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Infectious complications in home parenteral nutrition: A long-term study with peripherally inserted central catheters, tunneled catheters, and ports

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ABSTRACT

Objective: Home parenteral nutrition (HPN) has become a common therapy, with tunneled central venous catheters (CVCs) being the preferred route of administration. Peripherally inserted central catheters (PICCs) have been used increasingly, but whether they should be preferred over other types of CVCs is still controversial. The aim of this study was to evaluate catheter-related complications of CVC in patients receiving HPN.

Methods: All patients treated at our center for HPN from 2007 to 2017 were prospectively included. A specialized intravenous therapy team took care of these patients. Catheter-related bloodstream infections (CRBSI) were confirmed with positive, simultaneous, differential blood cultures drawn through the CVC and peripheral vein and then semiquantitative or quantitative culture of the catheter tip.

Results: In all, 151 patients received HPN during the 11-y study period. Of these patients, 95 were women (63%) and 55 were men (37%), with a mean age of 58 ± 13 y. Twenty-six were non-cancer patients (17%) and the remaining 125 patients had an underlying malignancy (83%). Regarding the CVC, 116 were PICCs, 18 Hickman, and 36 ports. Confirmed CRBSI per catheter-days showed 0.15 episodes per 1000 catheter-days for PICCs, 0.72 for Hickman, and 2.02 for ports. PICCs had less-confirmed CRBSIs per 1000 catheter-days than ports ($\varphi = 0.54$, $P = 0.005$), but no difference between PICCs and Hickman was found ($\varphi = 0.32$, $P = 0.110$). Confirmed episodes of CRBSI (2 versus 13%, $\chi^2 = 6.625$, $P = 0.036$) were more frequent with multilumen catheters.

Conclusions: In our setting, single-lumen PICC and Hickman catheters showed low infectious complications.

Introduction

Parenteral nutrition (PN) has become a common therapy for patients at home. National registries in North America, including 1251 patients enrolled from 29 sites from 2011 to 2014, showed that 28% of all patients expected to require home parenteral nutrition (HPN) indefinitely [1]. The last analysis of Spain's national registry showed 220 patients and 229 episodes of HPN registered from 37 centers, which represents a rate of 4.7 patients per million habitants per year [2]. Currently, the leading cause for need of HPN is cancer in adults and congenital intestinal disorders in children [2,3]. Prognosis and survival in the medium and long term are better with HPN than with an intestinal transplant, so this must be reserved for those patients presenting severe complications of PN [4]. The standardization of care and the development of good educational programs may contribute to an improvement in the results, with emphasis on the caregiver who may be an important contributor of the quality of life for these patients [5].

European guidelines for the choice of central venous access for HPN stated that a tunneled central catheter was preferred over other types of central catheters [6]. However, in the last Canadian registry [3], the use of tunneled catheters decreased from 64.3% to 38% and was no longer the most frequently chosen vascular access. In contrast, the proportion of peripherally inserted central catheters (PICCs) increased from 21.6% to 52.9% [3].

One of the most frequent complications in HPN is catheter-associated blood infection, affecting >10% of these patients, with

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catheter-related infections per 1000 PN-days ranging from 0.35 to 0.91 in adults [7]. Patients with implanted ports or double-lumen catheters had more catheter-related infections than those with PICC or tunneled central catheters or single-lumen catheters in the North America National registry [7]. Although PICCs have shown a diminished rate of catheter-related infections in some hospitalized patients, such as intensive care unit patients and children [8,9], reported data in HPN have shown conflicting results: On the one hand, a previous study showed that patients with PICCs for HPN had an increase of catheter-related infections compared with other central venous catheters (CVC) [10], and a recent study also showed higher infectious rates for PICCs compared with Hickman catheters in patients with intestinal failure receiving HPN [11].

On the other hand, previous experience has shown that PICCs may be a good alternative to other CVC for HPN [12,13]. The aim of the present study was to prospectively evaluate a cohort of patients with HPN attended at our center for 11 y, focusing on catheter-related complications, especially infections.

Patients and methods

Design and endpoints of the study

This was an observational, prospective study that included all patients attending our center for HPN from January 2007 to December 2017. A specialized intravenous therapy team (ITT) took care of these patients from the beginning of the study. Our hospital is a reference center for delivering HPN in its coverage area, which comprises a population of 566 445 individuals. As HPN is fully reimbursed in our community, private prescription for HPN also is negligible.

The primary endpoint of the study was the number of catheter-related infections that occurred with each type of CVC. Secondary endpoints included the subanalysis of infections depending on single-lumen versus multilumen catheters, the occurrence of other complications such as vein thrombosis, catheter-tip displacement, total lumen occlusion, and catheter removal.

The local ethics committee approved the study and written informed consent was obtained from the participants.

Composition and delivering of HPN

Composition of PN followed European guidelines [14]. In brief, we prepared PN at our hospital for individualized formulae, and whenever possible, commercial "ready-to-use" (RTU) bags also were employed (Smofkabiven Fresenius SE & Co. KGaA health care group, Bad Homburg, Germany, and Olimel Baxter Ltd. Deerfield, IL, USA). In both cases the daily aim was 20 to 35 kcal/kg, with a proportion of 3 to 6 g/kg for glucose, 1 g/kg for amino- acids, and <1 g/kg for lipids, with 7 to 10 g/d of essential fatty acids. Vitamins and trace elements were also added by the hospital pharmacy for those patients unable to take these supplements. PN was infused on an intermittent schedule primarily at nighttime. All patients and, when needed, some of their relatives, were appropriately trained for adequate manipulation of both the central catheter and PN infusion pumps and connections. After nutrition infusion, patients were instructed to use heparin (3 mL of 20 IU/mL commercial vials) through their catheters. For those active patients who were able to care for their PICC, a polyethylene extension tube (Vygon Corporation, Montgomeryville, PA, USA) was connected between the PICC and the nutrition system, to avoid rendering them one-handed. Patients were followed up every 15 d at the beginning of the program, and every 1 to 3 mo thereafter. A complete blood test was performed at that moment as well as a clinical history and examination. Catheter inspection was also done at our clinic at the same time. Moreover, whenever needed, patients also came for inspection of their catheter, particularly if suspecting any complication, whether or not they had a scheduled interview.

Central venous catheters

The choice of CVC was not randomized but based on the patient's responsible physician, always taking into account the underlying disease, the expected duration of HPN, and the possibility of a safe procedure for obtaining a venous access. A Hickman CVC was preferred for those patients with non-malignant disease who were initially expected to need long-term PN (>6 mo of HPN administration). A PICC catheter was indicated for those patients initially expected to need HPN for <6 mo, such as those in the advanced stages of malignant disease and at least receiving second-line chemotherapy or those with no further treatments in palliative care. However, for the last 5 y of the study, based on our previous experience [13], PICCs also were considered for longer periods (>6 mo) of HPN infusion. Port-a-caths also were used for HPN in those patients with cancer who already had these devices and in whom survival was expected to be short (<6 mo) and PN was not contraindicated with concomitant chemotherapy infusion. If the latter was the case, then ports were used for chemotherapy and a simultaneous PICC was used for HPN. PICC catheters were also indicated for those patients with Hickman or port removal after a complication, especially if difficulty in obtaining these CVCs again for technical reasons. Multilumen catheters were chosen when patients needed medication in addition to PN (except for small doses of intravenous [IV] analgesia).

Ports and Hickman catheters were implanted in the Intervention Radiology Department, a high expertise one with >1000 implants per year, using fluoroscopy guidance and local anesthesia. PICCs were implanted at the ITT clinic, with the patient under local anesthesia and the technician using ultrasound guidance (for the first 5 y, ultrasound was performed in those patients in whom venous access was not expected to be easy after inspection by an expertise nurse with >1000 implants per year, and for the last 5 y, ultrasound was routinely employed for all insertions). Most of the implanted PICCs were of silicone composition (Cook Medical, Bloomington, IN, USA; Vygon Corporation, Montgomeryville PA, USA; Arrow International Incorporation, Reading, PA, USA; Bard Medical, Covington, GA, USA) or carbotane (B. Braun España, Barcelona, Spain), and some were power PICCs of polyurethane composition (Bard Medical, Covington, GA, USA; Wacrees, Medcomp Pro, Madrid, Spain). Maximal barrier precautions were maintained for all catheter insertions.

Catheter-related infections and other complications

Local catheter infections were defined as exit-site infections (defined as redness, swelling, tenderness, with an erythema of more than twice the diameter of the catheter), tunnel infections, or pocket infections.

Catheter-related bloodstream infections (CRBSIs) were suspected when a febrile episode in a patient with HPN occurred, especially when there was no apparent source for an infection except the catheter itself, and all patients with fevers were instructed to come to the hospital to have blood cultures performed. CRBSI was confirmed by isolation of the same microorganism from quantitative pair blood cultures from both the catheter lumen and the blood peripherally drawn, and after catheter-tip removal with positive semiquantitative cultures (roll-plate Maki technique) and only in the case of negative semiquantitative

culture was quantitative culture with sonication was also performed [15,16].

Venous thrombosis was evaluated by ultrasonography when compatible symptoms and signs were reported by patients. No routine screening for venous thrombosis was performed in otherwise asymptomatic patients.

Statistical analysis

A sample size analysis performed with Ene 3.0 software and based on previous results to detect a significant difference in catheter infections [13]. Forty-nine patients in each group were needed for both $\alpha = 0.05$ and $1 - \beta = 0.8$.

Results are expressed as means ± SD unless otherwise stated. The Kolmogorov–Smirnov statistic was applied to continuous variables. Logarithmic or square-root transformations were applied as needed to ensure a normal distribution of the variables. Comparisons between the different groups at baseline were performed by independent *t* test for continuous variables or the Mann–Whitney U test for non-normal distributed variables, and by χ^2 test or Fisher's exact test for discontinuous variables. For more than two groups, comparisons were performed by using univariate analysis of variance for continuous variables with post hoc Tukey's significant difference test (HSD) or Kruskal–Wallis test for non-normal distributed variables, and using the χ^2 test for discontinuous variables, as needed. Time-dependent events were analyzed by the log-rank test and multivariate Cox proportional hazards test. Analyses were performed using SPSS version 18 (SPSS Inc, Chicago, IL, USA). $P < 0.05$ was considered statistically significant.

Results

In all, 151 patients received HPN during the 11-y study period. Of these, 95 were women (63%) and 55 men (37%), aged 58 ± 13 y. Regarding the patients' underlying disease, 26 were non-cancer patients (17%) and the remaining 125 had an underlying malignancy (83%). Specific diagnoses are presented in Table 1.

Regarding the implanted CVCs, 170 were registered: 116 were PICCs, 18 were Hickman, and 36 were ports. Table 2 summarizes catheter distribution among patients, as well as other clinical characteristics. Ports and PICCs were used more frequently in patients with cancer and single-lumen catheters were more frequently PICCs (Table 2). Ultrasound guidance was employed for 94 PICC insertions. (This has been routine practice since 2011.) There were no total catheter obstructions requiring removal of the CVC; however, one PICC needed to be removed because of tip displacement. Only one episode of deep vein thrombosis (0.6%) was recorded in a patient with a PICC.

Catheter infections

Confirmed CRBSI by culture (Table 3) was found in three patients with PICCs (3%), three with Hickmans (17%), and seven with ports (19%; $\chi^2 = 11.135$, $P = 0.004$). However, after catheter removal, two PICCs, one Hickman, and one port did not show positive culture of catheter tip (Table 3). Catheter removal was considered the best option for CRBSI diagnosed with quantitative paired blood cultures in all patients except for three cases of ports with negative coagulase staphs that were salvaged after IV antibiotic, catheter lock, and subsequent negative blood cultures (Table 3).

Total catheters-days were 20 495 for PICCs, 4167 for Hickman, and 2970 for ports. Confirmed CRBSI per catheter-days were 0.15 episodes per 1000 catheter-days for PICCs, 0.72 for Hickman, and 2.35 for ports, respectively. PICCs had less confirmed CRBSI per 1000 catheter-days than ports ($\varphi = 0.57$, $P = 0.002$); however, no statistical difference was found between PICCs and Hickman catheters ($\varphi = 0.32$, $P = 0.110$).

When considering single-lumen versus multilumen catheters (selecting only PICCs and Hickman for the analysis), confirmed episodes of CRBSI by blood cultures (2% versus 13%, $\chi^2 = 6.625$, $P = 0.036$) and also after catheter tip cultures (0% versus 13%, $\chi^2 = 14.679$, $P = 0.005$) were more frequent with multilumen catheters.

Multivariate Cox proportional hazards test, after introducing type of catheter, age and sex of patient, number of catheter lumens, and underlying oncologic disease as covariates, showed that only the multilumen catheter (Wald = 4.468, hazard ratio, 5.556; $P = 0.035$) was associated with a confirmed CRBSI (−2 log likelihood = 30.194, $\chi^2 = 5.557$, $P = 0.018$).

Table 1
Underlying diseases of included patients (N = 151)

Non-cancer	26
Inflammatory bowel disease	5
Systemic sclerosis with GI involvement	2
Olgilvie syndrome	1
Chronic encephalopathy	1
Short intestine with intestinal failure	6
Idiopathic intestinal lymphangiectasia	1
Intestinal amyloidosis	1
Peritoneal fibrosing syndrome	3
Cerebral palsy with GI pseudobstruction	1
Idiopathic GI pseudobstruction	1
Protein-losing enteropathy	2
Ménétrier's disease	1
Radiation enteritis	1
Cancer	125
GI neoplasia	*84*
Esophageal cancer*	8
Gastric cancer with PC or obstruction	35
Pancreatic cancer with PC or obstruction	10
Hepatocarcinoma with encephalopathy	2
Intestinal adenocarcinoma with PC	1
Neuroendocrine tumor with obstruction	3
Appendicular carcinoma	1
Colorectal cancer with PC	23
Rectal cancer with radiation enteritis	1
Gynecologic neoplasia	*26*
Cervix carcinoma with PC	1
Müllerian carcinoma with PC	1
Breast cancer with PC	3
Ovarian cancer with PC	18
Fallopian tube carcinoma with PC	2
Endometrium cancer with PC	1
Others	*15*
Bladder cancer with PC	4
Bladder cancer with cutaneous fistula	1
Bone sarcoma with PC	1
Sézary lymphoma with GI involvement	1
Lung cancer with GI involvement	1
Head & neck cancer*	3
GVHD after leukemia	4

GI, gastrointestinal; GVHD, graft-versus-host disease; PC, peritoneal carcinomatosis
*Enteral nutrition and/or prosthesis not feasible.

Discussion

Previous experience showed that PICC use for HPN was a good alternative to tunneled central catheters [12,13,17] when patients were supported by a highly specialized team [18,19]. Results from the present study demonstrated that PICC use for HPN is associated with less episodes of CRBSI than ports, and similar to Hickman catheters.

Table 2
Type of catheters employed for home parenteral nutrition (N = 170)

	PICC (n = 116)	Hickman (n = 18)	Ports (n = 36)	*P*-value
Women (%)	67 (58)	10 (56)	27 (75)	
Men (%)	49 (42)	8 (44)	9 (25)	0.157
Cancer patients (%)	93 (80)	9 (50)	33 (92)	
Non-cancer patients (%)	23 (20)	9 (50)	3 (8)	0.002
Single-lumen catheters (%)	100 (87)	10 (56)	NA	
Multilumen catheters	15 (13)	8 (44)	NA	0.001
Catheter-days (median ± IQR)	70 ± 175	63 ± 280	66 ± 94	0.507

IQR, interquartile range

Table 3
Confirmed CRBSI by culture

Type of catheter	Microorganism in blood culture	Antibiotic therapy
PICC	*Klebsiella pneumoniae*	Ceftazidime
	Staphylococcus epidermidis[*]	Vancomycin
	Coagulase-negative Staphylococci[*]	Vancomycin
Hickman	*Coagulase-negative Staphylococci* and *Actynomices*	Vancomycin and meronem Piperacillin-tazobactam
	Enterococcus faecalis	Vancomycin
	Staphylococcus epidermidis[*]	
Ports	*Staphylococcus hominis*	Ceftazidime
	Staphylococcus epidermidis[†]	Vancomycin
	Staphylococcus epidermidis[†]	Vancomycin
	Staphylococcus epidermidis[†]	Vancomycin
	Coagulase-negative Staphylococci	Vancomycin
	Candida albicans[*]	Amphotericin B
	C. glabatra	Amphotericin B

CRBSI, catheter-related bloodstream infections; PICC, peripherally inserted central catheter
[*]Positive blood culture but negative catheter-tip culture.
[†]Salvage of catheter, no tip culture performed.

The present results are in agreement with a recent study conducted in 250 cancer patients with 269 PICCs that found a low incidence of CRBSI, thrombosis, and mechanical complications; a long catheter life span; and a low probability of catheter removal because of complications [20]. Another recent study showed that PICCs resulted in fewer CRBSIs (1.05/1000 catheter-days) than Broviac catheters in HPN patients with intestinal failure [21]. The latter study included 204 catheters (133 Broviac and 71 PICCs) inserted in 196 adult patients with a mean follow-up of 140 d for PICCs. Venous thrombosis rate was low (0.4 of 1000 catheter-days) but occurred only with PICCs [21], as it did in the present study. These numbers are lower than those reported for hospitalized patients [22] or for oncologic patients [23].

On the other hand, a previous study showed that patients using PICCs for HPN had a significant increase of catheter-related infections compared with other central venous access devices [10]; however, the study was retrospective and false-negative results may have occurred. It contrasts with our methodology, because we performed a prospective study in which patients were told to always communicate any event regarding a possible catheter-related complication and whenever a febrile episode occurred, the patient was referred to our center for evaluation, where blood or catheter cultures were taken as needed to confirm or refute CRBSI.

Christensen et al. recently demonstrated a higher risk and shorter time to first CRBSI in PICC compared with Hickman catheters in a study of 136 patients with intestinal failure and HPN [11]. However, these patients needed a total of 295 catheters (169 Hickman catheters and 126 PICCs) over a 6-y period, which comprises a higher rate of catheter replacement than the aforementioned studies, as well as ours. Nevertheless, in our setting there is a highly specialized team, including an ITT, integrated in our department, which was created before the beginning of our study. Therefore, the present results are not applicable to other clinical settings in which a lack of such a specialized team may compromise patients' adequate training regarding the management of HPN and CVC care and identification of its possible complications. Moreover, the majority of the patients in the present study had an underlying malignancy, which differs from the cohort of the study by Christensen et al. [11].

Santarpia et al. [24] studied the prevalence of CRBSI and infecting agents in 172 adult patients on HPN. The study population consisted of 127 cancer (74%) and 45 (26%) non-cancer patients, similar to our cohort, for a total of 53 818 (median 104; range 14–1080) CVC-days. They found an infection rate of 1.74 of 1000 CVC-days with coagulase-negative *Staphylococci* as the most frequently infecting agent. They found no relationship with the type of catheter and infections, but only a small proportion of patients had PICCs (27 of 238) or Hickman catheters (37 of 238). This also could have driven a higher infection rate than in our patients with PICCs and Hickman, and similar to our patients with ports [24].

The present study was not subject to any possible bias regarding patient selection, as every patient in our clinical area who may need HPN is referred directly to our department. On the other hand, although this was a prospective study, a limitation was the lack of randomization when assigning the type of CVC. As stated previously, clinical judgment of the responsible clinician guided the choice as to type of CVC. Nevertheless, this did not result in any bias regarding catheter-days, and in fact, PICC catheter-days were similar to those with Hickman catheters, and only ports were more frequently used for the short term (as expected for the case of cancer patients with worse prognosis).

Although HPN for cancer patients with short life expectancy is controversial, incurable cancer patients may enter an HPN program if they are unable to meet their nutritional requirements by oral or enteral route and there is a risk for death due to malnutrition [14]. Furthermore, oncologic patients may have a better survival when the concomitant use of active antitumoral therapy with HPN is provided in the case of intestinal subocclusion [25].

PICCs also may have the disadvantage, because of its exit position, of rendering the patient one-handed, which may make self-care difficult. We have overcome this problem with silicone extension sets, but nevertheless quality of life was not measured in these patients, so this is another limitation of the present study, which should be addressed in future trials.

We have shown that multilumen catheters presented a higher rate of infections than single-lumen catheters, and in the multivariate analysis was the only associated variable with confirmed CRBSI. In agreement with the present results, Ross et al. [7] recently reported that patients with implanted ports or double-lumen catheters also had more CRBSIs than those with peripherally inserted or central catheters or single-lumen catheters, and Pichitchaipitak et al. also reported more infections with implanted ports, among other risk factors [26].

Conclusions

Single-lumen PICCs and Hickman catheters showed low infectious complications for the administration of HPN. Ports showed higher rates of infections and should not be used routinely for this purpose. Future randomized clinical trials should be conducted to definitively confirm the present results.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.nut.2018.06.016.

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