Central venous catheter-related infections in children on long-term home parenteral nutrition: incidence and risk factors

V. COLOMB, M. FABEIRO, M. DABBAS, O. GOULET, J. MERCKX, C. RICOUR
Hôpital Necker-Enfants Malades, Paris (Correspondence to: VC, Unité de Gastroentérologie et Nutrition, Fédération de Pédiatrie, Hôpital Necker-Enfants Malades, 149 rue de Sèvres, 75743 Paris Cédex 15, France)

Abstract—Background and aims: This study aimed to assess the incidence and etiology of central venous catheter (CVC) infections in children on home parenteral nutrition (HPN). Methods: 207 CVC-years were studied retrospectively in 47 children on HPN, aged 8.1 ± 5.0 years. Results: 125 CVC were used (means: 2.6 CVC/patient and 21 months utilization/CVC). Half of the hospitalizations (162) were due to proven CVC-related infections. The mean infection incidence was 2.1/1000 HPN days. The total population divided in two groups below and above this value: group one including 24 children, incidence ≤ 2.1 per 1000 days (mean: 0.83) and group two including 23 children, incidence > 2.1 per 1000 days (mean: 4.3). No differences were found between the two groups in terms of underlying disease, presence of ostomies, age at the time of HPN onset, or micro-organisms responsible. The only differences (p < 0.05) were the mean duration of HPN (longer in group one) and the delay between HPN onset and the first infection (longer in group one). Conclusions: This study does not highlight any risk factors for CVC infection. However, early CVC infections after HPN onset appear to predict a bad prognosis.

Key words: children; central venous catheter; infection; home parenteral nutrition

Introduction

Since the first reports in 1960s, the use of central venous catheters (CVCs) in the care of critically ill patients has increased rapidly. CVCs provide reliable and painless access to the central venous system for intravenous hydration, transfusions, drugs and short-term parenteral nutrition (PN). In case of chronic gut failure, long-term PN is necessary to provide protein–energy supplies which cannot be achieved by enteral feeding. Short bowel syndrome is the first indication for long-term PN, in children as in adults, whatever the underlying disease (1). Home PN (HPN) has developed in children from the late 1970s (2–4). It gives patients who depend on long-term PN the best possible quality of life (5–7) and is cost-sparing as compared to prolonged hospitalizations (8). However, HPN is high-risk technique. Among PN-associated complications, CVC-related infections are especially feared in children. Firstly, infections might lead to iterative CVC removal and/or deep venous thrombosis, that appear as a risk factor for CVC placement complications (9) and contribute to using up access to the central venous system. Secondly infections are a well known risk factor for the PN-associated liver disease (10–12). Thirdly, several studies have emphasized the cost of infectious complications of HPN (13,14).

This retrospective study aimed to assess the incidence of CVC-related infections in children on long-term HPN, in a single pediatric HPN centre. One major goal was to try to find out some risk factors, in order to improve the prevention.

Patients and methods

Patients

All CVC used for long-term PN (at least 6 months) in the 47 children belonging to the Necker-Enfants Malades Hospital HPN centre at the time of study (July 1998) were studied. Indications for HPN are summarized in Table 1. At the time of study, the mean age of the population was 8 years, 52% of the children had been on HPN for more than 4 years and 30% for more than 8 years (Table 2). For each patient, the following items were recorded: underlying disease and presence of a stomia (%), number of CVC-related infections and microorganisms found, age at the time of study (years), age at HPN onset (months), HPN duration (years), delay between HPN onset and the first infection (months) (per 1000 HPN days), presence of a nurse at home for CVC handling.

Catheters

CVCs were single lumen cuffed silicone central venous Broviac-type catheter (15), inserted into the superior venous.
vena cava above the right atrium through a jugular vein and tunneled subcutaneously–cutaneous exit of the catheter being on the anterior chest wall in the midclavicular line.

**Familial requirements for HPN and parents’ teaching**

Whatever medical indication, the nutrition team assessed that the family was suitable for HPN before a child’s HPN program was planned. A single-parent family was not considered as a contraindication for HPN (4), provided that social help and home nursing assistance were organized. The teaching program began as soon as the decision of HPN was taken, during the period when at least one parent or both were resident in the hospital. The mean duration of the teaching programme was 2 to 3 weeks (4, 6). One single specialized nurse has been responsible for parents’ teaching from the beginning of our pediatric HPN centre. All the families were taught the following guidelines for CVC handling. The CVC is always handled under sterile surgical conditions (hand washing and scrub with foaming 4% povidone iodine, surgical dressing). Before the beginning of infusion and after completion of infusion, the CVC is flushed with 10 mL of sterile saline serum. The CVC cap, as well as the CVC tubing junction, are swathed with sterile swabs moistened with 1% povidone iodine. The dressing at the catheter exit site is changed each second day. The site is cleaned with 10% povidone iodine and closed occlusively with a sterile air-permeable gauze pad. The use of the CVC for any drug injections at home (even antibiotics) is avoided. Blood draws from the CVC are authorized only in specialized hospital units. Baths in swimming pools are forbidden.

**Nutrients**

Before 1995, HPN consisted of binary admixtures including glucose, amino acids, electrolytes, trace elements and vitamins, lipid emulsions being administered separately on a Y-line (4). From 1995, all-in-one admixtures were provided to all HPN patients. Admixtures were manufactured and delivered to patients weekly, with disposables. Bags were stored at 4°C from their production to their delivery to patients. The rhythm of parenteral formula delivery was cyclic, usually 12–24 hours nightly.

**Monitoring and follow up**

Once discharged from hospital, a regular out-patient follow up was planned. A 24 h, hot, telephone contact was provided by the nutrition team, in close contact with general practitioners and regional non-specialized hospital units in order to deal with emergencies.

**Attitude toward signs of infection**

Parents were taught about the symptoms of catheter-related sepsis and monitored the child’s temperature daily. They had to contact their general practitioner and the hospital immediately in case of fever or any other signs of infection. Once a catheter-related sepsis was suspected, the child was hospitalized, central venous and peripheral blood samples were taken for bacterial cultures. In the absence of obvious alternative sites of primary infection, antibiotic treatment against *Staphylococcus aureus* including Vancomycin and another antibiotic (usually Rifamycin) was started and delivered through the catheter, awaiting the results of blood cultures.

**Criteria for infection diagnosis**

CVC-related infection was diagnosed in one of the following conditions: positive blood cultures from both the CVC and a peripheral vein for the same microorganism; more than one positive blood culture from the CVC for the same organism (even with a negative blood culture from a peripheral vein); infection at the exit site of the CVC with a positive site culture, with or without positive blood cultures; positive culture of the CVC tip upon CVC removal.

**Treatment of infections**

In case of positive blood cultures, antibiotics were selected according to the microorganism found and to the antibiogram, and were maintained over 8 to 15 days. In case of negative blood cultures and in the absence of biological infection criteria, the treatment was stopped at day 3. The criteria to perform a cardiac ultrasonography were: isolation of a *Staphylococcus aureus*, persistence of fever after a 48 h antibiotic treatment or persistence of positive blood cultures despite adequate antibiotics. In the absence of secondary septic localization, persistence of positive blood cultures suggested the

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**Table 1** Indications for HPN in the 47 children

<table>
<thead>
<tr>
<th>Indications</th>
<th>Number of cases</th>
<th>% of the total HPN population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short bowel syndrome</td>
<td>19</td>
<td>40.5</td>
</tr>
<tr>
<td>Chronic intestinal pseudo-obstruction</td>
<td>10</td>
<td>21</td>
</tr>
<tr>
<td>Intractable diarrhea</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>3</td>
<td>6.5</td>
</tr>
<tr>
<td>Hirschsprung disease</td>
<td>3</td>
<td>6.5</td>
</tr>
<tr>
<td>AIDS</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>3</td>
<td>6.5</td>
</tr>
</tbody>
</table>

**Table 2** Characteristics of HPN population

<table>
<thead>
<tr>
<th>Range</th>
<th>M ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at the time of study (years)</td>
<td>0.75–18</td>
</tr>
<tr>
<td>Age at HPN onset (months)</td>
<td>4–183</td>
</tr>
<tr>
<td>HPN duration (years)</td>
<td>0.5–14.2</td>
</tr>
</tbody>
</table>
contamination of the CVC and repair kits were used to replace the longest possible external portion of the CVC. The catheter was removed only in the case of fungal infection, exit-site cellulitis or tunnel infection, secondary infection (endocarditis, osteitis or arthritis) or unsuccessful antibiotic treatment.

Statistical analysis

Comparison of the means was performed using the Wilcoxon’s test for unpaired data. A $P$ value of less than 0.05 was considered significant.

Results

Two hundred and seven (207) CVC years were studied. One hundred and twenty five (125) CVC were used in 47 patients with a mean of 2.6 CVC per patient. The mean CVC lifespan was 21 months ($21 \pm 20$ months, range 0.2–113 months). The duration of the first CVC was similar to the second ($24 \pm 20$ versus $28 \pm 35$ months respectively).

Over the 207 CVC years, 162 infections occurred. Although only 22% of CVC infections–of which half were exit-site infection–led to CVC removal, infections were responsible for 44% of CVC removal. Specific CVC repair kits were used to treat 15 infections unresponsive to antibiotics.

Half of the PN-related hospitalizations (162) were due to CVC-related infections ($7 \pm 5$ per child, for $8.5 \pm 4$-day periods). The organisms responsible were

\begin{table}[h]
\centering
\begin{tabular}{|l|c|c|}
\hline
Organisms & Septicemia (a) & Exit-site infections (b) \\
\hline
\textit{Staphylococcus epidermidis} & 67 & 7 \\
\textit{Staphylococcus aureus} & 5 & 64 \\
Other Gram positive Cocci & 9 & 0 \\
Gram negative Bacilli & 16 & 22 \\
Fungi & 3 & 7 \\
\hline
\end{tabular}
\caption{Organisms responsible for CVC-related infections}
\end{table}

(a) Out of which 8 pluri-microbial infections.
(b) Out of which 1 pluri-microbial infection.

Table 4 Comparison of 2 groups of children who presented with a mean sepsis incidence $\leq 2.1/1000$ HPN days and $>2.1/1000$ HPN days respectively

<table>
<thead>
<tr>
<th></th>
<th>Group 1 ($\leq 2.1/1000$ d)</th>
<th>Group 2 ($&gt;2.1/1000$ d)</th>
<th>Statistics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>24</td>
<td>23</td>
<td>NS</td>
</tr>
<tr>
<td>Incidence of CVC-related</td>
<td>$0.83 \pm 0.65$</td>
<td>$4.3 \pm 2.0$</td>
<td>$P &lt; 0.05$</td>
</tr>
<tr>
<td>Infections (per 1000 HPN days)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at the time of study (years)</td>
<td>$9.0 \pm 5.4$</td>
<td>$7.0 \pm 4.3$</td>
<td>NS</td>
</tr>
<tr>
<td>Age at HPN onset (months)</td>
<td>$32.5 \pm 47.0$</td>
<td>$28.8 \pm 37.9$</td>
<td>NS</td>
</tr>
<tr>
<td>HPN duration (years)</td>
<td>$5.3 \pm 4.0$</td>
<td>$3.5 \pm 2.7$</td>
<td>$P &lt; 0.05$</td>
</tr>
<tr>
<td>Delay between HPN onset and the first infection (months)</td>
<td>$13.5 \pm 15.9$</td>
<td>$4.3 \pm 3.6$</td>
<td>$P = 0.001$</td>
</tr>
<tr>
<td>Help of a nurse at home (% per group)</td>
<td>58%</td>
<td>52%</td>
<td>NS</td>
</tr>
<tr>
<td>Immune deficiency (%)</td>
<td>21%</td>
<td>21%</td>
<td>NS</td>
</tr>
<tr>
<td>Short bowel (%)</td>
<td>56%</td>
<td>46%</td>
<td>NS</td>
</tr>
<tr>
<td>Presence of a stoma (%)</td>
<td>37</td>
<td>26</td>
<td>NS</td>
</tr>
<tr>
<td>Micro-organism (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>-\textit{Staphylococcus epidermidis} &amp; 76</td>
<td>70</td>
<td>NS</td>
<td></td>
</tr>
<tr>
<td>-Gram negative bacilli</td>
<td>10</td>
<td>19</td>
<td></td>
</tr>
</tbody>
</table>

Discussion

This study, which describes CVC-related infections in children on long term-HPN is, to our knowledge, one of the largest pediatric studies ever performed on this issue with regard to both the number of patients involved and the very long duration of HPN usage. Although indications for HPN have not changed over the last 15 years in our centre (4), HPN mean duration has increased threefold over this period. This is due to the large number of cases of definitive gut failure as short bowel syndrome secondary to extensive intestinal resection, unadapted short bowel (16), intractable diarrhea of infancy (17) or severe chronic intestinal pseudo obstruction (18). Several other pediatric HPN

\textit{Staphylococcus epidermidis} in 67% blood cultures and \textit{S. aureus} in 64% cutaneous infections (Table 3). Twenty five percent of infections occurred over the first HPN year and 44.5% over the first 2 HPN years. The incidence of CVC-related infections (148 with positive blood cultures and 14 exit-site or tunnel infections) was 2.1/1000 HPN days (or 1.476 days, or 0.78 per patient-year). When the distribution of the entire study population below and above this mean value was examined, it appeared that a bi-modal distribution spontaneously split the population into 2 equal groups of patients (Table 4). Group one (defined by a sepsis incidence $\leq 2.1/1000$ HPN days) included 24 children with a sepsis incidence of $0.83 \pm 0.65/1000$ days, and group two (defined by a sepsis incidence $>2.1/1000$ HPN days) included 23 children with a sepsis incidence of $4.3 \pm 2.0/1000$ days. Seven children in group one did not present with any CVC-related infections during the period studied (their mean HPN duration was 2.6 years, the longer HPN duration without infection being 6.4 years). The two groups differed only by the HPN duration–longer in group one, ($P < 0.05$) – and by the delay between HPN onset and the first infection – longer in group one, ($P < 0.05$) – (Table 4).
teams have described similar HPN durations (19, 20). The increase in HPN duration in our centre did not lead to a proportional increase in the number of CVCs per child, but on the contrary, to an increase in the mean lifespan of each CVC, from 16.5 months in our first study (4) to 21.2 months in the current study. This might be explained by improvement in the management of CVC-related complications.

Infections are by far the most frequent CVC-related complications. The infection incidence in our survey – 2.1 per 1000 HPN days – is in the same range as data given by other pediatric studies, which varied from 1 to 4 per 1000 HPN days (19–22). This confirms that CVC-related infections are more frequent in children than in adults, in whom CVC infection incidence range from 0.3 to 1.3 per 1000 days (23–25). However, criteria used to define a ‘CVC-related infection’ might differ from one study to another, making the comparison between studies difficult. Coagulase-negative (Epidermidis) Staphylococcus accounted for about 70% of micro-organisms involved in our study, this ratio being stable over the last 15 years in our centre (4). Interestingly, the incidence of CVC-related infections due to S. aureus, Gram-negative bacilli and fungi is lower than in other pediatric populations on HPN in Europe or North America (6,19–21). It must be emphasized also, that many infections occurred during the first 2 years of HPN, this observation being shared with other pediatric teams (19, 21). Since most pediatric HPN programmes begin in children aged less than 1 year, the higher incidence of infections might be attributed partly to young children specific risk factors. Moreover, the improvement in quality of CVC handling by the families with time might be another explanation.

The fact that our population split into two groups of children of similar size with significantly different CVC infection incidence, led us to compare these two groups. We failed to show any differences between them in term of underlying disease, presence of ostomies, age at the time of HPN onset, involvement of a nurse in the CVC handling or micro-organisms responsible for infection. Several other pediatric studies failed also to identify specific risk factors for CVC infection apart from age at first infection (21). However, our two groups differed in the mean duration of HPN; the longer HPN duration in the group one (5.3 years, versus 3.5 for the group two) being associated with a lower incidence of CVC infection. The other highly significant difference is the delay between HPN onset and the first infection (13.5 months for the group one versus 4.3 for the group two). These results may point up the same phenomenon: one might hypothesize that some children present from the beginning of HPN a higher risk of CVC infection, that leads to early infections and numerous episodes over the first months of HPN. Since no specific risk factors emerged from the comparison of our two groups, it is still impossible to identify high-risk patients and to apply personalized preventive measures from the beginning of HPN. Unfortunately, only 7/47 children never had a CVC-related infection, thus it was impossible to compare statistically these 7 patients with 40 others. Nevertheless, our data suggest that the early occurrence of CVC infections (over the first 6 months of HPN) might predict future repeated infections and should lead to a greater family training.

References


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