Peritoneal Dialysis International, Vol. 34, pp. 162–170
doi: 10.3747/pdi.2013.00275

0896-8608/14 $3.00 + .00

ORIGINAL ARTICLES

32 YEARS' EXPERIENCE OF PERITONEAL DIALYSIS–RELATED PERITONITIS IN A UNIVERSITY HOSPITAL

Sadie van Esch,[1] Raymond T. Krediet,[2] and Dirk G. Struijk[1]

Nephrology[1] and Renal Unit,[2] Academic Medical Centre, Amsterdam, Netherlands

♦ ***Background:*** **Peritonitis in peritoneal dialysis (PD) patients can lead to technique failure and contributes to infection-related mortality. Peritonitis prevention and optimization of treatment are therefore important in the care for PD patients. In the present study, we analyzed the incidence of peritonitis, causative pathogens, clinical outcomes, and trends in relation to three major treatment changes that occurred from 1979 onward: use of a disconnect system since 1988, daily mupirocin at the exit-site since 2001, and exclusive use of biocompatible dialysis solutions since 2004.**

♦ ***Methods:*** **In this analysis of prospectively collected data, we included peritonitis episodes from the start of PD at our center in August 1979 to July 2010. Incident PD patients were allocated to one of four groups: Group 1 – 182 patients experiencing 148 first peritonitis episodes between 1979 and 1987, before the introduction of the disconnect system; Group 2 – 352 patients experiencing 239 first episodes of peritonitis between 1988 and 2000, before implementation of daily mupirocin application at the catheter exit-site; Group 3 – 79 patients experiencing 50 first peritonitis episodes between 2001 and 2003, before the switch to biocompatible solutions; and Group 4 –118 patients experiencing 91 first peritonitis episodes after 2004. Cephradine was used as initial antibiotic treatment.**

♦ ***Results:*** **In 32 years, 731 adult patients started PD, and 2234 episodes of peritonitis in total were diagnosed and treated. Of those episodes, 88% were cured with medical treatment only, and 10% resulted in catheter removal. In 3% of the episodes, the patient died during peritonitis. Median time to a first peritonitis episode increased from 40 days for group 1 to 150 for group 2, 269 for group 3, and 274 for group 4. The overall peritonitis rate and the gram-positive and gram-negative peritonitis rates showed a time-trend of decline. However, the duration of antibiotic treatment increased over time, with groups 3 and 4 having the longest duration of treatment, accompanied by a higher percentage of antibiotic switch. Increased resistance to cephradine was found for coagulase-negative *Staphylococcus*.**

♦ ***Conclusions:*** **Peritonitis rates declined significantly over the years because of several changes in PD treatment. However, the need to change the initial antibiotic increased because of diminished antibiotic susceptibility rates over time. Nevertheless, the cure rate was high and remained stable during the entire period analyzed, and the death rate remained low. Consequently, peritonitis is a manageable complication of PD that cannot be considered a contraindication to this mode of renal replacement therapy.**

Perit Dial Int **2014; 34(2):162–170 www.PDIConnect.com**
epub ahead of print: 01 Mar 2014 doi:10.3747/pdi.2013.00275

KEY WORDS: Infection; peritonitis; peritonitis outcomes.

Chronic peritoneal dialysis (PD) treatment without the occurrence of peritonitis is impossible. Although most cases of peritonitis follow a rather benign course with appropriate antibiotic treatment, some episodes are complicated by hospitalization and temporary or permanent loss of the PD catheter. Severe and long-lasting peritonitis probably leads to peritoneal membrane failure and hence the need to discontinue PD and switch to hemodialysis. In a recent study in 709 incident PD patients participating in the Netherlands Cooperative Study on the Adequacy of Dialysis, infections were the reason for a switch to hemodialysis in 10% – 18% during the first 3 years of PD,

Correspondence to: S. van Esch, Nephrology, Academic Medical Centre, Meibergdreef 9, Amsterdam 1105 AZ Netherlands.
s.vanesch@amc.uva.nl
Received 24 October 2013; accepted 31 December 2013

depending on duration of treatment (1). Moreover, peritonitis contributes to a significant portion of infectious-related mortality in PD patients (2). Peritonitis prevention and optimization of peritonitis treatment are therefore important aims in the care of PD patients.

In 1979, chronic PD was started as a renal replacement therapy in our center. In the years thereafter, three important treatment changes were realized. First, we switched to disconnect (twin bag) systems in 1988; second, application of mupirocin at the catheter exit site was implemented in 2001; and third, biocompatible dialysis solutions have been used in all patients since 2004. Since 1979, 731 adult patients have been started on PD and a total of 2234 episodes of peritonitis have been diagnosed and treated. The aims of present study in this cohort were to analyze the incidence of peritonitis, the causative pathogens, the clinical outcomes, and the trends in the above findings in relation to the three major treatment changes.

METHODS

PATIENTS

All patients 18 years of age and older who were treated with PD at the Academic Medical Center from 1979 to July 2010 were included in the study. From the day PD was started, all peritonitis data were collected prospectively in a large database. The data include patient characteristics, start and duration of every peritonitis episode, causative organisms, dialysate leukocyte counts, type and duration of antibiotic treatment, antibiotic resistance, and outcome of the peritonitis, which could be cure, change of PD catheter, transfer to hemodialysis, or death. The time in months from PD start to the first episode of peritonitis was computed. Primary kidney disease was classified into 9 main categories according to the codes of the European Renal Association – European Dialysis and Transplant Association. Patients with two or more pathogens isolated from the cultures in a peritonitis episode were considered to have polymicrobial peritonitis. A relapse of peritonitis was defined when the same organism or a culture-negative peritonitis episode was identified within 4 weeks of completing appropriate antibiotic therapy for a previous episode.

PERITONITIS DIAGNOSIS AND TREATMENT PROTOCOL

In patients with any combination of cloudy effluent, abdominal pain, and fever, a sample of the effluent was obtained for a cell count with differential, Gram stain, and culture. Peritonitis was defined as the presence of two of three criteria: namely, clinical symptoms, effluent cell count exceeding 100 cells/μL, and a positive culture. Those criteria were developed by Vas and colleagues (3) and are confirmed in the current guidelines of the International Society for Peritoneal Dialysis (4). Except for the first cell count after presentation, all counts were performed in peritoneal effluent after the long dwell. Patients who were not admitted to the hospital were instructed to bring the first clear night bag to the outpatient clinic. Initial treatment consisted of a first-generation cephalosporin, which was combined with gentamicin when the patient was clinically ill and needed hospitalization. Cephradine was the first-generation cephalosporin used. It was replaced by cephalothin after cephradine was removed from the market in 2008. When hypersensitivity reactions occurred, vancomycin was given. Antibiotic treatment thereafter could be adjusted according to the resistance of the causative organism. Treatment duration was 1 week after cultures became negative and cell counts reached less than 100 cells/μL. The protocol was published in 1985 and has not been changed since (5).

STATISTICAL ANALYSIS

To analyze possible associations between categorical data, the chi-square test was applied. For continuous variables, a Kruskal–Wallis or Mann–Whitney test was used. Results are expressed as means and standard deviations, or medians and ranges.

For the analysis of clinical outcomes and peritonitis incidence in relation to the three major changes in PD treatment, 4 groups of incident PD patients were formed:

- Group 1 consisted of 182 patients who started PD between 1979 and 1987—thus, before the introduction of disconnect systems. These 182 patients experienced 148 first peritonitis episodes.
- Group 2 consisted of 352 patients who started PD between 1988 and 2000—that is, before implementation of daily mupirocin at the catheter exit-site. They experienced a total of 239 first peritonitis episodes.
- Group 3 contained 79 patients who started PD between 2001 and 2003, before the switch to the sole use of biocompatible solutions, and they experienced 50 first peritonitis episodes.
- Group 4 consisted of the remaining 118 patients, who started PD after 2004 and who experienced 91 first peritonitis episodes.

The Jonckheere trend test was used to analyze linear trends in the peritonitis incidence over time, and

the Kendall tau was used to calculate the correlation coefficient. All statistical analyses were performed using SPSS for Windows (version 19.0: IBM, Armonk, NY, USA). A p value less than 0.05 was considered significant.

RESULTS

GENERAL

Between August 1979 and July 2010, 731 patients 18 years of age and older (57% men) started treatment with PD. Median age at PD start was 52 years (range: 18 – 87 years). Diabetic nephropathy was the cause of renal failure in 22% of the patients. Table 1 provides further details.

Death was the reason for PD discontinuation in 38% of the patients, followed by switch to hemodialysis (29%) and renal transplantation (28%). In 3% of patients, PD was able to be stopped because of return of kidney function, and 3% of the patients transferred to another hospital and were lost to follow-up. Causes of death were classified as cardiovascular (29%), infectious complications (22%), treatment refusal (11%), and unidentified (35%) when the patient died suddenly at home, probably from cardio- or cerebrovascular causes.

PERITONITIS INCIDENCE AND OUTCOMES

No peritonitis occurred in 203 of the 731 patients (28%). The remaining 528 patients experienced 2234 peritonitis episodes in total. Median time from the start of PD to a first peritonitis episode was 128 days (range: 0 – 3450 days). Relapsing peritonitis accounted for 301 of the 2234 episodes (13%). Of the remaining 1933 episodes, cultures identified a single organism in 71% and polymicrobial infection in 21%; 9% of episodes were culture-negative. The peritonitis rate declined to 1.4 episodes per patient–year in 1989 (1 year after the introduction of the twin-bag system) from 4.4 episodes per patient–year in 1979. The rate further declined to 0.95 episodes per PD–year in 2010, as shown in Figure 1.

Most of the peritonitis episodes (88%) were cured by antibiotic treatment. Catheter removal was required in 10% of the episodes. In 3%, the patient died during peritonitis. Analysis of cause of death in those episodes showed that 45% (n = 30) died from peritonitis, and 6% (n = 4) died from other infections. Death from cardiovascular causes during peritonitis occurred in 33% (n = 22) of the patients.

TABLE 1
Demographic and Baseline Clinical Characteristics of Incident Peritoneal Dialysis (PD) Patients Treated During the Study Period

	Patient group				
Characteristic	1 Single bag	2 Twin bag	3 Twin bag and mupirocin	4 Twin bag, mupirocin, and biocompatible	Overall
Time period	1979–1987	1988–2000	2001–2003	2004–2010	1979–2010
Patients (n)	182	352	79	118	731
Sex (men:women)	96:86	213:139	43:36	67:51	419:312
Mean age (years) at PD start	49±15	52±16	53±17	54±17	52±16[a]
Cause of ESRD (%)					
Glomerulonephritis	26	16	11	12	17[a]
Interstitial nephritis[b]	19	10	10	3	11[a]
Cystic kidney disease	6	7	5	7	7
Congenital[c]	1	1	6	3	2[a]
Renal vascular disease	8	19	17	21	16[a]
Diabetic nephropathy	21	23	18	21	22
Other multisystem diseases	9	9	11	12	10
Other or unknown	11	14	22	21	15[a]
Modality (APD:CAPD)	1:181	19:332	25:54	52:21	105:625[a]

ESRD = end-stage renal disease; APD = automated PD; CAPD = continuous ambulatory PD.
[a] $p < 0.05$ (analysis of variance).
[b] Includes pyelonephritis, drug induced nephropathy, and urolithiasis.
[c] Other congenital and hereditary kidney diseases.

CAUSATIVE PATHOGENS

Table 2 shows the distribution of causative pathogens in all peritonitis episodes. Most of the peritonitis episodes were caused by gram-positive organisms (57%). The organism most often cultured was coagulase-negative *Staphylococcus* [CNS (30%)], followed by *S. aureus, Streptococcus* species, and *Enterococcus* species. In 11% of all peritonitis episodes, gram-negative organisms such as *Pseudomonas* species, *Escherichia coli,* and others were found. Fungi were the cause of peritonitis in 1% of episodes.

Figure 2 shows PD catheter removal for all peritonitis episodes, by organism, but with the exclusion of polymicrobial peritonitis. Peritonitis caused by fungi (38%) and *Pseudomonas* (32%) resulted in the greatest catheter loss, followed by *S. aureus*. Culture-negative peritonitis resulted in 4% of catheter loss. Catheter removal was required in 9% of non-relapsing peritonitis episodes and in 14% of relapsing peritonitis ($p < 0.01$).

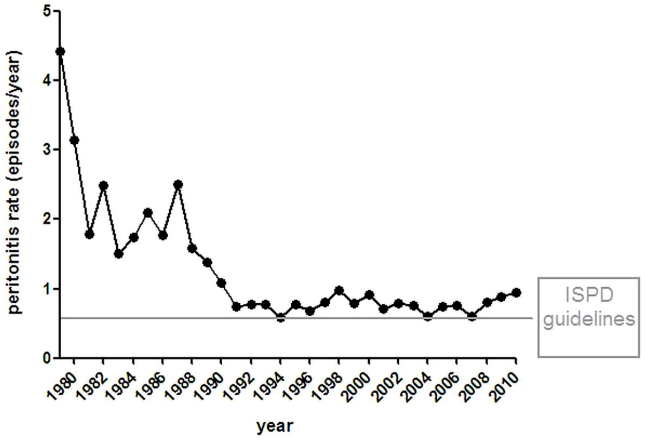

Figure 1 — Peritonitis incidence per year. ISPD = International Society for Peritoneal Dialysis.

TABLE 2
Distribution of Causative Pathogens in Peritonitis

Organism	[*n* (%)]
Overall	2234 (100)
Gram-positive	
CNS	681 (30)
Staphylococcus aureus	342 (15)
Streptococcus sp.	149 (7)
Enterococcus sp.	32 (1)
Others	88 (4)
Gram-negative	
Pseudomonas sp.	53 (2)
Escherichia coli	44 (2)
Others	152 (7)
Fungi	24 (1)
Mycobacterium	2 (0.1)
Others	16 (1)
Polymicrobial	429 (19)
Culture-negative	222 (10)

CNS = coagulase-negative *Staphylococcus*.

ANALYSIS OF PERITONITIS EPISODES IN RELATION TO THE THREE TREATMENT CHANGES

Table 1 shows the baseline characteristics of the 4 patient groups. Over the years, patients were older at the start of PD, and more patients started automated PD than continuous ambulatory PD. The causes of end-stage renal disease were different in the groups.

Median time in days to a first peritonitis episode was 40 for group 1, 150 for group 2, 269 for group 3, and 274 for group 4 ($p < 0.01$). Figure 3 shows the Kaplan–Meier analysis for time to a first peritonitis episode in the patient groups. Table 3 summarizes peritonitis outcome, antibiotic treatment, and antibiotic switches in incident patients with a first peritonitis. Compared with group 2, the single-bag group (group 1) had a lower percentage of catheter removal. Median duration of antibiotic treatment increased over time, with the longest duration of treatment observed in groups 3 and 4. Those longer times were accompanied by a higher percentage of antibiotic switch, as Table 3 shows.

Trends in resistance to flucloxacillin by *S. aureus* did not change significantly over time. The resistance to cephradine by CNS increased to 5.8% in group 3 from 0.8% in group 1. The susceptibility of *Pseudomonas* to aminoglycosides showed no change.

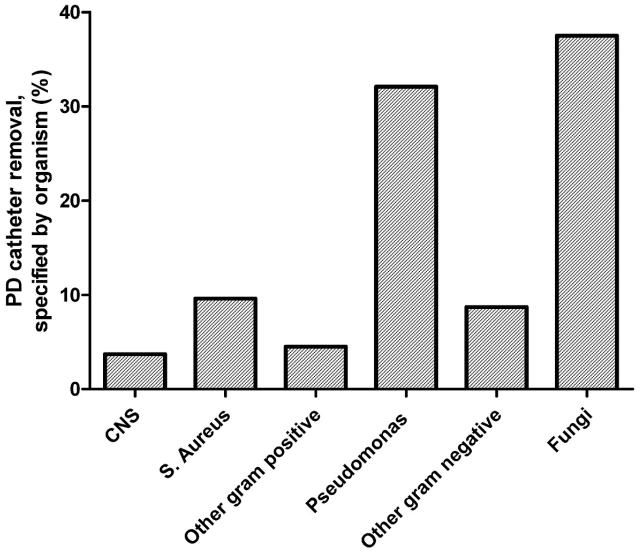

Figure 2 — Peritoneal dialysis (PD) catheter removal, by organism. CNS = coagulase-negative *Staphylococcus*; S. aureus = *Staphylococcus aureus*.

Table 4 compares peritonitis rates between the groups. The rates of *S. aureus* and *S. epidermidis* peritonitis declined significantly over time ($p = 0.01$). After the sole use of biocompatible dialysis solutions, gram-negative peritonitis attributable to *E. coli* declined ($p = 0.03$); however, no decrease in peritonitis caused by *Pseudomonas* species was observed. A time-trend of decline was found for the rate of relapsing peritonitis ($p \leq 0.01$).

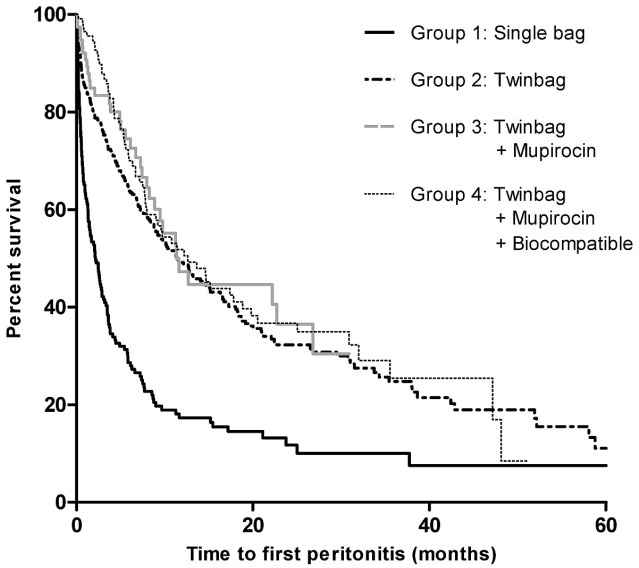

Figure 3 — Time to first peritonitis per group, maximal follow-up of 5 years.

DISCUSSION

In the present study, 32 years' experience of 2234 PD-related peritonitis episodes in a large university hospital were analyzed. Over those years, three important changes were made in the care of PD patients: specifically, use of a disconnect system since 1988, daily mupirocin at the exit-site since 2001, and use only of biocompatible dialysis solutions since 2004.

A significantly declining trend was observed in the overall peritonitis rate, and in episodes caused by both gram-positive and gram-negative organisms. Our findings confirm those of other, much smaller studies of the dramatic effects that the use of disconnect systems, which started in 1988, have had on the peritonitis incidence (6–10). The decreases were especially marked for CNS and *S. aureus* peritonitis.

The introduction of daily mupirocin application at the catheter exit site in 2001 led to a further reduction in *S. aureus* infections, not only at the exit-site, but also as peritonitis. A Cochrane analysis by Strippoli *et al.* (11) published in 2004 reported that nasal mupirocin reduced exit-site and tunnel infection, but not peritonitis.

TABLE 3
Peritonitis Outcomes and Antibiotic Treatment Duration and Switch in the Study Patients[a]

	Patient group			
Variable	1 Single bag (*n*=148)	2 Twin bag (*n*=239)	3 Twin bag and mupirocin (*n*=50)	4 Twin bag, mupirocin, and biocompatible (*n*=91)
Time period	1979–1987	1988–2000	2001–2003	2004–2010
Peritonitis outcome (%)				
Cure	94	86	92	90
Catheter removal[b]	3.4	12.1[c]	4.0	8.8
Death during peritonitis	2.7	2.1	4.0	1.1
Antibiotic treatment[b]				
Median duration (days)	13	14	16[d]	16[e]
Switch (%)	30	41[f]	70[g]	67[h]

[a] Groups include only incident patients experiencing their first peritonitis.
[b] $p < 0.05$.
[c] $p < 0.01$ compared with group 1.
[d] $p = 0.02$ compared with groups 1 and 2.
[e] $p < 0.01$ compared with groups 1 and 2
[f] $p = 0.04$ compared with group 1.
[g] $p < 0.01$ compared with groups 1 and 2.
[h] $p < 0.01$ compared with groups 1 and 2.

TABLE 4
Time Trends for Peritonitis in the Study Patients[a]

Variable	Mean peritonitis rate (episodes/PD year), by patient group			
	1 Single bag (*n*=182)	2 Twin bag (*n*=352)	3 Twin bag and mupirocin (*n*=79)	4 Twin bag, mupirocin, and biocompatible (*n*=118)
Time period	1979–1987	1988–2000	2001–2003	2004–2010
All episodes	3.22	1.30	0.89	0.95[b]
Gram-positive episodes	2.39	0.87	0.71	0.65[b]
Staphylococcus aureus	0.79	0.23	0.05	0.03[b]
S. epidermidis	1.23	0.35	0.35	0.13[b]
Gram-negative episodes	0.51	0.51	0.28	0.30[b]
Escherichia coli	0.20	0.20	0.21	0.04[c]
Pseudomonas species	0.06	0.06	0.02	0.06
Culture-negative	0.47	0.21	0.10	0.14
Relapsing	0.32	0.11	0.04	0.15[b]

[a] Groups include only incident patients experiencing their first peritonitis.
[b] $p \leq 0.01$.
[c] $p = 0.03$.

However, that conclusion was based on only one trial performed in 1996 with intranasal mupirocin. It can be hypothesized that compliance by patients is higher for topical than for intranasal mupirocin. Recently, Xu *et al.* (12) published a systematic review of studies that compared mupirocin treatment with placebo or no treatment. Those authors also found that mupirocin treatment was effective in preventing exit-site infection and peritonitis.

The total abandonment of conventional dialysis solutions in 2004 was associated with a further reduction in the rates of gram-positive and *E. coli* peritonitis, but no change in the incidence of culture-negative, gram-negative, and overall peritonitis was observed. Recently, Cho *et al.* performed a systematic review of randomized controlled trials to evaluate the benefits and harms of biocompatible solutions compared with conventional solutions in PD patients (13). That review showed that the use of biocompatible PD solutions might result in better preservation of urine output and residual renal function and might improve inflow pain. A decline in peritonitis episodes was not found, nor an improvement in technique and patient survival. However, it must be appreciated that outcomes in the various studies of this issue have been highly inconsistent. The results of our long-term observational study suggest that biocompatible solutions might have some protective effect against some, but not all micro-organisms.

Since 2004, more patients started with automated PD than with continuous ambulatory PD, a change that was not associated with a lower overall peritonitis incidence. The literature contains conflicting data about treatment modality and risk of peritonitis. Some studies showed that automated PD is associated with a lower peritonitis risk (14,15); other studies found no difference (16–18).

Despite the decline in peritonitis incidence, our center often failed to achieve the goal set by the International Society for Peritoneal Dialysis (4) of a peritonitis rate no more than 1 episode every 18 months (0.67 episodes per year at risk). That finding might be due to the continuation of PD after a few episodes of uncomplicated peritonitis. In addition, the low socio-economic status of many of our patients might have played a role. However, some papers report the same high incidence of peritonitis (10,19,20). Reporting bias cannot be excluded as a potential factor in lower peritonitis rates, because authors tend to publish success rather than failure, as hypothesized by Davenport (10). In contrast to the improved results for peritonitis incidence, the duration of antibiotic treatment for a peritonitis episode increased to 16 from 13 days, and that increase was accompanied by a higher percentage of antibiotic switch. Because the initial antibiotic was changed according to the resistance of the causative organism, we examined resistance for the two major causes of peritonitis in our series: CNS and *S. aureus*. Increased resistance to cephradine was found for CNS; *S. aureus* was not tested. Many other authors showed increased resistance of CNS

to methicillin, and consequently to first-generation cephalosporins (9,21–23). With respect to flucloxacillin, *S. aureus* showed no difference in the rate of resistance over time. All isolates were susceptible to vancomycin. The International Society for Peritoneal Dialysis (4) recommends a first-generation cephalosporin as the initial empiric antibiotic for gram-positive coverage, but underlines the importance of looking at the local history of sensitivities for the organisms causing peritonitis. Given our observations in the present study of significant changes in the antibiotic susceptibility of the main gram-positive pathogen causing peritonitis, re-evaluation of our current treatment protocol is indeed warranted.

Over the years, our cure rate has been high and stable, and the rate of death during peritonitis has remained low. Catheter removal was stable over the years, with the exception of a lower catheter removal rate in the early years of PD. We speculate that the latter observation is related to the high incidence of CNS peritonitis, which often has a relatively mild clinical course and usually does not require catheter removal. In contrast, catheter removal rates were significantly higher when peritonitis was caused by a single gram-negative organism or fungus than when the cause was a single gram-positive organism, which is consistent with results in other studies (23–26). Peritonitis caused by fungi (38%) and *Pseudomonas* (32%) resulted in the greatest catheter loss. Our relatively low catheter removal rates in fungal peritonitis contrast with those of most studies (27–30) and with the International Society for Peritoneal dialysis recommendation, which advises catheter removal immediately after fungi are identified by microscopy or culture (4). Our group always followed another policy (31), in which medical treatment with intraperitoneal amphotericin and flucytosine was initiated and then continued for 4 weeks. In *Candida albicans* peritonitis, this treatment is effective in 60% of cases. It is not appropriate for fungal peritonitis caused by other fungi or yeasts, however. A pitfall with the above regimen is that the dialysis effluent may remain turbid because of a high, amphotericin-induced cell number, which could erroneously suggest that the medical treatment is not effective. Ignorance of that fact and unjustified fear of inducing peritoneal membrane damage might be reasons for considering primary catheter removal.

In almost half the patients who died during peritonitis (46%), the cause of death was assigned to the peritonitis. Other infections and cardiovascular problems were the most important causes in 6% and 33% of deaths respectively. Boudville *et al.* (32) reported similar results in 250 patients who experienced an episode of peritonitis in the 30 days before death, except that the percentage of deaths attributable to peritonitis was lower at 28%. The authors of that paper touched on the problem of reporting a cause of death. Because no standard definition of peritonitis-associated mortality has yet been established, the approach to a diagnosis of peritonitis-associated death is variable and subjective. As a consequence, the prevalence rates presented in the literature vary. Systemic inflammation may predispose to cardiovascular disease, as reported by others (33,34). Although peritonitis cannot always be considered a systemic inflammation, the potential for inflammation could be an additional explanation for the high percentage of cardiovascular causes of death during peritonitis.

The present study has a number of limitations. First, it is a single-center study, which makes the results difficult to apply to other centers. However, in a single-center study, data are more complete, and accuracy is more easily checked than is possible with registry data. Second, although the peritonitis episodes were thoroughly prospectively documented in an extensive peritonitis database, data collection was not part of a general prospective study in which all imaginable parameters were collected. Hence, we were not able to distinguish the possible effects of nutrition status, patient education, and socio-economic status on peritonitis incidence and outcome. Also, data about exit-site infections were not prospectively collected.

One of the strengths of this study is the large number of peritonitis episodes that were collected during 32 years of PD practice. Another is that our initial antibiotic treatment protocol has not changed over the years. Moreover, the percentage of culture-negative episodes was just 9%. That observation underlines the high standard for culture methods in our medical microbiology laboratory, making the culture results very accurate.

CONCLUSIONS

The practice of PD with respect to peritonitis has improved significantly over the years because of implementation of a disconnect system and daily mupirocin application at the exit site. A clear positive effect of the use of biocompatible solutions could not be found. Still, our peritonitis rates are higher than guideline recommendations and need to be improved. Moreover, because of decreased rates of antibiotic susceptibility that developed over time, our initial empiric antibiotic treatment—consisting solely of a first-generation cephalosporin—declined in effectiveness.

Yet the cure rate was and has remained stable and high, and the rate of death during peritonitis was and has remained low. Those observations show that peritonitis is a manageable complication of PD that cannot be considered a contraindication to this mode of renal replacement therapy.

DISCLOSURES

The authors have no financial conflicts of interest to declare.

REFERENCES

1. Kolesnyk I, Dekker FW, Boeschoten EW, Krediet RT. Time-dependent reasons for peritoneal dialysis technique failure and mortality. *Perit Dial Int* 2010; 30:170–7.
2. Pérez Fontán M, Rodriguez–Carmona A, Garcia–Naveiro R, Rosales M, Villaverde P, Valdes F. Peritonitis-related mortality in patients undergoing chronic peritoneal dialysis. *Perit Dial Int* 2005; 25:274–84.
3. Vas S, Low D, Layne S, Khanna R, Dombros N. Microbiological diagnostic approach to peritonitis in CAPD patients. In: Atkins RC, Thomson NM, Farrell PC, eds. *Peritoneal Dialysis*. Edinburgh, UK: Churchill Livingstone; 1981: 264–71.
4. Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, *et al*. Peritoneal dialysis–related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423. [Erratum in: *Perit Dial Int* 2011; 31:512]
5. Boeschoten EW, Rietra PJ, Krediet RT, Visser MJ, Arisz L. CAPD peritonitis: a prospective randomized trial of oral versus intraperitoneal treatment with cephradine. *J Antimicrob Chemother* 1985; 16:789–97.
6. Daly C, Campbell M, Cody J, Grant A, Donaldson C, Vale L, *et al*. Double bag or Y-set versus standard transfer systems for continuous ambulatory peritoneal dialysis in end-stage renal disease. *Cochrane Database Syst Rev* 2001; (2):CD003078.
7. Korbet SM, Vonesh EF, Firanek CA. Peritonitis in an urban peritoneal dialysis program: an analysis of infecting pathogens. *Am J Kidney Dis* 1995; 26:47–53.
8. Holley JL, Bernardini J, Piraino B. Infecting organisms in continuous ambulatory peritoneal dialysis patients on the Y-set. *Am J Kidney Dis* 1994; 23:569–73.
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.
10. Davenport A. Peritonitis remains the major clinical complication of peritoneal dialysis: the London, UK, peritonitis audit 2002–2003. *Perit Dial Int* 2009; 29:297–302.
11. Strippoli GF, Tong A, Johnson D, Schena FP, Craig JC. Antimicrobial agents for preventing peritonitis in peritoneal dialysis patients. *Cochrane Database Syst Rev* 2004; (4):CD004679.
12. Xu G, Tu W, Xu C. Mupirocin for preventing exit-site infection and peritonitis in patients undergoing peritoneal dialysis. *Nephrol Dial Transplant* 2010; 25:587–92.
13. Cho Y, Johnson DW, Badve SV, Craig JC, Strippoli GF, Wiggins KJ. The impact of neutral-pH peritoneal dialysates with reduced glucose degradation products on clinical outcomes in peritoneal dialysis patients. *Kidney Int* 2013; 84:969–79.
14. de Fijter CW, Oe LP, Nauta JJ, van der Meulen J, Verbrugh HA, Verhoef J, *et al*. Clinical efficacy and morbidity associated with continuous cyclic compared with continuous ambulatory peritoneal dialysis. *Ann Intern Med* 1994; 120:264–71.
15. Sanchez AR, Madonia C, Rascon–Pacheco RA. Improved patient/technique survival and peritonitis rates in patients treated with automated peritoneal dialysis when compared to continuous ambulatory peritoneal dialysis in a Mexican PD center. *Kidney Int Suppl* 2008; (108):S76–80.
16. Oo TN, Roberts TL, Collins AJ. A comparison of peritonitis rates from the United States Renal Data System database: CAPD versus continuous cycling peritoneal dialysis patients. *Am J Kidney Dis* 2005; 45:372–80.
17. Nessim SJ, Bargman JM, Austin PC, Nisenbaum R, Jassal SV. Predictors of peritonitis in patients on peritoneal dialysis: results of a large, prospective Canadian database. *Clin J Am Soc Nephrol* 2009; 4:1195–200.
18. Martin LC, Caramori JC, Fernandes N, Divino–Filho JC, Pecoits–Filho R, Barretti P on behalf of the Brazilian Peritoneal Dialysis Multicenter Study BRAZPD Group. Geographic and educational factors and risk of the first peritonitis episode in Brazilian Peritoneal Dialysis study (BRAZPD) patients. *Clin J Am Soc Nephrol* 2011; 6:1944–51.
19. Kavanagh D, Prescott GJ, Mactier RA on behalf of the Scottish Renal Registry. Peritoneal dialysis–associated peritonitis in Scotland (1999–2002). *Nephrol Dial Transplant* 2004; 19:2584–91.
20. Moraes TP, Pecoits–Filho R, Ribeiro SC, Rigo M, Silva MM, Teixeira PS, *et al*. Peritoneal dialysis in Brazil: twenty-five years of experience in a single center. *Perit Dial Int* 2009; 29:492–8.
21. Berns JS, Tokars JI. Preventing bacterial infections and antimicrobial resistance in dialysis patients. *Am J Kidney Dis* 2002; 40:886–98.
22. Kan GW, Thomas MA, Heath CH. A 12-month review of peritoneal dialysis–related peritonitis in Western Australia: is empiric vancomycin still indicated for some patients? *Perit Dial Int* 2003; 23:465–8.
23. Kim DK, Yoo TH, Ryu DR, Xu ZG, Kim HJ, Choi KH, *et al*. Changes in causative organisms and their antimicrobial susceptibilities in CAPD peritonitis: a single center's experience over one decade. *Perit Dial Int* 2004; 24:424–32.
24. Bunke CM, Brier ME, Golper TA. Outcomes of single organism peritonitis in peritoneal dialysis: gram negatives versus gram positives in the Network 9 Peritonitis Study. *Kidney Int* 1997; 52:524–9.

25. Troidle L, Gorban–Brennan N, Kliger A, Finkelstein F. Differing outcomes of gram-positive and gram-negative peritonitis. *Am J Kidney Dis* 1998; 32:623–8.
26. Krishnan M, Thodis E, Ikonomopoulos D, Vidgen E, Chu M, Bargman JM, *et al*. Predictors of outcome following bacterial peritonitis in peritoneal dialysis. *Perit Dial Int* 2002; 22:573–81.
27. Goldie SJ, Kiernan–Troidle L, Torres C, Gorban–Brennan N, Dunne D, Kliger AS, *et al*. Fungal peritonitis in a large chronic peritoneal dialysis population: a report of 55 episodes. *Am J Kidney Dis* 1996; 28:86–91.
28. Wang AY, Yu AW, Li PK, Lam PK, Leung CB, Lai KN, *et al*. Factors predicting outcome of fungal peritonitis in peritoneal dialysis: analysis of a 9-year experience of fungal peritonitis in a single center. *Am J Kidney Dis* 2000; 36:1183–92.
29. Prasad KN, Prasad N, Gupta A, Sharma RK, Verma AK, Ayyagari A. Fungal peritonitis in patients on continuous ambulatory peritoneal dialysis: a single centre Indian experience. *J Infect* 2004; 48:96–101.
30. Miles R, Hawley CM, McDonald SP, Brown FG, Rosman JB, Wiggins KJ, *et al*. Predictors and outcomes of fungal peritonitis in peritoneal dialysis patients. *Kidney Int* 2009; 76:622–8.
31. Struijk DG, Krediet RT, Boeschoten EW, Rietra PJ, Arisz L. Antifungal treatment of *Candida* peritonitis in continuous ambulatory peritoneal dialysis patients. *Am J Kidney Dis* 1987; 9:66–70.
32. Boudville N, Kemp A, Clayton P, Lim W, Badve SV, Hawley CM, *et al*. Recent peritonitis associates with mortality among patients treated with peritoneal dialysis. *J Am Soc Nephrol* 2012; 23:1398–405.
33. Rost NS, Wolf PA, Kase CS, Kelly–Hayes M, Silbershatz H, Massaro JM, *et al*. Plasma concentration of C-reactive protein and risk of ischemic stroke and transient ischemic attack: the Framingham study. *Stroke* 2001; 32:2575–9.
34. Fine A. Relevance of C-reactive protein levels in peritoneal dialysis patients. *Kidney Int* 2002; 61:615–20.