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ORIGINAL ARTICLE

Prevention and treatment of implanted central venous catheter (CVC) - related sepsis: A report after six years of home parenteral nutrition (HPN)

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Abstract—Catheter-related sepsis is a serious and common complication in patients receiving home parenteral nutrition (HPN). Prevention measures, prevalence of infections, types of agents and implanted central venous catheters (CVC), effectiveness of antibiotic therapy have been evaluated in 221 patients consecutively followed in our unit from January 1995 to December 2000. The clinical diagnosis of catheter-related infection was made using well-defined criteria. Patients were divided into two groups: A and B, receiving instructions with different modalities: standard (A) and detailed (B), respectively. Sixty CVC-related sepsis occurred in 32 (14%) patients. A multivariate analysis showed that the duration of HPN ($P<0.001$; OR = 0.9), type of catheter ($P=0.009$; OR = 0.12) and type of disease ($P=0.033$; OR = 4.92) significantly influence catheter infection. The type of implanted CVC (159 port-a-cath in 153 patients and 71 tunnelled in 68) seems to affect the infection rate, this being lower in tunnelled ($P=0.03$). Infection rate was lower in B vs A group ($P<0.001$) with all types of catheters, suggesting the preventive role of very careful training. In particular, the incidence of CVC-related sepsis was 6/1000 days of HPN (i.e. 6/1000 days of catheterization) in Group A and 3/1000 in Group B. Systemic and antibiotic lock therapy was performed with an 83% successful rate. Gram-positive bacteria were the most frequent CVC infection agents, which are usually eradicated by antibiotic therapy lasting 7 days.

Key words: venous catheter; infections; prevention; treatment; HPN

Introduction

Home parenteral nutrition (HPN) is widely used to prevent or correct malnutrition both in oncologic and non-oncologic patients (1, 2). Despite its proved efficacy, HPN is burdened with some complications: the most serious and frequent being catheter-related sepsis (3–5). Recent studies reveal that common skin commensals, such as Staphylococci, are frequently responsible for central venous catheter (CVC)-related infections; fungi and Gram-negative organisms are other, less frequent, possible pathogens (6, 7). Nowadays, after short-term systemic, antibiotic and catheter-lock therapy, most infections are completely resolved and use of implanted CVC restored (8).

The purpose of this retrospective study was to examine in a sample of cancer- and non-cancer-bearing patients on HPN in Naples district (South Italy): (1) the prevalence of CVC infections, (2) infection rate according to the type of implanted CVC, (3) the effect of strict preventive measures on CVC infections, (4) effectiveness of antibiotic therapeutic protocols on the occurred infections.

Patients and methods

Two-hundred-twenty-one consecutive patients (96 M, 125 F; 72% oncologic, 28% non-oncologic) were followed for 11,192 days of treatment between January 1995 and December 2000 at the outpatient clinic of the Clinical Nutrition Unit of the University Hospital Federico II in Naples. Patient age averaged 58 ± 18 years (min 27, max 78) and BMI $20.1 \pm 3.8\,kg/m^2$ (min 15.2, max 22.8).

Patients have been divided into two groups:

1. Group A = 110: 39 M, 71 F; aged 58 ± 16 years (min 29, max 74); BMI $20.6 \pm 3.2\,kg/m^2$ (min 16.2, max 21.8); 81 oncologic, 29 not, followed from January 1995 to December 1998 (6573 days of HPN).
2. Group B = 111: 57 M, 54 F; aged 57 ± 19 years (min 27, max 78); BMI $19.4 \pm 2.8\,kg/m^2$ (min 15.0, max 21.7); 78 oncologic, 33 not, followed from January 1999 to December 2000 (4619 days of HPN).

In the large majority of cases, parenteral nutrition (PN), with daily infusions, was started few days after CVC implant, days of HPN approximately corresponding to days of catheterization.

Before starting HPN, Group A patients, and/or their care givers, were given an information sheet and received oral instructions from the nutritional team, attending two training sessions on the use of CVC when HPN started; Group B patients, and/or their care givers, instead, were given more detailed written instructions on the aseptic management of CVC and how to avoid and recognize complications, attended regularly at least six both theoretical and practical training sessions carried out by the nutritional team, and, when possible, were monthly followed up in the clinic in order to examine CVC conditions, to inspect the area of insertion and to check their compliance to the given instructions.

In detail, instructions for Group B patients focused on six main points:

1. *Personal and environmental hygiene*: Modalities and duration of washing hands, using a nail brush and an aseptic soap; using a sterile bearing surface; using sterile gloves, disposable coats and cups during the management of HPN.
2. More accurate procedure to prepare, under sterility, the solution and eventual additions to the nutritional solution (i.e. vitamins, trace elements, insulin, etc.)
3. Instructions about procedures to maintain sterility at the beginning and at the end of infusions.
4. Use of special silicone perforable caps, to be applied at the end of catheter, instead of rigid unscrewable caps.
5. More care of CVC while not in use (skin cleansing, sterile bandage).
6. How to recognize signs and symptoms of potential septic complications and how to receive first care.

The use of a mask, sterile gloves and a cap during the management of HPN was mandatory for both groups, but periodically recommended to patients in Group B.

Finally, Group B patients were carefully advised that CVCs for HPN were to be used for PN only.

Rare exceptions were allowed on the occasion of other i.v. treatments for selected patients with limited peripheral venous access.

The diagnosis of systemic infection was made according to the following traditional criteria (9, 10):

- increased body temperature and shivering during the infusion of parenteral nutrition,
- identification of the same pathogen in peripheral blood and catheter cultures,
- elevated white blood cell count,
- exclusion of other possible sources of infection.

When CVC infection was suspected, parenteral nutrition was given by peripheral route and CVC used only for lock therapy, until central access was restored. All septic episodes were separate infections because the identified pathogens were always different from the previous ones; only in few cases, the same organism was cultured from the same catheter but later than 2 months after discontinuation of the antibiotic therapy.

Type of implanted CVC was in

1. Group A: 91 port-a-cath in 86 patients, 26 tunnelled in 24.
2. Group B: 68 port-a-cath in 67 patients and 45 tunnelled in 44.

Patients were hospitalized on 10 occasions, when catheter removal was necessary, i.e. culture results yielded fungi or multiple infections or home antibiotic therapy failed to eradicate the organism.

Systemic i.v. antibiotic and lock therapy was performed for 7 consecutive days, according to the results of blood cultures, and use of CVC restored after negative results of blood cultures were obtained; details are shown in Table 3.

Lock therapy consisted in intra-catheter injection of the antibiotic diluted with 1–2 ml of heparinized saline solution in the ports and 2–3 ml in the tunnelled catheters. Total amounts were 3 ml of diluted antibiotic solution in the port-a-caths and 5 ml in the tunnelled in order to completely fill the subcutaneous reservoir in the ports and both the catheter lumen and the subcutaneous tunnelled tract in tunnelled catheters. Lock therapy was administered in bolus, once or twice a day, according to the drug used (Table 3).

Statistical analysis

Data are expressed as mean $\pm$ S.D. Age and BMI differences between groups A and B were tested using unpaired *t*-test. Differences in the rate of infections between groups were tested using χ^2 analysis and considered significant when $P<0.05$.

A multivariate analysis has been performed with logistic regression, using number of infections as dependent variable; sex, type of catheter, type of disease and group (A or B) as categorial covariates; duration of HPN and age as non-categorical ones. Forward stepwise analysis has also been performed.

Results

Sixty CVC-related infections occurred in 32 patients. In Group A, 45 cases of CVC infection were recorded in 23 patients (six oncologic) corresponding to 21% of the whole group. In Group B, only 15 CVC infections were recorded in nine patients (one oncologic), i.e. 8% of the whole group ($P<0.001$ Group A vs Group B).

The type of infected implant was 27 port-a-cath and six tunnelled in Group A and 10 port-a-cath and one tunnelled in Group B. One-hundred-eighty-nine patients

Table 1 Characteristics of HPN patients, number of infections and their incidence in the two groups of patients, A and B, differently trained

Group	A	B	*P*
Total patients	110	111	N.S
Age	58±16	57±19	N.S
Sex (M/F)	39/71	57/54	N.S
BMI	20.6±3.2	19.4±2.8	N.S
Patients never infected	87 (79%)	102 (92%)	0.011
Infected patients	23 (21%)	9 (8%)	0.011
With one infection	13	4	N.S
With two infections	5	4	N.S
With three infections	3	1	N.S
With five infections	1	0	N.S
With eight infections	1	0	N.S
Total infections (*n*)	45	15	0.000
Incidence (*n*/HPN days)	6.8/1000	3.2/1000	0.000

(86%) had no infections corresponding to 87 patients (79%) in Group A and 102 patients (92%) in Group B (A vs B: $P = 0.01$). General data on infections and incidences are summarized in Table 1.

According to the type of implanted CVC, 37 infections were observed in those patients with 159 implanted port-a-cath and seven in patients with 71 tunnelled catheters, corresponding, respectively, to an infection rate of 23% of implanted ports and 10% of tunnelled catheters, the difference being significant ($P = 0.03$) in the whole population and in particular, in Group B ($P = 0.05$).

In particular, in Group A, 27 port-a-cath and six tunnelled catheter infections were recorded, corresponding to 30% and 23% infection rates, respectively; in Group B, the incidence was 15% (10/68) and 2% (1/45) for port-a-cath and tunnelled, respectively (Tables 2a and 2b).

While comparing Groups A and B, there was a significant decrease in infection rate either with port-a-cath ($P = 0.04$) and tunnelled implanted ($P = 0.01$) catheters.

The overall annual incidence of CVC infections (number of infections/1000 days of HPN) significantly decreased from more than 6/1000 in Group A to less than 3/1000 in Group B, the difference being significant ($P < 0.001$).

Furthermore, in Group A, two major septic complications, i.e. septic shock during manoeuvres for blood sampling from CVC were also recorded and accordingly treated.

As far as pathogens were concerned *Staphylococcus epidermidis* was responsible for 33/60 infections (55%); other Gram-positive occurred in 11/60 (18%); Gram-negative accounted for 15% (9/60), whereas fungi only 2% (1/60). Finally, six cases (10%) were polymicrobial.

In conclusion, Gram-positive bacteria represented 73% of the isolated pathogens. Systemic and antibiotic lock treatment was performed according to the results of blood cultures as summarized in Table 3. Bacteria involved in Group B infections (14 *S. epidermidis* and 1 *Escherichia coli*) were all eradicated, while in Group A,

Table 2a Type of catheters used for Groups A and B†

	Port-a-cath	Tunnelled	*P*
Group A	91 (78%)	26 (22%)	0.000
Group B	68 (60%)	45 (40%)	0.004
Total	159 (69%)	71 (31%)	0.000
Infected	37 (23%)	7 (10%)	0.032

†Absolute number (relative percentage); *P* expresses the difference between groups.

Table 2b Number and type of catheters, total infections and their incidence, according to the type of catheter: port-a-cath and tunnelled in Groups A and B, respectively

	Port-a cath			Tunnelled			Infection rate
	Total (*n*)	Infected (*n*)	%	Total (*n*)	Infected (*n*)	%	*P* (port vs tunn)
Group A	91	27	30*	26	6	23**	NS
Group B	68	10	15*	45	1	2**	0.051
Total	159	37	23	71	7	10	0.032

*A vs B $P = 0.044$. **A vs B $P = 0.014$.

seven infections (6 polymicrobial and 1 *Candida albicans*) were *a priori* considered not treatable with antibiotics. After antibiotic therapy, infections were completely resolved in 50 cases (83%) and use of CVC restored after a negative control blood culture from CVC.

CVC was immediately removed in one case due to mycotic infection (*C. albicans*), in six patients because of multiple infections and in other three (two *Serratia marcescens* and one *Xanthomonas* spp.) due to antibiotic resistance; as previously mentioned all patients were in Group A. Removed catheters were port in seven cases and tunnelled in three. The average duration of the replaced catheter before the occurrence of a new infection with a different organism was 192±120 days (min 63, max 365) and several pathogens were involved (*S. epidermidis* in most of the cases). When CVC removal was necessary, catheter tip was cultured to confirm the cause of infection and the same pathogen present in the blood was always observed.

A multivariate analysis with logistic regression, carried out using number of infections as dependent variable, showed that the duration of HPN ($P < 0.001$; OR = 0.9), type of catheter ($P = 0.009$; OR = 0.012), and type of disease ($P = 0.033$; OR = 4.92) significantly influence catheter infection (Table 4). Using a forward stepwise analysis, days of HPN turned out to be the major determinant of CVC infection, followed by group (A or B) ($P = 0.013$).

Discussion

Catheter-related bloodstream infection is a severe and the most frequent complication of HPN, being a common cause of hospitalization (11, 12). In the past, the general approach to catheter-related infections in

Table 3 Antibiotic treatment in the 50 successfully treated infections

Infections (*n*)	Groups		Pathogens	Antibiotic therapy			
	A (*n*)	B (*n*)		Antibiotics	Daily dose: Lock	Daily dose: Systemic (i.v.)	Days of treatment
33	19	14	*S. epidermidis*	Clindamicine	300 mg × 2	600 mg × 2	7
10	10	0	*S. aureus*, *S. auricolaris*, *S. werneri*, *S. sanguis*, *S. sciuri*, *S. hominis*	Teicoplanine	100 mg × 1	200 mg × 1	7
5	5	0	*S. liquefaciens*, *E. cloacae*, *B. diastasonis*	Netilmicine	150 mg × 1	150 mg × 2	7
2	1	1	*E. coli*, *S. haemoliticus*	Piperacilline	500 mg × 2	2 g × 2	7

Table 4 Results of multivariate analysis performed with logistic regression using number of infection as dependent variable[†]

Tested variables	*P*	OR	Confidence interval
Age	0.20	0.97	0.93–1.01
Sex	0.20	1.90	0.70–5.15
Disease	0.033	4.92	1.13–21.3
Days of HPN	0.000	0.97	0.95–0.98
Group	0.46	0.70	0.27–1.82
Type of catheter	0.0092	0.12	0.02–0.59

[†]Using a forward stepwise analysis, the variable group significantly influences CVC infection rate ($P = 0.01$).

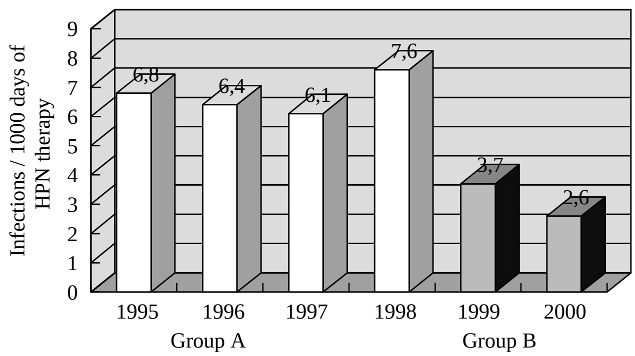

Fig. 1 Annual incidence of CVC infections in Group A (1995–1998; white bars) and in Group B (1999–2000; black bars). Group A vs Group B average incidence: $P < 0.05$.

patients receiving HPN was CVC removal and its replacement after systemic antibiotic treatment (13, 14).

In the last few decades, new available antibiotics as well as lock therapy, because of high drug concentrations in the catheter's lumen (8), have shortened the duration and increased the success rate of treatment of infected CVC (4, 15). Therefore, nowadays most of the infected catheters can be sterilized by antibiotic and local care (16); hence a treatment attempt is worthwhile with some well-known contraindications, i.e. polymicrobial or fungal infections where prompt CVC removal is advisable (17).

Prevention plays a fundamental role in the management of CVC infections in patients on HPN and the nutritional team, including nursing and local care, can effectively reduce infection rates and severity thus increasing catheter longevity (16, 18, 19).

Also in our experience, it appears that strict adherence to protocols and close monitoring lead to a decreased sepsis rate with increased catheter longevity (Fig. 1).

The careful information given to the patients leads to a significant decrease of CVC-related sepsis both in oncologic and in non-oncologic patients and with both types of implanted catheters.

Furthermore, the experience gained by the team plays a central role confirming that HPN is not a common treatment and must be performed by well-trained, experienced teams, in particular, to prevent and treat major complications such as sepsis (5, 19).

The nutritional team has, therefore, a central role in the training of patients and/or their care givers (both nurses or relatives), in particular, emphasizing thorough attention to the aseptic management of implanted catheters (19).

The majority of these infections in our outpatient's population was due to Gram-positive organisms susceptible to either Clindamicine or Netilmicine according to microbiological reports; Teicoplanine was a reasonable alternative to this combination in case of bacterial resistance.

Following multivariate analysis, also the use of port-a-cath appeared as a determinant of catheter infection, its role being important.

Therefore, implanted port-a-cath seems to be associated with a higher risk than tunnelled catheters, the difference being statistically significant ($P = 0.03$). On the other hand, this result does not mean that use of port-a-cath catheters is not advisable.

In some cases and, above all in oncologic patients, port-a-cath had been previously implanted and also used for chemotherapy, and only subsequently for HPN.

Tunnelled catheters had usually been implanted specifically for HPN, therefore a more limited manipulation was guaranteed under these circumstances. Furthermore, tunnelled catheters have a subcutaneous tunnelled tract (about 5–10 cm) that lengthens the distance between external skin and bloodstream, thus reducing the likelihood of germ entry; moreover, they have a dacron cuff that inhibits migration of micro-organisms by stimulating growth of surrounding tissue, providing a natural anchor for the catheter (1). Nevertheless, careful instructions were able to improve infection rate in patients on HPN either with tunnelled or port-a-cath implanted catheters. On the other hand, a longer proportion of patients in Group B used a tunnelled catheter, suggesting that the choice of implantable catheter was perhaps more appropriate in the consideration of long-term HPN.

Few data are available about host factors that contribute to HPN infections (20, 21). In our study, age, sex, clinical condition, cultural level did not appear to have a role as predictive factors for CVC infection (data not shown). On the other hand, type of disease significantly influences CVC infection rate. Duration of HPN is the main predictor of infection, followed by type of catheter and type of disease; besides, the improved training of patients and care givers and the experience gained over time by the nutritional team are able to influence the infection rate of implanted CVC.

The choice of catheters to be implanted also seems to play a role giving priority to the use of tunnelled more than port-a-cath catheters (22). Furthermore, in our population, Gram-positive bacteria are frequently responsible for CVC infections; these infections can be treated, particularly when due to a single pathogen, and in these cases, short-term antibiotic lock therapy, associated with systemic treatment, allows complete recovery of the central catheter after only 7 days of treatment. The concomitant presence of Gram-negative bacteria as well as fungi required catheter removal (15, 23).

Unfortunately, several factors limited our study: (1) the small number of antibiotics tested by the microbiological service; (2) consequently, few antibiotics turned out to be active against isolated germs; (3) few tested antibiotics were available in injectable formulations.

However, this retrospective study increased our experience on the treatment of CVC infections also as far as the selection of antibiotics to be used is concerned. In fact, by early 2001, no more than a single antibiotic for lock and systemic treatment is used, but a combination of two or plus antibiotics with different mechanisms, site and spectrum of action, in order to avoid bacterial resistance. In particular, drugs with more specific spectrum and lower MIC are currently used for antibiotic lock therapy and those with wider spectrum for systemic therapy.

In conclusion, HPN patients need clear information about what are infectious complications as well as clear and continuous instructions on the use of implanted catheter by a well-trained team. Tunnelled catheters also in our experience show a lower risk of infection.

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References

1. Kemp L, Burge J, Choban, Harden J, Mirtallo J, Flancbaum L. The effect of catheter type and site on infection rates in total parenteral nutrition patients. J Parenter Enteral Nutr 1994; 18(1): 71–74
2. Bijma R, Girbes A R, Kleijer D J, Zwaveling J H. Preventing central venous catheter- related infection in a surgical intensive-care unit. Infect Control Hosp Epidemiol 1999; 20(9): 618–620
3. Lucet J C, Hayon J, Bruneel F, Dumoulin J L, Joly-Guillou M L. Microbiological evaluation of central venous catheter administration hubs. Infect Control Hosp Epidemiol 2000; 21 (1): 40–42.
4. Schierholz J, Lefering R, Neugebauer E, Beuth J, Konig D P, Pulverer G. Central venous catheters and bloodstream infection. JAMA 2000; 283(4): 477–478; discussion 478–494
5. Bijma R, Girbes A R, Kleijer D J, Zwaveling J H. Preventing central venous catheter-related infection in a surgical intensive-care unit. Infect Control Hosp Epidemiol 1999; 20(9): 618–620.
6. Gastmeier P, Weist K, Ruden H. Catheter-associated primary bloodstream infections: epidemiology and preventive methods. Infection 1999; 27(Suppl): S1–S6
7. Sitges-Serra A, Girvent M. Catheter related bloodstream infections. World J Surg 1999; 23(6): 589–595
8. Rupp M E, Ulphani J S, Fey P D, Mack D. Characterization of *Staphylococcus epidermidis* polysaccharide intercellular adhesin–hemagglutinin in the pathogenesis of intravascular catheter-associated infection in a rat model. Infect Immun 1999; 67(5): 2656–2659
9. Messing B, Man F, Colimon R, Thuillier F, Beliah M. Antibiotic-lock technique is an effective treatment of bacterial catheter-related sepsis during parenteral nutrition. Clin Nutr 1990; 9: 220–225
10. Dobbins B M, Kite P, Wilcox M H. Diagnosis of central venous catheter related sepsis, a critical look inside. J Clin Pathol 1999; 52 (3): 165–172
11. Lugauer S, Regenfus A, Boswald M, Martus P, Geis C, Bechert T, Greil J, Guggenbichler J P. A new scoring system for the clinical diagnosis of catheter-related infections. Infection 1999; 27(Suppl 1): S49–S53
12. Fletcher S J. Central venous catheter related infection. Anaesth Intens Care 1999; 27(4): 425
13. Douard M C, Ardoin C, Payri L, Tarot J P. Infectious complications of long term intravenous devices: incidence risk factors diagnostic tools. Pathol Biol (Paris) 1999; 47(3): 288–291
14. Rannem T, Ladefoged K, Tvede M et al. Catheter-related septicemia in patients receiving home parenteral nutrition. Scand J Gastroenterol 1986; 21: 455–460
15. Fleming C R, Witzke D J, Beart R W. Catheter-related complications in patients receiving home parenteral nutrition. Ann Surg 1980; 192: 593–599
16. Kullberg B J, De Pauw B E. Therapy of invasive fungal infections. Neth J Med 1999; 55(3): 118–127
17. Carratala J, Niubo J, Fernandez-Sevilla A, Juve E, Castellsague X, Berlanga J, Linares J, Gudiol F. Randomized, double-blind trial of an antibiotic-lock technique for prevention of Gram-positive central venous catheter-related infection in neutropenic patients with cancer. Antimicrob Agents Chemother 1999; 43(9): 2200–2204
18. Buckman A L, Moukarzel A, Goodson B, Herzog F, Pollack P, Reyen L, Alvarez M, Ament M E, Gornbein J. Catheter-related infections associated with home parenteral nutrition and predictive factors for the need for catheter removal in their treatment. J Parenter Enteral Nutr 1994; 18(4): 297–302
19. Bach A. Prevention of infections caused by central venous catheters, established and novel measures. Infection 1999; 27(Suppl 1): S11–S15
20. Faubion W C, Wesley J R, Khalidi N, Silva J. Total parenteral nutrition catheter sepsis: impact of the team approach. J Parenter Enteral Nutr 1986; 10(6): 642–645
21. Tokars J I, Cookson S T, McArthur M A, Boyer C L, McGeer A J, Jarvis W R. Prospective evaluation of risk factors for bloodstream infection in patients receiving home infusion therapy. Ann Intern Med 1999; 131(5): 340–347
22. Hannan M, Juste R N, Umasanker S, Glendenning A, Nightingale C, Azadian B, Soni N. Antiseptic bonded central venous catheters and bacterial colonisation. Anaesthesia 1999; 54(9): 868–872
23. Yu W L, Linn C W, Wang D Y. *Serratia marcescens* bacteremia: clinical features and antimicrobial susceptibilities of the isolates. Chung Hua Min Kuo Wei Sheng Wu Chi Mien I Hsueh Tsa Chih 1998; 31(3): 171–179

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