Development of *Clostridium difficile* Colitis in Peritoneal Dialysis Patients Treated for Peritonitis

Editor:

Since 2000, the incidence of *Clostridium difficile* infection has increased significantly in hospital and ambulatory care settings alike (1). This increase in *C. difficile* infection also affects peritoneal dialysis (PD) patients and, given the close association of the gastrointestinal tract and the peritoneal cavity, may create serious complications in the treatment of PD-associated peritonitis.

Anecdotal evidence from our PD program suggested a high rate of *C. difficile* colitis in our patients treated for peritonitis. Comorbid *C. difficile* infection caused considerable discomfort for our patients, a need for more medications, and in one case, a need for hospitalization. A review of the literature resulted in limited data on the risk for *C. difficile* infection in PD-associated peritonitis. Thus, we sought to evaluate risk factors for the development of this infection in our patients on PD treated for peritonitis and the effect of *C. difficile* infection on duration of treatment, relapse rates, and need for hospitalization. The identification of risk factors would add valuable knowledge to improve management of the complications of peritonitis.

METHODS

From 1 July 2010 to 31 July 2011 in our PD program, 9 patients developed peritonitis, 4 of whom developed *C. difficile* colitis during peritonitis treatment.

All patients were on continuous cycling PD, and none were institutionalized. A retrospective chart review of the latter 4 patients and of all patients treated for peritonitis was completed. Infection with *C. difficile* was documented in a positive stool polymerase chain reaction assay for toxin A or B. Differences between patients who developed *C. difficile* infection and those who did not were tested by the chi-square and t-test, as appropriate.

RESULTS

Significant differences in treatment duration and in the number of antibiotics administered were the major findings of the review. The average length of treatment for patients without *C. difficile* was 18.1 days; it was 25.3 days for patients with *C. difficile* ($p = 0.03$). All of the peritonitis episodes complicated by *C. difficile* had involved at least 1 change of antibiotics; only 25% of peritonitis episodes without *C. difficile* had such a change ($p = 0.02$). We observed no significant difference in mean age, proportion using proton pump inhibitors, or prevalence of diabetes in the patient groups. Two patients (50%) with *C. difficile* had received intravenous antibiotics during their treatment; only 1 patient (10%) without *C. difficile* had received intravenous therapy ($p = 0.10$). Table 1 presents the demographic and treatment variables.

DISCUSSION

Rates of *C. difficile* infection are increasing in hospitals and communities because of increased antibiotic use, emergence of new virulent *C. difficile* strains, and an aging patient population with increased comorbidities (2). This increased rate of infection has a great effect on health care because of increased lengths of hospital stay and increased costs (3). The increasing incidence of *C. difficile* in the general population will become a growing problem in our PD patients. Patients on PD may have an increased risk associated with development of *C. difficile* infection, because such an infection may interfere with their renal replacement therapy. Despite the importance of *C. difficile* prevention in our patients, little information is available in the literature about PD-specific risk factors for development of this infection or about its complications, highlighting the need for studies.

Multiple changes of antibiotic regimen and longer duration of antibiotic therapy were significantly associated with development of *C. difficile* infection in our study population. Those findings correlate with results in the general population of hospitalized patients, which showed that both the number of antibiotics and the days on antibiotics were independently associated with *C. difficile* infection (4). A longer duration of therapy may contribute to the development of *C. difficile*

TABLE 1
Demographic and Treatment Variables by Group

Variable	Overall	Peritonitis episodes		<i>p</i> Value
		With <i>C. difficile</i>	Without	
Patients (<i>n</i>)	16	4	12	
Age (years)	52.9	60.3	50.4	0.58
Race [<i>n</i> (%)]				
White	15 (94)	3 (75)	12 (100)	
Asian	1 (6)	1 (25)	0 (0)	
Change in antibiotics [<i>n</i> (%)] ^a	7 (43.8)	4 (100)	3 (25)	0.02
Average antibiotic changes (<i>n</i>) ^b	1.07	3.25	0.27	0.01
Hospitalization ^c	9 (56.3)	3 (75)	6 (50)	0.44
Diabetes mellitus	2 (12.5)	1 (25)	1 (8.3)	0.42
Intraperitoneal antibiotic use only	6 (37.5)	2 (50)	4 (33.3)	0.11
Intravenous antibiotic use	3 (18.8)	2 (50)	1 (8.3)	0.10
Proton pump inhibitor use	6 (37.5)	2 (50)	4 (33.3)	0.77
Total duration of antibiotics (days)	20.1	25.3	18.1	0.03

^a Excludes narrowing of antibiotics.

^b Change in therapy or addition of antibiotic to selected therapy.

^c Hospitalization during treatment for peritonitis.

infection because of greater enteric flora depletion and thus increased susceptibility to *C. difficile* overgrowth, with consequent infection. However, it may also be that having concurrent *C. difficile* infection necessitates longer treatment with antibiotics for persistent or severe peritonitis.

Infection with *C. difficile* may cause persistent peritonitis because of the effects of the clostridial toxins, which cause damage to the gastrointestinal barrier, potentially allowing enteric bacterial to translocate into the peritoneal cavity (5). With the use of dextrose in dialysate and the general immunocompromised state of patients with kidney failure, the translocated bacteria can easily seed the susceptible peritoneal cavity. This added exposure may cause a secondary microbial infection after antibiotics have already been narrowed based on the initial culture data, leading to deficient antibiotic coverage and a subsequent need for treatment change and longer duration. Prolongation of infection can increase the risk of detrimental peritoneal membrane changes and cause increased severity of symptoms, requiring hospitalization for an infection that can usually be managed with home therapy.

We did not find a difference between the patient groups in the use of intraperitoneal (IP)-only compared with IP plus oral or intravenous antibiotics. It might be thought that the IP route used in treatment of peritonitis would not have the same risk of *C. difficile* development; however, IP medications are absorbed systemically (6) and thus may carry a risk at least similar to that with the oral route. Notably, we observed a trend to less *C. difficile* infection in patients not receiving intravenous antibiotics.

We were unable to evaluate complications of *C. difficile* infection in our small patient population. We do know that one patient required hospitalization after developing *C. difficile* colitis because of a need for increased supportive care and the morbidity of the diarrheal symptoms. No patient who had *C. difficile* infection experienced a relapse or had to abandon PD as their renal replacement therapy, but long-term follow-up has not yet been completed.

Our study highlights possible risk factors associated with the development of *C. difficile* infection in PD patients treated for peritonitis, including longer duration of antibiotics and multiple changes in the antibiotic regimen. But drawing conclusions from such a small group of patients is difficult, indicating a need for larger multicenter studies to better characterize the prevalence of concurrent *C. difficile* infection and the factors associated with *C. difficile* infection in PD patients. Better characterization of the risk can result in

earlier treatment of *C. difficile* and earlier use of measures aimed at preventing spread, such as contact precautions and avoidance of alcohol-based hand sanitizer. In detecting *C. difficile* early, it may be possible to prevent potential sequelae from the infection—which can include refractory peritonitis and changes to the peritoneal membrane—and ultimately to prevent changes leading to technique failure.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

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