

# Fungal Peritonitis in Iranian Children on Continuous Ambulatory Peritoneal Dialysis

## A National Experience

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**Introduction.** Fungal peritonitis (FP), causing catheter obstruction, dialysis failure, and peritoneal dysfunction, is a rare but serious complication of peritoneal dialysis. In this study, the frequency and risk factors of FP are evaluated in children who underwent peritoneal dialysis.

**Materials and Methods.** A retrospective multicenter study was performed at the 5 pediatric peritoneal dialysis centers in Iran from 1971 to 2006, and FP episodes among 93 children were reviewed. Risk ratios were calculated for the clinical and demographic variables to determine the risk factors of FP.

**Results.** Ninety-three children aged 39 months on average were included in study. Sixteen out of 155 episodes of peritonitis were fungi infections, all by *Candida albicans*. The risk of FP was higher in those with relapsing bacterial peritonitis ( $P = .009$ ). Also, all of the patients had received antibiotics within the 1 month prior to the development of FP. Catheters were removed in all patients after 1 to 7 days of developing FP. Six out of 12 patients had catheter obstruction and peritoneal loss after the treatment and 5 died due to infection.

**Conclusions.** Fungal peritonitis, accompanied by high morbidity and mortality in children should be reduced by prevention of bacterial peritonitis. Early removal of catheter after recognition of FP should be considered.

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## INTRODUCTION

Fungal Peritonitis (FP) is a rare but serious complication of continuous ambulatory peritoneal dialysis (CAPD). The reported incidence is 3% to 6% in children,<sup>1-3</sup> and 1% to 15% in adults.<sup>4-8</sup> It leads to catheter obstruction, abscess formation,

peritoneal adhesion dialysis failure, peritoneal dysfunction and death.<sup>4,7,9</sup>

The most important known risk factors of FP are previous bacterial peritonitis, prior use of antibiotics, and previous peritonitis caused by gram-negative organisms.<sup>2,7,10</sup> Early catheter removal and antifungal

therapy have been proposed for treatment this complication<sup>7,11-16</sup>; however, the efficacy of nystatin for prophylaxis is still debatable.<sup>8,17</sup> The aim of this study was to determine the prevalence, possible risk factors, and the outcome of FP in children receiving CAPD.

## MATERIALS AND METHODS

A retrospective multicenter study was performed at all the 5 centers for pediatric peritoneal dialysis in Iran (Ali-Asghar Children's Hospital, Children's Hospital Medical Center, and Mofid Children's Hospital in Tehran; Namazi Hospital in Shiraz; and Alzahra Hospital in Isfahan) with 93 pediatric patients from 1971 to 2006. They were 43 girls and 50 boys. The hospital records of the patients younger than 16 years who had been receiving CAPD were reviewed and cases of FP were selected for further investigation. Fungal peritonitis was diagnosed by the recorded clinical signs of peritonitis and at least 2 documented positive cultures of dialysate fluids for fungi. Fungi were cultured on blood agar in 37°C for at least 7 days and fungal colonies were diagnosed by light microscopy at all centers. Relapsing bacterial peritonitis was defined as an infection with the same causative organism within 2 weeks after completion of an antibiotic treatment course and documentation of at least 1 negative

dialysate culture.<sup>18</sup> Risk ratios (RRs) were calculated to determine the risk factors of FP in children with CAPD. Statistical analyses were performed by Fisher exact test. A *P* value less than .05 was considered significant.

## RESULTS

A total of 866.46 months had been taken for the treatment of peritonitis episodes in the children on CAPD in the 5 centers. Sixteen out of 155 episodes of the peritonitis (10.3%) were fungal, all caused by *Candida albicans*, which occurred in 12 patients (12.9%). The Table shows the clinical characteristics of 12 patients whose dialysate fluid was positive for yeasts or *Candida*. The median age of these children was 27 months and half of them were girls. The underlying kidney diseases were cystinosis in 2 patients, dysplastic kidney disease in 2, hemolytic uremic syndrome in 2, multicystic dysplastic kidney/nephronophtisis in 2, diffuse mesengeal sclerosis in 1, polycystic kidney disease in 1, and asphyxic thoracic syndrome in 1. The etiology was unknown in 1 patient.

The patients had neither history of the gastrostomy tube insertion nor of immunosuppressive therapy. In 4 patients, the FP cases were the first peritonitis episodes that began within 3 days to 12 months after starting CAPD. Several episodes of bacterial

Clinical Characteristics of Patients With Fungal Peritonitis\*

Episode of FP	Sex	Age, mo	Weight, kg	Duration of CAPD, mo	Peritonitis Episodes Prior to FP	Time of FP, mo	Time of Catheter Removal, mo	Outcome
1	G	36	10.0	0.5	2	.1	0.5	Deceased
2†	B	12	6.0	12	0	...	...	CAPD
3†	B	27	8.0	27	0	...	...	CAPD
4†	B	28	9.0	28.6	1‡	28.6	...	No dialysis modality
5	B	12	7.5	0.74	0	...	0.5	Recovery of native kidney
6	G	55	13.3	0.4	0	...	0.4	Hemodialysis
7	G	48	10.5	3	2‡	1	...	Hemodialysis
8	G	28	10.0	1.4	2‡	.4	0.5	Deceased
9	G	16	6.0	3.1	1	.3	1.5	Deceased
10	B	2	3.3	7.2	4‡	.2	1	Deceased
11§	B	24	10.5	0.7	0	...	...	CAPD
12§	B	29	11.0	5.7	1	2	5	Hemodialysis
13	G	84	13.5	4.6	2	2.3	3	Hemodialysis
14	B	9	10.5	2	3	1	...	CAPD
15	B	11	10.5	2	0	4	2	Deceased
16	G	11	6.0	24	5	2.5	...	Deceased

\*FP indicates fungal peritonitis; CAPD, continuous ambulatory peritoneal dialysis; G, girl; and B, boy. Ellipses indicate the missed data.

§The last episode occurred simultaneously with the FP.

†,‡,|| These episodes occurred in a same patient.

peritonitis had happened in the earlier months before FP, including 5 episodes by gram-negative bacteria, 3 by gram-positives, and 2 with negative culture results. All episodes of FP had occurred after 1 month being treated with antibiotics. Peritonitis rate prior to fungal infection was lower than that as the overall cases (0.09 versus 0.17 episodes per patient-month).

Six patients were treated with amphotericin B, intraperitoneally or intravenously, for 2 to 3 weeks and fluconazole was given to only 2 patients as an adjuvant therapy. Catheters were removed in all patients after 1 to 7 days of developing FP. Half of the patients were terminated to catheter obstruction and loss of peritoneal access, and 5 died due to infection.

Patients in whom the onset of the first bacterial peritonitis had occurred earlier than 1 month from the start of dialysis had a greater risk of developing FP (RR = 4.70; 95% confidence interval [CI], 1.37 to 16.38;  $P = .009$ ). Prior use of antibiotics was a factor present in all of the patients ( $P = .007$ ). The risk of FP was not significantly higher in the patients with relapsing peritonitis (RR = 1.70; 95% CI, 0.50 to 5.30;  $P = .37$ ), age less than 5 years (RR = 3.45; 95% CI, 0.46 to 24.9;  $P = .28$ ), dialysis in the first week of catheter implantation (RR = 4.10; 95% CI, 0.55 to 30.17;  $P = .16$ ), and straight type of Tenckhoff catheter (RR = 3.15; 95% CI, 0.73 to 13.59;  $P = .11$ ).

## DISCUSSION

Fungal peritonitis is a rare complication of CAPD that is accompanied by high morbidity and mortality rates. Although in a large multicenter survey, Warady and colleagues found the incidences of FP in both children and adults to be similar, in our patients, the frequency of pediatric FP was five times as higher as that in other studies.<sup>1-3</sup> Younger age is associated with a higher risk of FP. This might be due to higher risk of bacterial peritonitis predisposing to FP.<sup>2,19-21</sup> However, our limited data failed to show the influence of age.

Previous studies have suggested the role of recent bacterial infection, especially with gram-negative organisms, in the development of FP.<sup>2,7,10</sup> We only found a significant higher RR of FP in those with bacterial peritonitis during the first month of starting CAPD. Albeit nonsignificant, the RRS were high for both early usage of catheter

and straight type of Tenckhoff catheter. These may be secondary to the increase risk of bacterial peritonitis. Reviewing the literature, no relation was found between the type of the catheter and the risk of FP. However, twin-bag disconnect system has been reported to significantly reduce the risk of this infection.<sup>22</sup> Peritoneal dialysis catheters are susceptible to the development of infections because of the frequent manipulating required and high dextrose concentration of the indwelling dialysis fluid.<sup>20</sup> *Candida* species are able to grow into the dialysis catheter and form a surrounding biofilm. The incidence of FP has been reported lower among patients on automated peritoneal dialysis, because of fewer numbers of disconnections.<sup>23</sup> However, Warady and colleagues reported a similar rate of FP in patients on CAPD and automated peritoneal dialysis.<sup>3</sup>

In the current study, *Candida* species were the responsible fungi for one-third of first episodes of peritonitis. The risk of candidiasis is enhanced by indwelling catheter, abdominal surgery, hyperglycemia, prolonged hospitalization, broad-spectrum antimicrobial therapy, malnutrition, and azotemia.<sup>24</sup> Most of the cases in this study had failure to thrive and all had the history of prior antibiotic administration. Antibiotics suppress the normal bacterial flora of the skin, and thus, allow the overgrowth of *Candida*. In addition, some antibiotics cause a decrease in neutrophils that can kill *Candida* (eg, sulfonamides) or diminish the neutrophils' phagocytosis potential (eg, aminoglycosides).<sup>25</sup>

Half of our patients died and the remainder had to change their maintenance dialysis into to hemodialysis (because of outflow obstruction or loss of peritoneal adequacy) or could not have any other modalities (in cases of very small children). This figure shows the high mortality and morbidity of FP that could have been preventable by rational usage of antibiotics, improving nutrition by consulting specialized nutritionists, feeding by gastrostomy tube in malnourished infants, not changing the normal bacterial flora that prevent *Candida* colonization, using infrequent disconnection system of peritoneal dialysis for very young children and infants, using newer nondextrose dialysates, and early removal of the catheter. The recommended treatment protocol of FP in 2000 was either removing catheter and

maintaining patient on hemodialysis for at least 4 to 6 weeks or leaving original unobstructed catheter in place while administering antifungal agents intraperitoneally or intravenously for at least 4 to 7 days. The catheter would have been removed in the case of no response to the treatment.<sup>26</sup> In contrast, the protocol in 2005 has changed by emphasizing on early removal of the catheter in FP. Lack of a substitution of CAPD for infants and young children with a weight less than or equal to 10 kg was the reason of choosing the second option of 2000 protocol.<sup>27</sup> The few numbers of children and absence of a uniform protocol of therapy in our series were the limitations in this study that preclude a more definite conclusion.

### CONCLUSIONS

Fungal peritonitis is accompanied by high morbidity and mortality in children who receive CAPD and should be reduced by prevention of bacterial peritonitis. Prompt removal of catheter after recognition of FP should be considered.

### CONFLICT OF INTEREST

None declared.

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