attendings, fellows, and residents at the Long Island Jewish Medical Center, which is an 827-bed tertiary care teaching hospital that is part of the North Shore–Long Island Jewish Health System. The primary outcome measure was the rate of local tissue injury resulting from use of VM via PIV access. The study was approved by the hospital institutional review board (study #13–583A), which waived requirement for informed consent.

Protocol for Administration of VM via PIV Access

In cooperation with the Department of Pharmacy, medical and nursing staff developed a written protocol for administration of VM via PIV access. The protocol was reviewed and approved by the hospital pharmacy and therapeutics committee and the MICU nursing leadership. The MICU nursing staff received in-service training before rollout of the protocol, which included training on the recognition of PIV access extravasation and the type of line that could be used. The MICU housestaff teams were given specific instructions concerning the protocol during their MICU rotations.

TABLE 1. Summary of the Requirements for PIV Access Used for Infusion of VM

Vein diameter >4 mm measured with ultrasonography
Position of PIV access documented to be in the vein with ultrasonography before starting infusion of VM
Upper extremity only, contralateral to the blood pressure cuff
Intravenous line size 20 gauge or 18 gauge
No hand, wrist, or antecubital fossa PIV access position
Blood return from the PIV access prior to VM administration
Assessment of PIV access function every 2 hours as per nursing protocol
Immediate alert by nursing staff to the medical team if line extravasation, with prompt initiation of local treatment
72 hours maximum duration of PIV access use

NOTE: **Abbreviations:** PIV, peripheral intravenous; VM, vasoactive medication.

A summary of the requirements for PIV access for VM use is summarized in Table 1.

Patient Management

The decision to initiate treatment with VM was made by the clinical management team. The standard concentrations of VM for use via PIV access were: norepinephrine 8 mg or 16 mg/250 mL normal saline, dopamine 400 mg or 800 mg/250 mL D5W, and phenylephrine 80 mg or 160 mg/500 mL normal saline. If the attending or fellow in charge of the case decided that VM should be administered through PIV access, peripheral access was established that conformed to the requirements of the protocol, and VM was administered via PIV access for as long as there was clinical indication or until PIV access suitable for VM administration was no longer feasible. If the patient received VM via PIV access, a second PIV access site was established in case of failure of the primary PIV site. If no PIV access could be inserted, the patient received CVC access. The decision to use VM via CVC access was made by the clinical management team, as was the type, dose, and duration of the VM use via PIV access or CVC access. Vasopressin was not used via PIV access. Dobutamine was used via PIV access but not recorded in our results, as it has no α-mediated vasoconstrictor effect. Dobutamine was not used concomitantly with other vasoactive medication through the same PIV access. If PIV access was not established using standard technique by nursing staff, medical residents or critical care fellows inserted PIV access using real-time ultrasound guidance. The PIV access use for VM could also be used for other medications providing they were compatible with the VM. Only 1 type of VM was infused through the PIV access.

As indicated in Table 1, the nursing staff examined the PIV access site every 2 hours and checked that blood could be aspirated from the line. The aspiration of the line requires several seconds of discontinuation of VM use, which we considered to have no clinical relevance. If the nursing staff identified extravasation of the PIV access site through which VM was infusing, they notified the medical housestaff, who promptly initiated treatment with local injection of phentolamine and local application of nitroglycerin paste as described in Table 2. The extravasation site was examined for tissue injury on a shift basis by the nursing staff, and on bedside rounds by the attending and fellow for at least 48 hours following PIV access removal. Tissue injury was defined as any erythema, blistering, skin breakdown, or necrosis in the site of extravasation.

Data were collected prospectively by an investigator (J.C.-G.) and entered into a standard data-collection sheet for quality and safety assessment for the initial 13 months of the study. In the subsequent 7 months of observation, data were collected from retrospective chart review. The initial 13 months of data collection were performed as an ongoing safety analysis project; the subsequent 7-month review was performed as an additional quality assessment project. The deidentified data included patient demographics, patient disease characteristics, use of VM, and VM via PIV access complications.

Statistical Analysis

The statistical analysis was performed using SPSS 21 (Statistical Package for the Social Sciences; IBM, Armonk, NY). Continuous variables are presented as mean ± standard deviation.

RESULTS

Characteristics of patients who received VM via PIV access are presented in Table 3. During the study period, there were 2462 admissions to the MICU, and 267 CVCs were inserted by the MICU team, 170 of which were triple-lumen catheters and 97 were large-gauge catheters for hemodialysis or plasmapheresis. Of the total admissions, 953 cases received VM; 783/953 (82%) received VM via PIV access, and 170/953 received VM via CVC access (18%). For VM use, an 18-gauge PIV catheter was used in 192/783 (25%), a 20-gauge catheter was used in 590/783 (75%), and a 22-gauge catheter was used in 1/783 of interventions.

TABLE 2. Treatment of VM via PIV Access Extravasation

1. The VM via PIV infusion is stopped immediately.
2. Residual medication is aspirated through the PIV access, and the catheter is removed.
3. The extent of the extravasation is outlined to provide a baseline for monitoring.
4. Two vials, each containing 5 mg of phentolamine, are reconstituted with 5 mL of normal saline per vial to yield a final concentration of 1 mg/mL.
5. The phentolamine solution is injected in 0.5- to 1-mL aliquots in 5 separate injections around the leading edge of the extravasation, using separate 25-gauge or 27-gauge needles for each injection.
6. Nitroglycerin paste (2.5 cm) is applied to the area of extravasation.
7. A medication occurrence report is filled out for review by the quality committee.

NOTE: **Abbreviations:** PIV, peripheral intravenous; VM, vasoactive medication.

TABLE 3. Demographic and Disease Characteristics of the Study Population

	Total Study Group
No. of patients	734
Age, y	72 ± 15
Gender	
Male	398 (54%)
Female	336 (46%)
SAPS II score	75 ± 15
Patients on mechanical ventilation	235 (32%)
Patients on hemodialysis	90 (12%)
MICU mortality	177 (23%)
Use of VM via PIV access	783
Extravasations of VM via PIV access	19 (2%)
Total MICU admissions during study period	2,462

NOTE: **Abbreviations:** MICU, medical intensive care unit; PIV, peripheral intravenous; SAPS II, simplified acute physiology score II; VM, vasoactive medication.

Catheter length was 30 mm, 45 mm, or 48 mm depending on availability. The 22-gauge catheter, which was a deviation from standard protocol, infiltrated shortly following insertion. We did not formally record the anatomic position of the PIV access in the standard data-collection sheet; anecdotally, the majority of PIV accesses were placed in the upper arm basilic or cephalic vein. The duration of VM via PIV access was 49 ± 22 hours. Central intravenous access was required in 95/734 (13%) of patients who initially had VM via PIV access. These catheters are included in the 170 triple-lumen CVCs that were inserted by the MICU team during the study period. The type and highest dose of VM administered via PIV access are presented in Table 4.

A total of 734 patients received VM via PIV access during the 20-month study period; 49 of these patients required 2 or more PIV access insertions, as the initial and/or subsequent site timed out at 72 hours, resulting in a total of 783 separate interventions. Infiltration of the PIV access site occurred in 19/783 (2%) of interventions. All of them were identified by nursing staff with prompt response using local injection of phentolamine and application of nitroglycerin paste at the site of the extravasation. There was no tissue injury at the site of VM extravasation. Sixteen of the extravasations occurred with norepinephrine infusions and 3 with dopamine infusions. There were no infections of the PIV access sites used for VM. Use of phentolamine and nitroglycerin paste was not associated with hypotension, as defined as mean arterial pressure less than 65 mm Hg.

DISCUSSION

Our study demonstrates that administration of VM via PIV access is feasible, carries a low rate of complications, and offers an alternative to CVC access. There are several elements that may have allowed safe use of VM via PIV access. We developed a protocol that involved a multidisciplinary team. The hospital pharmacy performed an extensive literature search and formulated the initial protocol with the MICU attending staff. The protocol was then subjected to iterative process improvement by a hospital committee and nursing leadership in the MICU. Before program rollout, the MICU nursing staff were educated and trained to use the protocol. This was a key component of the program, as the nurses were responsible for many of the line insertions, line maintenance, and identification of infiltration. Although we did not perform any formal measurement of the impact of PIV access use on nursing workflow, we note that leadership and frontline nurses have been enthusiastic about the implementation of VM via PIV access. The MICU housestaff teams were given an in-service instruction concerning the importance of prompt initiation of local treatment in case of infiltration of the PIV access site. Specific elements of the protocol that may have improved safety were the use of ultrasonography to insert difficult PIV access and confirmation of all PIV access insertions using ultrasonography by the MICU housestaff. The requirement for frequent checks of PIV access function, prompt recognition of infiltration, and specific antidote to extravasation were important elements of safety. The low rate of PIV access extravasation (2%) may be related to the use of ultrasonography to guide PIV access insertion in patients who had challenging anatomy (eg, obesity, edema, recreational drug use, history of multiple PIV insertions), and ultrasonography was used to check that the PIV access was well positioned before VM infusion.

There were early literature reports that subcutaneous extravasation of catecholamines could result in local ischemic injury both in human patients and animal models.[1–5] Local phentolamine injection has been identified as a specific antidote to block the local ischemic injury.[6–15] More recently, there have been anecdotal reports showing that local application of nitroglycerin paste blocks ischemic injury in the pediatric population.[5,16,17] With this information, our

TABLE 4. Frequency, Highest Dose, and Complications of Vasoactive Medication Administered via PIV Access

Norepinephrine	
Interventions	506
Dose, μg/kg/min, mean ± SD	0.70 ± 0.23
PIV access extravasations	16
Dopamine	
Interventions	101
Dose, μg/kg/min, mean ± SD	12.7 ± 5.23
PIV access extravasations	3
Phenylephrine	
Interventions	176
Dose, μg/kg/min, mean ± SD	3.25 ± 1.69
PIV access extravasations	0

NOTE: **Abbreviations:** PIV, peripheral intravenous; SD, standard deviation.

protocol included the requirement of prompt treatment of local extravasation with phentolamine and nitroglycerin paste at the site of VM via PIV access extravasation. In theory, both phentolamine and nitroglycerin might cause hypotension. In our study, administration of both phentolamine and nitroglycerin paste was not associated with more hypotension nor did it increase requirements for VM.

Multilumen small bore CVCs may be used for several reasons, some of which need to be reconsidered. First, before introduction of the VM via PIV access protocol, a common indication for triple lumen CVC insertion in our MICU was the perception that VM could only be administered through CVC access, for fear of local tissue injury should extravasation of the VM occur through the PIV access site. Our results indicate that VM use is not an automatic indication for CVC insertion. Second, a possible indication for CVC insertion is to measure central venous pressure for the purpose of guiding volume resuscitation in patients with hemodynamic failure. As the utility of central venous pressure monitoring has been called into serious question,[18–20] we do not consider this indication for CVC use to be valid. Third, CVC access may be required due to anatomic constraints (ie, there is no suitable PIV site). Fourth, there may be need for such a large number of intravenous medications that PIV access cannot support. Fifth, there is occasional situation where the patient requires use of medications where extravasation of PIV access would cause local tissue injury without local antidote (eg, certain chemotherapeutic agents). The continued need for CVC access in some patients is reflected in the finding that 13% of our study patients who received VM via PIV access eventually required triple-lumen CVC insertion. However, our results indicate that the rate of CVC use may be reduced by using PIV access for VM administration.

Our study has some methodological limitations. Study design was single center and observational. The focus of this study was to examine the safety of VM via PIV access. We cannot comment on its effectiveness, indications, or influence on patient outcome nor on why some patients required CVC insertion whereas others did not. The decision to administer VM was made by the clinical team, as was the route of its administration and concentration, without any input from the investigators. We did not collect data on who performed the PIV access insertion (medical or nursing staff), demographics, and disease characteristics of the CVC group, nor to what extent ultrasonography was used to guide PIV insertion. We did not attempt to define whether there were any factors that identified risk for PIV access extravasation, nor did we evaluate for any differences between the PIV and CVC group in terms of demographics and disease characteristics. Lacking a control group, we cannot say definitively that VM via PIV access is safer than VM via CVC. Being a single-center study, it is not possible to say that the results are transferable to another clinical environment; this applies particularly to the use of ultrasonography, which is a user-dependent skill. We cannot determine which, if any, component of the protocol was responsible for the safe use of VM via PIV access. The rate of PIV access extravasation was low, so it is possible that a larger sample size is required to identify incidents of tissue necrosis from extravasation of VM delivered via PIV access despite the use of local antidote.

CONCLUSIONS

The delivery of VM via PIV access is safe and feasible. Tto reduce the risk of extravasation leading to possible local tissue injury, we developed a protocol that emphasized close cooperation between the nursing and medical staff, routine use of ultrasonography, rapid identification of extravasation of the PIV access, and prompt response to local extravasation of VM using phentolamine and nitroglycerin paste. This approach offers a means of reducing CVC use, in both intensive care unit (ICU) and non-ICU settings, including hospital wards and emergency departments. Clinicians should no longer consider administration of norepinephrine, dopamine, or phenylephrine to be an automatic indication for CVC access. This study focused on the safety of VM administered via PIV access, with emphasis on local complications related to extravasation, and should be considered a preliminary single-center study that demonstrates that administration of certain vasoactive medications may not universally require central venous access. A broader study regarding assessment of safety and efficacy will require a multicenter design.

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