Peritonitis in a Pediatric Dialysis Unit: Local Profile and Implications

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ABSTRACT: **Background:** Peritonitis is a major complication of chronic peritoneal dialysis therapy. It is recommended that each center monitor infection rates in order to define the local microbiological profile and implement an appropriate empiric antibiotic regimen.

Objectives: To analyze the microbiologic profile of peritonitis in our pediatric dialysis unit and identify local predisposing factors.

Methods: In this retrospective study we reviewed the files of children treated with chronic PD during the 10 year period 1997–2007.

Results: Eighty peritonitis episodes were recorded in 29 children (20 male, 9 female) aged 0.1–18.5 years (median 11.75) treated with peritoneal dialysis for 6–69 months (median 19) for a total of 578 patient-months. The annual peritonitis rate was 1.66/patient. The main pathogens were coagulase-negative *Staphyloccocus* (32.5%) and *Pseudomonas* spp. (16%), which were also cultured in most cases (64–69%) from the exit site during the 3 months preceding peritonitis. No peritonitis occurred in 31% of the patients (median age 12.5 years). All patients less than 5 years old had at least one peritonitis episode. Contaminating conditions (gastrostomy, enuresis, diaper use), found in 44% of the study group, and first infection within 6 months from starting PD were significantly associated with an increased peritonitis rate ($P = 0.01$, $P = 0.009$, respectively). Recurrent peritonitis led to a switch to hemodialysis in 18% of patients. There were no deaths.

Conclusions: The risk factors for peritonitis in our study were: first infection within less than 6 months from starting treatment, *Pseudomonas* exit-site colonization, and contaminating conditions (gastrostomies, diaper use, enuresis). These susceptible subgroups as well as very young age (< 5 years) at starting PD should be especially targeted during training of caregivers and follow-up to prevent later complications.

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PD = peritoneal dialysis

Peritoneal dialysis is the main modality of renal replacement therapy in children. Rates of use range from 65% to 59% in patients less than 20 years old and up to 87% in patients under the age of 5 [1,2]. Two-thirds of the failures with this technique are due to recurrent peritonitis [3]. Peritonitis may have a considerable impact, both short and long term, leading to increased hospitalization, loss of peritoneal membrane function warranting a change in renal replacement therapy, and inadequate dialysis [4]. Peritonitis, with a mortality risk of at least 1%, is also the leading cause of death in children on chronic PD [3-5].

The reported annual rate of peritonitis in children on chronic peritoneal dialysis is 0.77–0.96 episodes per patient-year or one episode of peritonitis every 18 patient-months [4,6]. Rates in adults are lower and range from 0.36 to 0.55 episodes per patient-year [7].

The 2005 guidelines of the International Society of Peritoneal Dialysis recommend yearly monitoring of infection rates at each center in order to define the local microbiologic profile and institute an appropriate empiric antibiotic regimen [8,9]. The identification of risk factors and implementation of specific preventive measures would improve the outcome of patients treated with PD [9].

The aims of the present study were to analyze the microbiologic profile of PD-associated peritonitis at our center and to identify predisposing factors in our patient population.

PATIENTS AND METHODS

The study group comprised all patients under the age of 19 who were treated with chronic peritoneal dialysis for at least 3 months during the 10 years since our center opened its pediatric dialysis unit (1997-2007).

In our center, highly trained pediatric surgeons introduce double-cuffed curled peritoneal catheters for chronic PD. The procedure is performed under general anesthesia in the operating room after whole-body cleansing with antiseptic soap and intravenous administration of antibiotics (usually cefamezine). The exit site is positioned laterally to midline and oriented downward and always outside the diaper area or away from gastrostomy tubes, if present. PD is delayed for at

least 2 weeks from peritoneal catheter insertion, and during this time the patient and caretaker undergo training by a dialysis nurse and a representative from the manufacturer of the device. A double-bag system is used in patients receiving continuous ambulatory peritoneal dialysis, and a Home-choice® (Baxter, UK) or Sleep-safe® (Fresenius Medical Care, Germany) cycler is used in patients on automated peritoneal dialysis. Routine exit-site care consists of changing the exit-site dressing every day after cleaning with sterile saline solution and thorough drying. No prophylactic exit-site antibiotic application was used during the study period.

Peritonitis is diagnosed in accordance with ISPD guidelines: namely, the presence of at least two of the following three conditions in patients on chronic PD: a) symptoms of peritoneal inflammation, b) cloudy peritoneal effluent with more than 100 cells/mm^3 (> 50% neutrophils), and c) bacteria identified in peritoneal fluid by gram's stain or culture [7,10]. Initial empiric therapy with cefamezine-ceftazidime was used, as stipulated in the pediatric ISPD guidelines [10]. Until 2001, initial empiric therapy for suspected peritonitis consisted of intraperitoneal cefamezine and amikacin.

At every routine follow-up visit in the dialysis unit the exit site is examined and a culture swab is obtained if redness, discharge, or granulation tissue is observed, regardless of symptoms. Mupirocin or gentamicin was applied according to exit-site findings and culture result, and not routinely.

The demographic, clinical and laboratory data of the study patients were recorded from the medical charts. The total number of peritonitis episodes and the total length of PD therapy (months) in the study group were calculated. The peritonitis rate was expressed as the number of infectious episodes per patient-year of PD therapy. Individual peritonitis rates were calculated similarly for each patient. Early-onset peritonitis was defined as a first infectious episode within 6 months of the start of chronic PD therapy.

For every peritonitis episode, the causative pathogen (if identified) and antibiogram were recorded. Positive exit-site culture results and temporal relationship with peritonitis episodes were recorded for all patients in the study group.

STATISTICAL ANALYSIS

Because of the small sample size, non-parametric Mann-Whitney test or ANOVA (non-paired) *t*-test was used to compare continuous variables across groups.

RESULTS

Thirty-one patients met the inclusion criteria and the full medical records for data retrieval were available in 29: 20 males (67%) and 9 females (33%). The primary renal diseases were: dysplastic kidneys/obstructive uropathy in 14, congenital nephrotic syndrome in 4, congenital tubulopathy in 3, acquired glomerulonephritis in 7, and cortical necrosis due to severe hypoxic-ischemic perinatal event in 1. Demographic and dialysis-associated characteristics are given in Table 1. One patient had moderate mental retardation due to Joubert syndrome; no other comorbidities were found in the study group. Almost a half (44%) of the study group had contaminating conditions including diaper use or enuresis (20.5%) or a combination of gastrostomy (percutaneous endoscopic gastrostomy) and enuresis or diaper use (17%).

Table 1. Demographic and PD-related data of the study population

	No. (%) (range)
No. of patients	29
Males (%) / Females (%)	20 (67) / 9 (33)
Age at PD start (yrs)	
Median (range)	11.75 (0.1–18.5)
Patients ‹ 5 years (% of whole group)	7 (24)
PD duration (mos)	
Median (range) for whole group	19 (6–69)
Patients › 12 months on PD (%)	16 (55)
Type of PD	
APD / CAPD-CCPD	18 (62) / 11 (38)
No. of PD catheters used	48
Median no. of catheters/patient	1
% of patients with › 1 PD catheter	34
Patients with PEG/enuresis or diapers	13 (44%)
PEG only	2 (7)
Enuresis or diapers only	6 (20.5)
PEG+enuresis or diapers	5 (17)

APD = automated peritoneal dialysis (cycler-assisted) performed during sleep hours, CAPD = continuous ambulatory peritoneal dialysis, CCPD = combination of nightly APD and CAPD during the day, PEG = percutaneous gastrostomy

There were 80 episodes of peritonitis during a total period of 578 patient-months of PD therapy. The duration of chronic PD ranged from 6 to 69 months (median 19 months) and was similar for the different age groups. The median time from the start of PD to the first peritonitis episode was 2.5 months (range 1–42). The calculated annual peritonitis rate was 1.66 or one infection for every 7.2 patient-months. The median number of peritonitis episodes per patient was 1.2.

MICROBIOLOGIC PROFILE

The pathogens responsible for the peritoneal and exit-site infections are presented in Table 2. In 14 peritonitis episodes (17.5%) no bacteria were isolated.

Cultures of the catheter exit-site discharge were positive for 140 samples; 65.5% grew gram-positive bacteria (mainly coagulase-negative *Staphylococcus*), and 35.5% grew gram-negative bacteria, mainly (75%) *Pseudomonas* spp. (data not shown). For those peritonitis episodes caused by *Pseudomonas* spp. and by CONS, the same bacteria (identical antibiogram)

ISPD = International Society of Peritoneal Dialysis

CONS = coagulase-negative *Staphylococcus*

Table 2. Microbiologic profile of PD-associated peritonitis and exit-site infections in the study group

	No. of peritonitis episodes (%)	Same exit-site bacteria in previous 3 mos (%)
Total	80	25 (31)
Gram-positive		
Total	45 (56)	
CONS	26 (32.5)	18 (69)
S. aureus	3 (4)	
Others*	16 (20)	
Gram-negative		
Total	21 (26)	
Pseudomonas spp+	13 (16)	9 (69)
Others#	8 (10)	
No growth	14 (17.5)	

Table 3. Peritonitis rates and associated factors

	Whole group	No peritonitis	With peritonitis	Early-onset peritonitis*	Late-onset peritonitis*
No. of patients	29	9	20	14	6
Median age at PD start (yrs)	11.3	12.5	11.2	9.3	12.6
Median PD length (mos)	19	13**	19.5**	11.5	26.5
Median annualized peritonitis rate	1.66	0	1.93	3†	1†
No. (%) of patients with PEG/diapers	13 (45)	1 (11)††	12 (60)††	8 (57)	4 (66)

* Early-onset peritonitis = infection occurring within the first 6 months from starting PD vs. late-onset after 6 months

** Not statistically significant (P = 0.2)

† Significant ($P = 0.0092$)

†† Significant ($P = 0.01$)

were identified at the exit site during the 3 months preceding the infection in 69% and 64% of cases, respectively.

The antibiotic sensitivity profile (data not shown) did not include any methicillin-resistant *Staphylococcus aureus* species or extended-spectrum beta-lactamase producing Enterobacteriaceae; 44.4% of CONS were methicillin-resistant *Staphylococcus epidermidis*.

RISK FACTORS FOR PERITONITIS

Peritonitis rates and associated factors are shown in Table 3. Age at the start of PD was similar among subgroups. However, none of those aged less than 5 years when beginning PD was peritonitis free during PD therapy (data not shown).

Nine children (31% of the study group) – 7 boys and 2 girls, aged 5.9–13.4 years (median age 12.5 years) and treated with chronic PD for a median of 13 months (range 6–26) – did not have peritonitis at any time during dialysis treatment. Although this group's median length of chronic PD was slightly shorter, 13 versus 19.5 months, this difference was not statistically significant.

Fourteen patients (48%) had early-onset peritonitis. Their median age at starting PD was not significantly younger than in the late-onset group: 9.6 vs. 12.6 years ($P = 0.7$) but their subsequent peritonitis rate was significantly higher: 3 vs. 1 peritonitis/patient-year ($P = 0.0092$). Of note, the early-onset peritonitis group had a shorter median length of PD therapy.

Thirteen patients (45%) in our cohort had a contaminating condition (PEG, enuresis or diaper use). These contaminating factors were significantly more common among patients with peritonitis (60%) than among those without (11%) ($P = 0.01$). There was no difference in peritonitis rate by dialysis modality: APD vs. CAPD (data not shown).

Sixteen of the 28 patients in the study group (57%) eventually underwent kidney transplantation. Of the remainder, 7 are still on chronic peritoneal dialysis and 5 (18%) were switched to hemodialysis because of recurrent peritonitis.

DISCUSSION

Peritonitis is the Achilles heel of PD therapy in children awaiting renal transplantation. Although children are given high priority on transplantation waiting lists, preservation of the peritoneal membrane for the long term (including return to dialysis in case of graft failure) takes precedence. Therefore, it is essential that the dialysis team keeps the occurrence of peritonitis to a minimum and treats all episodes promptly [11].

The incidence of peritonitis in our study group was 1.66 episodes/patient-year or one episode for every 7.2 months of dialysis, which is almost twice the rate reported in the literature [4,12,13]. The median length of therapy in our study group, 19 months, was longer than in some reports on pediatric patients [12] but comparable to others [13]. A longer period of dialysis therapy might cause fatigue with resultant lower adherence to aseptic technique standards and increased exposure to infections [4,12].

APD, which was used in most of our patients (64%), and the 4 week delay from peritoneal catheter insertion to starting PD (in line with the recommendations) did not confer any protection against frequent peritonitis, as also reported elsewhere [14].

The microbiologic profile of peritonitis in our patients differed from other reports. In our study, *S. aureus* accounted for only 4% of the isolates compared to 15–38% in earlier studies, and *Pseudomonas* spp. accounted for 16% of the isolates compared to 3–8% in earlier studies [15,16]. This trend for increased prevalence of gram-negative infections in chronic PD patients was recently highlighted by a comprehensive

PEG = percutaneous endoscopic gastrostomy
APD = automated peritoneal dialysis
CAPD = continuous ambulatory peritoneal dialysis

worldwide study [17]. However, *Haemophilus parainfluenzae* was not among the causative pathogens in our PD-associated peritonitis series, as described elsewhere [18].

We also found an increased rate of gram-negative exit-site colonization (34.5%), with *Pseudomonas* spp. accounting for half these cases. This finding could possibly be explained by the greater exposure to moistness in our subtropical climate and warrants extra attention to proper care of the exit site (thorough drying).

In our center, *Pseudomonas* might effectively predict impending peritonitis since it was cultured from the exit site in 69% of *Pseudomonas*-induced peritonitis episodes. Therefore, its identification should prompt early and aggressive eradication attempts or earlier catheter replacement [6,11]. The association of exit-site colonization by a certain type of bacteria and its later appearance as the cause of the peritonitis described for *Pseudomonas* cannot be regarded as significant for CONS since it is a common colonizing bacterium of the skin.

Our empiric antibiotic protocol was ineffective against CONS infection, which was found in 32.5% of peritonitis episodes, but patients were switched to vancomycin only after the culture results were obtained. Nevertheless, there were no cases of sepsis, serious infectious complications, or death. This finding may be explained by the relatively low virulence of CONS. The lack of significant nephrotoxicity reported in PD patients treated for peritonitis with intraperitoneal cefazoline-amikacin [19], together with our finding of a relatively high incidence of *Pseudomonas* spp. peritonitis, suggests that this combination is the appropriate empiric therapy, as proposed recently [20].

Other possible factors specific to our population that could explain the observed high peritonitis rate are:

- **Young age** (< 5 years), widely reported to increase susceptibility to peritonitis during chronic PD [4,12,15,21], was found in 24% of our cohort. Indeed none of these patients was peritonitis free. However, older patients did not display the expected decrease in infection rate [4,22]. This fact might reflect patients' attempts at performing the PD procedure independently, improper technique, and compliance problems in this age group [23].
- **Early-onset peritonitis** occurred in almost half (46%) of our patients and was significantly associated with frequent peritonitis episodes during continuing chronic PD therapy. A similar association was reported in adult patients on chronic PD therapy, including a high subsequent rate of peritonitis, technique failure (with switch to hemodialysis) and high risk of death [24]. In most of these cases the pathogens were gram-positive bacteria, mainly CONS, indicating that the technique was not applied properly [11,12]. Although 10–20% of pediatric patients starting dialysis have been reported to develop peritonitis early in the course of chronic PD [4,13], the impact of this event on further PD-related infections has not been described in pediatric patients. Therefore, early-onset peritonitis in pediatric patients should alert physicians to the need for intensified patient and caretaker training to prevent further infections.
- **PEG and/or need for diapers or enuresis**, found in almost half of our patients, are recognized contaminating factors associated with increased bacterial colonization [4,13,17,21] and gram-negative peritonitis in young patients [20]. Significantly, patients with these contaminating devices had threefold higher peritonitis rates.
- **Infrequent PD catheter replacement** (only a third of our patients had reinsertion of PD catheter) might have contributed to the high recurrence rate of peritonitis in this study.

Despite the high rate of infections in our cohort, the rate at which patients were switched to permanent hemodialysis (18%) was similar to other reports: 15–30% [1,3,15]. Importantly, no deaths occurred in our cohort compared to the 1–15% mortality reported in other studies [15,25].

In view of the high incidence of peritonitis recorded in PD patients in our dialysis unit, retraining families after every peritonitis episode, application of mupirocine or gentatrim (according to the causative pathogen of peritonitis) to the exit site, and a short course (7–10 days) of oral ciprofloxacin in cases of persistent *Pseudomonas* exit-site colonization were undertaken after the study period. Although not yet thoroughly analyzed, the results seem positive.

CONCLUSIONS

The occurrence of peritonitis within 6 months of starting PD predicts increased susceptibility to infections during the rest of the PD course. We speculate that if patients can be kept infection free during the first months of PD treatment, they may stay peritonitis free later on. This can be achieved by thorough training of patients and caregivers, with careful attention to proper exit-site care and connection technique, particularly in patients at high risk of peritonitis – namely, young age at PD start, diaper use, or PEG feeding. Exit-site colonization with *Pseudomonas* may serve as a red flag for impending peritonitis, which requires prompt and aggressive care. Initial empiric therapy with the combination cefamezine-aminoglycoside is still appropriate in centers with low rates of *S. aureus* infection.

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