J Vasc Access 2014; 15 (4): 251-256
DOI: 10.5301/jva.5000220

ORIGINAL ARTICLE
OPEN ACCESS

Safe administration of vancomycin through a novel midline catheter: a randomized, prospective clinical trial

Jona V. Caparas[1], Jian-Ping Hu[2]

[1] IV Team Coordinator, New York Hospital Queens, New York, NY - USA
[2] PICC Nurse, New York Hospital Queens, New York, NY - USA

ABSTRACT

Background: **According to the 2011 Infusion Nursing Standards of Practice, the low pH of intravenous vancomycin requires that it be administered through a central line. However, a careful review of the literature and a retrospective analysis of the experience at New York Hospital Queens (NYHQ) did not support the position of the Standards.**

Purpose: **A prospective, controlled, randomized clinical trial was conducted to determine if intravenous vancomycin could be safely administered through a novel midline catheter (POWERWAND®, Access Scientific, San Diego, CA).**

Methods: **Patients scheduled to receive short-term (<6 days) intravenous vancomycin were randomly assigned to receive treatment through either a peripherally inserted central catheter (PICC) or the midline study device. Complications and the costs of insertion were recorded.**

Results: **The two groups did not differ significantly with respect to total complications (17.9% with PICCs vs. 19.9% with the midline), phlebitis (0% vs. 0%) or thrombosis (0% vs. 0%). One suspected catheter-associated bloodstream infection did occur in the PICC group. Insertion costs were $90.00 less per insertion in the midline group.**

Conclusions: **Short-term intravenous vancomycin can be safely and cost-efficiently administered in the deep vessels of the upper arm using the midline study device.**

Key words: **Infusion-phlebitis, INS Standards, Midline, pH, Phlebitis, Vancomycin**

Accepted: January 12, 2014

INTRODUCTION

The 2011 CDC Guidelines for the Prevention of Intravascular Catheter-Related Infections state, "Midline catheters are associated with lower rates of phlebitis than short peripheral catheters and with lower rates of infection than CVCs" (1). As part of an evidence-based effort to reduce central line-associated bloodstream infections (CLABSIs), in December 2011 the Vascular Access Team (VAT) at New York Hospital Queens began inserting a novel midline catheter (POWERWAND®, Access Scientific, San Diego, CA), using the accelerated Seldinger technique (2-4). In the first year, performance of the device was excellent, with 93% of 906 midlines lasting through completion of therapy and zero bloodstream infections (BSIs) (5).

Despite these excellent outcomes, patient selection was initially limited due to criteria established by the Infusion Nursing Society in the 2011 Standards of Practice. The Standards recommend that central lines, not midlines (a subcategory of peripheral catheters), be used for "infusates with pH less than 5 or greater than 9" (6). Since vancomycin (pH 3.9) is the most commonly administered antibiotic at NYHQ for the treatment of methicillin-resistant *Streptococcus aureus*, large numbers of patients requiring intravenous vancomycin received peripherally inserted central catheters (PICCs) instead of midlines.

When a pharmacist questioned the Standards, noting that the pH of normal saline ranges from 4.5 to 7.0 (USP) and that erythromycin (pH 6.5-7.5) is far more phlebitogenic than vancomycin, the VAT decided to explore the topic further.

A detailed review of the 13 references cited in the Standards on the association of pH and thrombophlebitis revealed the following: Three of the references referred back to the Standards, five made no reference to pH whatsoever, one included no references and no data and four addressed pH only in connection with parenteral nutritional infusates (7-19). One of the self-referring articles

did contain a 1968 internal reference to buffering 5% dextrose solutions in order to reduce phlebitis (20). However, not one article or internal reference addressed the pH of any medication as the sole and only cause of phlebitis.

In light of these findings, a more extensive review of the topic was undertaken. This led to the discovery that there are no well-conducted human outcome studies in the English literature to suggest that pH, in and of itself, causes phlebitis. There are numerous studies, on the other hand, demonstrating that multiple other factors contribute to infusion-related thrombophlebitis (e.g., anatomic location, gender, experience of the inserter, etc.) (21-33). Even more striking, perhaps, was the discovery of three published studies and one 2013 poster presentation—totaling 1848 patients—attesting to the safe intravenous administration of vancomycin through peripheral (including midline) catheters (32, 34-36). In fact, one of these studies (Roszell) demonstrated a lower mean and maximum phlebitis score with vancomycin than with other antibiotics. A second study (Mowry) demonstrated the "protective" effect of vancomycin in patients receiving amiodarone, as patients receiving both medications actually had fewer incidents of phlebitis than patients receiving amiodarone alone. This latter study further demonstrated 7.3 times less phlebitis with vancomycin than with the control group. None of the 1,848 cases reported in the literature suffered tissue injury as a result of vancomycin infiltration.

This research prompted the VAT to explore whether, after placement of the midline study device for other indications, physicians at NYHQ had decided to use it for intravenous administration of vancomycin. A retrospective survey found 22 patients who had received vancomycin through the midline catheter. Duration of therapy ranged from 2 to 19 days. No adverse outcomes were reported. In this connection it should be noted that at NYHQ, vancomycin is routinely administered through short peripheral intravenous catheters for 3-5 days.

Ultimately, three factors—(1) uncertainty about the evidence for the Standards' pH restrictions, (2) the presence of multiple published human studies attesting to the safety of peripherally administered vancomycin and (3) a record at NYHQ of safe peripheral and midline administration of vancomycin—prompted the following prospective, randomized clinical trial comparing administration of vancomycin via PICCs with administration of vancomycin via a novel midline catheter.

ETHICAL CONSIDERATIONS

The IRB/Ethics Committee deemed approval unnecessary in light of the fact that PICCs, midlines and peripheral intravenous catheters, all properly consented, were being used routinely to administer vancomycin at New York Hospital Queens.

METHOD

Patients requiring short-term intravenous vancomycin—more than one dose and less than 6 days of treatment—were referred to the VAT and, after inclusion versus exclusion was decided, randomly assigned (based on odd/even terminal digit of their medical records number) to receive either the midline study device or a PICC (Teleflex Medical, Research Triangle Park, NC). Patients with contraindications to vancomycin or the intended VAD, or whose renal status precluded vascular access in the upper arm, were excluded. If vancomycin therapy was extended beyond 5 days, physicians were advised to administer subsequent doses via a PICC. Understandably, clinical circumstances did not always allow for this change of routes.

Midlines and PICCs were inserted according to manufacturers' directions for use. Preparation included 2% chlorhexidine and maximum sterile barrier protection; lines were dressed with a chlorhexidine impregnated sponge and transparent semipermeable dressing and secured using a mechanical catheter securement device. All VADs were inserted in the basilic, brachial or cephalic vein of the upper arm using ultrasound guidance.

Nurses administering vancomycin were instructed to check for line patency and functionality by aspirating for blood and flushing the line with preservative-free normal saline. If it flushed, but blood return could not be demonstrated, the line was assessed with ultrasound to determine its position. Only if the line flushed easily and intraluminal position could be confirmed was vancomycin administered.

Vancomycin was given by infusion pump over a minimum of 60 minutes, at a concentration of 4 mg/mL, either once or twice daily.

Patients were observed at least once daily. All device-related complications were recorded.

A comparative analysis of operational costs to deliver vancomycin by means of the midline study device versus a PICC was also undertaken.

RESULTS

There were no significant differences between the two groups with respect to age, gender, administration of other antibiotics and average number of days on vancomycin. The average age of the PICC group was 69 years; the average age of the midline group was 72 years. Vancomycin was administered along with other antibiotics in 92% of the PICC group and in 93% of the midline group (Tab. I).

A total of 54 patients were enrolled. There were no significant differences in the average or median catheter dwell-times. Twenty-nine patients received one or more midline, totaling 174 catheter-days, with an average

TABLE I - SAMPLE CHARACTERISTICS

	Midline Group	PICC Group	p-Value
Number of patients	29	25	
Number of catheters	30	28	
Average age (years)	72	69	0.15*
% male/female	31%/69%	52%/48%	0.17*
% receiving multiple antibiotics	93%	92%	1.00†
Average days on vancomycin	3.7	4.6	0.13*
% vancomycin >5 days	29%	32%	0.77†

*Wilcoxon two-sample test.
†Fisher's exact test.

TABLE II - CATHETER PERFORMANCE

	Midline Group	PICC Group	p-Value
Average catheter dwell-time	5.8 days	6.3 days	0.94*
Range dwell-time	1-12 days	1-25 days	
Median dwell-time	5 days	5 days	0.51*
Total complications	19.9%	17.9%	1.00†
Bloodstream infection			
Confirmed	0	0	
Suspected	0	1 (3.6%)	0.46‡
Thrombosis	0	0	
Phlebitis	0	0	
Infiltration	3 (10%)	0	0.24‡
Dislodgment	2 (6.6%)	4 (14.2%)	0.40‡
Leak	1 (3.3%)	0	1.00‡

*Wilcoxon two-sample test.
†Fisher's exact test.
‡Unpaired *t*-test.

TABLE III - COST COMPARISON

Insertion Costs	PICC	Midline
Maximum barrier kit	$161.00	$149.00
Tip locator (navigator)	$47.00	$0.00
X-ray	$31.00	$0.00
Total	$239.00	$149.00
	Net Savings	$90.00

PICC = peripherally inserted central catheter.

midline dwell-time of 5.8 days (range = 1-12 days; median = 5 days). Twenty-five patients received one or more PICC, amounting to 176 catheter-days, with an average PICC dwell-time of 6.3 days (range = 1-25 days; median = 5 days).

There was no significant difference in total complications between the PICC and study device groups (Tab. II).

Total complications were 17.9% for patients with PICCs, including one (3.6%) "suspected BSI"—that is, fever without identified source, resolved with line removal—and four (14.2%) dislodgments. Thirty-two percent (32%) of PICC patients received intravenous vancomycin for greater than 5 days.

Total complications were 19.9% for patients with midlines, including one (3.3%) "leak" and two (6.6%) dislodgments. In addition, three (10.0%) Grade I infiltrations (INS Infiltration Scale) occurred in the midline group. The average age of the three patients with infiltrations was 91 years; the average dwell-time of the midline at the time of infiltration was 10 days. Twenty-nine percent (29%) of midline patients received intravenous vancomycin for greater than 5 days. There were no confirmed or suspected BSIs in the midline group.

Thrombosis and phlebitis rates were zero in both groups.

There were two culture-proven, PICC-related CLABSIs in patients enrolled in this study. However, both infections occurred outside the perimeter of the study itself. The two patients were each admitted with a PICC which, after 6 and 12 days, respectively, became infected; subsequent to PICC removal, these two patients were randomized into the midline group.

Table III shows the cost comparison between the study device and the double-lumen PICC used at NYHQ. This does not include the $80.00 per dose cost of alteplase, because it was used intermittently to treat various degrees of occlusion in PICCs. The net savings realized from placing the midline study device instead of a PICC was $90.00 per insertion.

DISCUSSION

Although a small study, the results confirm that short-term intravenous vancomycin can be safely administered through the midline study device. Even in this population of aged patients receiving multiple other antibiotics, phlebitis did not occur. This finding comports with the published literature, wherein peripherally administered intravenous vancomycin has proven less phlebitogenic and in one study "protective," as compared with other antibiotics and medications (32, 34-36). Since "the concentration of a toxicant in contact with the cells lining

the inside of the vessel and the duration of that exposure" (not pH) are primary determinants of vessel injury, placement of the midline study device in the deep vessels of the upper arm, where greater hemodilution occurs, likely contributed to the absence of phlebitis (37).

Extravasation of vancomycin into the tissues of the upper arm has long been a concern. Graphic photographs of "vancomycin extravasations" are often cited. However, of the two cases most frequently shown, one was an allergic reaction (not a direct toxic effect) and the other was "capillary leak syndrome" in the dorsal vein of a foot (38, 39). Both cases resolved uneventfully upon withdrawal of vancomycin. The published literature suggests that vancomycin infiltrations do not commonly cause tissue injury. Roszell, for example, reported that vancomycin infiltrations resulted in outcomes identical to "other antibiotics," namely, Grade 0-2 infiltrations only (32). In the current study, it is unclear whether vancomycin was infusing when one of the midline infiltrations occurred. (Two of the three infiltrations clearly occurred days after vancomycin administration had ceased.) What is clear, however, is that no tissue damage resulted from any infiltration. Of course, infiltration/extravasation must always be a concern to clinicians. But that concern should prompt patency and functionality checks, not necessarily placement of a more dangerous access device.

The PICCs in this study functioned well. The four reported dislodgments were caused by confused patients who intentionally discontinued their lines. The one "suspected" BSI, however, foreshadows one of the very real risks of central venous access—CLABSI. Two confirmed cases of PICC-associated BSI directly preceded matriculation of those same two patients into this trial; this underscores a major risk of central venous access and the original impetus for the present study. Coupled with the knowledge that silent deep vein thrombosis occurs in 19.4%-37% of PICC patients, clinicians are obliged to weigh the risks and benefits of PICC placement carefully (40-43).

LIMITATIONS

The principal limitation of this study is its small sample size. A larger prospective, randomized trial of this nature would undoubtedly be worthwhile. Additionally, the method of randomization was imperfect, though well-suited for the actual clinical conditions of the trial. Strict adherence to sequencing—that is, determination of inclusion versus exclusion, followed by rigid assignment of treatment—was implemented so as to mitigate any potential bias.

CONCLUSION

Specifically as regards intravenous vancomycin, the question must be asked is: Do the benefits of PICC placement outweigh the risks of DVT and CLABSI? Previous studies have demonstrated the safety of the midline study device with respect to infection and thrombosis (4). The present study (along with four other published reports) confirms the low risk of phlebitis from peripherally administered vancomycin (5, 32, 34-36). Therefore, the benefits of PICC placement for vancomycin administration—namely, diminished risk of phlebitis—can clearly be achieved using the midline, with less risk of DVT or CLABSI.

Administration of short-term vancomycin is not a valid indication for PICC insertion. Midline administration of short-term vancomycin, in the deep vessels of the upper arm, is equally safe, less expensive and less risky.

ACKNOWLEDGMENTS

The authors would like to thank Agility Clinical, Inc. and Zachary J. Berl for their assistance with statistical analysis of the data.

Financial support: None.

Conflict of interest: The authors disclose no conflict of interest.

Address for correspondence:
Jona Caparas
New York Hospital Queens Flushing
New York, USA
jeanie1109.jc@gmail.com

REFERENCES

1. O'Grady NP, Alexander M, Burns LS, et al. CDC guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2011;39(4):S3, S5.
2. Stoker R. Accelerated Seldinger technique. Managing Inf Cont. 2009;March:32-35.
3. Dawson RB, Moreau NL. Midlines—an essential tool in CLABSI reduction. Infect Control Today. 2013;17(3):42-45.
4. Warrington WG, Penoyer DA, Kamps T, et al. Outcomes of using a modified Seldinger technique for long term

intravenous therapy in hospitalized patients with difficult venous access. JAVA. 2012;17(1):24-31.
5. Caparas J. Staff Education/Training Aids Implementation of Advanced Midline Catheter. Scientific Poster, presented at: INS Annual Convention & Industrial Exhibition; May 2013.
6. Gorski LA, Eddins J, Hadaway L, et al. Infusion nursing standards of practice (revised 2011). JIN. 2013;34(1S): S37-S38.
7. McGoldrick M. Infection prevention and control. In: Alexander M, Corrigan A, Gorski L, et al. Infusion Nursing: An Evidence-Based Approach. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2010:204-228.
8. Bullock-Corkhill M. Central vascular access device access and insertion. In: Alexander M, Corrigan A, Gorski L, et al. Infusion Nursing: An Evidence-Based Approach. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2010:480-494.
9. Cheung E, Baerlocher MO, Asch M, Myers A. Venous access: a practical review for 2009. Can Fam Physician. 2009;55(5):494-496.
10. Hadaway L. Infusion therapy equipment. In: Alexander M, Corrigan A, Gorski L, et al. Infusion Nursing: An Evidence-Based Approach. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2010:391-436.
11. Perruca R. Peripheral vascular access. In: Alexander M, Corrigan A, Gorski L, et al. Infusion Nursing: An Evidence-Based Approach. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2010:456-479.
12. Mirtallo J, Canada T, Johnson D, et al; American Society for Parenteral and Enteral Nutrition. Safe practices for parenteral nutrition: practice guidelines for safe practice for parenteral nutrition. J Parenter Enteral Nutr. 2004; 28(6):S39-S70.
13. Isaacs JW, Millikan WJ, Stackhouse J, Hersh T, Rudman D. Parenteral nutrition of adults with a 900 milliosmolar solution via peripheral veins. Am J Clin Nutr. 1977;30(4): 552-559.
14. Pettit J, Wyckoff M. Peripherally Inserted Central Catheters: Guidelines for Practice. 2nd ed. Glenview, IL: National Association of Neonatal Nurses: 2007.
15. Gura KM. Is there still a role for peripheral parenteral nutrition? Nutr Clin Pract. 2009; 24(6):709-717.
16. Krzywda EA, Meyer D. Parenteral nutrition. In: Alexander M, Corrigan A, Gorski L, et al. Infusion Nursing: An Evidence-Based Approach. 3rd ed. St. Louis, MO: Saunders/Elsevier; 2010:316-350.
17. Hayden BK, Goodman M. Chemotherapy: principles of administration. In: Cancer Nursing: Principles and Practice. 6th ed. Boston, MA: Jones & Bartlett; 2005:352-412.
18. Oncology Nursing Society. Chemotherapy and Biotherapy: Guidelines and Recommendations for Practice. 2nd ed. Pittsburgh, PA: ONS; 2005.
19. Bishop L, Dougherty L, Bodenham A, et. al. Guidelines on the insertion and management of central venous access devices in adults. Int J Lab Hematol. 2007;29(4): 261-278.
20. Fonkalsrud EW, Murphy J, Smith FG Jr. Effect of pH in glucose infusions on development of thrombophlebitis. J Surg Res. 1968;8(11):539-543.
21. Lewis GBH, Hecker JF. Infusion thrombophlebitis. Br J Anaesth. 1985;57(2):220-233.
22. Tagalakis V, Kahn SR, Libman M, Blostein M. The epidemiology of peripheral vein infusion thrombophlebitis: a critical review. Am J Med. 2002;113(2):146-151.
23. Campbell L. I.v.-related phlebitis, complications and length of hospital stay: 1. Br J Nurs. 1998;7(21):1304-1306, 1308-1312.
24. Harrigan CA. A cost-effective guide for the prevention of chemical phlebitis caused by the pH of the pharmaceutical agent. NITA. 1984;7(6):478-482.
25. Maki DG, Ringer M. Risk factors for infusion-related phlebitis with small peripheral venous catheters. A randomized controlled trial. Ann Intern Med. 1991;114(10): 845-854.
26. Monreal M, Quilez F, Rey-Joly C, et al. Infusion phlebitis in patients with acute pneumonia: a prospective study. Chest. 1999;115(6):1576-1580.
27. Cicolini G, Bonghi AP, Di Labio L, Di Mascio R. Position of peripheral venous cannulae and the incidence of thrombophlebitis: an observational study. J Adv Nurs. 2009; 65(6):1268-1273.
28. Tripathi S, Kaushik V, Singh V. Peripheral IVs: factors affecting complications and patency—a randomized controlled trial. J Infus Nurs. 2008;31(3):182-188.
29. Hawes ML. A proactive approach to combating venous depletion in the hospital setting. JIN. 2007;30(1):33-44.
30. Kirschner R. Contrast media—phlebitis implications. US Radiology. 2010;2(1):27-30.
31. Kokotis K. Preventing chemical phlebitis. Nursing. 1998; 28(11):41-46.
32. Roszell S, Jones C. Intravenous administration issues. JIN. 2010;33(2):112-118.
33. Jones ER. Relationship between pH of intravenous medications and phlebitis: an experimental study. NITA. 1982; 5(4):273-276.
34. Lanbeck P, Odenholt I, Paulsen O. Antibiotics differ in their tendency to cause infusion phlebitis: a prospective observational study. Scand J Infect Dis. 2002;34(7): 512-519.
35. Mowry JL, Hartman LS. Intravascular thrombophlebitis related to the peripheral infusion of amiodarone and vancomycin. West J Nurs Res. 2011;33(3):457-471.
36. Balliad P, Peterson S. Midline Catheter Reduces Infiltrations for Coronary Artery Bypass Graft Patients. Scientific Poster, presented at: INS Annual Convention & Industrial Exhibition; May 2013.
37. LaRue GD, Peterson M. The impact of dilution on intravenous therapy. JIN. 2011;34(2):117-123.
38. Bohm NM, Wong JG. Bullous dermatosis associated with vancomycin extravasation. Am J Med Sci. 2012;343(2): 117-119.

39. Hoelen DWM, Tjan DHT, van Vugt R, van der Meer YG, van Zanten AR. Severe local vancomycin induced skin necrosis. Br J Clin Pharmacol. 2007;64(4): 553-554.
40. Periard D, Monney P, Waeber G, et al. Randomized controlled trial of peripherally inserted central catheters vs. peripheral catheters for middle duration in-hospital intravenous therapy. J Thromb Haemost. 2008;6(8):1281-1288.
41. Bonizzoli M, Batacchi S, Cianchi G, et al. Peripherally inserted central venous catheters and central venous catheters related thrombosis in post-critical patients. Intensive Care Med. 2011;37(2):284-289.
42. Prandoni P. Prophylaxis of catheter-related thrombosis in cancer patients. Lancet. 2009;373(9663):523-524.
43. Chopra V, Flanders SA, Saint S. The problem with peripherally inserted central catheters. JAMA. 2012;308(15): 1527-1528.