Fungal peritonitis (FP) is an infrequent cause of peritonitis in peritoneal dialysis (PD), but it has high morbidity and mortality. We analyzed the experience with FP in a single PD unit over a 24-year period.

We identified 671 episodes of peritonitis that occurred in 496 patients during the study period. Of these episodes, 23 (3.4%) were FP episodes occurring in 21 patients. In the FP episodes, the patients’ mean time on PD was 29.2 ± 27 months. In 5 episodes, the patients had experienced a peritonitis episode within the preceding month, and in 11 episodes, the patients had used antibiotics within the preceding month. The FP diagnosis was made a mean of 3.17 ± 3 days after the diagnosis of peritonitis, and in 1 patient, the diagnosis was made after death. Candida spp. were isolated in 82.6% of patients. In 91.3%, the peritoneal catheter was removed. After the FP diagnosis, 15 patients dropped out of PD, but in only 8 patients (34.7%) was drop-out related to FP. In 4 patients, drop-out occurred because of peritoneal membrane failure, and 4 patients (17.4%) died. Time on PD was significantly higher in the group of patients that dropped out of PD because of the FP (45.7 ± 31 months vs. 19 ± 18 months, p = 0.02).

Fungal peritonitis is a rare cause of peritonitis in PD patients, but it is associated with high morbidity and mortality. Longer time on PD is the main factor in technique failure and mortality.

**Key words**
Fungal peritonitis
per cubic millimeter, a differential white blood cell count showing more than 50% polymorphonuclear cells, and symptoms related to peritonitis (7).

**Isolation of fungi from PD effluent**

“Catheter-related peritonitis” was defined as peritonitis associated with an exit-site or tunnel infection with the same organism (7). “Death related to peritonitis” was defined as death of a patient who had active peritonitis or was admitted with peritonitis, or who died within 2 weeks of a peritonitis episode (7).

**Statistical analysis**

Results are expressed as mean ± standard deviation, and p < 0.05 was considered statistically significant. The chi-square test was used to compare proportions, and the Mann–Whitney U-test, to compare continuous variables. Logistic regression analysis was used to study risk factors associated with technique failure and death.

**Results**

Between January 1980 and December 2004, 671 episodes of peritonitis occurred in 496 patients being treated with PD. We identified 23 FP episodes (3.4%) in 21 patients. Table I shows the characteristics of the patients with FP. In 5 FP episodes (21.7%), the patient had had a bacterial peritonitis within the preceding month. In 11 episodes (47.8%), antibiotics had been administered within 1 month before the FP. Oral nystatin or fluconazole prophylaxis had been given in 3 of these patients.

The clinical presentation of the FP was varied, with abdominal pain in 20 episodes (87%), poor or slow outflow in 17 (74%), fever in 12 (52%), diarrhea in 4 (17%), and constipation in 1 episode. In 2 episodes, the only complaint was outflow failure. The causative fungus was identified within a mean of 3.17 ± 3 days (range: 0 – 13 days) after the diagnosis of peritonitis. In 1 patient, the diagnosis was made at autopsy.

Table II shows the fungal species isolated. Candida spp. were isolated in 19 episodes (82.6%). In 2 episodes (8.7%), the fungi were not classified. Two patients each had 2 episodes of FP. The fungi isolated in those episodes were C. albicans and C. tropicalis in one patient, and C. glabrata and Alternaria sp. in the other. In 3 patients, the peritonitis was catheter-related.

Antifungal therapy was initiated as soon as the diagnosis of FP was made—or earlier, if FP was suspected. The initial agent and the route of administration varied (Table III). Fluconazole and flucytosine IP were used in most episodes (59%), because that antifungal regimen became the empirical treatment for FP in 1997. In 9 episodes with FP attributable to Candida spp., the antifungal agent was changed to amphotericin B because of poor response to the initial agent: fluconazole and flucytosine (n = 5), fluconazole (n = 1), fluconazole and ketoconazole (n = 2), or ketoconazole and flucytosine (n = 1). The mean duration of antifungal treatment was 29.4 ± 16 days. One patient did not receive antifungals because the FP diagnosis was made after death.
In 2 episodes, the peritoneal solution was changed to bicarbonate/lactate to increase peritoneal defense and immunity (8), and in one case, the peritoneal effluent did not become clear after the change. The peritoneal catheter was removed in 21 of the 23 FP episodes (91%). In the other 2 patients, the catheter was left in place—in one case, because response to the antifungal treatment was good; in the other, because the FP diagnosis was made only after death. The mean time between the diagnosis of peritonitis and catheter removal was 4 ± 6 days. The catheter was removed before the diagnosis of FP in 4 patients, and at diagnosis in another 4 patients. Most catheters were removed after diagnosis, usually after 2 – 3 days of specific FP treatment, so as to remove the catheter with local inflammation at its lowest. When possible, a new peritoneal catheter was inserted after 4 – 6 weeks of specific treatment for FP.

Hospitalization [mean duration: 21.8 ± 15 days (range: 4 – 60 days)] was required in 19 patients (83%). At the time of the FP episode, 15 patients (65.2%) dropped out from PD, but in only 8 cases (34.7%) was the drop-out related to the FP. Four patients (17.4%) were transferred to hemodialysis because of peritoneal membrane failure, and 4 patients (17.4%) died. The remaining 7 patients preferred to be transferred to hemodialysis because the patient or the family was discouraged with PD. One patient with peritoneal membrane failure decided to remain on a combination of PD and once-weekly hemodialysis, although transfer to hemodialysis was indicated. All patients whose FP episode occurred within the first year on PD (n = 8) were able to remain on PD. Patients who dropped out of PD because of the FP (n = 8) had a longer duration on PD before the FP diagnosis than did patients who resumed PD (45.7 ± 31 months vs. 19 ± 18 months, p = 0.02). Logistic regression analysis showed that other factors—age, prior antibiotic use, time since the last episode of peritonitis, presence of abdominal pain, delay in FP diagnosis, antifungal treatment duration, catheter removal, and time between diagnosis and catheter removal—were not related to technique failure or death.

Discussion
Because FP represents an infrequent complication in patients receiving chronic PD, fungi are often forgotten as a cause of peritonitis. In our series, the incidence of FP was 3.4%, similar to that noted in previous reports (1,3,4,6).

Peritonitis is the main cause of technique failure in PD patients, resulting in death in 1% – 6% of episodes, with FP being responsible for the highest (25%) mortality rates (7). In the present study, the proportion of patients that dropped out of PD because of FP was 34.7%, and the FP-related mortality rate was 17.4%. In accord with previous reports (4,6), we found a high rate of hospitalization (83%), with a mean duration of 21 days, confirming the high morbidity associated with FP.

Most FP episodes are preceded by use of antibiotics (3). Antibiotic use within 3 months prior to FP has previously been associated with technique failure (4). In the present study, 47.8% of patients received antibiotics in the month before their FP episode, but we found no association between antibiotic use and technique failure or death. The prophylactic use of an antifungal agent (either nystatin or fluconazole) during antibiotic therapy to prevent FP remains a controversial issue (9–11) and is recommended only in high-risk units (FP rate > 10%). Prophylaxis is not a common practice in our unit.

Among the clinical factors studied, we found that longer duration on PD before a diagnosis of FP was the main risk factor for technique failure: patients that dropped out of PD had spent more time on PD than those who returned to PD after an FP episode (45.7 ± 31 months vs 19 ± 18 months, p = 0.02). As our group previously reported (12), the vulnerability of peritoneal function to infectious episodes is higher in long-term PD and is mainly expressed by loss of ultrafiltration capacity, probably because of a higher degree of peritoneal fibrosis. That factor may explain our findings. In addition, Lo et al. (5) demonstrated

<table>
<thead>
<tr>
<th>Initial antifungal agent</th>
<th>Episodes [n (%)]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluconazole IP + 5-fluorocytosine IP</td>
<td>13 (59)</td>
</tr>
<tr>
<td>Fluconazole PO</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Fluconazole IP</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Fluconazole IP + Fluconazole PO</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Fluconazole IP + Ketoconazole PO</td>
<td>2 (9)</td>
</tr>
<tr>
<td>Ketoconazole PO + Fluorocytosine IP</td>
<td>1 (4.5)</td>
</tr>
<tr>
<td>Amphotericin B IV</td>
<td>2 (9)</td>
</tr>
</tbody>
</table>

IP = intraperitoneal; PO = oral; IV = intravenous.
that a PD duration of more than 26 months is an additional risk factor for mortality.

In our series, a longer time between the diagnosis of peritonitis and the identification of the fungus and initiation of an antifungal agent was not associated with technique failure. However, obtaining a prompt diagnosis of FP is very important because of the rareness of fungus as a peritonitis cause. The major problem is that identification of the fungus usually takes several days. In our series, the mean FP diagnosis delay was 3.17 ± 3 days. New diagnostic techniques have been developed in the last few years, but identification of fungi remains problematic. In the present study, 2 fungi were never classified, and 7 Candida spp. were undetermined. Candida spp. were the most commonly found organism, at 82.6%. In other reported series (2,3,4,6), non albicans species were more frequently isolated than was C. albicans. The high number of undetermined Candida spp. in our series means that we could not perform a statistical analysis differentiating the mortality rate between Candida and non Candida species. Previous series have revealed non-significant differences (4).

In some studies, the presence of abdominal pain has been related to greater technique failure (4). Abdominal pain was present in 87% of our patients, and we observed no correlation with technique failure or mortality. In contrast, poor dialysate outflow has been described as an occasional sign (6%) of peritonitis (1), and poor outflow was reported in 74% of our cases. In 2 patients, it was the only complaint.

Optimal treatment for FP remains a controversial issue, but catheter removal after identification of the fungus appears to reduce technique failure and mortality (4,6). Most reports (3,13) suggest that early catheter removal followed by antifungal therapy is associated with a high rate of return to PD and the lowest mortality. In contrast, the use of antifungals alone, without catheter removal, has been associated with lower cure rates. However, the optimal time for catheter removal is still not clear. Some studies suggest that immediate catheter removal after diagnosis is mandatory (4). In our unit, the peritoneal catheter was removed in 91% of cases, but at very different times depending on response to therapy. We usually try 2 – 3 days of specific treatment after FP diagnosis, so as to remove the catheter when peritoneal inflammation is lowest, to reduce the likelihood of further intra-abdominal adhesions. In our experience, the time between FP diagnosis and catheter removal did not influence technique failure or mortality. The role of bicarbonate-based PD solutions in the treatment of FP remains unclear, and further studies are needed. Our study is limited in that it was restricted to a single center and a low number of cases.

Conclusions
Fungi are a rare cause of peritonitis in patients receiving PD, but fungal peritonitis is associated with high morbidity and mortality. Longer time on PD is the main factor associated with technique failure and death.

References
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