Research Report

The Safety of Midline Catheters for Intravenous Therapy at a Large Academic Medical Center

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Abstract

Background: Midline catheters (MCs) have arisen as alternatives to peripherally inserted central catheters (PICCs) for both general intravenous therapy and extended outpatient parenteral therapy. However, there is a lack of data concerning the safety of medication therapy through midline for extended durations. **Objective:** The purpose of this study is to evaluate the safety of MCs for extended intravenous use. **Methods:** This was a retrospective cohort study evaluating patients who received intravenous therapy through an MC at a tertiary care academic medical center. The primary end point was the incidence of composite catheter-related adverse events that included local events, catheter dislodgment, infiltration, catheter occlusion, catheter-related venous thromboembolism, extravasation, and line-associated infection. **Results:** A total of 82 MC placements and 50 PICC placements were included; 50 MCs were for outpatient parenteral antimicrobial therapy, and 32 were for inpatient intravenous use. There were 21 complications per 1000 catheter-days in the outpatient group and 7 complications per 1000 catheter-days in the PICC group ($P = 0.91$). The median time to complication in both groups was 8 days. The antimicrobial classes commonly associated with complications were cephalosporins, carbapenems, and penicillins. **Conclusion and Relevance:** Our results suggest that intravenous therapy with MCs is generally safe for prolonged courses that do not exceed 14 days as compared with PICC lines, which can be placed for months. There is still limited evidence for the use of MCs between 14 and 28 days of therapy. This study can help guide our selection of intravenous catheters for the purpose of outpatient antimicrobial therapy.

Keywords

midline catheter, OPAT, antimicrobial therapy, parenteral antibiotics, catheter complications

Introduction

Peripherally inserted central catheters (PICCs) and tunneled central venous catheters (CVCs) have historically been common routes for the receipt of extended-duration intravenous antimicrobial therapy, facilitating discharge from acute care hospitals. Midline catheters (MCs) are peripheral catheters that are inserted above the antecubital fossa and terminate in a large peripheral vein in the axillary region; they are becoming popular alternatives.[1] Previous literature has shown that MCs may have a lower risk of catheter-associated infections when compared with CVCs and are on average $90.00 cheaper per insertion than PICCs.[2] The maximum approved in situ time for an MC is 28 days. The 2018 Infectious Diseases Society of America clinical practice guidelines for the management of outpatient parenteral antimicrobial therapy (OPAT) recommend that MCs may be used in adults needing courses of OPAT for less than 14 days (weak recommendation, very low-quality of evidence).[3,4] There is very limited evidence for the use of MCs for greater than 14 days of therapy.

Previous research in the safety of various antimicrobial agents and catheter types suggests that MCs are an independent risk factor for catheter-related complications.[5] In a

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previously published prospective cohort study, MCs were associated with a statistically significant increase in catheter complications when compared with PICCs (adjusted incidence rate ratio [aIRR] = 9.44; 95% CI: 2.12-41.97). In another study, the percentage of complications of vancomycin infused through an MC was 17.9% versus 19.9% when infused through PICCs.[2] Whereas previous studies have reported the median in situ times of catheters, median time to complication has not been reported. As such, there is still little evidence regarding the safety of OPAT through an MC, and the optimal duration of therapy is not known.

The objectives of this study are to evaluate the safety of extended intravenous therapy of antimicrobials via MC as compared with PICC lines. Outcomes of interest were any catheter-related adverse events, including serious events such as extravasation of antimicrobial agents, catheter-related thromboembolic events, and catheter-related infections.

Methods

Study Design

This was a single-center, retrospective chart review that was conducted at NYU Langone Health, an 825-bed tertiary care academic teaching hospital. Because of the retrospective and observational nature of this project done for quality improvement, it was exempt from review by our institutional review board. Electronic charts of patients with MCs or PICCs placed from November 2017 to July 2018 were reviewed.

All patients ≥18 years of age discharged on outpatient intravenous therapy with an MC were included. A random sample of patients during the same time frame who received an MC as inpatients, identified by procedure notes in the electronic health record, were also studied. Any patient who was lost to follow-up prior to removal of MC was excluded. Patients were analyzed based on whether they were inpatients or outpatients for their intravenous therapy. Adult patients discharged on outpatient intravenous therapy with a PICC for a maximum duration of 4 to 6 weeks were included as a comparator group.

Data collection included patient demographics, risk factors for catheter-related adverse events, anticoagulation and/or antiplatelet therapy, in situ time of the midline, site of placement, and total number of medications infused through the catheter. Medication information collected included medication type, duration of therapy, and vesicant properties.

Outcomes

The primary outcome was incidence of composite catheter-related adverse events that included local events, catheter dislodgment, infiltration, catheter occlusion, catheter-related venous thromboembolism, extravasation, and line-associated infection. Local events were defined as phlebitis (any redness, tenderness, swelling, or bruising around the site of MC insertion), bruising, or local irritation. Catheter dislodgment was inadvertent displacement or removal of the MC prior to completion of therapy. Infiltration was when fluid was infused into the tissues surrounding the venipuncture site. Extravasations were defined as the infiltration of a vesicant or chemotherapeutic drug into the surrounding IV site. Catheter-associated bloodstream infections were defined as the presence of bacteremia attributed to an intravenous catheter.

Risk factors of catheter-related adverse events were defined from patient and procedure-related factors. Histories of obesity (defined by an encounter BMI ≥ 30 kg/m^2), peripheral neuropathy, peripheral vascular disease, lymphedema, and Raynaud's disease were collected. Data on catheter gauge, the use of ultrasound during placement, and the service placing the line were also collected. Anticoagulation therapy was defined as the administration of oral or parenteral therapeutic anticoagulants, including intravenous or subcutaneous heparin, low-molecular-weight heparin, direct oral anticoagulants, and/or vitamin K antagonist.

Statistical Analysis

Patient characteristics were represented as medians with interquartile ranges (IQRs) for continuous variables and percentages for categorical variables. Statistical analysis was performed between outpatient MC versus PICC groups. Categorical variables were described as frequencies with proportions and compared using a χ^2 or Fisher exact test. Continuous variables were described as medians with IQRs and analyzed using the Mann-Whitney *U* test. A 2-sided α of $<.05$ was considered to be statistically significant. Complications were described using a composite rate of the number of complications per 1000 catheter-days in order to be able to measure a risk of MCs with different in situ times and allow a standard measure to compare with other studies.[6] A Poisson regression model was used to generate incident rate ratios (IRRs) of adverse events. Statistical analyses were performed using SPSS version 25 (IBM, Armonk, NY)

Results

A total of 82 MC placements were reviewed in patients who received an MC for intravenous therapy; 50 of these MCs were for outpatient intravenous therapy, and 32 MCs were for inpatient therapy. A total of 50 PICC placements for the purpose of OPAT were also reviewed. Baseline characteristics, presence of risk factors for complications, and concurrent anticoagulation and antiplatelet therapy are shown in

Table 1. Baseline Characteristics.[a]

Characteristics	Midline		PICC Outpatient (n = 50)	*P* Value (Midline vs PICC Outpatient)
	Inpatient (n = 32)	Outpatient (n = 50)		
Age, years, median (IQR)	67 (53-76)	66 (48-80)	61 (45-72)	0.25
Male	21 (66)	25 (50)	20 (40)	0.32
Weight, kg, median (IQR)	72 (62-88)	71 (61-86)	81 (63-98)	0.13
Risk factors for complications				
Obesity	7 (22)	10 (20)	19 (38)	0.05
Peripheral neuropathy	3 (9)	5 (10)	3 (6)	0.72
Peripheral vascular disease	3 (9)	4 (8)	6 (12)	0.51
Lymphedema	0 (0)	2 (4)	1 (2)	1.00
Raynaud's disease	0 (0)	1 (2)	1 (2)	1.00
Concurrent anticoagulant	6 (19)	6 (12)	11 (22)	0.18
In situ time, days, median (IQR)	7 (4-12)	13 (9-19)	29 (18-39)	$P < 0.01$
Site of catheter placement				
Basilic vein	14 (44)	30 (60)	33 (66)	0.53
Cephalic vein	9 (28)	11 (22)	2 (4)	0.01
Brachial vein	9 (28)	9 (18)	15 (30)	0.16

Abbreviations: IQR, interquartile range; PICC, peripherally inserted central catheter.
[a]All values reported as n (%) unless otherwise noted.

Table 1. Table 1 also gives details about the placement and timing of MCs.

Inpatients

The median age of inpatients was 67 (IQR = 53-76) years. Seven (22%) MCs were placed in obese patients. The median in situ time was 7 (IQR = 4-12) days for a total catheter time of 298 days. A total of 14 (44%) MCs were placed in the basilic vein, followed by 9 (28%) MCs each in the brachial and cephalic veins. All MCs were 4-French catheters placed by a dedicated venous access team and confirmed by ultrasound. One medication was administered through 8 (25%) catheters, 2 in 11 (34%), and 3 or more in 13 (41%). The median duration of each medication administered through the line was 2 (IQR = 1-6) days. The most common medications infused through midline were electrolytes (ie, magnesium, potassium), vancomycin, and cephalosporins. The full list of medications infused is listed in Table 2. Of a total 96 medications, 20 (21%) that were infused are documented vesicants.

There were 7 complications, for a rate of 23 complications per 1000 catheter-days. The median time to a complication was 8 (IQR = 6-11) days. Tables 3 and 4 give specific data about catheter-related complications. Five of these 7 complications required a new catheter, whereas none required a complete change in therapy. The most common complications seen were local events followed by catheter dislodgment. No extravasations or catheter-associated infections were documented. The most common medications associated with complications after adjusting for total administrations were piperacillin/tazobactam (4 of 6 courses) and cephalosporins (4 of 9 courses). All piperacillin/tazobactam administrations were infused as an extended infusion over 4 hours per institutional policy.

Seven MCs remained for 14 days or greater. Of these MCs, 1 catheter experienced a complication. Full description of medications infused through the midline are described in Table 4. The patient with the complication experienced phlebitis from the catheter 15 days into therapy. The primary team flushed the line, and the dressing was changed with resolution of irritation.

Outpatients

The median age was 66 (IQR = 51-80) years in the MC group and 61 (IQR = 45-72) years in the PICC group. Ten (20%) MCs were placed in obese patients and 19 (38%) PICCs were placed in obese patients ($P = 0.05$). Rates of other risk factors for complications were similar between the 2 groups. The median in situ time was 13 (IQR = 9-19) days for a total of 707 catheter-days in the MC group. The median in situ time was 29 (IQR = 18-39) days for a total of 1424 catheter-days in the PICC groups ($P < 0.01$). A total of 30 (60%) MCs were in the basilic vein, followed by 11 (22%) in the cephalic, and 9 (18%) in the brachial vein; 33 (66%) PICCs were in the basilic vein, followed by 15 (30) in the brachial vein, and 2 (4) in the cephalic vein. All MCs were 4-French catheters, and all catheters except one had placement confirmed by ultrasound. All MCs except one were placed prior to discharge by the venous access team. All PICCs were 5-French catheters with placement confirmed by ultrasound. All PICCs except one

Table 2. Medication Characteristics.[a]

Characteristics	Midline		PICC Outpatient (n = 50)	*P* Value (Midline vs PICC Outpatient)
	Inpatient (n = 32)	Outpatient (n = 50)		
Number of medications infused				
1	8 (25)	45 (90)	34 (68)	0.01
2	11 (34)	3 (6)	13 (26)	0.01
3 or more	13 (41)	2 (4)	3 (6)	1.00
Duration of medication administration, days, median (IQR)	2 (1-6)	10 (6-14)	26 (14-38)	<0.01
Medication classes: anti-infectives				
Cephalosporins	9 (28)	27 (54)	19 (38)	0.05
Carbapenems	4 (13)	20 (40)	15 (30)	0.15
Vancomycin	14 (44)	3 (6)	14 (28)	0.01
Penicillins	6 (19)	4 (8)	13 (26)	0.04
Antifungals	6 (19)	0 (0)	2 (4)	0.50
Aminoglycosides	1 (3)	2 (4)	0 (0)	0.10
Antivirals	3 (9)	0 (0)	1 (2)	1.00
Monobactams	2 (6)	1 (2)	0 (0)	0.47
Daptomycin	0 (0)	2 (4)	3 (6)	1.00
Other	7 (22)	0 (0)	1 (2)	1.00
Medication classes: others				
Electrolytes	15 (47)	0 (0)	0 (0)	
Diuretics	6 (19)	0 (0)	0 (0)	
Sedatives	3 (9)	0 (0)	0 (0)	
Antiarrhythmics	3 (9)	0 (0)	0 (0)	
Corticosteroids	3 (9)	0 (0)	0 (0)	
Analgesics	2 (6)	0 (0)	0 (0)	
Phenylephrine	1 (3)	0 (0)	0 (0)	
Other	9 (28)	0 (0)	0 (0)	
Documented vesicant	23/96 (24)[b]	7/59 (12)[b]	18/67 (27)[b]	0.04

Abbreviations: IQR, interquartile range; PICC, peripherally inserted central catheter.
[a]All values are reported as n (%) unless otherwise noted. Other anti-infectives: levofloxacin, linezolid, metronidazole, sulfamethoxazole/trimethoprim, tigecycline. Other medications: albumin, esmolol, unfractionated heparin, levothyroxine, metoclopramide, ondansetron, pantoprazole, thymoglobulin.
[b]Denominator is over total number of medications.

were placed prior to discharge by the venous access team, with 1 PICC being placed by interventional radiology. A total of 45 (90%) MCs received only 1 medication during the course of therapy. Median medication administration time was 10 (IQR = 5-13) days. Cephalosporins (54%) and carbapenems (40%) were the 2 most common medication classes administered through an MC.

The number of documented complications in the MC group was 15, and the complication rate was 21 complications per 1000 catheter-days. Seven of these required a new catheter, and 6 resulted in either a switch to oral antibiotics or discontinuation of therapy altogether. Median time to complication was 10 (IQR = 5-12) days. The most common complications documented were local events, followed by catheter dislodgment and infiltrations. No extravasations or line infections were noted. The most common medications associated with complications after adjusting for total administration were carbapenems (40%) and cephalosporins (22%). In this group, no piperacillin/tazobactam administrations were infused as extended infusion.

The number of documented complications in the PICC group was 10, and the complication rate was 7 complications per 1000 catheter-days. Two of these complications required a new catheter, and 1 resulted in a switch to oral antibiotics earlier than anticipated. Median time to complication was 10 (IQR = 7-20) days. The most common complications documented were local events, followed by catheter occlusion, 1 catheter dislodging, and 1 central line–associated bloodstream infection. The most common medications associated with complications were carbapenems, penicillins, cephalosporins, and vancomycin.

When comparing the complication rates between groups, though there were numerically higher complication rates between midlines and PICCs (21 vs 7 complications per 1000 catheter-days), this was not statistically significant (aIRR = 1.06; 95% CI = 0.40-2.77; $P = 0.91$).

Table 3. Complications.[a]

Complications	Midline		PICC Outpatient (n = 50)	*P* Value (Midline vs PICC Outpatient)
	Inpatient (n = 32)	Outpatient (n = 50)		
Documented complications	7 (22)	15 (30)	10 (20)	0.25
Local events	3 (43)	6 (40)	5 (50)	0.75
Catheter dislodging	2 (29)	6 (40)	1 (10)	0.11
Infiltration	1 (14)	5 (33)	0 (0)	0.06
Catheter occlusion	1 (14)	1 (7)	2 (20)	0.56
Catheter-related VTE	0 (0)	2 (13)	0 (0)	0.50
Extravasation	0 (0)	0 (0)	0 (0)	—
Line infection	0 (0)	0 (0)	1 (10)	1.00
Need for new catheter	5 (71)	7 (47)	2 (20)	0.17
Need for change in therapy	0 (0)	6 (40)	1 (10)	0.18
Readmission for catheter-related complications	N/A	3 (20)	2 (20)	1.00
Time to complications, days, median (IQR)	8 (6-11)	8 (5-12)	8 (7-20)	0.46

Abbreviations: IQR, interquartile range; PICC, peripherally inserted central catheter; VTE, venous thromboembolism.
[a]All values reported as n (%) unless otherwise noted. Local events: phlebitis, bruising, or local irritation.

Table 4. Complication Details.[a]

Characteristics	Midline		PICC Outpatient (n = 10)	*P* Value (Midline vs PICC Outpatient)
	Inpatient (n = 7)	Outpatient (n = 15)		
Obesity	1 (14)	4 (27)	4 (40)	0.67
Peripheral neuropathy	0 (0)	3 (20)	1 (10)	0.63
Peripheral vascular disease	0 (0)	1 (7)	4 (10)	0.12
Concurrent anticoagulation	3 (43)	2 (14)	2 (10)	1.00
Site of catheter				
Basilic vein	3 (43)	8 (53)	7 (70)	0.41
Cephalic vein	2 (29)	4 (27)	0 (0)	0.13
Brachial vein	4 (57)	3 (20)	3 (30)	0.57
Number of medications infused				
1	1 (14)	13 (87)	6 (60)	0.13
2	2 (29)	2 (13)	3 (30)	0.36
3 Or greater	4 (57)	0 (0)	1 (10)	0.40
Medication classes				
Cephalosporins	4/9 (44)	6/27 (22)	4/19	0.32
Carbapenems	1/4 (25)	8/20 (40)	4/15	0.32
Vancomycin	1/13 (8)	1/3 (33)	3/14	0.33
Penicillins	4/6 (67)	0/4 (0)	3/13	0.10
Aminoglycosides	1/1 (100)	1/3 (33)	0/0	—
Daptomycin	0/0	0/2 (0)	1/3 (33)	0.48
Antifungals	2/6 (33)	0/0 (0)	0/2	—
Linezolid	1/2 (50)	0/0 (0)	0/0	
Metronidazole	1/2 (50)	0/0 (0)	0/0	
SMX/TMP	1/1 (100)	0/0 (0)	0/0	

Abbreviations: PICC, peripherally inserted central catheter; SMX/TMP, sulfamethoxazole/trimethoprim.
[a]All values reported as n (%) unless otherwise noted.

There were 21 MCs in situ for 14 days or more. The most common medications that were used for greater than 14 days were ceftriaxone (8) and ertapenem (5). A full description of medications infused through the MC are described in Table 4. Of these patients, only 1 catheter had a complication reported. This patient had an episode of midline dislodgment 5 days into therapy that was resolved by the infusion company, and therapy was continued until the MC was removed when therapy was completed 20 days after the date of placement.

There were 2 catheter-related thromboembolisms found in the MC outpatient group. Neither was in patients receiving concurrent anticoagulation at the time the thromboembolism was found, nor were they in patients with a history of deep-vein thrombosis or pulmonary embolism. One patient had a history of active malignancy and was found to have extensive deep-vein thromboses in the same arm in which the MC was placed, and systemic anticoagulation was started. The other patient had no history of VTE or malignancy and had her MC placed with no anticoagulation initiated.

Discussion

In this retrospective cohort study, we attempted to assess the safety of MCs in inpatient and outpatient cohorts. In the inpatient cohort, we found a complication rate of 23 complications per 1000 catheter-days. Similarly, in the outpatient cohort, we observed a complication rate of 21 complications per 1000 catheter-days. Both these complication rates are elevated compared with previously published literature, where rates of complications range between 11 and 15.6 complications per 1000 days.[6,7] Reported rates of MC complications when radiologically guided during insertion have been as low as 0.67 per 1000 days, though 99% of MCs placed in this study were ultrasound guided, with a total combined complication rate of 22 complications per 1000 catheter-days.[7] Other studies have not reported their results as a standardized composite rate but have reported a raw percentage of MC complications as high as 19.5%.[7,8] Carbapenems and cephalosporins were the most commonly administered outpatient medications, whereas vancomycin and cephalosporins were the most common inpatient medications.

Similarly, the overall incidence of complications in outpatients was 30%. However, when averaged out over 1000 catheter-days, these rates were comparable to what we encountered in inpatients. We had theorized that median longer in situ times of catheters and less frequent outpatient line maintenance would lead to increased rates of complications, but that does not seem to be the case because we observed similar incidence of complications in both inpatients and outpatients when complications were standardized over 1000 catheter-days.

Our overall incidence of PICC complications was 20%. However, when averaged out over 1000 catheter-days, the rate was 7 complications per 1000 catheter-days. This was not statistically different from the complication rate encountered with outpatient MCs. However, this complication rate seems to be higher than the rate of PICC complications reported in the literature. Rates of PICC complications are reported to be between 0.45 and 2.02 complications per 1000 catheter-days or a raw percentage of 5.8% to 21%.[6-8] In this study, PICCs had longer in situ times, and multiple medications were more often infused through them. This likely reflects a difference in indication, where PICC lines are preferred when courses of antibiotics are expected to be up to 4 weeks or more.

Limitations to this study include that it was a retrospective chart review combining inpatient records with outpatient infusion company records. This resulted in missing information such as medication concentrations, osmolarities, and infusion rates. Some details of complications such as infiltration scoring based on the Society of Infusion Nurses Infiltration Scale were not able to be collected. Furthermore, this study is a single-center study with a small sample size and lacks external validity. As such, this study is likely underpowered to detect a difference between groups. In this study, we attempted to assess the safety of previously reported high-risk medications such as vancomycin or daptomycin.[5] Of 17 total vancomycin administrations, only 2 (10%) MCs had catheter-related adverse events. The safety of daptomycin could not be assessed because of the low sample size of daptomycin patients. Adverse events may also be underreported in the outpatient setting because we relied on third-party reporting and chart review. Minor events may not be reported or documented and would be difficult to evaluate in a retrospective design.

Conclusion and Relevance

In conclusion, the use of MCs appears to be generally safe for prolonged intravenous therapy when compared with PICCs. Although the rates of complications are higher than currently reported rates of complications, severe complications associated with MCs were rare. We found 0 cases of catheter infection, 2 cases of catheter-related thrombosis, and 6 OPAT patients who required a change in or discontinuation of therapy in our cohort of 82 patients. Ideally, the duration of therapy in outpatients should be limited to no more than 14 days, similar to current OPAT guideline recommendations,[3] because the median time to complication was around 10 days. In patients requiring courses of OPAT for less than 14 days, the use of MCs seems safe, and further evaluation is needed for longer courses.

Authors' Note

This study was accepted for poster presentation at the American Society of Health System Pharmacy Midyear Conference, Anaheim, CA, in December 2018 (poster 12-286).

Declaration of Conflicting Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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