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TREATMENT OF FUNGAL PERITONITIS WITH A COMBINATION OF INTRAVENOUS AMPHOTERICIN B AND ORAL FLUCYTOSINE, AND DELAYED CATHETER REPLACEMENT IN CONTINUOUS AMBULATORY PERITONEAL DIALYSIS

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♦♦*Background:* **Fungal peritonitis (FP) is associated with significant mortality and high risk of peritoneal failure. The optimum treatment for peritoneal dialysis (PD)-associated FP remains unclear. Since January 2000 we have been treating FP with a combination of intravenous amphotericin B and oral flucytosine, together with deferred catheter replacement. We examined the clinical course and outcome of the FP patients treated with this approach (study group). An outcome comparison was also made to an alternatively treated historic cohort (control group).**

♦♦*Methods:* **This was a single-center retrospective study. The clinical course and outcome of 13 consecutive episodes of FP occurring in 13 patients treated between January 2000 and April 2005 with the study approach were examined. The patients were treated with an incremental dose of intravenous amphotericin B to a target dose of 0.75 – 1 mg/kg body weight/day, and oral flucytosine 1 g/day upon a diagnosis of FP at 3.77 ± 0.93 days from presentation. Replacement of the peritoneal catheter was intended after complete clearing of effluent, after which, antifungal chemotherapy was continued for another 1 – 2 weeks. Their outcome was compared with 14 historic controls that were treated between April 1995 and December 1999.**

♦♦*Results:* **Mean age of the study group was 58.7 ± 13.2 years; male-to-female ratio was 2:11; 6 (46.1%) were diabetic. All FP were caused by *Candida* species (*C. albicans*, 2; *C. parapsilosis*, 8; *C. glabrata*, 3). Two (15.4%) patients died before resolution of the peritonitis. The dialysate effluent cleared in 11 patients (84.6%) after 13.2 ± 3.3 days of treatment, but 2 patients died of acute myocardial infarction before catheter replacement. Nine patients had their catheters replaced at day 26.7 ± 7.7 of treatment; all 9 returned to PD after a total of 31 ± 12.2 days of antifungal chemotherapy. Reversible liver dysfunction was common with this regimen. When compared with the 14 cases in the historic control group (*Candida* species, 13; *Trichosporon*, 1), who were treated with amphotericin B, fluconazole, or a combination of the two, and the majority (78.6%) of whose catheters were removed before day 10 of presentation, the study group appeared to have a lower technique failure rate (30.8% vs 78.6%, $p = 0.013$) and similar all-cause mortality (30.7% vs 28.5%, p = NS), FP-related mortality (15.4% vs 28.5%, p = NS), and length of hospitalization (48.5 ± 30.2 vs 57.0 ± 37.7 days, p = NS). However, a significantly earlier commencement of antifungal treatment in the study group (3.8 ± 0.9 vs 5.8 ± 2.4 days, $p = 0.012$) could be an important confounder of outcome.**

♦♦*Conclusions:* **Combination of intravenous amphotericin B and oral flucytosine with deferred catheter replacement appears to be associated with a relatively low incidence of PD technique failure, without affecting mortality in patients suffering from FP due to yeasts in this preliminary study. Nonetheless, drug-induced hepatic dysfunction was common; close monitoring during treatment is of paramount importance. The reasons accounting for the observed distinctive outcome remain unclear and further study is required to confirm the results and to investigate for the underlying mechanism.**

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KEY WORDS: Amphotericin B; catheter; flucytosine; fungal peritonitis; outcome.

Peritonitis is one of the most frequent complications in patients receiving peritoneal dialysis (PD). Fungal peritonitis (FP) accounts for 1% – 15% of all episodes reported in the literature (1). The reported mortality for FP has been as high as 53%, and technique failure necessitating conversion to hemodialysis has been seen in up to 67% of cases (1,2). With respect to treatment, many antifungal agents and various combinations of them have been tried, with diverse outcomes being reported (3–12). In addition, some observational studies have suggested that catheter retention in patients suffering FP is associated with increased mortality. The overall cure rate in patients without catheter removal was estimated to be only about 10% (1). Nevertheless, the optimum

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antifungal chemotherapy regimen and timing of catheter removal remain unclear. In addition, other factors, such as the identity of the causative fungal organisms, might also affect treatment outcome (2,13).

Indeed, there is evidence in the literature suggesting that continuation of PD might help preserve peritoneal function and save patients from conversion to long-term hemodialysis (14,15). In this context and in view of the poor outcome and exceptionally high technique failure rate in our previous experience, and with the theoretical advantages of combining amphotericin B and flucytosine in the treatment of peritoneal infection with potential additive or synergistic effect against *Candida* and molds (13,16,17), we have, since January 2000, been treating our FP PD patients with a combination of intravenous amphotericin and oral flucytosine, and delayed catheter replacement.

Data on using this regimen for the treatment of FP are scarce. This study examines the clinical course and outcome of FP patients being treated with this recent approach. We also try to compare the outcome of these patients with an alternatively treated historic cohort.

PATIENTS AND METHODS

This was a single-center retrospective study performed at a regional dialysis center in Hong Kong. All PD-related FP episodes occurring between April 1995 and March 2005 were included into the study. That period was divided into two parts: period A (January 2000 – March 2005) and period B (April 1995 – December 1999). The study approach for the treatment of PD-related FP was used during period A.

The definition of FP used was the presence of cloudy peritoneal effluent with or without fever, abdominal pain with peritoneal effluent white cell count of 50/μL or greater, and positive culture for fungi from the peritoneal dialysate effluent on one or more occasions. Fungal culture was performed on Sabouraud medium and blood agar at 37°C for 7 days. If a *Candida* species was found, further identification of the *Candida* subtype was performed following the API *Candida* identification system. Fungal peritonitis as a secondary event or a complication of a major surgical condition, such as bowel perforation, intestinal obstruction, or ischemic bowels, was excluded from the study. Antibiotic-related FP was defined as a history of exposure to antibiotics within 1 month of the development of FP.

During period A there were 479 episodes of peritonitis and 13 episodes of FP in 13 patients among 480 patients with a total follow-up of 13 194.9 patient-months. One patient having peritonitis with mixed growth of organisms including C*andida* species secondary to ischemic bowels was excluded from the study. The overall peritonitis rate was 0.44 episodes/patient-year, with a FP rate of 0.012 episodes/patient-year. All these continuous ambulatory PD (CAPD) patients with FP were treated with a combination of intravenous amphotericin B deoxycholate and oral flucytosine, both given as a once-daily dose without immediate peritoneal catheter removal. Intravenous amphotericin B was given at a starting dose of 0.1 mg/kg body weight/day infused over 6 hours after a test dose of 1 mg, and it was gradually increased to a target dose of 0.75 – 1 mg/kg body weight/day over 4 days. During the administration of amphotericin B, daily doses of paracetamol 500 mg orally and hydrocortisone 25 mg intravenously were routinely given as pre-medications 30 minutes in advance. Flucytosine was given at a fixed dose of 1 g daily. The peritoneal catheter was kept *in situ* with continuation of PD. Catheter removal and replacement were intended either after clearing of dialysate effluent or at the discretion of attending nephrologists if they considered it necessary due to the condition of the patients. Amphotericin B and oral flucytosine were intended to be continued for another 1 – 2 weeks after catheter replacement, depending on patients' tolerability.

During period B there were 434 episodes of peritonitis and 14 episodes of FP in 14 patients among 330 patients with a total follow-up of 9405.4 patient-months. The overall peritonitis rate was 0.55 episodes/patient-year, with a FP rate of 0.018 episodes/patient-year. Most (11/14) patients had the peritoneal catheter removed and were switched to hemodialysis immediately after the diagnosis of FP. The average interval from presentation to the diagnosis of FP and catheter removal in these 11 cases was 5.9 ± 2.5 days. As flucytosine was not available in the locality at that time, patients were treated with regimens including oral fluconazole alone for 2 weeks in 2 cases, 3 weeks in 1 case, and 4 weeks in 3 cases; intravenous amphotericin B alone in 1 patient for 4 weeks, intravenous amphotericin B for 3 – 10 weeks (mean, 31.5 days) followed by oral fluconazole for 10 days to 16 weeks (mean, 48.3 days) in 6 patients; and a combination of amphotericin B and oral fluconazole in 2 patients for 19 and 47 days. Amphotericin B was administered intravenously in a similar fashion to patients treated during period A. Oral fluconazole was given as a 200 mg loading dose, followed by 100 mg daily.

Drug level and susceptibility tests for antifungal agents including amphotericin B and flucytosine were not available locally. Information retrieved and analyzed included clinical presentation, patients' demographic characteristics, underlying causes of renal failure, duration on dialysis, significant comorbidities, such as dia-

betes, cardiovascular disease resulting in acute myocardial infarction or requiring coronary intervention, cerebrovascular disease with cerebrovascular accident, and advanced liver disease with cirrhosis; antibiotic exposure within 1 month before FP, FP occurring *de novo* or complicating bacterial peritonitis, species of fungus causing peritonitis, catheter removal and time of removal, type of antifungal agents used, and treatment-related side effects. Patient mortality, technique failure rate, and duration of hospitalization were the outcome parameters. Technique failure was defined as failure to resume CAPD and included patients that did not survive the episode of FP.

STATISTICAL ANALYSIS

Results are expressed as mean ± standard deviation. Differences between groups were assessed using Fisher's exact test, chi-square test, Mann–Whitney U test, and Wilcoxon signed rank test when appropriate. A p value less than 0.05 was considered significant.

RESULTS

The baseline characteristics of the affected patients and characteristics of the FP episodes during the two study periods are shown in Table 1.

PERIOD A

There were 13 episodes of FP in 13 patients. Fungal peritonitis was caused by *Candida albicans*, *C. parapsilosis*, and *C. glabrata* in 2, 8, and 3 episodes. The underlying causes of renal disease were diabetes in 6 patients, chronic glomerulonephritis in 3 patients, and unknown in 4 patients. A majority (11/13) of the patients were using disconnecting twin-bag systems. Eight (61%) patients developed abdominal pain and 38.5% had fever with the peritonitis. The maximum daily doses of amphotericin B were 1 mg/kg in 3 patients and 0.75 mg/kg in 10 patients. After a mean duration of 13.2 ± 3.3 days of antifungal therapy, clearing of peritoneal dialysate effluent was observed in 11 (84.6%) patients, 10 of whom also had the fungal culture of their spent dialysate specimens turn negative. Two patients died, at days 6 and 18 of treatment respectively, before complete resolution of peritonitis. Among those 11 patients that responded with complete resolution of peritonitis, 2 died of acute myocardial infarction before catheter replacement at day 21 of treatment. Due to some logistic problems in arranging catheter replacement, there were time lags between resolution of peritonitis and catheter replacement. In the end, 9 patients had the peritoneal catheter removed after a mean of 26.7 ± 7.7 days of treatment; 8 of those patients underwent elective removal with simultaneous reinsertion of the peritoneal catheter, and 1 patient had urgent catheter removal due to catheter blockage requiring temporary hemodialysis and catheter reinsertion 3 months later. Of the nine removed catheters, only the one that had the positive growth in dialysate before catheter exchange grew the causative fungal organisms. Antifungal chemotherapy was continued for an additional 1 – 2 weeks after catheter removal in 8 patients. One patient had significant liver dysfunction and antifungal

TABLE 1
Baseline Clinical Characteristics of the Two Study Groups

	Period A Amphotericin B+flucytosine (n=13)	Period B Historic control (n=14)	p Value
Age (years)	58.7±13.2	59.4±10.9	NS
Sex (M/F)	2/11	9/5	<0.02
Duration on Peritoneal dialysis (months)	53.0±33.6	41.8±21.5	NS
Diabetics	6 (46.2%)	3 (21.4%)	0.06
CVA/cardiac	6 (46.2%)	3 (21.4%)	0.06
Liver disease	2 (15.4%)	0 (0%)	NS
FP complicating bacterial peritonitis	1 (7.7%)	2 (14.2%)	NS
Bacterial peritonitis within 1 month of FP	3 (23%)	3 (21.4)	NS
Antibiotic-related episodes	4 (30.8%)	10 (71.4%)	0.035
Candida FP	13 (100%)	13 (92.8%)	NS
Catheter *in situ* >10 days	13 (100%)	3 (21.4%)	<0.001
Time from presentation to commencement of antifungal therapy (days)	3.77±0.93	5.8±2.4	0.012

CVA = cerebrovascular accident; FP = fungal peritonitis; NS = not significant.

chemotherapy was stopped immediately after catheter replacement in that patient. The total duration of antifungal therapy was 31 ± 12.2 days in these 9 patients.

During the course of treatment, significant reversible increases in serum alanine aminotransferase (ALT), total bilirubin, and alkaline phosphatase (ALP) levels were commonly observed: 5 (38.5%) patients had abnormal ALT, 4 (30.8%) patients had abnormal serum bilirubin levels, and 7 (53.8%) patients showed more than a 50% rise in serum ALP. Mean elevations in ALT, bilirubin, and ALP were 26.4 ± 51.2 IU/L, 11.9 ± 23.8 µmol/L, and 135 ± 261 IU/L, respectively. Because of these increases, early cessation of flucytosine was required in 2 patients and complete cessation of both amphotericin B and flucytosine after catheter replacement was necessitated in 1 patient. In addition, confusion was noted in a patient who required a dose reduction of amphotericin B, from 1 mg/kg to 0.75 mg/kg. There was, however, no significant bone marrow toxicity or electrolyte imbalance observed.

PERIOD B

The 14 episodes of FP in 14 patients were caused by *Candida albicans* in 1, *C. tropicalis* in 1, *Trichosporon* in 1, and *C. parapsilosis* in 11 episodes. No common environmental source of *C. parapsilosis* was identified during epidemiologic study. Compared to patients in period A, patients in period B did not differ significantly in age, duration on CAPD, comorbidities, including diabetes, significant cerebrovascular and cardiovascular disease, and liver disease; or proportion of *de novo* FP episodes and proportion of episodes caused by *Candida* species. However, male patients were predominant in the control group, and antibiotic-related episodes accounted for the majority of FP during this period before the introduction of oral nystatin antifungal prophylaxis in our unit, which was started in late 1999. The average time from presentation to diagnosis of FP and commencement of antifungal treatment was also significantly longer in group B compared with group A (5.8 ± 2.4 vs 3.8 ± 0.9 days, $p = 0.012$). In addition, significantly fewer patients in the historic control group (period B) had the catheter *in situ* for more than 10 days compared with period A (21.4% vs 100%, $p < 0.001$).

COMPARISON OF OUTCOME BETWEEN THE TWO STUDY GROUPS

All-cause mortality during period A was 30.7%, with 4 deaths, 2 of which (15.4%; 1 due *C. parapsilosis* and 1 due *C. albicans*) were directly related to FP. During period B, 4 patients (3 from *C. parapsilosis* and 1 from *C. tropicalis*) died of FP-related complications, with an all-cause mortality rate of 28.5%; 3 of these patients received fluconazole alone and 1 received combination therapy with amphotericin and fluconazole. There were no significant differences between periods A and B in terms of all-cause mortality (30.7% vs 28.5%, p = NS) or FP-related mortality (15.4% vs 28.5%, p = NS). In addition, there was also no difference in mean duration of hospitalization for FP between patients treated in periods A and B (48.5 ± 30.2 vs 57.0 ± 37.7 days, p = NS).

Concerning technique survival, all the 9 surviving patients of the study group were able to continue CAPD after their episodes of FP; overall technique failure rate was 30.7% in this group. In contrast, only 3 (21.4%) patients in the control group were able to resume CAPD, and 7 patients required permanent conversion to hemodialysis due to peritoneal failure with adhesion and abscess formation. The overall technique failure rate for the control group was significantly higher than for the study group (78.6% vs 30.7%, $p = 0.013$).

DISCUSSION

Fungal peritonitis is associated with high mortality and morbidity. The optimum treatment for this important complication is unclear. Uncertainty and controversy remain in terms of the choice, route, and total dose of antifungal therapy, as well as the indication for and timing of catheter removal. With catheter *in situ* being identified as a mortality risk factor in some retrospective studies and cases series, it has been suggested that early catheter removal is essential for successful treatment of FP and that the catheter should be removed promptly once the diagnosis of FP is established (2–4). However, these conclusions and recommendations are limited by the fact that the studies underlying the arguments are largely retrospective and observational, various different combinations of antifungal regimens were used, and the numbers of patients involved in individual regimens were small.

On the other hand, there is also evidence in the literature showing that continuation of PD might be beneficial in patients with FP (12,14,15). Indeed, there were a few studies showing that peritoneal lavage might reduce peritoneal adhesion and technique failure rate, although rapid peritoneal exchanges might be undesirable due to their negative impact on leukocyte function (18). In this respect, there were some studies in the literature reporting successful treatment without catheter removal. In particular, there was a case series study on the use of a combination of amphotericin B and flucytosine,

both intraperitoneally, for the treatment of FP, in which successful outcome was achieved in 6 of 9 patients without catheter removal and, in the end, 8 of the 9 patients were able to return to PD (12).

Theoretically, removal of the catheter could stop continuous seeding of organisms embedded in its associated biofilm that might otherwise perpetuate the infection (19). On the other hand, continuation of PD could allow continuous drainage of inflammatory debris or material that might otherwise predispose to peritoneal adhesion and abscess formation (13).

In the present study, delayed catheter removal does not seem to be associated with increased mortality. Despite the higher prevalence of baseline comorbidities, including diabetes and cardiovascular disease, the study group being treated with combination amphotericin B and flucytosine with delayed catheter removal was not found to have significantly higher mortality compared with the historic control group, in which most of the patients had their catheters removed soon after the diagnosis of FP. This mortality rate is not particularly high, even compared with the reported figures in other studies and especially in context of the long duration of dialysis in our patients (3–12).

The corollary to this observation is that outcome, rather than being dictated solely by the timing of catheter removal, is determined by a complex interplay of multiple factors, especially the availability of an antifungal regimen that can achieve effective killing of the causative fungal organism, leading to sterilization of the peritoneum.

Amphotericin B is a broad-spectrum effective antifungal agent for systemic candidiasis. Nevertheless, probably due to its poor water solubility and high protein binding, its penetration to the peritoneum and dialysate by intravenous administration is modest and variable; the penetration ratio is only about 0.41 (20,21). It has therefore been suggested that a dose of 0.5 – 1.0 mg/kg body weight/day is likely to be required to obtain adequate peritoneal drug levels above minimum inhibitory concentration for many of the common fungal pathogens (21). On the other hand, flucytosine is a small and highly water-soluble molecule with good oral bioavailability and peritoneal penetration, but its use as a single therapy is limited by rapid development of fungal resistance. Therefore, amphotericin B and flucytosine could, theoretically, be a reasonable combination. For one thing, this combination give rises to a low overall drug resistance potential, which is especially relevant in view of emerging resistance to imidazoles and the limited availability of sensitivity tests for antifungal agents in many localities (22). Furthermore, it could ascertain an adequate fungicidal activity in the peritoneum. In addition, this combination could possibly provide an additive or synergistic effect against *Candida* and *Cryptococcus*, as shown by some studies, although this finding has been disputed by other studies (16,23). Apart from systemic administration, there have been studies showing successful outcome using intraperitoneal administration of this combination, possibly delivering high local drug concentration to the peritoneum. However, the intraperitoneal use of amphotericin B has been limited by the common occurrence of chemical peritonitis, which has been reported in more than 80% of patients receiving such treatment in a study (12). In addition to leukocytosis of the dialysate, patients with chemical peritonitis might also have clinical signs and symptoms of peritonitis, in which case distinguishing it from superimposing bacterial peritonitis or persistent FP would be complex and problematic. Furthermore, its possible predisposition to the development of peritoneal fibrosis would also be a concern (12,24). So far, there have not been any effective measures available in the face of this problem.

Apart from conventional antifungal agents, there are new antifungals, including newer triazoles and echinocandins, that show promising results in the treatment of FP (25–28). Echinocandin is a new class of antifungal agent exhibiting a broad spectrum of antifungal activity by inhibiting the synthesis of β-(1,3)-D-glucan, a component of fungal cell walls. Caspofungin is the first available in this class. It is fungicidal against yeasts and appears to be highly active against *C. albicans* biofilms in *in vitro* study (29). New azoles such as ravuconazole, voriconazole, and posaconazole possess a broader spectrum against pathogenic yeasts, dimorphic fungi, and opportunistic moulds compared to fluconazole, and these azoles may even have greater *in vitro* activity than amphotericin, flucytosine, itraconazole, and fluconazole against many of the fluconazole-sensitive *Candida* species (30). However, the data on using these new agents in the treatment of FP remain very limited and are available only in the form of isolated case reports. Further studies are required to examine their exact efficacy and impact on clinical outcome in the treatment of PD-related FP.

Indeed, the combination of intravenous amphotericin B and oral flucytosine has been recommended as an initial therapy in patients suffering from FP (31). This is especially relevant given the observed shift in the pathogenic organisms causing FP. Historically, *C. albicans* has been the dominant causative species. Nevertheless, as in our study, non-*albicans Candida* species, *C. parapsilosis* in particular, have emerged to be the most prevalent

pathogens in the development of FP in recent reports (2,4,32,33). The fact that many of these non-*albicans Candida* species are relatively insusceptible to fluconazole and the possibility that individual *Candida* species might even display high minimum inhibitory concentration to newer triazoles or echinocandins have rendered initial treatment of FP with a combination of broad-spectrum antifungals highly desirable (34).

From this study, it seems that, for patients with FP due to a sensitive fungal organism, it is possible to resolve that FP with amphotericin B and flucytosine, even without catheter removal. In addition, patients being treated with this combination and delayed catheter removal appear to have better preservation of peritoneal function. However, the exact reasons accounting for this appealing outcome remain unclear. It might be attributed to early start of antifungal chemotherapy, the change of drug regimen, the continuation of PD, or the timing of catheter removal. In recent years, as we have become more vigilant of possible FP in patients showing negative microscopy on the initial spent dialysate specimen analyses, dialysate effluent specimens have been sent on a daily basis until resolution of the peritonitis or identification of the causative organism. This strategy led to an early diagnosis of FP by direct microscopic examination in group A while awaiting culture results. It is plausible that the consequent early start of antifungal chemotherapy might have played a role in the improved clinical outcome. Furthermore, due to its lack of supply in the locality before 2000, oral flucytosine was not included in the antifungal regimen of the control group, and therefore the antifungal regimens of the two study groups were not directly comparable. Therefore, it remains unknown whether treatment with the same combination of amphotericin B and flucytosine, but early catheter removal, could achieve a similar or even better outcome. Moreover, all these patients received pre-medication with intravenous hydrocortisone during the administration of amphotericin B, raising the question of its possible role in reducing peritoneal inflammation and subsequent adhesion in the study group. Nevertheless, it is probably of doubtful significance since this pre-medication was also employed in the controls, who also received amphotericin B.

Apart from all these uncertainties, there are also major limitations in this study. First, this is only a small retrospective study and the two study groups were not entirely comparable in many aspects. Second, drug levels and sensitivity tests were not available in this study. It is therefore difficult to clarify the treatment-and-response relationship. Third, the exact efficacy of this treatment approach for individual fungal pathogens and the associated risk-to-benefit ratio could not be delineated. Without monitoring the drug levels, it has also been impossible to have drug titration in order to ensure a therapeutic peritoneal drug level with minimal toxicity. As in our cases, it took more than a week to achieve resolution of peritonitis with this treatment regimen. It might not be easy to predict what may turn out to be the response in the early treatment period, although the identity of the causative organism would provide some clues on the likelihood of response. Outcome would also be affected by tolerance of individual patients to the prolonged antifungal treatment.

In conclusion, the findings in the present study suggest that delayed catheter removal does not necessarily lead to excessive mortality. Combination therapy with intravenous amphotericin B and oral flucytosine might result in successful resolution of peritonitis, possible eradication of infection, and preservation of peritoneal function, even without early catheter removal. This approach might, therefore, represent a viable option in select patients with FP due to susceptible organisms, including many of the *Candida* species, especially in those patients deemed unsuitable or undesirable for hemodialysis, and in financially constrained healthcare settings where the cost of hemodialysis is of major concern. This treatment strategy, however, appears to require a prolonged duration of antifungal treatment, and the optimal duration of treatment remains to be defined. It also necessitates close monitoring of the patient's clinical condition, nutritional status, and treatment side effects. Regular monitoring of drug levels and susceptibility testing should be incorporated into the protocol whenever possible. In this context, the length of hospitalization and overall treatment cost incurred by the prolonged treatment course could be a concern. Nevertheless, it did not appear to be a major issue in this study, in which the patients of period A actually showed a nonsignificant trend toward shorter length of hospitalization, possibly due to a vast reduction in the development of complications such as bowel adhesion and abscess formation compared to the historic controls. In addition, the daily acquisition cost for amphotericin B deoxycholate and flucytosine were also low. Case selection is, however, important and clinicians should be judicious in this process. Early catheter removal would be required if the patient deteriorates or serious intra-abdominal pathology is suspected. Experience of individual centers in managing this type of patient might impact the final treatment outcome. Before this approach might be widely adopted, further studies including drug level monitoring and susceptibility testing are warranted to verify

the results and to investigate the role of catheter removal, antifungal regimen, and their interrelationship in patient mortality and PD technique survival in PD patients suffering from this important complication.

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