Catheter-Related Infections in Continuous Hemodiafiltration in Intensive Care Patients

Taka-aki Nakada a, Hiroyuki Hirasawa a, Shigeto Oda a, Hidetoshi Shiga a, Kazuya Nakanishi a, Ken-Ichi Matsuda a, Masataka Nakamura a, Masayuki Shima b, Masaharu Watanabe c

Department of aEmergency and Critical Care Medicine, bPublic Health, Graduate School of Medicine, Chiba University, and cDivision of Clinical Laboratory, Chiba University Hospital, Chiba, Japan

Abstract

Background/Aims: Infection control is of key importance especially in the application of long-term continuous hemodiafiltration (CHDF) involving invasive vascular catheterization to critically ill patients. We investigated hemodialysis catheter-related infections in long-term CHDF.

Methods: We examined catheter infections in 54 patients who were admitted to the intensive care unit and underwent CHDF for 2 weeks or longer.

Results: With a total of 155 catheters (1,071 catheter days) studied, catheter colonization and catheter-related bloodstream infection were noted with an incidence rate of 4.8 and 2.7 per 1,000 catheter days, respectively. No difference in catheter colonization rate was observed depending on the catheterization sites or duration of catheterization. Infections were identified in 39 patients (72%) and blood culture positivity was noted in 25 patients (46%).

Conclusions: Since the majority of cases requiring long-term CHDF are complicated with a variety of infections, it is difficult to control infections associated with hemodialysis catheters separately from infections of other types.

Systemic infection control should serve as a strategy finally leading to successful control of catheter-related infection.

Introduction

Continuous hemodiafiltration (CHDF) is a blood purification therapy expected to achieve a wide spectrum of clinical efficacy including: renal support (correction of body fluid balance, electrolyte balance and acid-base balance as well as removal of metabolic waste products); removal of causative humoral mediators of organ failure(s), and careful nutrition control by removal of excess water [1–3]. Accordingly, this therapy has been widely applied in current critical care [4, 5]. CHDF has to be continued for a considerably long time in some critical cases that have failed to improve early.

Infection is a problem common among critically ill patients requiring critical care, although their clinical conditions may widely vary. Infection control is of key importance especially in the application of long-term CHDF involving invasive vascular catheterization to critically ill patients who need prolonged intensive care due to conditions such as organ failure(s).
In the present study, we investigated hemodialysis catheter-related infections in long-term CHDF.

Patients and Methods

During 5 years (between January 1998 and December 2002), a total of 1,851 patients were admitted to an 8-bed medical/surgical intensive care unit (ICU) at Chiba University Hospital, including 343 patients who underwent CHDF. Of these 343 patients, 54 who underwent CHDF for 2 weeks or longer were included in the present study.

Continuous Hemodiafiltration

To provide vascular access for CHDF, 7- to 9-french flexible double-lumen catheters (DLUO710YK, Medikit Co., Ltd., Japan) were used in infants and children, and 12-french flexible triple-lumen catheters (blood access triple-lumen catheter; Arrow International Inc., Reading, Pa., USA) in adults. All these catheters are non-heparin-coated and made of polyurethane. The structure of all these catheters is side-by-side lumen and side-hole type.

CHDF using the above-mentioned catheters was conducted consecutively, 24 h/day, until the therapy was no longer indicated for the patient. A polymethylmethacrylate membrane hemofilter (Hemofeel CH-1.0; Toray Medical Co., Ltd., Tokyo, Japan) was mainly used for CHDF. Nafamostat mesilate (Futhan; Torii Pharmaceutical Co., Ltd., Tokyo, Japan) was used as anticoagulant and its dose was adjusted as necessary to maintain an activated coagulation time of approximately 150 s. The hemodiafiltration system was monitored using a personal bedside console for CHDF (JUN-500; Ube Medical Co., Ltd., Tokyo, Japan).

Insertion and Care of Catheters

All hemodialysis catheters used in the present study underwent sterilization with 10% povidone iodine twice or more and were inserted at the bedside by experienced ICU physicians each wearing a cap, mask, and sterile gloves to prevent infection. The insertion site was also sterilized with 10% povidone iodine. The same treatment was applied at each dressing change. The hemodialysis catheters were inserted into the internal jugular, subclavian, or femoral veins. A film-type dressing with good vapor permeability (Bioclusive H; Johnson & Johnson, Cincinnati, Ohio, USA) was used to dress the catheter insertion site. We checked the insertion site every day and replaced dressing upon contamination with blood or partial detachment from the skin. The hemodialysis catheters were not used to infuse blood or for total parenteral nutrition. A catheter was removed when it was no longer needed; when catheter occlusion or insufficient blood flow was noted, or upon the development of fever or the appearance of erythema at the catheter insertion site suspicious of catheter-related infection. When the catheter was removed due to suspected catheter-related infection, a new catheter was inserted at a different site 24 h after catheter removal or even later, whenever possible. Neither regular catheter replacement (including wire-guided changes) nor insertion of a new catheter at the same site was performed throughout the study.

Microbiology

After removal, all hemodialysis catheters were subjected to microbiological culture test by the roll-plate method (semiquantitative culture) [6]. A blood culture test was performed regularly twice a week, and also when bacteremia was clinically suspected from the symptoms such as fever and chills.

Definitions of Infection

In the present study, catheter-associated infections were defined according to the standardized criteria generally adopted in recent studies [7-9].

Catheter Colonization. Significant growth of microorganisms (≥ 15 colony-forming units) from a catheter segment, as assayed by semiquantiative culture.

Catheter-Related Bloodstream Infection. Isolation of the same organism from a blood culture and from a semiquantiative culture of a catheter segment, accompanied by clinical symptoms of bloodstream infection without any other apparent source of infection.

Statistical Analysis

All data are expressed as mean ± SD. Statistical differences in catheterization duration were analyzed by Student’s t test. A p value of <0.05 was considered significant. The estimation of time to occurrence of catheter colonization was based on the Kaplan-Meier estimate. The log rank test was used to compare these estimations. For the statistical analysis, a computerized package (Dr. SPSS II; SPSS, Chicago, Ill., USA) was used.

Results

Table 1 summarizes the characteristics of the patients studied (42 men and 12 women, aged 51.6 ± 23.4 years). The mean duration of ICU stay was 29.9 ± 16.4 days and the mean duration of CHDF was 25.2 ± 16.6 days. Upon ICU admission, the mean APACHE II score was 22.9 ± 9.9 and the mean number of failing organs was 2.9 ± 1.4. Mortality was 63%. A wide variety of clinical conditions were observed at ICU admission. The major surgical operations performed on the patients prior to ICU admission included abdominal surgery (12 patients), thoracic surgery (4 patients), and pediatric surgery (3 patients). The medical causes of ICU admission were fulminating hepatic failure (8 patients), severe acute pancreatitis (6 patients), hematologic or collagen disease (6 patients), pneumonia (5 patients), cardiac failure (4 patients), and intoxication (1 patient). Infections were identified in 39 patients (72%). The main focus of infection varied from patient to patient, including pneumonia (19 patients), panperitonitis (8 patients), skin and soft tissue cellulitis (3 patients), enteritis (2 patients), and mediastinitis (1 patient). Blood culture was positive in 25 patients (46%).

Table 2 shows blood purification and extracorporeal cardiopulmonary support performed in the present study. CHDF was performed alone in 32 patients, and in the remaining 22 patients, in combination with other blood purification therapies and extracorporeal cardiopulmo-
### Table 1. Characteristics of patients

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male:female</td>
<td>42:12</td>
</tr>
<tr>
<td>Age, years</td>
<td>51.6 ± 23.4 (0–81)</td>
</tr>
<tr>
<td>Length of ICU stay, days</td>
<td>29.9 ± 16.6 (14–65)</td>
</tr>
<tr>
<td>Time on CHDF, days</td>
<td>25.2 ± 11.4 (14–64)</td>
</tr>
<tr>
<td>APACHE II score</td>
<td>22.9 ± 9.9</td>
</tr>
<tr>
<td>Number of failing organs</td>
<td>2.9 ± 1.4</td>
</tr>
<tr>
<td>Mortality</td>
<td>34 (63%)</td>
</tr>
</tbody>
</table>

**Clinical condition on admission to the ICU**

**Surgical**
- Abdominal: 12
- Thoracic: 4
- Pediatric: 3
- Others: 5

**Medical**
- Fulminant hepatic failure: 8
- Severe acute pancreatitis: 6
- Hematologic/collagen disease: 5
- Pneumonia: 4
- Cardiac failure: 3
- Intoxication: 1

**Cases of infection**
- Total: 39 (72%)

**Main focus of infection**
- Pneumonia: 19
- Peritonitis: 8
- Cellulitis: 3
- Enteritis: 2
- Mediastinitis: 1
- Other: 1
- Unknown: 5

**Blood culture-positive cases**
- Total: 25 (46%)

### Table 2. Blood purification and extracorporeal cardiopulmonary support performed

<table>
<thead>
<tr>
<th>Blood purification and cardiopulmonary support</th>
<th>Clinical diagnosis</th>
<th>Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>CHDF only</td>
<td>Acute renal failure, hypercytokininemia, etc.</td>
<td>32</td>
</tr>
<tr>
<td>CHDF+SPE</td>
<td>Fulminant hepatic failure, TTP, HPS, TEN, etc.</td>
<td>7</td>
</tr>
<tr>
<td>CHDF, HFCHDF+SPE</td>
<td>Fulminant hepatic failure</td>
<td>8</td>
</tr>
<tr>
<td>CHDF+SPE, DHP</td>
<td>Postoperative hepatic failure</td>
<td>1</td>
</tr>
<tr>
<td>CHDF, DHP, LCAP</td>
<td>Intoxication</td>
<td>1</td>
</tr>
<tr>
<td>CHDF, PCPS</td>
<td>Pneumonia, congenital diaphragmatic hernia</td>
<td>2</td>
</tr>
<tr>
<td>CHDF, PD, PCPS</td>
<td>TOF, congenital diaphragmatic hernia</td>
<td>2</td>
</tr>
</tbody>
</table>

**TTP = Thrombotic thrombocytopenic purpura; HPS = hemophagocytic syndrome; TEN = toxic epidermal necrolysis; TOF = trilogy of Fallot; SPE = slow plasma exchange; HFCHDF = high-flow dialysate CHDF; DHP = direct hemoperfusion; LCAP = leukocytapheresis; PCPS = percutaneous cardiopulmonary support.**

### Table 3. Insertion site of hemodialysis catheter and frequency of catheter colonization

<table>
<thead>
<tr>
<th>Insertion site</th>
<th>Blood access catheter (catheter days)</th>
<th>Colonized catheter</th>
<th>Frequency of catheter colonization (/1,000 catheter days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Femoral vein</td>
<td>118 (1,071)</td>
<td>6</td>
<td>5.6</td>
</tr>
<tr>
<td>Jugular vein</td>
<td>27 (285)</td>
<td>1</td>
<td>3.5</td>
</tr>
<tr>
<td>Subclavian vein</td>
<td>10 (108)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Total</td>
<td>155 (1,464)</td>
<td>7</td>
<td>4.8</td>
</tr>
</tbody>
</table>

**Clinical diagnosis**

- Acute renal failure, hypercytokininemia, etc.
- Fulminant hepatic failure, TTP, HPS, TEN, etc.
- Fulminant hepatic failure
- Postoperative hepatic failure
- Intoxication
- Pneumonia, congenital diaphragmatic hernia
- TOF, congenital diaphragmatic hernia
Figure 1 shows the actuarial survival curve for catheter colonization in the femoral and jugular veins. A Kaplan-Meier analysis estimating the risk of catheter colonization according to the duration of catheterization demonstrated no significant difference between these two catheter insertion sites (p = 0.558, log-rank test).

Figure 2 summarizes the duration of catheterization and the number of catheter changes for colonized and non-colonized hemodialysis catheters. The mean duration of catheterization was 9.3 ± 6.7 days for non-colonized catheters, while that for colonized catheters was 11.3 ± 8.3 days. No significant difference in the duration of catheterization was observed between colonized and non-colonized catheters (p = 0.44). In cases with catheter colonization, the number of catheter changes was 0–7 times in total and colonization was noted with either the 1st, 2nd, or 3rd catheter.

Thirty-two hemodialysis catheters (21%) were removed due to the development of fever suspicious of catheter-related infection. The removal of 20 catheters resulted in a subsequent decline in fever but this was not the case with the remaining 12 catheters. Catheter colonization was confirmed in 7 of the 20 catheters, the removal of which lowered the patient’s fever.

Table 4 shows the pathogenic organisms identified and the timing of culture positivity for each case of catheter colonization. Catheter culture was positive in a total of 6 patients, including patient 2 in whom both hemodialysis catheters placed at different times proved to be culture-positive. In all except patient 6, both catheter and blood cultures identified an identical pathogenic organism. In patients 1 and 2, an identical pathogenic organism had already been identified in blood culture before catheter culture was conducted and proved to be positive. Hemodialysis catheters had to be placed in these 2 patients who had already developed bacteremia upon ICU admission. In patients 3–6, on the other hand, an identical pathogenic organism was detected in both catheter and blood cultures conducted at the same time, which demonstrated hemodialysis catheter-related bloodstream infection. Thus, the incidence rate of hemodialysis catheter-related bloodstream infection was calculated to be 2.7/1,000 catheter days.
Table 4. Pathogenic organisms and timing of positive culture

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Pathogenic organism (hemodialysis catheter)</th>
<th>Pathogenic organism (blood)</th>
<th>Timing of positive culture</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MRSA</td>
<td>MRSA</td>
<td>Earlier in blood than catheter</td>
</tr>
<tr>
<td>2</td>
<td>Candida albicans Staphylococcus epidermidis</td>
<td>C. albicans S. epidermidis</td>
<td>Earlier in blood than catheter</td>
</tr>
<tr>
<td>3</td>
<td>Enterococcus faecalis</td>
<td>E. faecalis</td>
<td>Same time</td>
</tr>
<tr>
<td>4</td>
<td>Burkholderia cepacia</td>
<td>B. cepacia</td>
<td>Same time</td>
</tr>
<tr>
<td>5</td>
<td>MRSA</td>
<td>MRSA</td>
<td>Same time</td>
</tr>
<tr>
<td>6</td>
<td>MRSA</td>
<td>(–)</td>
<td>Same time</td>
</tr>
</tbody>
</table>

MRSA = Methicillin-resistant *Staphylococcus aureus*.

Discussion

In recent years, due to its expected wide spectrum of clinical efficacy, CHDF has been widely applied in the treatment of a variety of clinical conditions encountered in critical care [1, 3–5]. At the same time, infection, especially treatment-related iatrogenic infection, is an important problem in the management of critically ill patients.

We therefore investigated infections in patients undergoing CHDF. Since prolonged catheterization is reported to be a risk factor of catheter-related infections [9, 10], we first investigated the duration of hemodialysis catheter placement per catheter in 100 patients who recently underwent CHDF at our institution. As a result of this preliminary study, the duration of hemodialysis catheter placement per catheter was found to be longer in patients undergoing CHDF for 14 days or longer compared with those undergoing this therapy for a shorter period. Based on this observation, in the present study we included 54 patients who underwent CHDF for 14 days or longer over the past 5 years.

Since the definition of catheter-related infections as well as their diagnostic methodologies are still controversial, it is difficult to compare the incidence rates of catheter-related infections reported so far [8, 9]. Nevertheless, patients requiring treatment in an ICU are equivocally reported to constitute a high-risk group of catheter-related infections [8, 11]. As for ICU patients, the incidence rates of catheter colonization and catheter-related bloodstream infection have been reported to be 8–31/1,000 catheter days [12] and 1.5–19/1,000 catheter days [13–16], respectively. Actually, however, reports on hemodialysis catheter-related infections in ICU patients are still limited [16, 17]. One such report identified no significant difference in the incidence rates of catheter colonization and catheter-related bloodstream infection between hemodialysis and central venous catheters [16]. When compared with these previously reported values, both the catheter colonization rate (4.8/1,000 catheter days) and the catheter-related bloodstream infection rate (2.7/1,000 catheter days) calculated for hemodialysis catheters in the present work were smaller.

We next investigated the relationship between the catheterization site and infection. In general, the incidence rate of infection associated with central venous catheters placed in the subclavian vein tends to be smaller than the value for such catheters placed in the femoral vein [18]. Also, placement of central venous catheters in the jugular vein reportedly tends to reduce catheter-related infection compared with catheter placement in the femoral vein [7]. In the present study hemodialysis catheter colonization rates are 5.6/1,000 catheter days (femoral vein) and 3.5/1,000 catheter days (jugular vein). In the actuarial survival risk (Kaplan-Meier) method, no significant difference was observed between catheter colonization and the venous site of insertion. In the present study, we placed the majority of hemodialysis catheters in the femoral vein because most of the study subjects were critically ill and needed placement of a central venous catheter (e.g., Swan-Ganz catheter) in the jugular or subclavian vein prior to placement of a hemodialysis catheter, which limited the placement site for the hemodialysis catheter [19]. The second reason is that, whenever possible, we try to avoid hemodialysis catheter placement in the subclavian vein due to its potential risk of serious complications including stenosis, perforation, and thrombogenesis.

While prolonged placement of central venous catheters is considered to be a risk factor for catheter-related infec-
Hemodialysis Catheter-Related Infections in Long-Term CHDF

Hemodialysis Catheter-Related Infections in Long-Term CHDF
References


