Prevention and management of peritonitis and exit-site infection in patients on continuous ambulatory peritoneal dialysis

V. Vargemezis and E. Thodis

Division of Nephrology, Democritus University of Thrace, Greece

Introduction

Peritoneal dialysis (PD) is an important and lifesaving form of renal replacement therapy for more than 100,000 patients worldwide. Peritonitis, catheter exit-site, and tunnel infections are serious problems in PD patients. Peritonitis accounts for 15–35% of hospital admissions, is the major cause (40–45%) of transfer to haemodialysis (technique failure), and finally is associated with mortality (7–10% of deaths) either as a primary or contributing factor [1]. In the early 1980s peritonitis incidence was high, with rates as high as 6.3 episodes per patient year. During the 1980s and early 1990s the peritonitis rate dropped to 1.1–1.3 episodes per patient year. With improvements in connection technology (introduction of Y-set and double-bag systems) the peritonitis rates declined further to around 0.5 episodes per patient year [2].

Peritonitis

Aetiology

Using appropriate culture techniques, an organism can be isolated from the peritoneal fluid in over 90% of cases in which symptoms and signs of peritonitis and an elevated peritoneal fluid neutrophil count are present. Most episodes (>75%) are due to a single organism. In contrast to surgical peritonitis and spontaneous bacterial peritonitis, the most common organisms (50–65%) are Gram-positive [3].

Although unusual, fungal peritonitis has been reported in different series to account for 3–10% of CAPD peritonitis. Candida species have contributed to 75–80% of fungal peritonitis, although many species have been reported. Anaerobic peritonitis and multi-organism infections (more than one Gram-negative organism), suggest bowel perforation. Finally, mycobacterial peritonitis is rare, but may be more common in countries where mycobacterial infections are epidemic.

Potential routes of infection

The most common routes of infection and the common type of organisms causing peritonitis during CAPD are as follows:

(i) Contamination at connection sites (Staphylococcus epidermidis, Staphylococcus aureus, acinetobacter).
(ii) Pericatheter (exit-site or tunnel infection) (S.epidermidis, S. aureus, pseudomonas, proteus, yeast).
(iii) Transmural (through the gut wall) (multiple organism in association with anaerobes and fungi).
(iv) Haematogenous (streptococcus, mycobacterium).
(v) Ascending (through the vagina) (pseudomonas, yeast).

Table 1. Incidence of organisms isolated in patients with peritonitis [2,4,8,12,13]

<table>
<thead>
<tr>
<th>Organism</th>
<th>%</th>
<th>Episodes/patient year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gram-positive</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Staphylococcus epidermidis</td>
<td>30–45</td>
<td>0.17–1.04</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>10–20</td>
<td>0.09–0.15</td>
</tr>
<tr>
<td>Streptococcus sp.</td>
<td>5–10</td>
<td>0.04–0.14</td>
</tr>
<tr>
<td>Other Gram-positive</td>
<td>&lt;5</td>
<td>0.01–0.02</td>
</tr>
<tr>
<td>Gram-negative</td>
<td>10–20</td>
<td>0.09–0.15</td>
</tr>
<tr>
<td>Pseudomonas</td>
<td>3–8</td>
<td>0.01–0.06</td>
</tr>
<tr>
<td>Candida and other fungi</td>
<td>3–10</td>
<td>0.01–0.07</td>
</tr>
<tr>
<td>Mycobacterium tuberculosis</td>
<td>&lt;1</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Culture negative</td>
<td>5–20</td>
<td>0.10–0.20</td>
</tr>
</tbody>
</table>
Predisposing factors

Risk factors for the development of peritonitis identified higher rates for children, African Americans, Native Canadians, and those with a history of substance abuse or a lower socioeconomic status. Recent studies have identified immunosuppression and HIV-positive status, long-term antibiotic use, the intake of gastric acid inhibitors and (mainly for children on CAPD) upper respiratory tract infections, although the latter factor is not clear. The strongest dialysis-related factors are the type of connection system and staphylococcal nasal carriage.

It is now well known that 50% of PD patients are nasal carriers for *S. aureus*. Compared with non-carriers, carriers have a 2–6-fold higher incidence of *S. aureus* peritonitis, while the same germ accounts for 50% of exit-site infections. However, the development of disconnect systems has led to a shift in the relative importance of *S. aureus* compared with *S. epidermidis*. Studies evaluating CAPD-related peritonitis in association with ‘flush before fill’ techniques reported a significant reduction in the rate of *S. epidermidis* infections but no change in the number of episodes caused by *S. aureus* [5]. Strategies that treat nasal carriage (nasal mupirocin or cyclical rifampin), or treat the exit-site to prevent *S. aureus* exit-site infection (mupirocin) dramatically reduce the incidence of *S. aureus* peritonitis (see below, Prevention) [6].

Management of peritonitis

The Ad Hoc Advisory Committee on Peritonitis Management recommendations for the management of peritonitis are depicted in Figure 1 [7].

Exit-site infection

Exit-site infection (ESI) is a troublesome catheter-related complication of PD. During the 1990s the overall probability of developing ESI was 46% at 1 year and 70% at 3 years on CAPD. Not infrequently ESI leads to peritonitis (30–50%) and catheter loss (15–57%). ESI can develop irrespective of the type of catheter and the mode of exit-site care [8].

Incidence data

The reported incidence of organisms responsible for exit-site infections in patients on PD is *S. aureus* 25–85%, mixed organisms including *S. aureus* 16–35%, enteric Gram-negatives in 7–11% and fungal agents in 1–3% of cases [9].

Treatment of exit-site infections

Traditionally treatment duration has been 2–4 weeks, with any adjustment in therapy being made when the culture sensitivities are known. Current recommendations for the treatment of exit-site infections include topical chlorhexidine and mupirocin for erythema alone with no discharge, cephalosporin or vancomycin for Gram-positive bacteria in combination with rifampicin for persistent Gram-positive infection, ciprofloxacin for Gram-negative infections and catheter removal in combination with systemic antifungal therapy for fungal infections [10].

Prevention

Peritonitis and exit-site infections are serious problems for PD patients and major causes of hospitalization, catheter loss, and transfer to haemodialysis. In terms of prevention there are general instructions such as careful selection of patients, and training by experienced nurses. Other general aspects include the use of a twin-bag system, the spike assist device for APD and aggressive nutritional intervention for PD patients, especially for children [11].

While catheter-related infections (exit-site infections, tunnel infections) are major causes of peritonitis and *S. aureus* is the main cause of these complications, increasing evidence accumulated during the 1990s indicating that prophylaxis against *S. aureus* carriage may reduce the risk of catheter-related peritonitis. Staphylococcal infections predominate in those untreated, but Gram-negative infections have also been reported. Attempts were made to reduce *S. aureus* burden and infections with administration of systemic antibiotics (e.g. prophylactic oral trimethoprim–sulfamethoxazole, cyclic rifampin, and a combination of cyclical oral rifampin with daily mupirocin ointment applied to the exit-site region). Although these studies showed that it was possible to eradicate *S. aureus* temporarily and to reduce the infection rate at the same time, several clinical problems such as
resistance to antimicrobial therapy, colonization of the nose, and adverse effects of systemic antibiotic treatment occurred. Bernardini et al. [6] and Thodis et al. [12], reported that daily application of mupirocin cream to the catheter exit-site reduced both exit-site infections by 91% and peritonitis by 67% caused by \textit{S. aureus}, compared with historical controls. These studies contribute to the growing body of evidence that daily local application of mupirocin cream at the exit-site significantly reduces catheter related infections due to \textit{S. aureus} and some authors recommend that all PD patients apply mupirocin cream at the catheter exit-site as part of their daily exit-site care [12].

Fungal peritonitis is a devastating complication in PD patients, often leading to catheter loss (40–60%) and permanent transfer to haemodialysis (25–50%). Mortality rates associated with fungal peritonitis are high in children and adults (20–45%). While many trials have studied the effect of prophylaxis, only one was prospective and randomized, giving nystatin (500,000 U four times a day), during the administration of antibiotics [13]. The authors reported a decreased incidence of Candida peritonitis (1.9 vs 6.4 per 100 peritonitis episodes and 0.66 vs 1.43 per 100 antibiotic prescription for any indication) with this prophylaxis [13].

\section*{Conclusion}

In summary, in the last decade some progress has been made in prevention and management of PD catheter-related complications (exit-site, tunnel infections-peritonitis). This includes newer connection techniques, prophylaxis to prevent \textit{S. aureus} infections, nystatin prophylaxis with prolonged or frequent antibiotic administration and careful selection of patients. Close attention to training techniques with constant reinforcement of aseptic procedures is always important. Clearly, we still have a way to go before saying that catheter-related infection risk is minimal in PD patients.

\section*{References}