CAMPYLOBACTER PERITONITIS COMPLICATING PERITONEAL DIALYSIS: A REVIEW OF 12 CONSECUTIVE CASES

Terry King-wing Ma,¹ Kin Ping Lee,² Kai Ming Chow,¹ Wing Fai Pang,¹ Bonnie Ching Ha Kwan,¹
Chi Bon Leung,¹ Cheuk Chun Szeto,¹ and Philip Kam-tao Li¹

Division of Nephrology,¹ Department of Medicine and Therapeutics, and Department of Microbiology,²
Prince of Wales Hospital, Chinese University of Hong Kong, Hong Kong SAR, PR China

◆ **Background:** Peritoneal dialysis–associated peritonitis secondary to *Campylobacter* organisms is uncommon. Few studies have assessed either treatment or clinical outcomes.

◆ **Methods:** We reviewed all *Campylobacter* peritonitis episodes occurring in a single dialysis unit from 1994 to 2011.

◆ **Results:** During the study period, 12 episodes of *Campylobacter* peritonitis (0.45% of all peritonitis episodes) were recorded. Diarrhea was uncommon (8.3%). The overall primary response rate was 91.7%; the complete cure rate was 75.0%. Among 6 patients who failed to respond to standard antibiotics by day 5, all improved after administration of an oral macrolide (erythromycin or clarithromycin). Of those 6 patients, 5 experienced a complete cure, and 1 patient experienced relapse of culture-negative peritonitis. No patient required Tenckhoff catheter removal or temporary hemodialysis support. The 30-day mortality was 0%.

◆ **Conclusions:** *Campylobacter* peritonitis might not respond to first-line conventional antibiotics, and an oral macrolide is recommended if *Campylobacter* is confirmed. The findings from our analysis do not support the use of fluoroquinolone, which is associated with a high resistance rate.

Perit Dial Int 2013; 33(2):189–194 www.PDConnect.com
epub ahead of print: 02 Oct 2012 doi:10.3747/pdi.2011.00323

KEY WORDS: *Campylobacter*; peritonitis; macrolides; resistance.

Peritonitis is a serious complication of peritoneal dialysis (PD), and treatment for peritonitis is initiated before the causative organism is known. The common protocol includes an empiric combination of a first-generation cephalosporin and a second drug for gram-negative coverage, as recommended in the latest

International Society for Peritoneal Dialysis (ISPD) guideline (1). Nevertheless, culture of the PD effluent remains imperative to guide the choice of antibiotics. In particular, given the rising incidence of gram-negative organisms (2–4), including drug-resistant organisms (4–7), identification and sensitivity testing are indicated to guide the choice of therapy.

Campylobacter organisms are uncommon as a cause of peritonitis, but these organisms typically have resistance to beta-lactam antibiotics, including penicillin and most cephalosporins. Use of first-line treatment recommended by the ISPD guideline is usually inadequate to cover infections secondary to *Campylobacter*, underscoring the need to identify the causative organisms.

Given the small number of cases and literature reports on *Campylobacter* peritonitis (8,9), the optimal treatment remains uncertain. The latest ISPD guideline has no specific recommendations for the management of *Campylobacter* peritonitis (1). To provide epidemiologic and clinical information about this condition, we report our single-center experience of managing *Campylobacter* peritonitis in 12 Chinese PD patients.

METHODS

This retrospective study included adult patients who were receiving PD between 1994 and August 2011 at our center. All consecutive PD patients presenting with peritonitis at our center were reviewed to locate all episodes of peritonitis secondary to *Campylobacter* species. For each episode of infection, the antibiotics used, duration of treatment, and patient outcomes were recorded in detail.

The diagnosis of peritonitis complicating PD was based on at least two of the following criteria: abdominal pain or cloudy PD effluent, leukocytosis in effluent (white blood cell count of at least 100/mm³), or positive gram-stain or culture from effluent (1). Bacterial culture

Correspondence to: K.M. Chow, Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong SAR, PR China.

Chow_Kai_Ming@alumni.cuhk.net

Received 22 December 2011; accepted 7 March 2012

of PD effluent in our unit was performed using the BacT/ALERT system with SA and SN bottles (bioMérieux, Marcy l'Etoile, France) and, after December 2010, the BACTEC FX system with Aerobic Plus and Lytic Anaerobic bottles (Diagnostic Systems, Sparks, MD, USA), all following the manufacturer's instructions. Species identification was performed using the API Campy identification system (bioMérieux). Antibiotic sensitivity was determined by the disc diffusion method according to the Clinical and Laboratory Standards Institute guideline.

Initial antibiotics (Table 1) generally involved intraperitoneal administration of a third- or fourth-generation cephalosporin, plus or minus intermittent vancomycin every 5 days, or cefazolin by continuous administration, plus an aminoglycoside or ceftazidime. During the review period, two clinical trials on monotherapy using cefepime or imipenem/cilastatin were conducted at our center (10,11).

"Primary response" was defined as resolution of abdominal pain, clearing of dialysate, and a neutrophil count in PD effluent of less than 100/mm³ on day 10 with antibiotics alone. "Complete cure" was defined as complete resolution of peritonitis by antibiotics alone without relapse or recurrence within 4 weeks of therapy completion.

RESULTS

From 1994 to 2011, 2665 episodes of PD-related peritonitis were recorded at our center. The overall peritonitis rate was 0.51 episodes per year or 1 episode in 23.5 patient-months of follow-up. We identified 12 episodes of *Campylobacter* peritonitis, accounting for 0.45% of all peritonitis episodes. Table 2 shows baseline demographic data for the 12 patients (5 women, 7 men) experiencing *Campylobacter* peritonitis. All 12 were on

continuous ambulatory PD. Species isolation was available in 9 patients (Table 2), with *C. fetus* (66.7%) being more common than *C. jejuni* (33.3%).

All 12 patients had cloudy effluent, with a mean initial white cell count of 2474/mm³ (median: 1985/mm³). Only 1 patient (patient 8) had diarrhea before the development of *Campylobacter* peritonitis; his stool culture was negative for *Campylobacter*. Four patients (33.3%) had diabetes mellitus. Two patients had documented colonic diverticulosis. Two patients had chronic hepatitis B liver disease, and one had chronic hepatitis C disease. The remaining patients had no apparent risk factors for *Campylobacter* infection.

Table 3 and Figure 1 summarize the clinical course and treatment outcomes of *Campylobacter* peritonitis episodes. Notably, half the patients with *Campylobacter* peritonitis showed no clinical improvement after 5 days of treatment. Among those patients, the initial antibiotics included intraperitoneal cefazolin, vancomycin, cefepime, ceftazidime, netilmicin, and gentamicin. All patients responded after the addition of an oral macrolide, either erythromycin or clarithromycin, for 14 days after the causative organism was identified. Among patients who started with cefazolin and ceftazidime (with or without gentamicin), 4 of 9 (44.4%) responded well and required no change of treatment; 1 had *C. fetus* bacteremia. Summarizing, the overall primary response rate was 91.7%, and the complete cure rate was 75.0%. No patient required Tenckhoff catheter removal or temporary hemodialysis support. The 30-day mortality was 0%.

We further analyzed the microbiologic profile of *Campylobacter* isolates in our series (Table 2). All *Campylobacter* species in our series were sensitive to macrolides such as erythromycin. On the other hand, the rate of resistance to fluoroquinolone was high, with 80.0% of the isolates being resistant to ciprofloxacin.

TABLE 1
Standard Peritonitis Treatment Protocols at Various Times in the Unit

Period	Protocol ^a
January 1994 to December 1995	Vancomycin + ceftazidime
January 1996 to December 1995	Cefepime ± vancomycin
January 1996 to July 1998	Vancomycin + ceftazidime or cefepime ^b
August 1998 to October 1998	Cefoperazone/sulbactam
November 1998 to March 1999	Vancomycin + cefepime
April 1999 to February 2001	Cefazolin + netilmicin
March 2001 to February 2002	Imipenem/cilastatin or cefazolin + ceftazidime ^b
March 2002 to present	Cefazolin + ceftazidime

^a All antibiotics were administered intraperitoneally unless the patient had features of systemic sepsis.

^b Randomized controlled trials were underway to compare the two protocols (10,11).

TABLE 2
Baseline Characteristics of the Peritoneal Dialysis (PD) Patients and the *Campylobacter* Organisms

Pt ID	Age (years)	Sex	Primary renal diagnosis	Duration of PD (months)	Significant comorbidity	Species	Susceptibility Sensitive	Resistant
1	61	Female	Unknown	75	Hepatitis B cirrhosis	NA	NA	NA
2	48	Female	IgA nephropathy	26	None	NA	NA	NA
3	47	Female	Unknown	83	None	NA	E, IME, NET	CIP
4	75	Male	Diabetic nephropathy	30	Adrenal insufficiency, chronic hepatitis B	<i>C. fetus</i>	E	CIP
5	46	Female	Lupus nephritis	45	None	<i>C. jejuni</i>	E	CIP
6	77	Female	Unknown	29	Diverticulosis	<i>C. fetus</i>	E	CIP
7	50	Male	Diabetic nephropathy	32	Gastrectomy, chronic hepatitis C	<i>C. fetus</i>	E, CIP	No
8	70	Male	Diabetic nephropathy	25	None	<i>C. jejuni</i>	E	CIP
9	66	Male	Hypertension	40	Chronic obstructive airway disease	<i>C. fetus</i>	E, IME	CIP
10	66	Male	IgA nephropathy	76	Diabetes mellitus	<i>C. fetus</i>	E, CIP	No
11	61	Male	IgA nephropathy	50	Diverticulosis	<i>C. jejuni</i>	E	CIP
12	71	Male	APKD	22	None	<i>C. fetus</i>	E	CIP

Pt = patient; NA = not available; IgA = immunoglobulin A; E = erythromycin; IME = imipenem; NET = netilmicin; CIP = ciprofloxacin; APKD = adult polycystic kidney disease.

DISCUSSION

To our knowledge, the present study reports the largest case series of *Campylobacter* peritonitis complicating PD. The first case of *Campylobacter* peritonitis was reported in a 61-year-old man on PD who developed *C. fetus* peritonitis in 1982 (12). Altogether, fewer than 30 cases of PD-associated *Campylobacter* peritonitis have been reported in the literature (9). Such reports are critical because they permit clinicians to manage this specific PD complication more appropriately.

Several findings from this series of *Campylobacter* peritonitis are noteworthy. First, infection with this organism is rare. We encountered only 12 cases in 17 years, accounting for 0.45% of all peritonitis episodes. It would be extremely difficult to conduct randomized trials to ascertain the optimal treatment for *Campylobacter* peritonitis.

Second, *Campylobacter* peritonitis presents no differently than other organisms causing bacterial peritonitis. A smaller case series of 8 patients from one center suggested that diarrhea occurs more commonly (87.5%) in *Campylobacter* peritonitis (8). Our data show that 8.3% of the patients reported diarrhea before peritonitis. Diarrhea can be both a predisposing factor and a presenting symptom in peritonitis. Hence, it is not possible to rely on clinical features to predict that *Campylobacter* is the causative organism.

Third, the clinical response to conventional empiric antibiotics is variable. For instance, 4 patients with *C. fetus* peritonitis (patients 4, 6, 7, 9) responded to intraperitoneal cefazolin or ceftazidime with or without gentamicin. By contrast, other patients treated with intraperitoneal cefazolin and ceftazidime, with or without the addition of vancomycin or gentamicin, failed to respond by day 5. In other words, we observed a much less favorable response of *Campylobacter* peritonitis to cefazolin than was reported by Elshafie *et al.* (9), whose 3 cases of *Campylobacter* peritonitis were all susceptible to cefazolin (9). Earlier studies have reported effective regimes including cefazolin (9), erythromycin plus tobramycin (13), clarithromycin (14), imipenem (15), meropenem (16), gentamicin plus ciprofloxacin (17), vancomycin plus norfloxacin (18), vancomycin plus netilmicin and ciprofloxacin (19), and vancomycin plus gentamicin (20). Interestingly, all 6 patients who failed to respond by day 5 in our series (Table 3) improved after administration of an oral macrolide (erythromycin or clarithromycin); 5 achieved a complete cure, and 1 patient experienced relapse of culture-negative peritonitis.

The encouraging treatment response of *Campylobacter* peritonitis to macrolide bears an important implication, because those agents are not routinely considered in peritonitis. For instance, macrolides do not appear in the list of antibiotic drugs with dosing recommendations in

TABLE 3
Summary of Clinical Outcomes after *Campylobacter* Peritonitis

Pt ID	Initial antibiotic	Species	Response by day 5	Change antibiotics after confirming <i>Campylobacter</i> peritonitis	Primary response (by day 10)	Catheter removal	30-Day mortality	Relapse or recurrent peritonitis within 30 days
1	Imipenem/cilastatin + vancomycin	NA	Yes	No	Yes	No	No	No
2	Cefoperazone/sulbactam + netilmicin	NA	Yes	No	Yes	No	No	No
3	Cefepime + netilmicin	NA	No	Imipenem/cilastatin and oral erythromycin	Yes	No	No	No
4	Cefazolin + ceftazidime	<i>C. fetus</i>	Yes	No	Yes	No	No	Culture-negative peritonitis: response to another course of cefazolin and ceftazidime
5	Cefazolin + ceftazidime, followed by gentamicin	<i>C. jejuni</i>	No	Oral erythromycin	Yes	No	No	No
6	Cefazolin + ceftazidime	<i>C. fetus</i>	Yes	No	Yes	No	No	No
7	Cefazolin + ceftazidime, followed by gentamicin	<i>C. fetus</i>	Yes	No	Yes	No	No	No
8	Cefazolin + ceftazidime + gentamicin	<i>C. jejuni</i>	No	Oral erythromycin	Yes	No	No	No
9	Cefazolin + ceftazidime ^a	<i>C. fetus</i>	Yes	No ^b	Yes	No	No	<i>C. fetus</i> peritonitis: response to ceftazidime and gentamicin
10	Cefazolin + ceftazidime, followed by vancomycin, gentamicin	<i>C. fetus</i>	No	Oral clarithromycin	Yes	No	No	No
11	Cefazolin + ceftazidime	<i>C. jejuni</i>	No	Oral clarithromycin ^c	No	No ^b	No	Culture-negative peritonitis: response to cefazolin and ceftazidime
12	Cefazolin + ceftazidime	<i>C. fetus</i>	No	Oral clarithromycin	Yes	No	No	No

^a Patient 9 initially received intravenous cefazolin and ceftazidime (followed by intraperitoneal ceftazidime); he was subsequently confirmed to have *C. fetus* bacteremia.

^b Patient 9 had an erythromycin allergy.

^c *Campylobacter* was identified (from dialysis effluent saved on day 10) at 3 weeks after the onset of peritonitis; the patient refused Tenckhoff catheter removal.

Figure 1 — Flow diagram of clinical outcomes after *Campylobacter* peritonitis. “Relapse” is defined as an episode that occurs within 4 weeks of completion of therapy for a previous *Campylobacter* peritonitis with the same organism (or culture-negative). Two relapse episodes were culture-negative, and one relapse episode was confirmed to be *Campylobacter* peritonitis.

the two most recent ISPD guidelines (1,21). Based on our experience, if a PD patient has confirmed *Campylobacter* peritonitis and does not respond to the usual empiric antibiotics, oral macrolide therapy should be initiated. Ciprofloxacin is unlikely to be beneficial because of a high resistance rate (up to 80% in our unit). On the other hand, a practical problem is that macrolide would not be the usual drug of choice for nephrologists, who noted slow clinical response in peritonitis and the initial reporting of gram-negative organisms from PD fluid. Early identification of *Campylobacter* organisms seems to be important to alert nephrologists to the potential role for macrolides.

The major limitation of the present review is the small number of cases and the fact that the data come from a single center. It is not clear whether the low resistance rate of the *Campylobacter* organisms recovered from our patients can be extrapolated to other dialysis centers. If similar patterns of resistance are observed elsewhere, the use of oral macrolide for *Campylobacter* peritonitis should be encouraged, because the pharmacokinetics (including serum and dialysate concentration measurements) have been validated in PD patients receiving

oral clarithromycin treatment (14). Clinical clues with respect to the source of *Campylobacter* organisms were also not available in most of our cases. Recommendations to prevent this particular peritonitis are therefore difficult to make.

CONCLUSIONS

Our analyses of data for 12 patients with *Campylobacter* peritonitis from a single unit showed excellent treatment response to oral macrolide. The prognosis for this complication appears to be satisfactory after identification of the causative organisms and appropriate antibiotic treatment.

ACKNOWLEDGMENT

This study was supported in part by the Richard Yu Peritoneal Dialysis Research Fund.

DISCLOSURES

The authors have no relevant financial interests to declare.

REFERENCES

- Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, et al. on behalf of International Society for Peritoneal Dialysis. Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423. [Erratum in: *Perit Dial Int* 2011; 31:512]
- Szeto CC, Leung CB, Chow KM, Kwan BC, Law MC, Wang AY, et al. Change in bacterial aetiology of peritoneal dialysis-related peritonitis over 10 years: experience from a centre in South-East Asia. *Clin Microbiol Infect* 2005; 11:837–9.
- Zelenitsky S, Barns L, Findlay I, Alfa M, Ariano R, Fine A, et al. Analysis of microbiological trends in peritoneal dialysis-related peritonitis from 1991 to 1998. *Am J Kidney Dis* 2000; 36:1009–13.
- Szeto CC, Chow KM. Gram-negative peritonitis—the Achilles heel of peritoneal dialysis? *Perit Dial Int* 2007; 27(Suppl 2):S267–71.
- Szeto CC, Chow KM, Leung CB, Wong TY, Wu AK, Wang AY, et al. Clinical course of peritonitis due to *Pseudomonas* species complicating peritoneal dialysis: a review of 104 cases. *Kidney Int* 2001; 59:2309–15.
- Valdés-Sotomayor J, Cirugeda A, Bajo MA, del Peso G, Escudero E, Sánchez-Tomero JA, et al. on behalf of the Grupo de Estudios Peritoneales de Madrid. Increased severity of *Escherichia coli* peritonitis in peritoneal dialysis patients independent of changes in *in vitro* antimicrobial susceptibility testing. *Perit Dial Int* 2003; 23:450–5.
- Szeto CC, Chow VC, Chow KM, Lai RW, Chung KY, Leung CB, et al. *Enterobacteriaceae* peritonitis complicating peritoneal dialysis: a review of 210 consecutive cases. *Kidney Int* 2006; 69:1245–52.
- Wood CJ, Fleming V, Turnidge J, Thomson N, Atkins RC. *Campylobacter* peritonitis in continuous ambulatory peritoneal dialysis: report of eight cases and a review of the literature. *Am J Kidney Dis* 1992; 19:257–63.
- Elshafie SS, Asim M, Ashour A, Elhiday AH, Mohsen T, Doiphode S. *Campylobacter* peritonitis complicating continuous ambulatory peritoneal dialysis: report of three cases and review of the literature. *Perit Dial Int* 2010; 30:99–104.
- Li PK, Ip M, Law MC, Szeto CC, Leung CB, Wong TY, et al. Use of intraperitoneal cefepime as monotherapy in treatment of CAPD peritonitis. *Perit Dial Int* 2000; 20:232–4.
- Leung CB, Szeto CC, Chow KM, Kwan BC, Wang AY, Lui SF, et al. Cefazolin plus ceftazidime versus imipenem/cilastatin monotherapy for treatment of CAPD peritonitis—a randomized controlled trial. *Perit Dial Int* 2004; 24:440–6.
- Vernon SE, Dominguez C. *Campylobacter* and peritoneal dialysis. *Ann Intern Med* 1982; 96:534.
- Wens R, Dratwa M, Potvliege C, Hansen W, Tielemans C, Collart F. *Campylobacter fetus* peritonitis followed by septicemia in a patient on continuous ambulatory peritoneal dialysis. *J Infect* 1985; 10:249–51.
- Verbanck JJ, Verlinde AM, Verbanck MI, Claessens MM, Vandewiele IA, Segaert MF, et al. *Campylobacter jejuni* II peritonitis in a CCPD patient: cure by oral clarithromycin. *Perit Dial Int* 1999; 19:85–6.
- Van den Eden EJ, Cabuy A, Daelemans R, Verhaegen J, Lins RL. *Campylobacter jejuni* peritonitis during chronic ambulatory peritoneal dialysis (CAPD). *Perit Dial Int* 1990; 10:177–8.
- Inoue K, Kitamura H, Nagasawa Y, Kawada N, Isaka Y, Rakugi H. *Campylobacter fetus* peritonitis in a patient with an unused embedded subcutaneous peritoneal catheter. *Perit Dial Int* 2010; 30:253–4.
- Lee YC, Huang YT, Sheng WH, Hsueh PR. Simultaneous peritoneal dialysis-associated peritonitis and bacteremia due to ceftriaxone-resistant *Campylobacter fetus*. *Perit Dial Int* 2011; 31:366–8.
- Kubota M, Ishiguro N, Tomino Y, Koide H. *Campylobacter fetus* subspecies *fetus* peritonitis in continuous ambulatory peritoneal dialysis. *Nephron* 1993; 65:487–8.
- Adedeji A, Subudhi CP, Gokal R, Hutchison AJ, Kerr JR. *Campylobacter jejuni* bacteremia, peritonitis, and exacerbation of chronic pancreatitis in a patient on CAPD: case report and literature review. *Perit Dial Int* 2000; 20:794–6.
- Binukrishnan S, Howse M, Neal T, Ahmad R. A case of *Campylobacter jejuni* peritonitis in a patient undergoing peritoneal dialysis. *J Med Microbiol* 2001; 50:935.
- Piraino B, Bailie GR, Bernardini J, Boeschoten E, Gupta A, Holmes C, et al. on behalf of the ISPD Ad Hoc Advisory Committee. Peritoneal dialysis-related infections recommendations: 2005 update. *Perit Dial Int* 2005; 25:107–31.