DIALYSIS AND TRANSPLANTATION
ORIGINAL SCIENTIFIC PAPERS

Adv Clin Exp Med 2008, **17**, 2, 167–172
ISSN 1230-025X

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Peritonitis in 203 Children Treated with Peritoneal Dialysis in Poland During 2000–2003

Zapalenie otrzewnej u 203 dzieci leczonych metodą dializy otrzewnowej w latach 2000–2003 w Polsce

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Abstract

Background. Between Jan. 1, 2000, and Jan. 1, 2003, 203 children with end-stage renal failure were treated with peritoneal dialysis (PD) at the 13 pediatric dialysis centers in Poland.
Objectives. The aim of the study was a prospective analysis of peritonitis etiology, incidence rates, and outcome in Polish children treated with peritoneal dialysis.
Material and Methods. Of the 203 children, 107 commenced dialysis during the analyzed period. The children were aged 1 week to 18 years. The majority were treated by automated PD (91% APD, 9% CAPD). The total duration of dialysis was 4521 months. The incidence of peritonitis, its relapse rates, causative agents, and complications were analyzed.
Results. During the three-year period, 202 primary episodes of peritonitis and 40 relapses were observed (18.9% relapse rate). The overall national incidence of peritonitis in the pediatric centers was 1 episode per 22.39 patient-months or 0.53 episodes per patient-year. Peritonitis-free survival time was 17 months. Gram-positive organisms were the major causative agent, with *Staphylococcus aureus* and *Staphylococcus epidermidis* predominating. while Gram-negative rods accounted for 18.6% of episodes, with *Pseudomonas* species prevailing. Fungal infections were rare. 14.6% of cultures were negative. The highest relapse rates were noted following *Acinetobacter*, *E. coli*, and staphylococcal infections. The majority of children recovered and continued peritoneal dialysis, though 5.4% required catheter removal and reinsertion. Four children died and 15 (6.4%) were transferred to hemodialysis.
Conclusions. The incidence of peritonitis in children on APD is comparable to the adult population. Contact contamination remains the most common cause of peritonitis in children on APD. Further improvement of outcome should be aimed at decreasing the relatively high relapse rate, the main cause of catheter loss (**Adv Clin Exp Med 2008, 17, 2, 167–172**).

Key words: peritonitis, peritoneal dialysis, children, end-stage renal disease.

Streszczenie

Wprowadzenie. W okresie 1.01.2000–1.01.2003 r. leczono 203 dzieci ze schyłkową niewydolnością nerek za pomocą dializy otrzewnowej w 13 pediatrycznych ośrodkach dializacyjnych.

Cel pracy. Analiza czynników etiologicznych, częstotliwości występowania oraz wyników leczenia zapalenia otrzewnej w populacji dzieci dializowanych w Polsce.
Materiał i metody. Spośród 203 dzieci leczonych dializą otrzewnową 107 rozpoczęło dializoterapię w okresie obserwacji. Wiek dzieci wynosił od 1 tygodnia życia do 18 lat. Większość chorych (91%) stosowała automatyczną dializę otrzewnową (ADO). Sumaryczny okres dializoterapii wynosił 4521 pacjentomiesięcy. Dane zbierano w sposób prospektywny. Na ich podstawie określono czynniki etiologiczne, częstość występowania, wskaźniki nawrotów oraz wyniki leczenia zapalenia otrzewnej w polskiej populacji dzieci dializowanych.
Wyniki. W okresie 3 lat odnotowano 202 epizody zapalenia otrzewnej, po których wystąpiło 40 nawrotów (wskaźnik nawrotów – 18,9%). Częstość występowania zapalenia otrzewnej w polskich pediatrycznych ośrodkach dializacyjnych wynosiła 1 epizod na 22,39 pacjentomiesięcy lub 0,53 epizodów na rok. Średni okres przeżycia bez zapalenia otrzewnej wynosił 17 miesięcy. Bakterie Gram-dodatnie (z przewagą infekcji *S. aureus*, *S. epidermidis*) były przyczyną 61%, bakterie Gram-ujemne 18,6% (z przewagą infekcji *Pseudomonas*), a grzyby 3% zapaleń otrzewnej. Czynnika etiologicznego nie zidentyfikowano w przypadku 14,6% epizodów infekcyjnych. Nawroty zapalenia otrzewnej obserwowano najczęściej po zakażeniach gronkowcowych oraz wywołanych pałeczkami *Acinetobacter* i *E. coli*. Większość dzieci (92,2%) wyzdrowiała i po wyleczeniu kontynuowała dializę otrzewnową. 5,4% chorych wymagało usunięcia i ponownego założenia cewnika Tenckhoffa. Czworo dzieci zmarło, a 15 (6,4%) zrezygnowało z tej metody leczenia.
Wnioski. Częstotliwość występowania zapalenia otrzewnej w populacji dzieci dializowanych w Polsce jest zbliżona do obserwowanej w populacji dorosłych. Zanieczyszczenie kontaktowe bakteriami Gram-dodatnimi jest najczęstszym sposobem zakażenia płynu dializacyjnego u dzieci dializowanych metodą ADO. Poprawa wyników leczenia zapalenia otrzewnej powinna być ukierunkowana na zmniejszenie stosunkowo dużej liczby nawrotów i wynikających z nich częstych wymian cewników Tenckhoffa (**Adv Clin Exp Med 2008, 17, 2, 167–172**).

Słowa kluczowe: zapalenie otrzewnej, dializa otrzewnowa, schyłkowa niewydolność nerek, dzieci.

Peritoneal dialysis (PD) is a frequently chosen method of renal replacement therapy for children with end-stage renal failure. Peritoneal dialysis is not limited by the child's size or age and it can be performed at home, giving relative independence from the hospital and freedom for school attendance and social contacts. The most important limitation of this mode of dialysis is its infectious complications. Peritonitis may lead to fibrosis of the peritoneal membrane with a potential risk of technique failure, future surgical interventions, or sclerosing encapsulating peritonitis. An essential part of the care of children treated with long-term PD is the constant monitoring of center incidence rates of peritonitis, its causative agents, and their antibiotic sensitivity. In January 1, 2000, the Polish Pediatric Peritoneal Dialysis Group began prospective registration of all peritonitis episodes observed in children treated at the 13 pediatric dialysis centers in Poland via an electronic database. Data concerning the start of PD, its duration, time of peritonitis, causative agents and their antibiotic sensitivity, therapy, and outcome were collected. This paper presents the incidence rates, causative agents of peritonitis, and its outcome in Polish children on long-term peritoneal dialysis over a three-year period.

Material and Methods

Between January 1, 2000, and January 1, 2003, 203 children with end-stage renal failure were treated with peritoneal dialysis (PD) at 13 pediatric dialysis centers in Poland. There were 103 girls and 100 boys aged 1 month to 20 years (mean: 9.6 ± 6.2 years). The time on dialysis ranged from 3–36 months (mean: 21 ± 11 months), with a total of 4521 patient-months. Ninety-six patients were already on PD in January 2000 (prevalent patients) and 107 PD patients initiated dialysis during the observation period (incident patients). The majority of patients (91%) were on automated PD (APD). The incidence of peritonitis, its relapse rates, causative agents, and outcome were analyzed. The incidence of peritonitis is presented as cohort-specific peritonitis incidence for the total 203 PD patients, cohort-specific peritonitis incidence for the 107 children starting dialysis during observation period, and peritonitis-free survival according to Kaplan-Meier life-table analysis. The effects of age and sex of the patients and the center size on the relative risk of adverse final outcomes were assessed by multivariate logistic regression analysis. The model was assumed to be significant at $p < 0.05$. A peritonitis relapse was defined as the recurrence of peritonitis within the same organism within four weeks after termination of antibiotic treatment. Outcome of peritonitis was classified as recovery with continuation of PD, death, or technique failure if the patient was transferred to HD. Catheter removal rates and relapse rates were calculated for the different causative agents.

Results

During the observation period, 202 episodes of peritonitis developed in the children on long-term peritoneal dialysis followed by 40 relapses of

Table 1. National peritonitis incidence rates in a cohort of 203 children on long-term peritoneal dialysis treated in Poland during a three-year period (Jan 1, 2000–Jan 1, 2003)

Tabela 1. Częstość występowania zapalenia otrzewnej u dzieci polskich w 13 pediatrycznych ośrodkach dializacyjnych w latach 2000–2003

	Incidence of peritonitis (Występowanie zapalenia otrzewnej)
Prevalent patients Jan. 1, 2000–Jan. 1, 2003 (Liczba obserwowanych pacjentów)	1/22.39 patient – months
Patients commencing dialysis Jan. 1, 2000–Jan. 1, 2003 (Liczba pacjentów rozpoczynających dializy 1.01.2000–1.01.2003)	1/24.5 patient – months
Gram-positive peritonitis in prevalent patients (Gram-dodatnie zapalenie otrzewnej)	1/35.1 patient – months
Gram-negative peritonitis in prevalent patients (Gram-ujemne zapalenie otrzewnej)	1/110 patient – months

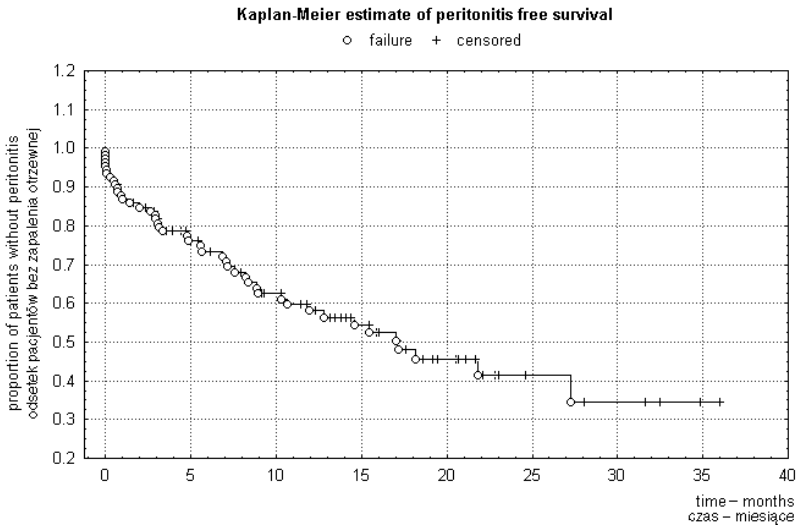

Fig. 1. Peritonitis-free survival for 107 children commencing peritoneal dialysis in Poland between Jan. 1, 2000, and Jan. 1, 2003 (median peritonitis-free survival: 17 months)

Ryc. 1. Krzywa przeżycia bez zapalenia otrzewnej dla 107 dzieci rozpoczynających dializę otrzewnową w Polsce w okresie od 1. 01.2000–1.01.2003 r.

the same etiology. Among the cohort of 107 patients commencing dialysis during the observation period, 84 episodes were observed, followed by 18 relapses. One hundred two patients remained peritonitis free during the observation period. Eighty-five percent of infectious events developed in 61 of the total 203 of children (30%) dialyzed. Peritonitis episodes were independent of age, sex, and center size. Patients over 15 years had a higher incidence of peritonitis, but this did not reach statistical significance (hazard ratio: 1.7, 95%*CI*: 0.9–3.3, $p = 0.12$). The cohort-specific incidence of peritonitis for 203 patients at 13 pediatric centers was 1 episode per 22.39 patient-months or 0.53 episodes per patient-year. The cohort-specific incidence of peritonitis for the 107 patients commencing PD between the observation period was 1 episode per 24.5 patient-months or 0.49 episodes per patient-year (Table 1). Median time of peritonitis-free survival was 17.04 months. At one year from the start of dialysis, 60% of the children were peritonitis free and at two years 40% had not developed any infectious complication (Fig. 1).

Gram-positive microorganisms were the major causative agents (61.6%), with *Staphylococcus aureus* (22%) and *Staphylococcus epidermidis* (20%) predominating. Gram-negative rods accounted for 18.6% of episodes, with *Pseudomonas* species prevailing. Fungal infections were rare (2.5%). Relapsing peritonitis was most frequently observed following staphylococcal, *Acinetobacter*, and *E. coli* infections. The overall relapse rate was 19.8% (Table 2). Catheter removal was performed 28 times, usually following staphylococcal relapses (15 episodes), fungal (6 episodes), or *Pseudomonas* (2 episodes) infections (Table 3). The outcomes of 223 (92.2%) episodes were favorable, with further continuation of PD therapy. Recovery was achieved in 13 (5.4%) of these episodes following catheter removal and reinsertion. Overall, 15 patients discontinued peri-

Table 2. Distribution of causative organisms of peritonitis and their relapse rates in 203 children on long-term peritoneal dialysis

Tabela 2. Czynniki etiologiczne zapalenia otrzewnej u dzieci dializowanych oraz wskaźniki nawrotów

Etiology of peritonitis (Etiologia zapalenia otrzewnej)	Causative agents (Czynniki etiologiczne) %	No. of episodes (Liczba zdarzeń)	No. of relapses (Liczba nawrotów)	Relapse rate (Wskaźnik nawrotów) %
Gram(+)	61.6	120	29	24.2
S. aureus	22.3	43	11	25.6
S. epidermidis	20.7	39	11	28.2
Streptococcus	9.5	19	4	21
Other G(+) (Inne G(+))	9.1	19	3	15.7
Gram + and Gram (–)	2.1	5	0	
Gram(–)	18.6	38	7	18.4
Pseudomonas	4.5	11	0	
E. coli	3.7	7	2	28.5
Klebsiella	2.5	6	0	
Acinetobacter	2.5	3	3	100
Other G(–) (Inne G(–))	5.4	11	2	18.1
Fungi (Grzyby)	3	6	0	
Eosinophilic (Eozynofilowe)	1	2	0	
Unknown (Nieznane)	15.5	31	4	12.9
Total (Suma)	100	202	40	19.8

Table 3. Outcome of 242 peritonitis episodes in 203 children on long-term peritoneal dialysis

Tabela 3. Zejście 242 epizodów zapalenia otrzewnej u dzieci leczonych dializą otrzewnową w Polsce w latach 2000–2003

Outcome of 242 peritonitis episodes (Zejście 242 epizodów zapalenia otrzewnej)	No. of episodes (Liczba epizodów)	%
Recovery with continuation of PD (Wyzdrowienie i kontynuacja dializy otrzewnowej)	223	92.2
Technique failure (Niepowodzenia techniczne dializy)	15	6.2
Death (Zgon)	4	1.6
Catheter removal (Usunięcie cewnika)	28	11.6
removal and reinsertion (wymiana)	13	5.4
removal and transfer to HD (usunięcie cewnika i przeniesienie na HD)	15	6.2

toneal dialysis following peritonitis and were transferred to hemodialysis. Four patients died (1.6%).

Discussion

The incidence rate of peritonitis for both patients already on PD at the beginning of the three-year period analyzed (prevalent patients) and for those commencing dialysis during it (incident patients) was relatively low and similar to reports of other national registries in Europe and Asia [1–4] and lower than those reported for regional registries [5, 6]. The low incidence rates are probably due to the predominant use of automated PD in children and the fairly uniform educational standards used by the Polish centers. Nevertheless, the

calculated median peritonitis-free survival time of 17 months requires improvement, as the mean waiting time for kidney transplantation for children in Poland is 24 months. Lower incidence rates are possible to achieve in children and have been claimed by single-center studies and some national registries [7, 8].

Young age, nasal *S. aureus* colonization, small center size, poor educational programs, and environmental factors have been implicated as risk factors for the development of peritonitis in children [1, 9]. However, they do not fully explain the uneven distribution of peritonitis among the dialysis population. Frequent episodes develop in a small group of patients, the majority remaining peritonitis free for long periods of time or demonstrating single infectious complications. In the cohort of children of the present study, 85% of infectious events developed in just 61 (30%) of the total of 203 children dialyzed. The incidence of peritonitis was independent of both patient age and sex and center size. The most peritonitis prone were adolescents, though the higher incidence of peritonitis in patients > 15 years did not have statistical significance. These patients, known for their noncompliance, frequently perform exchanges on their own, avoiding the control of their caretakers. The majority of infections in the present cohort of mainly APD patients was associated with contact contamination, as 71% of the recognized causative organisms were Gram-positive agents. This study confirms the predominance of Gram-positive infections in Europe reported by the International Pediatric Peritonitis Registry (IPPR), but does not confirm the high proportion of coagulase-negative staphylococci noted by the Registry for Eastern Europe [10]. In fact, the distribution of causative agents was nearly identical to that reported by the global registry for the rest of Europe, with an equal proportion of *S. aureus* (22%) and *S. epidermidis* (21%) organisms [10]. This suggests that general environmental factors probably have an important influence, as daily exit-site practices and the types of Tenckhoff catheters differed according to region and among centers. Further improvement in peritonitis incidence rates may be achieved in centers with prevalent Gram-positive infections through wider implementation of *S. aureus* prophylactic measures and reeducation programs for caretakers.

Gram-negative causative agents accounted for 22% of peritonitis episodes. The incidence of this infectious complication is probably fairly stable in countries with moderate climates. Reports from a single Polish center demonstrated that over the last 15 years the incidence rates of Gram-negative peritonitis have remained stable at 1/87 patient-months, with a significant decline in Gram-positive infections (from 1/19 to 1/39 patient-months) [11]. For those centers with low overall incidence rates of peritonitis, this group of causative agents has gained increasing importance. Gram-negative infections are also seen more frequently in centers treating higher numbers of young children, who have been shown to be at higher risk of acquiring GNP [9].

Variations in PD practices also contribute to the different global distribution of Gram-negative peritonitis [10]. Gentamycin or ciprofloksacin exit-site prophylaxis may be a potential prophylactic measure for peritonitis of this etiology [12]. Culture-negative peritonitis accounted for 18% of all episodes. Though this is acceptable by quality control programs, lower rates have been reported in USA (11%) and other countries [1, 9, 13]. The present national survey also noted a relatively high rate of relapsing peritonitis (19%). Though recurrence rates previously reported by pediatric centers have ranged from 10 to 30%, later studies have noted lower values (7–13%) [1, 10]. The recurrence rate was highest for both *S. epidermidis* (28%) and *S. aureus* (25%) infections. Relapsing peritonitis is regarded to be catheter related, with biofilm playing a key role [14]. In the cohort of patients of the present study, reassessment of both initial treatment and indications for early catheter removal are therefore necessary. Among the Gram-negative infections, *Acinetobacter* and *E. coli* infections relapsed frequently, though the numbers are too small to draw any conclusions.

The final outcome of peritonitis was favorable for the majority of children. The findings of the present study do not confirm the observation of the IPPR of a worse outcome of peritonitis due to technique failure (20%) in Eastern Europe. These observations were based on a relatively small number of 40 episodes reported by four centers [10]. The outcome of this larger series of 242 peritonitis episodes showed that recovery with continuation of PD was achieved following 92.2% of episodes, though 13 patients required catheter removal and reinsertion (5% episodes). The high technique failure rate reported by the IPPR may be a result of the unusually high incidence of *S. epidermidis* infections reported (38%) by the centers. Coagulase-negative staphylococcal infections, according to the present authors' observations, were associated with a high risk of recurrence and resultant frequent catheter removal. In the present cohort of 203 children, PD was discontinued permanently in 7.8% of cases, in 15 children (6.2%) due to technique failure and in 4 (1.6%) due to death. Three of the patients died following septic infection (one child with active SLE, one with

generalized amyloidosis, and one with fulminant staphylococcal pneumonia) and one child due to fungal peritonitis.

The authors conclude that this three-year survey of Polish pediatric dialysis centers demonstrated that the incidence of peritonitis in children on APD is comparable to that of the adult population. Contact contamination remains the main cause of peritonitis in this cohort of children on APD, and a further decrease of incidence rates should be aimed at prophylactic measures for staphylococcal infections. Improvement of outcome should be aimed at decreasing the relatively high relapse rate, the main cause of catheter loss.

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Conflict of interest: None declared

Received: 15.01.2008
Revised: 13.02.2008
Accepted: 20.03.2008