

Evaluation of the safety of a novel peripheral vasopressor pilot program and the impact on central line placement in medical and surgical intensive care units



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<https://doi.org/10.1093/ajhp/zxac144>

Purpose. The purpose of this quality improvement project was to evaluate the safety and feasibility of peripheral vasopressor administration in an attempt to minimize the placement and improve early removal of unnecessary central lines to reduce central line–associated bloodstream infection (CLABSI) rates.

Methods. A retrospective chart review was conducted on patients who received vasopressors via peripheral infusion over 3 months, starting at the time of guideline implementation.

Results. We identified 129 vasopressor orders among 79 patients that were administered peripherally. Among these orders, 3 events were documented as possible extravasation events. Forty-five patients (57%) did not require central line placement due to increasing vasopressor requirements. Standard utilization ratio data suggest minimal central line impact of the protocol implementation. December 2020 to February 2021 was associated with a large second peak of coronavirus disease 2019 (COVID-19) in our region. Utilization of central lines was less than predicted in December 2020 to February 2021 in 2 of our 3 intensive care units (ICUs); however, the differences were statistically significant on only 3 occasions. In the third ICU, utilization was greater than predicted, but this unit housed a majority of the most critically ill patients with COVID-19.

Conclusion. This study suggests that short-term use of select vasopressors at conservative doses is safe for peripheral administration and points toward efficacy at preventing central line placement. Further analysis is required to confirm efficacy.

Keywords: central venous catheter, peripheral vasopressor, quality improvement, vasoactive agents, vasopressor agents

Central line–associated bloodstream infections (CLABSIs) are associated with increased mortality and healthcare costs, with costs averaging approximately \$46,000 per case.¹ Many of these cases are preventable with proper aseptic technique, site care, quick removal/minimized use, and management strategies, but the risk of infection in these patients still remains high depending on the site.¹ Even with placement under aseptic technique, CLABSI rates range from 0.8 to 4.1 cases per 1,000 central line days depending on location in the

hospital, with intensive care units (ICUs) on the lower end of the range. When nontunneled, lines may become a nidus for infection over 7 to 10 days as bacteria migrate, highlighting the importance of reducing initial placement and duration of use.¹ One of the most common indications for central lines at our institution is blood pressure support with intravenous (IV) vasopressors. Historically, vasopressors have been considered only appropriate for use via a central line owing to the risk of infiltration, extravasation, and subsequent necrosis. Practice at our

institution was to administer vasopressors via a central line, with the unwritten exception that only phenylephrine could be administered peripherally; however, this approach was rarely utilized. Newer literature has demonstrated that short-term use of select vasopressors is safe for peripheral administration at select doses and concentrations.²⁻⁴

Over the past couple years, our institution has continuously reevaluated its total central line days and incidence of CLABSI as a result of increased rates. Although some of the increase in rates may have been related to the coronavirus disease 2019 (COVID-19) pandemic, interdisciplinary huddles along the Lean/Six Sigma framework identified opportunities to reduce central line placement in the critical care space related to IV vasopressors. An extensive literature search was conducted that confirmed concerns surrounding overuse of central lines based on the duration and dosage of vasopressors across some ICU patients. As such, the flagship hospital of the organization has been leading an initiative to decrease the total number of central line placements initially in the emergency department and ICU. The aim of this initiative is to decrease overall central line days and, hopefully, incidence of CLABSI. A secondary goal is to facilitate early removal of central lines, in which we hope this protocol will have an important role moving forward. As part of this initiative, the critical care committee for the hospital implemented a pilot program to allow peripheral administration of vasopressors in 3 of our ICUs. The purpose of this study was to evaluate the safety of peripheral administration of select vasopressors at select doses and concentrations and the impact on central line placement, with a focus on the feasibility of a peripheral vasopressor guideline. Herein we report the findings from this quality improvement project.

Methods

Peripheral vasopressor guideline document. After defining the issue at hand, a guideline document



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was developed for this pilot program, listing inclusion and exclusion criteria for patients for peripheral administration of vasopressors, and was passed through hospital-wide infection prevention, nursing, and critical care committees (see [eAppendix](#) for the guideline document). The goal was to create a framework to ensure safe use while also identifying patients who could be followed retrospectively as the pilot was put in place across our prespecified ICUs. Specifically, patients were included if they did not require a central venous catheter for any other reason, such as blood product resuscitation, poor access, or hypertonic fluid administration, and were expected to require low or moderate doses of a single vasopressor for at most 72 consecutive hours. The latter

determination was made subjectively by the provider approving use on the basis of the perceived severity of the indication for vasopressor use. If after 72 hours the patient still required a vasopressor, providers were allowed to use the alternate limb for an additional 72 hours. Patients were to be excluded if they required 2 or more vasopressors, if their vasculature would not support the placement of 2 peripheral IV sites, if the peripheral IV site did not have brisk blood return, and if the patient had limb restrictions. Ultrasound-guided line placement was not a requirement due to the potential for hindrance of use and sentiment from the nursing, provider, and IV therapy teams that brisk blood return was enough of a constraint with required monitoring.

Our guideline also included monitoring parameters for nurses and providers. Nurses were instructed to inspect the site of peripheral access 5 minutes after the start of infusion and at least every hour thereafter for early signs and symptoms of extravasation/infiltration. If extravasation/infiltration occurred, a provider was to be notified with use of appropriate management techniques. Finally, an important requirement of this protocol was the loading of specific extravasation reversal agents to automated dispensing cabinets in units included in the study.

After guideline implementation, it became clear that awareness of and attention to peripherally running vasopressors were highly variable among providers. To improve awareness of peripheral vasopressor administration and adherence to the guideline, several additional interventions were implemented. IV lines were tagged with labels that displayed “peripheral vasopressor,” and laminated signs were created for room doors identifying patients on a peripheral vasopressor and the time administration began. Additionally, providers and other floor staff went through informal training on the peripheral vasopressor guideline and how to order and document a peripheral

vasopressor in our electronic health record. Informal training included discussions at daily huddles, distribution of the guideline to affected units, and online training with a descriptive presentation followed by attestation that providers read the materials.

Study design. This quality improvement project was performed at Hartford Hospital, using the SQUIRE (Standards for Quality Improvement Reporting Excellence) guidelines for quality improvement reporting.⁵ This study was deemed “not research” by the Hartford HealthCare institutional review board (HHC-2021-0168).

Upon order verification, pharmacists were instructed to flag orders for peripheral vasopressors so that these orders could be reviewed for this study. A retrospective chart review was conducted on these patients, with data collection occurring shortly after the peripheral vasopressor order was identified.

Outcomes. The critical care council for the health system defined specific measures that would aid in ensuring primarily the safety but also the efficacy of the protocol. Our team determined that data should be collected over a period of 3 months, starting at the time of guideline implementation (December 2020 to February 2021). Data were collected on the vasopressor used, duration of peripheral administration, maximum dose infused peripherally, and time at maximum dose. For safety outcomes, we evaluated the incidence of extravasation events, defined as phlebitis, erythema, infiltration, skin blanching, and/or edema according to the bedside team, and the outcome of these events, specifically whether extravasation treatment was required. Nursing was required to document in an electronic medical record flowsheet the presence or absence of infiltration and, if infiltration was present, the severity of infiltration/extravasation. To evaluate the impact on central line placement, we collected data on the number of central lines that were placed because of an increased vasopressor requirement, extended duration, need for

a second vasopressor, or poor access or loss of access and, if a line was placed, the incidence of CLABSI.

Analysis. Descriptive statistics were used for safety outcomes data as this was not an a priori powered study. We used standard utilization ratio (SUR) to analyze the impact of our guideline on central line placement. SUR is a standardized approach that was developed by the National Healthcare Safety Network (NHSN) to track device utilization, and it adjusts for various facility-level factors that contribute to device use.⁶ SUR is calculated by dividing the number of observed device days by the number of predicted device days.⁶ A SUR greater than 1 indicates that more device days were observed than predicted, while a SUR less than 1 indicates that fewer device days were observed than predicted.⁶ The NHSN then uses a mid-*P* exact test associated with confidence intervals to assess the statistical significance of the difference from the expected utilization rate. Predicted device utilization days are calculated based on national aggregate NHSN data from 2015 and adjusted for risk by Centers for Disease Control and Prevention location, hospital beds, medical school affiliation type, and facility type. Further, observational safety data and SUR-based analysis of efficacy, although not specifically powered, were compiled and presented across the local critical care committee and system-wide critical care council. The goal was to have the team use data analysis to identify areas for improvement, verify safety outcomes, and assist with goals and measures for a larger study to be conducted following approval of the guideline for system-wide use. This would represent the final stage in our implementation of the DMAIC (Define, Measure, Analyze, Improve, Control) model and is currently underway with adequate power.

Results

Between December 2020 and February 2021, we identified 129 vasopressor orders among 79 patients for whom peripheral administration

was performed (Table 1). Data are reported as separate orders for 79 unique patients, as patients may have had orders discontinued and restarted in the same prolonged stay or been switched between vasopressors depending on indication. Norepinephrine and phenylephrine were the most commonly used vasopressors. The average maximum dose infused peripherally was below the maximum dose outlined in our protocol for all vasopressors except epinephrine, with 2 of the 3 epinephrine orders run above 0.1 µg/kg/min. Of the 129 peripheral vasopressor orders, 23 were run above the maximum dose stated in our guideline at some point during the 72-hour administration period. The average total duration of peripheral administration was less than 72 hours for all vasopressors. Seven orders were infused peripherally beyond 72 hours, but in each instance a peripheral IV site on the alternate limb was used (Table 2).

Three events were documented as possible extravasation events. These events were not specifically labeled as “extravasation” by the bedside team, and the patients did not require treatment for extravasation. One event was labeled as “phlebitis/erythema at access site,” with norepinephrine running at 6 µg/min at hour 28 of peripheral administration, and this infusion was continued without further intervention or documentation of phlebitis/erythema. Two events were labeled as “infiltration/skin blanched/edema <1 inch,” with phenylephrine running at 160 µg/min at hour 76 of peripheral administration and with norepinephrine running at 14 µg/min at hour 62 of peripheral administration. Similarly, both of these infusions were continued at alternate sites without further intervention or documentation of infiltration. No extravasation events were documented in the instances where a vasopressor was run above the maximum dose stated in our guideline.

Of the 79 patients included in this study, 45 (57%) did not require central

Table 1. Peripheral Vasopressor Use for All Patients Using the Peripheral Vasopressor Protocol^a

Vasopressor	No. of orders	Average total duration of peripheral administration, hours	Average maximum dose	Average time at maximum dose, hours
Norepinephrine	67	20	14.9 µg/min	5.3
Phenylephrine	58	17.8	119.9 µg/min	3.1
Vasopressin	1	18.2	0.03 units/min	17
Epinephrine	3	6.4	0.3 µg/kg/min	2

^aInfusion data while running vasopressor centrally are not included in this table for patients who required central line placement (ie, were unable to be weaned from the maximum peripheral dose or had exceeded the maximum duration without the ability to switch limbs).

Table 2. Duration of Peripheral Vasopressor Administration

Duration of peripheral administration	No. of orders
<24 hours	94
24-48 hours	25
48-72 hours	3
>72 hours	7

line placement due to increasing vasopressor requirements. No CLABSIs were documented among the 34 patients who did require central line placement. Table 3 shows SUR data on central line placement from before and after implementation of our guideline in December 2020. These data suggest that utilization of central lines was less than predicted in December 2020 to February 2021 in 2 of our 3 ICUs; however, observed differences were statistically significant on only 3 occasions. In ICU 2, utilization of central lines was greater than predicted in December 2020 and January 2021 but less than predicted in February 2021; these differences were not statistically significant. Of note, ICU 1 is a primary 16-bed medical ICU, ICU 2 is a 14-bed surgical/trauma ICU, and ICU 3 is a primary 12-bed medical ICU. Throughout the 2020 calendar year, ICU 1 housed the most critically ill patients with COVID-19. ICU 3 served as a backup COVID-19 unit, with ICU 1 only accepting these patients during the largest peaks.

Discussion

This quality improvement project supports the feasibility of peripheral

vasopressor administration based on real-world implementation of our novel protocol. Our findings suggest that short-term use of select vasopressors is safe for peripheral administration at select doses and concentrations. Specifically, we were able to determine via a planned Six Sigma DMADV (Define, Measure, Analyze, Design, Verify) plan that it was indeed safe to continue on a larger scale. We chose the DMADV plan for this initial project phase as it represents a framework for implementation of a new process. Our final steps in the Six Sigma framework will be completed upon implementation and analysis of the protocol across the system utilizing a DMAIC model. As noted in the methods, after implementation, we developed signage and flags/tags for peripheral lines running vasopressors. As part of the quality improvement project, meetings were held to analyze and improve usage. Teams quickly realized that simply relying on pharmacist documentation and follow-up during rounds and provider documentation in the health system alone was not enough to achieve adequate awareness and monitoring. Nursing teams quickly suggested

additional measures that allowed the entire team to continuously evaluate safety with respect to line patency and infiltration events. Through a focused document, continuous reevaluation, and subsequent improvement, it is clearly feasible (with appropriate resources) to implement a similar protocol across multiple ICUs for future expansion.

Our findings are consistent with other recent literature demonstrating the safety of peripheral vasopressor administration.²⁻⁴ Specifically, one systematic review found that 3.4% of 1,382 patients who received a vasopressor via peripheral administration experienced extravasation.⁷ Similarly, another study identified a 4% extravasation rate with peripheral vasopressor administration in 202 patients.⁸ Although our sample size was relatively small in comparison to other studies, we did not find any events that were labeled as extravasation by the bedside team in our preliminary data pool. Our findings provide support for current literature demonstrating the safety of peripheral vasopressors when used for short durations at conservative doses. Apart from the sample size, other possible explanations for our lack of extravasation events include the strict dosing restrictions, deliberation during bedside rounds, and education for nursing and other bedside staff, as well as close monitoring of all infusion sites with timestamp labeling. During daily rounds, the team was required to comment on whether vasopressors were running peripherally so that all would be aware. This ensured that both pharmacists and providers tracked

Table 3. Standard Utilization Ratio Data From the 3 Intensive Care Units Included in This Study^a

Month	ICU 1		ICU 2		ICU 3	
	SUR (CI)	P	SUR (CI)	P	SUR (CI)	P
Dec. 2019	0.8 (0.7-0.91)	0.001	1.08 (0.95-1.22)	0.25	ND	ND
Jan. 2020	0.94 (0.83-1.07)	0.38	0.82 (0.71-0.95)	0.01	ND	ND
Feb. 2020	0.84 (0.73-0.96)	0.01	0.9 (0.77-1.05)	0.19	ND	ND
Mar. 2020	0.94 (0.83-1.07)	0.38	1.11 (0.97-1.27)	0.13	ND	ND
Apr. 2020	1.36 (1.22-1.51)	<0.001	1.2 (1.05-1.36)	0.001	1.29 (1.13-1.47)	0.0003
May 2020	1.31 (1.17-1.47)	<0.001	0.95 (0.82-1.1)	0.51	1.14 (0.99-1.31)	0.07
Jun. 2020	1.11 (0.98-1.26)	0.11	0.89 (0.77-1.03)	0.12	0.7 (0.58-0.84)	<0.001
Jul. 2020	0.83 (0.72-0.95)	0.01	1.02 (0.89-1.16)	0.8	0.75 (0.64-0.89)	0.0006
Aug. 2020	0.64 (0.55-0.75)	<0.001	1.03 (0.9-1.18)	0.67	0.89 (0.76-1.04)	0.16
Sep. 2020	0.67 (0.57-0.78)	<0.001	1.15 (1.01-1.3)	0.04	0.77 (0.65-0.91)	0.002
Oct. 2020	0.56 (0.47-0.66)	<0.001	1.09 (0.96-1.24)	0.21	0.62 (0.52-0.75)	<0.001
Nov. 2020	0.69 (0.59-0.8)	<0.001	0.95 (0.82-1.09)	0.46	0.59 (0.48-0.71)	<0.001
Dec. 2020	0.91 (0.8-1.03)	0.15	1.13 (0.99-1.28)	0.07	0.64 (0.53-0.76)	<0.001
Jan. 2021	0.99 (0.88-1.13)	1	1.09 (0.96-1.24)	0.18	0.86 (0.74-1.0)	0.06
Feb. 2021	0.8 (0.69-0.92)	0.002	0.93 (0.8-1.08)	0.37	0.8 (0.68-0.94)	0.01

Abbreviations: CI, confidence interval; ICU, intensive care unit; ND, no data; SUR, standard utilization ratio.

^aPeripheral vasopressor data were collected from December 2020 through February 2021. SURs with a P value of <0.05 were considered significant.

duration and monitoring of orders and nursing documented correct site care, route of administration, and adverse effects.

Previous studies have included retrospective analysis of vasopressors in a specific setting, such as the operating or emergency room; prospective randomized analysis of vasopressors in patients with sepsis; and meta-analysis of previously conducted trials.^{2-4,7,8} However, to our knowledge, none of the cited reports highlighted how the researchers went about improving practice, for example, through implementation of a novel guideline. Our report aims to build on prior studies while highlighting our own quality improvement initiatives on a multidisciplinary team across a health system. We include our guideline document, safety outcomes, and efficacy data as evidence and resources for other hospitals to support work toward safe, evidence-based practice in a manner that allows for continuous reevaluation and improvement.

From the aforementioned continuous reevaluation focusing on care of our patients, we gleaned that at our institution phenylephrine was previously considered the only safe vasopressor to run peripherally, with no dose or concentration limits explicitly defined. As this was a practice before the implementation of our peripheral vasopressor guideline, we noticed issues with guideline adherence after implementation of our pilot program, specifically with regard to phenylephrine administration above the maximum peripheral dose stated in the guideline. Despite this, we did not see any extravasation events at doses higher than those defined. A secondary concern regarding phenylephrine was overuse in patients with sepsis requiring peripheral vasopressors in medical ICUs. On the basis of the aforementioned previous practice, many patients would be started, and continued, on phenylephrine for sepsis resuscitation, in direct discordance with Surviving Sepsis Campaign recommendations.⁹

This will be formally evaluated in future research, but was a driver for implementation of a protocol outlining use of other peripheral vasopressors. Goals such as reduction of inappropriate phenylephrine use continue to emerge from interdisciplinary nursing, provider, and pharmacist meetings. Across the health system, an initial PDSA (Plan, Do, Study, Act) framework has stalled at the A phase. The goal of the workgroup is to use the final adequately powered upcoming system-wide study. As a team, the critical care council determined upon studying pilot program data that a larger study across the system would further identify areas for improvement as well as success. The next cycle is planned to be a longitudinal study across much of this fiscal year. At the end of the cycle, data will be presented at system-wide councils to determine future directions.

Our findings provide support for the safety of peripheral administration of vasopressors and potentially point toward the efficacy of implementing a

guideline document to reduce central line placement. However, this assumes that all patients included would have received vasopressors long enough to require a central line and were not just transiently hypotensive or responsive to rapid resuscitation. More than half of the patients included in this study did not require central line placement due to vasopressor requirements. Our SUR data on central line placement showed that central line utilization was less than predicted in 2 of our 3 ICUs for the entire study period, although the differences did not reach statistical significance. Several confounders likely contributed to increased central line placement during this time. For example, our patient population included trauma patients on a massive transfusion protocol, patients with COVID-19, and patients who were hemodynamically unstable secondary to sedation. The study period of December 2020 to February 2021 coincided with a large second wave of COVID-19 in our area after the initial peak in March to May 2020. In between these time periods, a significant drop was seen in the total volume of critically ill patients, which corresponded to uncharacteristically low SURs in our ICUs. Despite the second peak, after implementation of the pilot program, we were still able to come in below expected central line utilization rates. Additionally, the SUR data are based on NHSN data from 2015, which may not be the most reliable reference for current practice.

When comparing the period from December 2019 to February 2020 to the studied intervention period, a similar, if not higher, rate of central line usage could be seen (Table 3). This trend can likely be explained by COVID-19 peaks, as noted above. However, a clear trend was seen when looking at separate peaks in ICU 3, which was a new ICU as of April 2020. No concrete conclusions can be drawn about this unit as between-month SUR evaluations were not assessed for statistical significance, but there was a trend toward decreased SUR values from April 2020 to June 2020 and from December 2020 to February 2021. In the initial peak,

SUR values ranged from 0.7 to 1.29, while in the second peak the range was 0.64 to 0.86. Again, no statistical comparisons were performed, but these 2 periods of similar acuity and patient populations in the same ICU point toward trends to analyze in the future. A similar trend could also be noted for the same time periods in ICU 1.

There were a few limitations to this study. First, our study was conducted during the COVID-19 pandemic when central line utilization was greater than previously, which may have affected our findings, specifically with regard to central line placement. Next, our method of data collection was limited in that we relied on peripheral vasopressor orders being flagged in the electronic health record by a pharmacist. Therefore, we likely underestimated the number of peripheral vasopressor orders throughout our study. Additionally, we did not have an order set built into our electronic health record before this study, which not only would have made identification of peripheral vasopressor orders more reliable, but also would have standardized the ordering process. The lack of an order set also led to peripheral vasopressor orders being entered incorrectly. Because of this, some orders did not have the correct maximum dose for the vasopressor to be administered peripherally, which often resulted in the vasopressor being run above the maximum dose stated in our guideline. In addition to the lack of an order set and incorrect orders, our smartpump settings were not adjusted to reflect the new protocol. Pump changes would have impacted the entire 7-hospital health system with more than 2,400 beds in the region without an active protocol. Such changes are planned to be implemented once the protocol is accepted on a system-wide level. Inclusion of different pump settings may have prevented infusion above the maximum dose recommended, although it may have also caused delays in care in areas without an active protocol. Moving forward, we anticipate that an order set build will be completed and that when providers

see the order set among the options the volume of peripheral vasopressor orders will increase.

Finally, the retrospective design of this quality improvement project carried the limitation that we were not able to assess the impact of the intervention on our outcomes with adequate power. Another study anticipated to have a larger patient population across our health system is underway; however, this will still be retrospective in design. The primary outcomes for this study will include central line placement and days as well as CLABSI occurrence. Secondary endpoints will include safety, risk factors related to extravasation, length of stay in hospital and ICU, mortality, and adherence to Surviving Sepsis guidelines.⁹ We also aim to adequately power the study to detect reductions in central line placement. The final goal is to continue to demonstrate efficacy on a larger scale, working toward continuous improvement over multiple PDSA cycles and completion of the Six Sigma DMAIC model. However, a prospective, randomized study design will still be needed to confirm findings.

Conclusion

In conclusion, our quality improvement project suggests that peripheral administration of select vasopressors at conservative doses and for less than 72 hours is safe. Implementation of a peripheral vasopressor protocol is feasible across multiple ICU settings with guidance documents and frequent monitoring. While trends toward a reduction in central line placement were seen, we encountered confounding variables; in the future, our group aims to further reanalyze the impact of this initiative on central line usage and CLABSI occurrence across ICUs. We also plan to investigate the impact on length of stay in hospital and ICU, mortality, and adherence to Surviving Sepsis Campaign recommendations, where appropriate.

Disclosures

The authors have declared no potential conflicts of interest.

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