

• CLINICAL RESEARCH •

Catheter-related infection in gastrointestinal fistula patients

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Abstract

AIM: To study the incidence, bacterial spectrum and drug sensitivity of catheter-related infection (CRI) in gastrointestinal fistula patients.

METHODS: A total of 216 patients with gastrointestinal fistulae during January 1998 to April 2001 were studied retrospectively. Two hundred and sixteen catheters of the 358 central venous catheters used in 216 gastrointestinal fistula patients were sent for microbiology analysis.

RESULTS: Ninety-five bacteria were cultivated in 88 catheters (24.6%). There were 54 Gram-negative bacteria (56.8%), 35 Gram-positive bacteria (36.8%), and 6 fungi (6.4%). During the treatment of CRI, 20 patients changed to use antibiotics or antifungal, and all patients were cured. The mean time of catheters used was 16.9 ± 13.0 d.

CONCLUSION: CRI is still the common complication during total parenteral nutrition (TPN) treatment in patients with gastrointestinal fistulae, and Gram-negative bacteria are the main pathogens, and bacterial translocation is considered the common reason for CRI.

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INTRODUCTION

Total parenteral nutrition (TPN) support is one of the main treatments for gastrointestinal fistula patients, and central venous catheters (CVC) are widely used as the major route. Catheter-related infection (CRI) is a serious complication during TPN. This paper retrospectively reviewed patients with gastrointestinal fistulae complicated by CRI during TPN during January 1998 to April 2001, and studied the incidence, bacterial spectrum and drug sensitivity of CRI. There were special characteristics of CRI in gastrointestinal fistula patients.

MATERIALS AND METHODS

Patient data

Patient data were obtained from a retrospective review of 216 CVC of 358 CVC from 216 patients with gastrointestinal fistulae

in the surgical unit of Nanjing Jinling Hospital during January 1998 to April 2001.

Intervention

The catheters were removed and sent for microbiological culture and analysis, when the patients were clinically considered as CRI because of infection signs (e.g. tremble and fever) during TPN.

Diagnosis of CRI

Patients who had signs of infection and positive culture of CVC were diagnosed as CRI.

Statistical analysis

Patient data, culture of central venous catheters and drug sensitivity were collected and analyzed by the softwares of WHONET 5.0 and SPSS 10.0

RESULTS

Clinical data

In this study, 358 catheters were inserted in 216 gastrointestinal fistula patients. The number of male patients was 129, mean age was 42.5 ± 16.6 years, and that of female was 87, mean age was 43.9 ± 16.5 years. Two hundred and sixteen catheters were removed, and then the catheter tips and concurrent peripheral venous blood were sent for microbiological analysis when the patients had such infection signs as phricasmus, chill and fever. Of the catheters sent for microbiological analysis, 88 (24.6%) were confirmed to have infection by positive culture. Ninety-five bacteria were cultivated, and 8% were polymicrobes. Of the concurrent peripheral venous blood culture, 50 (14.0%) were confirmed to be positive. Fifty-two bacteria were cultivated, and 4% were polymicrobes. Twenty-four bacteria were cultivated from catheters and concurrent peripheral venous blood. The mean time of catheters used was 16.9 ± 13.0 d.

Treatment and outcome

All the 88 patients who were confirmed having CRI were cured. Five patients were self-cured without treatment of any antibiotics after CVC was removed. Among the other 83 patients who were treated by antibiotics, 63 were cured by antibiotics in 1-3 d, 16 changed to use antibiotics, and 4 were treated by antifungal drugs according to the drug sensitivity because of persistent infection.

Microbiological analysis

Ninety five bacteria were cultivated from 88 catheters. The bacterial spectrum is shown in Table 1. There were 54 Gram-negative bacteria (56.8%), 35 Gram-positive bacteria (36.8%), and 6 fungi (6.4%). Drug sensitivity test was performed in 77 of 95 bacteria. Drug sensitivity of 48 Gram-negative bacteria and 29 Gram-positive bacteria is shown in Table 2 and Table 3, respectively. The result of drug sensitivity test indicated severe drug resistance. The preferably sensitive antibiotics for Gram-negative bacteria were imipenem, amikacin, ciprofloxacin, ceftazidime and cefoperazone/sulbactam in turn, and those for Gram-positive bacteria were vancomycin, norfloxacin and ciprofloxacin.

Table 1 Organisms present in 88 catheters

Species of bacteria	No of bacteria	Percent (%)
Gram-negative bacteria		56.8
Enterobacteriaceae		
Enterobacter cloacae	6	6.3
Escherichia coli	5	5.3
Non- identified Gram-negative bacteria	4	4.2
Klebsiella pneumoniae	1	1.1
Non-ferment gram negative rods		
Pseudomonas	20	21.1
Acinetobacter baumannii	7	7.3
Bacterium aeruginosa	5	5.3
Corynebacterium diphtheriae	4	4.2
Acinetobacter lwoffii	2	2.1
Gram-positive bacteria		36.8
Staphylococcus epidermidis	9	9.4
Staphylococcus haemolyticus	7	7.3
Tetrads	4	4.2
Staphylococcus aureus	4	4.2
Enterococcus sp.	4	4.2
Streptococcus viridans	2	2.1
Staphylococcus hominis	2	2.1
Staphylococcus warneri	2	2.1
Staphylococcus simulans	1	1.1
Fungus		6.4
Candida	5	5.3
Saccharomyces	1	1.1
Total	95	100.0

DISCUSSION

Characteristics of CRI in gastrointestinal fistula patients

As the serious complication during TPN support, the incidence of CRI was as high as 23% in simple malnutrition patients in the early years of TPN^[1]. Due to the development in nurse technology and catheter materials, the incidence of CRI has gradually decreased to 2-6%^[2-4]. However, the CRI incidence in surgical critical patients was still as high as 21.1-34%, and its mortality was increased^[5,6]. Based on this report, the CRI incidence in gastrointestinal fistula patients was similar to that in critical patients, and higher than that in simple malnutrition patients. The mean time of catheters used was 16.9±13.0 d, and it was 17 d in other reports^[2,5,6]. So it is important to supervise the symptoms of gastrointestinal fistula patients during TPN, especially 17 d after catheters were inserted.

In most literature reports, Gram-positive bacteria like *S. epidermidis* and *S. aureus* were most frequently cultivated from catheters^[5-8]. Bacterial skin colonization at the catheter-skin interface at the time of insertion or afterward distal spread of the bacteria along the external catheter surface is the basic pathogenesis. However, Gram-negative bacteria are the most common organisms causing CRI of gastrointestinal fistula patients, and the orderly are Gram-positive bacteria and Fungi. Three reasons were considered for this phenomenon. First, the importance of catheter nursing has been cognized and the means for decreasing bacterial skin colonization, such as disinfection and dressing replacement were performed 3 times per week. Second, gastrointestinal fistula patients always were complicated with inflammation of abdomen, microorganisms especial Gram-negative bacteria could broadcast from abdominal abscess to blood and adhere to catheter-hub and colonize. Third, patient were commonly fasting once gastrointestinal fistula occurred. If long-term lack of food stimulation and direct lumen nutrition, mucous atrophy, height of villus decrease and

Table 2 Drug sensitivity test of 48 Gram-negative bacteria (%S)

Species of bacteria	n	AMK	AMP	CFP	CSL	PIP	CAZ	CRO	CXA	CIP	IPM
Pseudomonas	20	75	12.5	0	25	25	70	45	0	70.5	75
Acinetobacter baumannii	7	100	16.7	0	100	0	60	60	0	85.7	100
Enterobacter cloacae	6	75	0	100	75	50	75	80	33.3	50	100
Escherichia coli	5	0	0	0	100	0	0	0	0	0	100
Bacterium aeruginosa	5	40	0	20	80	20	60	20	0	60	80
Corynebacterium diphtheriae	4	75	0	50	100	0	75	50	25	75	100
Klebsiella pneumoniae	1	0	0	0	0	100	0	0	100	100	100
Summary	48	80	7.5	30	69.2	21.1	70.3	55.6	8.9	75.6	90

%S indicates drug sensitivity. AMK: Amikacin, AMP: Ampicillin, CFP: Cefoperazone, CSL: Cefoperazone/Sulbactam, PIP: Piperacillin, CAZ: Ceftazidime, CRO: Ceftriaxone, CXA: Cefuroxime axetil, CIP: Ciprofloxacin, IPM: Imipenem.

Table 3 Drug sensitivity test of 29 Gram-positive bacteria (%S)

Species of bacteria	n	AMK	AMP	SAM	CEP	CIP	ERY	NOR	PEN	PIP	VAN
Staphylococcus epidermidis	9	0	0	0	0	66.7	0	66.7	0	0	100
S. haemolyticus	7	50	0	20	25	50	16.7	60	0	0	100
S. aureus	4	100	0	0	0	25	33.3	75	0	0	100
Enterococcus sp.	4	0	0	0	0	100	0	0	0	0	100
S. hominis	2	0	0	0	0	50	0	0	0	60	100
S. warneri	2	0	0	100	0	100	100	0	0	100	100
S. simulans	1	0	0	100	100	0	0	0	0	0	100
Summary	29	50	0	18.2	16.7	56.2	21.4	66.7	11.8	10.2	100

%S indicates drug sensitivity. AMK: Amikacin, AMP: Ampicillin, SAM: Ampicillin/Sulbactam, CEP: cephalothin, CIP: Ciprofloxacin, ERY: Erythromycin, NOR: Norfloxacin, PEN: Penicillin, PIP: Piperacillin, VAN: Vancomycin.

barrier damage would arise, followed by bacterial translocation from gastrointestinal tract to the mesenteric lymph nodes even blood^[9-11]. Gram-negative bacterial translocation was considered to be the most common reason for the high incidence of CRI in gastrointestinal fistula patients. Several researches indicated that gut bacterial translocation might be the pathogenesis of catheter-related infection during TPN. Pierro *et al* found that in neonates and infants who were receiving long-term parenteral nutrition, enteric microorganisms including *Escherichia coli*, *Klebsiella*, *Candida species* and *enterococci* were the main microorganisms cultured from blood sample, and they figured out that CRI might be a gut-related phenomenon^[12]. Pappo *et al.* speculated that *Candida* sepsis during TPN might be the result of *Candida* translocation from the gut due to the combination of high-density *Candida* colonization and favorable local conditions in the gut induced by TPN and bowel rest^[13]. Another research indicated that patients with an extremely short remaining small bowel (shorter than 50 cm) receiving home TPN had a higher frequency of catheter-related sepsis, particularly by enteric microorganisms^[14]. Based on our research, Gram-negative bacterial translocation was considered to be the pathogenesis of CRI in gastrointestinal fistula patients. Absence of gastrointestinal integrality and extravasations of intestinal succus would induce abdominal or systemic infection once fistula occurs, and the best treatment to deal with fistulae and infection is more effective drainage. Without effective drainage, it is very difficult to control infection, even with antibiotics from low to high grade or narrow to broad spectrum. Abuse of antibiotic would result in arouse increase of drug resistance. Our study demonstrated that drug resistance of gastrointestinal fistula patients was high, and the preferably sensitive antibiotics for Gram-negative bacteria were imipenem, ceftazidime and cefoperazone/sulbactam, and those for Gram-positive bacteria were vancomycin, norfloxacin and ciprofloxacin.

Prevention and treatment of CRI

The methods for prevention of CRI included skin cleanout and antisepsis before catheter inserted, strictly disinfection system and operation during inserting, catheter nursing and dressing replacement after insertion, decreasing manipulation of catheter, and avoiding unnecessary device^[15-22]. Catheters must be removed once CRI occurred or clinically suspected to be, subsequently therapies of experiential antibiotics were supposed to utilize, though part of patients could self-cure without treatment of any antibiotics^[23-29]. Imipenem, ceftazidime and cefoperazone/sulbactam are the perfect choice for therapy of experiential antibiotics based on the result of drug sensitivity. If the infective symptom persisted after catheters were removed and antibiotics were utilized, drug resistance or *Candida* infection should be considered, and effective antibiotics or antifungal drugs should apply according to drug sensitivity. Intravenous glutamine or short-chain fatty acids could reduce central venous catheter related infection by reducing bacterial translocation from gut lumen^[30,31]. According to the advancement of gastrointestinal physiology, enteral nutrition has been confirmed to improve gut mucosa barrier and liver function and nutrition, reduce bacterial translocation and avoid infection complication of TPN^[32-34]. For avoiding CRI, enteral nutrition (EN) should be utilized, and the time of TPN should be reduced in gastrointestinal fistula patients. CRI is a severe complication in gastrointestinal fistula patients, and attention should be paid to its high incidence based on this retrospective study. Gram-negative bacteria with high drug resistance are the most common organisms causing CRI. Catheters must be removed and sent for microbiological analysis once CRI occurs, sensitive antibiotics for Gram-negative bacteria should be utilized. If the infective symptom persists, drug resistance or *Candida* infection should be considered, and effective antibiotics or antifungal

drugs should be applied according to drug sensitivity.

REFERENCES

- 1 Adal KA, Farr BM. Central venous catheter-related infections: a review. *Nutrition* 1996; **12**: 208-213
- 2 Peterson KK. Central line sepsis. *Clin J Oncol Nurs* 2003; **7**: 218-221
- 3 Safdar N, Kluger DM, Maki DG. A review of risk factors for catheter-related bloodstream infection caused by percutaneously inserted, noncuffed central venous catheters: implications for preventive strategies. *Medicine* 2002; **81**: 466-479
- 4 Memish ZA, Arabi Y, Cunningham G, Kritchevsky S, Braun B, Richards C, Weber S, Pereira CR. Comparison of US and non-US central venous catheter infection rates: evaluation of processes and indicators in infection control study. *Am J Infect Control* 2003; **31**: 237-242
- 5 Charalambous C, Swoboda SM, Dick J, Perl T, Lipsett PA. Risk factors and clinical impact of central line infections in the surgical intensive care unit. *Arch Surg* 1998; **133**: 1241-1246
- 6 Clarke DE, Raffin TA. Infectious complication of indwelling long-term central venous catheters. *Chest* 1990; **97**: 966-972
- 7 Page S, Abel G, Stringer MD, Puntis JW. Management of septicemic infants during long-term parenteral nutrition. *Int J Clin Pract* 2000; **54**: 147-150
- 8 Reimund JM, Arondel Y, Finck G, Zimmermann F, Duclos B, Baumann R. Catheter-related infection in patients on home parenteral nutrition: results of a prospective survey. *Clin Nutr* 2002; **21**: 33-38
- 9 Alverdy JC, Aoy E, Moss GS. Total parenteral nutrition promotes bacterial translocation from the gut. *Surgery* 1988; **104**: 185-190
- 10 Odetola FO, Moler FW, Dechert RE, Van Der Elzen K, Chenoweth C. Nosocomial catheter-related bloodstream infections in a pediatric intensive care unit: Risk and rates associated with various intravascular technologies. *Pediatr Crit Care Med* 2003; **4**: 432-436
- 11 Eizaguirre I, Aldamiz L, Aldazabal P, Garcia Urkia N, Asensio AB, Bachiller P, Garcia Arenzana JM, Ruiz JL, Sanjurjo P, Perez Nanclares G. Tissue antioxidant capacity and bacterial translocation under total parenteral nutrition. *Pediatr Surg Int* 2001; **17**: 280-283
- 12 Pierro A, van Saene HK, Donnell SC, Hughes J, Ewan C, Nunn AJ, Lloyd DA. Microbial translocation in neonates and infants receiving long-term parenteral nutrition. *Arch Surg* 1996; **131**: 176-179
- 13 Pappo I, Polacheck I, Zmora O, Feigin E, Freund HR. Altered gut barrier function to *Candida* during parenteral nutrition. *Nutrition* 1994; **10**: 151-154
- 14 Terra RM, Plopper C, Waitzberg DL, Cukier C, Santoro S, Martins JR, Song RJ, Gama-Rodrigues J. Remaining small bowel length: association with catheter sepsis in patients receiving home total parenteral nutrition: evidence of bacterial translocation. *World J Surg* 2000; **24**: 1537-1541
- 15 Wang FD, Cheng YY, Kung SP, Tsai YM, Liu CY. Risk factors of catheter-related infections in total parenteral nutrition catheterization. *Zhonghua Yixue Zazhi* 2001; **64**: 223-230
- 16 Rijnders BJ, Vandecasteele SJ, Van Wijngaerden E, De Munter P, Peetermans WE. Use of semiautomatic treatment advice to improve compliance with Infectious Diseases Society of America guidelines for treatment of intravascular catheter-related infection: a before-after study. *Clin Infect Dis* 2003; **37**: 980-983
- 17 Bong JJ, Kite P, Ammori BJ, Wilcox MH, McMahon MJ. The use of a rapid *in situ* test in the detection of central venous catheter-related bloodstream infection: a prospective study. *J Parenter Enteral Nutr* 2003; **27**: 146-150
- 18 Kamala F, Boo NY, Cheah FC, Birinder K. Randomized controlled trial of heparin for prevention of blockage of peripherally inserted central catheters in neonates. *Acta Paediatr* 2002; **91**: 1350-1356
- 19 Chang L, Tsai JS, Huang SJ, Shih CC. Evaluation of infectious complications of the implantable venous access system in a general oncologic population. *Am J Infect Control* 2003; **31**: 34-39
- 20 Shin JH, Kee SJ, Shin MG, Kim SH, Shin DH, Lee SK, Suh SP,

- Ryang DW. Biofilm production by isolates of *Candida* species recovered from nonneutropenic patients: comparison of blood-stream isolates with isolates from other sources. *J Clin Microbiol* 2002; **40**: 1244-1248
- 21 **Buchman AL**. Complications of long-term home total parenteral nutrition: their identification, prevention and treatment. *Dig Dis Sci* 2001; **46**: 1-18
- 22 **Widmer AF**. Management of catheter-related bacteremia and fungemia in patients on total parenteral nutrition. *Nutrition* 1997; **13**(4 Suppl): 18S-25S
- 23 **Dinc L**, Erdil F. The effectiveness of an educational intervention in changing nursing practice and preventing catheter-related infection for patients receiving total parenteral nutrition. *Int J Nurs Stud* 2000; **37**: 371-379
- 24 **McConnell SA**, Gubbins PO, Anaissie EJ. Do antimicrobial-impregnated central venous catheters prevent catheter-related bloodstream infection? *Clin Infect Dis* 2003; **37**: 65-72
- 25 **Shorr AF**, Humphreys CW, Helman DL. New choices for central venous catheters: potential financial implications. *Chest* 2003; **124**: 275-284
- 26 **Kaplan SL**, Deville JG, Yogev R, Morfin MR, Wu E, Adler S, Edge-Padbury B, Naberhuis-Stehouwer S, Bruss JB. Linezolid versus vancomycin for treatment of resistant Gram-positive infections in children. *Pediatr Infect Dis J* 2003; **22**: 677-686
- 27 **Harbarth S**, Sax H, Gastmeier P. The preventable proportion of nosocomial infections: an overview of published reports. *J Hosp Infect* 2003; **54**: 258-266
- 28 **Beathard GA**. Catheter management protocol for catheter-related bacteremia prophylaxis. *Semin Dial* 2003; **16**: 403-405
- 29 **Hanna HA**, Raad II, Hackett B, Wallace SK, Price KJ, Coyle DE, Parmley CL. Antibiotic-impregnated catheters associated with significant decrease in nosocomial and multidrug-resistant bacteremias in critically ill patients. *Chest* 2003; **124**: 1030-1038
- 30 **Ding LA**, Li JS. Effects of glutamine on intestinal permeability and bacterial translocation in TPN-rats with endotoxemia. *World J Gastroenterol* 2003; **9**: 1327-1332
- 31 **McAndrew HF**, Lloyd DA, Rintala R, van Saene HK. Intravenous glutamine or short-chain fatty acids reduce central venous catheter infection in a model of total parenteral nutrition. *J Pediatr Surg* 1999; **34**: 281-285
- 32 **Fatkenheuer G**, Buchheidt D, Cornely OA, Fuhr HG, Karthaus M, Kisro J, Leithauser M, Salwender H, Sudhoff T, Szelenyi H, Weissinger F. Central venous catheter (CVC)-related infections in neutropenic patients. Guidelines of the Infectious Diseases Working Party (AGIHO) of the German Society of Hematology and Oncology (DGHO). *Ann Hematol* 2003; **82**(Suppl 2): S149-157
- 33 **Alpers DH**. Enteral feeding and gut atrophy. *Curr Opin Clin Nutr Metab Care* 2002; **5**: 679-683
- 34 **Wang XB**, Ren JA, Li JS. Sequential changes of body composition in patients with enterocutaneous fistula during the 10 days after admission. *World J Gastroenterol* 2002; **8**: 1149-1152

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