ORIGINAL ARTICLE

PREVENTION AND TREATMENT OF PERITONEAL DIALYSIS-ASSOCIATED PERITONITIS IN PEDIATRIC PATIENTS

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Peritoneal dialysis (PD) is the preferred dialysis modality in children and adolescents aged less than 15 years. Peritoneal dialysis-associated peritonitis remains a major cause of morbidity and reason for dropout from the PD program, although the incidence of peritonitis seems to have decreased during the past few years. Improved patient care, more frequent use of automated peritoneal dialysis (APD), use of PD catheters with downward facing exit sites, and Staphylococcus aureus prophylaxis account for this decline in infectious complications. With respect to the isolated micro-organism in PD-associated peritonitis, a predominance of gram-positive germs is found in children. Recent registry data suggest a decrease in coagulase-negative staphylococci, with a relative increase in gram-negative peritonitis episodes. The empiric antibiotic treatment regimen using a first-generation cephalosporin or a glycopeptide in combination with a third-generation cephalosporin in a risk-stratified manner was suggested in the pediatric peritonitis treatment guidelines. This regimen is currently being evaluated in the International Pediatric Peritonitis Registry.


KEY WORDS: Peritonitis; children; therapy.

In most countries, chronic peritoneal dialysis (PD) is the preferred dialysis mode for children and adolescents below the age of 15 years. Infectious complications are still a major cause of morbidity or change to hemodialysis in this patient group. The incidence of PD-associated peritonitis varies widely, from 1 episode every 14.9 patient-months to 1 every 30 patient-months in the different pediatric patient populations analyzed, but is considerably elevated compared to the data obtained in adult patient populations in most studies, although this is not universal (1–3). Latest data indicate a worldwide decrease in peritonitis frequency, as demonstrated by the improvement reported by the NAPRTCS registry within the past 5 years, showing a decrease from 1 in 13 to approximately 1 episode per 18 patient-months (Warady B, personal communication). When analyzing peritonitis incidence in different centers, individual factors have to be considered (4). Most data are given as cohort-specific peritonitis incidence but, especially in view of the small scale of many pediatric programs, subject-specific peritonitis rates have to be taken into account. In the total population at risk, up to 40% of patients remain free of peritonitis episodes throughout their time spent on dialysis awaiting renal transplantation (4).

PREVENTION OF PERITONITIS

Peritoneal dialysis-associated peritonitis is a major cause of hospitalization in pediatric patients. The risk of acquiring enterococci with reduced susceptibility or resistance to vancomycin was shown to be associated with hospitalization (5). Therefore, prevention of peritonitis episodes is of utmost importance in every pediatric PD program.

Prevention starts with the design of the PD catheter and its positioning. Time to development of a first
peritonitis episode was significantly longer with doublecuffed swan-neck catheters with the exit pointing downward compared to all other types used in the NAPRTCS registry (1). Burying the catheter in the subcutis was reported to improve infection rates compared to historical controls in adult patients, but this could not be confirmed in a prospective study (6). Perioperative antibiotic prophylaxis reduced early peritonitis episodes in children (7).

Automated peritoneal dialysis (APD) interferes less with the lifestyle and education of children and adolescents and is therefore now the preferred PD modality. On theoretical considerations, APD should be associated with a lower risk of peritonitis due to fewer connections to the PD catheter. However, no study has addressed this issue in pediatric patients prospectively; there are only studies with historic controls or registry data available. The latter indicate a reduced peritonitis rate in pediatric PD patients on APD versus those on continuous ambulatory PD (CAPD) (1). Because APD is more often used in infants and young children, who are consistently reported to have a higher peritonitis incidence (1) even in prospective studies (2), the difference between CAPD and APD could be expected to be even more clinically significant. The importance of proper training of children and their caregivers in preventing peritonitis was demonstrated by Holloway et al. (8). That international survey showed that the longer the time spent on training in practical and theoretical aspects, the lower the subsequent peritonitis rate.

Exit-site infections (ESI) of PD catheters often progress to peritonitis via migration of the germs along the outer catheter surface. Staphylococcus aureus (SA) is the most frequent micro-organism involved in ESI. Nasal SA carriers were shown to be at increased risk for PD catheter-related infections in the adult population. In pediatric patients, the significance of nasal SA colonization in frequency of infectious complications of PD remains controversial, although up to 50% of the patients and/or caregivers were colonized with SA within 6 months (9). It seems to be important that, in 15%, SA could be colonized from the caregivers only. In adult studies, all spouses and patients had identical SA strains (10). Therefore, the caregivers have the potential to transmit their strains to the patients, increasing the risk of SA infections. In the adult population, mupirocin applied either to the nares or to the exit site decreased SA infectious episodes. This was not confirmed in a pediatric cohort study with historical controls (11). However, preliminary results of a randomized, placebo-controlled study in pediatric PD patients demonstrated a significant decrease in SA infections (Klaus G, EuroPD 2002). The different outcomes of the two pediatric studies might be explained by the design because, in the latter, colonized caregivers were also treated. Therefore, in accordance with the adult guidelines, prophylaxis using mupirocin is recommended for patients colonized with SA.

**MICRO-ORGANISM**

Peritonitis should be diagnosed based on the following accepted criteria: cell count more than 100 cells/μL, with ≥50% neutrophils. In contrast to adult patients, the most common micro-organisms obtained are gram-positive germs, with a predominance of coagulase-negative staphylococci and SA. These two germs accounted for about 60% of all primary peritonitis episodes in MEPPS (2), in which gram-negative organisms were found in 16%. The data available on the Web site of the International Pediatric Peritonitis Registry (IPPR) (www.peritonitis.org) suggest a shift from gram-positive to an increased incidence of gram-negative peritonitis episodes, which parallels findings in adults. Improved connection technology eliminating spike systems, programs for tracking peritonitis, SA prophylaxis, and the use of the new, more biocompatible dialysis solutions may account for the reduction in gram-positive peritonitis episodes. Fungal infections account for about 3% of peritonitis episodes in children (1,2), with Candida being the most common species. Prolonged or repetitive antibiotic treatment was identified as a risk factor for fungal peritonitis. Prophylaxis with nystatin (10000 units/kg body weight per day) reduces the risk of Candida peritonitis when given to patients on antibiotics (12).

**TREATMENT**

The year 2000 consensus guidelines of the International Society for Peritoneal Dialysis (ISPD) for the treatment of peritonitis in pediatric patients receiving PD (13) recommend an empiric antibiotic regimen based on posed risk factors, which were based mainly on clinical experience. In children aged younger than 2 years with severe abdominal pain, a history of methicillin-resistant SA infection, or carrier or recurrent or current ESI, initial treatment with a glycopeptide (i.e., vancomycin or teicoplanin) for the gram-positive spectrum was recommended; whereas in children without these risk factors, a first-generation cephalosporin should be applied intra-peritoneally. Both regimens are to be combined with a third-generation cephalosporin (i.e., ceftazidime) for gram-negative organisms. After 3 days, the antibiotic...
therapy should be modified according to culture results. In all susceptible organisms, the glycopeptide should be replaced by a first-generation cephalosporin to minimize glycopeptide use according to the emerging reduced susceptibility or resistance of enterococci to vancomycin seen at least in the adult population. An important drawback to the cephalosporin-based regimen is the resistance of enterococci, which account for approximately 5% of peritonitis episodes. In culture-negative peritonitis, the initial antibiotic combination should be continued for 14 days, if the peritonitis episode is responsive. In refractory peritonitis episodes, the catheter should be removed within (3–) 5 days. Failure to do so resulted in patient death (35%) and/or subsequent PD failure (32%) in adults (14). Early catheter removal is necessary in up to 90% of fungal peritonitis episodes treated with fluconazole and flucytosine. Catheter replacement can be moved within (3–) 5 days. Failure to do so resulted in refractory peritonitis episodes, the catheter should be re-

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