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Risk Factors Associated with Nosocomial Peritonitis in Children on Peritoneal Dialysis

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ABSTRACT

Background: Peritoneal dialysis is the most frequent dialysis method in children, and peritonitis is a frequent complication. The responsible organisms differ between nosocomial and community acquired peritonitis, they cause longer hospitalization time, and can lead to dialysis failure. **Objective:** The aim of the study was to describe the risk factors associated with nosocomial peritonitis in children with end-stage renal disease undergoing dialysis treatment. **Methods:** A nested case-control study was conducted in an academic medical center. **Subjects:** The basic cohort included all pediatric patients with end-stage renal disease undergoing continuous ambulatory peritoneal dialysis therapy and who were hospitalized for non-infectious causes during the study period, January 2008 to December 2009. Cases were subjects who developed nosocomial peritonitis during hospitalization, and controls were children free of nosocomial peritonitis. The final groups consisted of 10 cases and 35 controls. **Results**: There were 11 episodes of nosocomial peritonitis in 10 subjects (incidence rate, 6.6 cases per year of hospitalization). By multiple logistic regression analysis, the presence of congenital abnormalities of the kidney and urinary tract was the only risk factor significantly associated with nosocomial peritonitis (OR: 11.54; 95% CI: 1.86-71.59). **Conclusion:** Congenital abnormality of the kidney and urinary tract was a significant risk factor for nosocomial peritonitis in pediatric patients with end-stage renal disease undergoing peritoneal dialysis. (REV INVES CLIN. 2015;67:170-6)
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Key words: Peritoneal dialysis. Peritonitis. Nosocomial. Children. Congenital abnormality. Kidney. Urinary tract. Risk factor.

INTRODUCTION

Peritoneal dialysis (PD) is a widely used treatment modality for end-stage renal disease (ESRD) in pediatric patients[1,2]. Children with ESRD can depend on PD for several years, and sometimes it is the only available treatment. Infectious complications are the main cause of PD failure because of peritoneal fibrosis and, in some cases, death. Hence, the prevention of such complications is particularly important in this population[3-6].

The cause of peritonitis during PD is not always known. In the International Pediatric Peritonitis Registry study, no risk factors were identified in 72% of cases of

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community acquired peritonitis. Recognized causes are catheter contamination, exit-site/tunnel infection, and catheter perforation/leakage. The presence of a nasogastric tube, gastrostomy, or an ureterostomy has also been associated with peritonitis[6,7].

The incidence rate of peritonitis is a useful and easily measurable indicator for the quality and safety of PD practice. In a previous multicenter study, Monteon, et al. described a peritonitis incidence rate of one case per 24.8 months in adult patients with continuous ambulatory peritoneal dialysis (CAPD)[8]. Another Mexican study reported a peritonitis incidence rate of one case per 47 months in children undergoing automated peritoneal dialysis (APD)[9].

The North American Pediatric Renal Trials and Collaborative Studies (NAPRTCS) reported a global peritonitis incidence rate of 0.64 cases per 18.8 months[2].

Nosocomial infections complicate 3-21% of all hospitalizations[10,11]. Nosocomial peritonitis (NP) is uncommon in the adult population, complicating approximately 5% of hospitalized patients with CAPD[12]. In Mexico, Garcia, et al. reported that NP corresponded to 11.1% of total nosocomial infections in an adult population in a tertiary-care center[13]. To our knowledge, there is no published information on NP in children.

The aim of this study was to identify risk factors for NP in pediatric patients with ESRD undergoing dialysis therapy in a single center. We hypothesized that NP is more frequent in younger patients and in those with previous history of peritonitis, and is associated with dialysis-specific training of the personnel handling the dialysis procedure. Secondary objectives included the description of incidence rates, microbiological etiologies, and the morbidity associated with NP.

METHODS

A nested case-control study was performed that included pediatric patients with ESRD undergoing PD treatment and who required hospitalization due to non-infectious causes at the Children´s Hospital of Mexico (Hospital Infantil de Mexico) between January 2008 and December 2009. Cases were defined as patients with CAPD who developed peritonitis during their hospitalization. Control subjects were hospitalized patients with PD without NP.

We included patients aged ≤ 18 years with known ESRD diagnosis, who were in a CAPD program and receiving PD while hospitalized during the study period (January 2008 through December 2009).

We excluded patients with community acquired peritonitis, defined as patients with an admission diagnosis of peritonitis and without a history of hospitalization in the last 72 hours; patients who clearly had an infectious disease at admission; patients with acute kidney injury requiring acute dialysis; and patients under APD.

We collected data from the clinical records, including age, sex, cause of ESRD, reason for hospitalization, hospitalization ward, total number of hospitalization days before peritonitis onset, if there had been dialysis-specific training of the personnel handling the dialysis procedure, use of antibiotic prophylaxis during catheter insertion, peritoneal fluid culture results, previous history of peritonitis, and outcome related with the dialysis treatment.

Surveillance of nosocomial infections at our hospital is conducted by the epidemiology department; they perform an active and daily supervision of all vascular access sites, surgery wounds, catheters, drains, nosocomial infections, clinical outcomes, and microbiological results, in accordance with the guidelines of the Ministry of Health of Mexico regarding nosocomial infections[14].

Clinical diagnosis of peritonitis was made according to internationally accepted criteria, i.e., the presence of an effluent cell count ≥ 100 cells/mm^{3}ml, and ≥ 50% of polymorphonuclear cells of the total white blood cell count, in addition to other findings such as fever and nausea[15,16].

Nosocomial peritonitis was defined as a case of peritonitis diagnosed after 48 hours of hospitalization, without evidence that peritonitis was developing or incubating upon admission, according to the US Centers for Disease Control and Prevention criteria on nosocomial infections[17].

Statistical analysis

Analyses were performed using SPSS software version 15.0 (SPSS Inc., Chicago, IL, USA). Differences were

Table 1. Patient demographics

	Patients developing NP (n = 10)	Patients not developing NP (n = 35)
Gender (n, %)		
– Male	5 (50)	23 (66)
– Female	5 (50)	12 (34)
Age in years (mean ± SD)	9.20 ± 6.30	10.85 ± 5.59
Cause of renal disease (n, %)*		
– CAKUT	6 (60)	6 (17.14)
– Unknown	4 (40)	23 (65.71)
– Shock	0	4 (11.42)
– Other	0	2 (5.71)

*p value by Fisher p = 0.028 CAKUT vs. all other causes.
NP: nosocomial peritonitis; CAKUT: congenital abnormalities of the kidney and urinary tract.

considered significant when $p < 0.05$. The distribution of variables was analyzed by Kolmogorov-Smirnov test. Data were compared by Student´s *t* test, Mann Whitney test, chi-square or Fisher exact test, as appropriate. A multivariate model was created with logistic regression analysis for peritonitis-based risk profiles. The strategy of multivariate analysis included creating a best-fit model for the explored event and other variables to obtain adjusted estimations of the independent odds ratio and their 95% confidence intervals associated with these secondary variables. The incidence rate of NP was calculated as the number of events per year of hospitalization.

RESULTS

We collected data on 66 in-hospital PD patients during the study period. Of them, 21 were excluded from analysis: 13 patients because they had undergone acute PD due to acute kidney injury, three because they were dialyzed with APD, and five patients because they started the dialysis program during this hospitalization period.

There were 45 patients with 67 hospital admissions (1.5 per patient) and an overall hospitalization time of 604 days. There were 11 NP events in 10 subjects constituting the group of cases. The control group included 35 subjects with 56 admissions and who did not develop NP. Thus, the incidence rate of NP was 6.6 cases per year of hospitalization. Eight subjects had a previous history of peritonitis, with no significant differences between cases and controls (3/10 and 5/35, respectively; $p > 0.05$). Demographic data are described in table 1.

All patients had a two-cuff straight Tenckhoff catheter with a left-oriented exit site, which was placed by pediatric surgeons in the operating room under standard aseptic conditions. Antibiotic prophylaxis was used in 24 patients (53%), with no difference between cases and controls (5/10 and 19/35 respectively; $p > 0.05$). The most common antibiotics used were cephalothin in nine subjects (25.7%), and dicloxacillin in eight (22.8%); other antibiotics used were amoxicillin with clavulanic acid, ceftazidime, cefepime, vancomycin, and ampicillin.

The presence of congenital abnormalities of the kidney and urinary tract (CAKUT) as the cause of renal disease was more frequent among cases than controls (60 vs. 17%, respectively; $p = 0.028$). Three cases (30%) and three controls (8.6%) had a urinary catheter ($p = 0.113$). Two cases had ostomies; one had colostomy because of an anorectal malformation and the other had cystostomy because the child had Prune Belly syndrome; none of the controls had ostomies.

There were no significant differences in the reasons for hospital admission between both groups (Table 2). The main reasons for hospital admission were related to ESRD treatment adherence in 27 subjects (azotemia, acidosis, or electrolyte disturbances), followed by a change in dialysis modality in 10 subjects (patients are switched to CAPD if they acquire social insurance that provides dialysis supplies), and due to

Table 2. Cause of admission and dialysis modality

	Cases (n = 10)	Control (n = 35)
Cause of admission*		
– Water-electrolyte imbalance	7 (70%)	20 (57.14%)
– access failure	2 (20%)	8 (22.85%)
– Shock	0	5 (14.28%)
– Other	1 (10%)	2 (5.71%)
History of peritonitis*		
– Yes	3 (30%)	5 (14.28%)
– No	7 (70%)	30 (85.71%)
Antibiotic prophylaxis*		
– Yes	5 (50%)	19 (54.28%)
– No	5 (50%)	16 (45.71%)
Interval between hospitalization and catheter insertion†		
– Months (median, 25th, 75th percentile)	0.26 (0.19, 0.37)	1.5 (0.3, 7.0)

*Statistically non-significant by Fisher test.
†p = 0.009 by Mann Whitney test.

Table 3. Spectrum of organisms causing nosocomial peritonitis

Organism	Cases, n (%)	
Gram-positive		
– *Staphylococcus aureus*	2	3 (27%)
– *S. epidermidis*	1	
– *Streptococcus pneumoniae*	1	
Gram-negative		
– *Citrobacter freundii*	3	5 (45.4%)
– *Providencia rettgeri*	1	
– *Serratia marcescens*	1	
Yeast		
– *Candida albicans*	1	(9%)
No growth	2	(18.18%)

Table 4. Multivariate-adjusted odds ratio for factors associated with nosocomial peritonitis in dialysis children

		95% CI		
	OR	Low	High	p
Hospital ward				
– Nephrology ward vs. other	0.28	0.03	2.39	0.254
Previous history of peritonitis	1.92	0.29	12.45	0.490
Cause of renal disease				
– Urinary malformation vs. others	11.54	1.86	71.59	0.009
Gender				
– Female	2.92	0.54	15.85	0.212

OR: odds ratio.

other causes in eight subjects (including severe anemia, verapamil intoxication, seizures, surgical repair of interatrial communication, hypervolemia, and bone biopsy).

Peritoneal dialysis was performed exclusively by nurses. Only nephrology ward nurses were specifically trained for good PD practice, although no statistical differences were observed in the frequency of NP events when the different wards were analyzed (data not shown).

Etiology of nosocomial peritonitis

Causative organisms were identified by peritoneal-effluent culture in 9/11 (81.8%) cases (Table 3). Gram-negative bacteria were isolated in 5/11 NP events (45.4%), with *Citrobacter freundii* found in three cases and *Serratia marcescens* and *Providencia rettgeri* in one case each. Gram-positive bacteria were recovered in 3/11 of NP cases (27.27%). One case was caused by *Candida albicans*. The initial treatment was ceftazidime and vancomycin in 10/11 (91%) cases, and one case was treated with ampicillin, amikacin, and metronidazole.

Risk factors for nosocomial peritonitis

Risk factors analyzed by logistic regression model are shown in table 4. The risk for NP was similar in the different hospitalization wards where peritoneal dialysis was provided. Patients with CAKUT as the cause of renal disease were at a higher risk for developing NP (OR: 11.54; 95% CI: 1.86-71.59; p = 0.009).

The presence of urinary catheters and ostomies was more frequent in patients with CAKUT, although no urinary tract infections were diagnosed in these subjects. The use of prophylactic antibiotics at catheter placement was less frequent among cases with CAKUT than among cases without CAKUT (2/6 [33%] vs. 3/4 [75%], respectively; p = 0.01).

The interval between hospitalization and catheter insertion was longer in control subjects (median, 1.5 months) when compared to the NP group (median, 0.26 months) (Table 2).

With regards to the age group of subjects, 33% of patients with CAKUT and 72% of patients with other causes of ESRD were adolescents. Four patients required a change in dialysis modality to hemodialysis because of NP. There were no deaths.

DISCUSSION

There is a knowledge gap regarding nosocomial peritonitis in children.

In the study performed by Troidle, et al., NP complicated 5% of hospitalizations of adults with ESRD and CAPD[12]. In this study, we found that 22% of hospitalizations of children with ESRD and PD were complicated with NP. All events of peritonitis were treated according to the International Society of Peritoneal Dialysis Guidelines, with good clinical responses[5], though one patient lost the dialytic capability of the peritoneal cavity because of peritoneal fibrosis.

Our results show that hospitalized children with ESRD secondary to CAKUT undergoing PD treatment may be at a high risk for the development of NP (OR: 11.54; 95% CI: 1.86-71.59; p = 0.009). This is relevant because CAKUT is one of the main causes of ESRD in children[2,18,19]. According to data from the NAPRTCS 2011 Annual Report, 35.2% of patients needing dialysis because of ESRD had CAKUT. Our findings were similar, with 28.3% of subjects with ESRD secondary to CAKUT[2]. Children with CAKUT are prone to develop urinary tract infections and thus are frequently treated with prophylactic antibiotics. In our study, subjects with CAKUT had a higher frequency of urinary catheters and ostomies, and a lower frequency of prophylactic antibiotic use at the time of insertion of the Tenckhoff catheter. However, both variables included in the risk analysis showed no interaction effect, and the effect of CAKUT on overall risk was not modified by any of these variables (data not shown).

None of the patients with CAKUT had urinary tract infections in the discharge diagnoses, but they had a higher proportion of urinary catheter and ostomies, which can contribute to bacterial colonization[7].

The International Society of Peritoneal Dialysis Guidelines endorse the use of antibiotic prophylaxis in all children just before peritoneal catheter placement, with a single dose of first- or second-generation cephalosporin, but the choice of specific antibiotic can vary depending upon center-specific microbial susceptibility patterns[5,16].

In the study of Klaus, he mentioned that APD should be associated with a lower risk of peritonitis due to fewer connections to the PD catheter[20]. However, no study has addressed this issue in pediatric patients prospectively. Automated peritoneal dialysis is more often used in infants and young children, who are consistently reported to have a higher incidence of peritonitis. We excluded from this study the APD patients because in our program most of them receive CAPD due to financial reasons[20-22].

The spectrum of responsible microorganisms that we found differed from those reported for community acquired peritonitis, in which gram-positive bacteria are more frequently described (66%)[1,23]. Contrarily, gram-negative bacteria are more frequent in nosocomial peritonitis in adults[12,13], which is what we found in our pediatric patients. There were no significant differences between previously reported organisms in NP in adults and our results in children.

The frequency of microorganisms confirmed by culture was higher than those reported in other Mexican series (33%), being similar to rates reported in the USA and Europe[3,9,24].

The importance of the type of microorganism causing peritonitis lies in the severity of the event. Pérez-Fontan found that cases of peritonitis caused by fungi, enteric bacteria, *Staphylococcus aureus* and *Pseudomonas aeruginosa* were more severe[25]. Nosocomial bacteria tend to be more aggressive and resistant to antibiotics[12,26], and therefore their culture identification and antibiotic susceptibility analysis is of great importance for treatment selection.

The frequency of peritonitis in children on PD continues to exceed the rate in adults, and peritonitis remains the most common reason for change in dialysis modality in children, according to the guidelines established by the international Society for Peritoneal Dialysis (ISPD) in 2012[5].

Because of NP, four patients (40%) had PD failure and were switched to hemodialysis. According to the 2011

NAPRTCS Annual Report, 1,263 patients had to change from peritoneal dialysis to hemodialysis. In 28.3% of such patients, the reason for change was excessive infection, occurring primarily in the PD access (43%)[2].

According to the guidelines established by the ISPD in 2012, there are several suggested actions to prevent peritonitis in children undergoing PD. These actions are grouped in four intervention types: (i) catheter-related interventions, such as catheter selection and proper placement; (ii) antibiotic prophylaxis for catheter placement; (iii) prevention of contamination; and (iv) development of continuous quality improvement programs, such as the creation of an epidemiologic surveillance program, morbidity-discussion sessions in case of an event, and the standardization of the sustained use of prophylactic antibiotics[5].

Also, pediatric PD training is extremely important for nurses, patients, and caregivers. In our center, patient, caregiver, and nurse training is provided by dialysis-specialized nurses. In order to assure correct training, the trainee must achieve three objectives: safely perform all required procedures, recognize contamination and infection, and list all appropriate responses to contamination and infection. In our center, the most experienced, trained and capable nurses with respect to PD care are those who are staffed at the Nephrology Department, although this variable did not show differences in risk profile.

Hand-washing procedure is extremely important in preventing nosocomial infections and peritonitis[27,28]. There is a wide range of adherence of healthcare workers to hand hygiene recommendations (5-89%)[28] and it is recommended that training be periodically reinforced for the nurses and personnel who handle dialysis systems[29].

In conclusion, nosocomial peritonitis is a frequent complication in our pediatric peritoneal-dialyzed patients, affecting 22% of subjects in this study, with an incidence rate of 6.6 cases per year of hospitalization. Despite the small sample size, the only independent risk factor that we found associated with NP in this study was the presence of CAKUT. There is a lack of information about pediatric NP worldwide.

The limitations of our study are the small sample size, the retrospective approach and single-center involvement. Further studies of NP in children are needed to determine if interventions such as hand hygiene surveillance, known to be essential for the control of nosocomial infections[30,31], in addition to reinforcement of PD training, could reduce the incidence of this severe complication.

DECLARATION OF INTEREST

The authors declare no conflicts of interest.

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