ORIGINAL ARTICLE

# Peritoneal dialysis-related peritonitis in the years 2005–2007 among patients of the Peritoneal Dialysis Clinic of the Department of Nephrology, Transplantology and Internal Medicine, Pomeranian Medical University in Szczecin

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**KEY WORDS**

antibiotic therapy, Gram-positive and Gram-negative bacteria, peritoneal dialysis, peritoneal dialysis-related peritonitis

**ABSTRACT**

**INTRODUCTION** Peritoneal dialysis-related peritonitis (PDRP) is the most common complication of dialysis in patients undergoing continuous ambulatory peritoneal dialysis.

**OBJECTIVES** The study analyzes incidence of PDRP, pathogens responsible for the disease and response to treatment in patients at the Peritoneal Dialysis Clinic of the Department of Nephrology, Transplantology and Internal Medicine of Pomeranian Medical University and the Independent Public University Hospital N° 2 in Szczecin in the years 2005–2007.

**PATIENTS AND METHODS** Within 36 months, 20 peritonitis incidents have been diagnosed in 18 subjects of 89 patients undergoing peritoneal dialysis.

**RESULTS** The incidence of PDRP was 1 episode/32 patient-months with 45% of PDRP episodes caused by Gram-positive bacteria, 40% by Gram-negative bacteria, and 5% by fungi. *Staphylococcus aureus* was the most common pathogen among Gram-positive bacteria and so were equally *Klebsiella oxytoca* and *Enterobacter cloacae* among Gram-negative bacteria. A satisfactory percentage of successful standard therapy (80%) was achieved; in 20% of PDRP cases removal of the Tenckhoff catheter was necessary.

**CONCLUSIONS** A higher proportion of PDRP caused by Gram-negative bacteria has been observed as compared to the data from other centers. There was high susceptibility of the isolated strains to third-generation cephalosporins and chinolones. Low incidence of PDRP in the center and bacteriological profile of strains causing the disease confirm high qualifications and training quality of the patients and the correct insertion of dialysis catheters.

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**INTRODUCTION** Peritoneal dialysis-related peritonitis (PDRP) is the most common cause of increased morbidity and the most common complication of dialysis in patients undergoing continuous ambulatory peritoneal dialysis. It may lead to persistent loss of peritoneal function as a dialysis membrane. Peritonitis in dialyzed patients is largely caused by bacterial contamination of the peritoneal dialysis catheter, resulting from inappropriate approach to system connecting methods.[1] Infection is a consequence of underestimation of the aseptic rules during exchanges. Migration of Gram-positive bacteria through the digestive tract wall could also cause

**TABLE 1** Etiology of peritoneal dialysis-related peritonitis (Department of Nephrology, Transplantology and Internal Medicine, Pomeranian Medical University)

| Pathogen | Incidence (n = 20) |
|---|---|
| Gram-positive flora | |
| *Staphylococcus epidermidis* | 3 (15%) MRSE-1 |
| *Staphylococcus aureus* | 4 (20%) MRSA-0 |
| *Staphylococcus heamolyticus* | 1 (5%) MR |
| *Staphylococcus hominis* | 1 (5%) MR |
| Gram-negative flora | |
| *Escherichia coli* | 1 (5%) |
| *Klebsiella oxytoca* | 3 (15%) |
| *Enterobacter cloacae* | 3 (15%) |
| *Moraxella catarrhalis* | 1 (5%) |
| Fungi | |
| *Candida albicans* | 1 (5%) |
| Negative culture | 2 (10%) |

Abbreviations: MR – methicillin-resistant; MRSA – methicillin-resistant *Staphylococcus aureus*; MRSE – methicillin-resistant *Staphylococcus epidermidis*

peritonitis; PDRP is secondary to the inflammation within the abdominal cavity (diverticulosis, adult autosomal dominant polycystic kidney disease). Upper respiratory *Staphylococcus aureus* carriers are more prone to recurrent PDRP, presence of *Staphylococcus aureus* colonies on the skin near the catheter poses a risk for appearance of bacterial biofilm inside the catheter.[2]

Incidence of PDRP along with improvements in the catheter system and replacement equipment were changing with time; in 1982, 1–2 episodes were observed for 1 patient within 1 year (1 episode for 4–5 patient-months of treatment).[3,4] In the 1990s, incidence of this complication decreased to 1 episode for approximately 24 patient-months of treatment.[1] In the years 2002–2004, it was 1 episode for 24–34 patient-months[5,6]; in 2005, PDRP incidence remained stable at 1 episode for 24 months of treatment[7]. Among the pathogens causing PDRP, Gram-positive bacteria predominate; Gram-negative bacteria are responsible for approximately 20% of PDRP cases. Patients undergoing automated peritoneal dialysis (APD) are less exposed to the risk of PDRP as compared to the patients undergoing continuous ambulatory peritoneal dialysis (CAPD), in which exchanges are performed manually[1] (APD is the form of therapy, where the dialysis fluid in the peritoneal cavity is exchanged by a cycler, i.e. an automatic device, following the determined dialysis scheme).

The present study analyzes incidence of PDRP, pathogens causing the disease and response to treatment in patients attending the Peritoneal Dialysis Clinic of the Department of Nephrology, Transplantology and Internal Medicine, Pomeranian Medical University and the Independent Public University Hospital) N° 2 in Szczecin in the years 2005–2007.

**PATIENTS AND METHODS** Retrospective analysis was performed for all cases of PDRP from January 2005 to December 2007 in patients at the Peritoneal Dialysis Clinic of the Department of Nephrology, Transplantology and Internal Medicine of Pomeranian Medical University in Szczecin and the Independent Public University Hospital N° 2. In 2005, 23 patients were treated with peritoneal dialysis, 32 patients in 2006 and 34 in 2007. PDRP was diagnosed based on clinical symptoms (cloudy dialysate, abdominal pain, fever or subfebrile temperature), dialysate cytosis over 100 leukocytes/μl with a predominance of multinuclear granulocytes and positive dialysate cultures. All PDRP patients were hospitalized in the Department of Nephrology, Transplantology and Internal Medicine of Pomeranian Medical University in Szczecin. 12 peritonitis cases were diagnosed in 18 patients; a control group consisted of 15 patients undergoing peritoneal dialysis without peritonitis episodes in the years 2004–2007.

Since the distribution of the analyzed parameters was non-normal, as confirmed by the Shapiro-Wilk test, the non-parametric Mann-Whitney U test was used to compare values between the groups (i.e. mean diuresis, total Kt/V urea, weekly total creatinine clearance).

During the PDRP treatment the patients were switched from APD to CAPD (current recommendations do not indicate such a need).[7] The mean treatment duration was approximately 14 days; patients who demonstrated cytosis <100 leukocytes/μl and negative dialysate cultures were deemed recovered.

**RESULTS** Within 36 months, 20 peritonitis cases were diagnosed in 18 patients (including 5 subjects with diabetic nephropathy) of 89 patients (59 males and 30 females, mean age of 52.9 ±12.1 years) undergoing peritoneal dialysis. The mean cytosis in the PDRP group was 6828.47 ±1259.37 cells/μl, the mean WBC count was 10.08 ±3.12 × $10^9$/l, the mean C-reactive protein (CRP) level was 117.76 ±13.03 mg/l, the total Kt/V was 2.33 ±1.16, the weekly total creatinine clearance was 101.587 ±65.56 l/week/1.73 $m^2$ and the mean diuresis was 1096.667 ±947.26 ml. The mean time from the introduction of peritoneal dialysis to the PDRP episode was approximately 1 year (347 days). For comparison, in patients undergoing peritoneal dialysis with no PDRP episodes, the total Kt/V urea was 2.47 ±0.69, the weekly total creatinine clearance was 108.85 ±40.86 l/week/1.73$m^2$ and the mean diuresis was 1660.667 ±850.04 ml (statistically insignificant differences between both groups, $p > 0.05$). At baseline, both groups used peritoneal dialysis solutions with similar percent of fluids containing medium and high glucose levels and with icodextrin. Etiology of end stage renal disease was also similar both in patients with and without PRDP. The PDRP group included 5 (27.8%) patients and the group without PDRP 6 subjects (40%) with diabetic nephropathy. Glomerulonephritis was found in 3 patients from the former group (16.7%) and in 2 patients from the latter

**TABLE 2** Antibiotic sensitivity of Gram-positive bacteria causing peritoneal dialysis-related peritonitis

| | Cloxacillin | Amicacin | Erythromycin | Vancomycin | Fluorochinolones | Co-trimoxazole | Linesolide |
|---|---|---|---|---|---|---|---|
| *Staphylococcus aureus* (4) | + | + | 3 strains +<br>1 strain +/– | + | + | + | + |
| *Staphylococcus epidermidis* (3) | 2 strains –<br>1 strain + | 2 strains +<br>1 strain – | – | + | 2 strains +<br>1 strain – | 2 strains –<br>1 strain + | + |
| *Staphylococcus hominis* (1) | – | – | – | + | + | – | + |
| *Staphylococcus haemolyticus* (1) | – | – | – | + | + | + | + |

+ sensitive, – resistant

(13.3%). The number of end stage renal disease cases of unknown etiology in the PDRP group and in the control group was 4 (22.2%) and 3 (20%), respectively. Other nephropathies (hypertensive nephropathy, autosomal dominant polycystic kidney disease, lupus nephropathy, chronic pyelonephritis) were observed in 6 patients from the former group (33.3%) and in 4 patients from the latter (26.7%).

The incidence of PDRP was 1 episode/32 patient-months. 2 cases (10%) demonstrated negative dialysate cultures, all the remaining cultures (90%) were positive. The etiology of PDRP included Gram-positive bacteria in 9 cases (45%), Gram-negative bacteria in 8 cases (40%) and fungi in 1 case (5%). No mixed infection was observed. TABLE 1 shows PDRP etiology in the study group. The most common pathogen among Gram-positive bacteria was *Staphylococcus aureus* found in 20% of PDRP cases, while among Gram-negative bacteria they were equally *Klebsiella oxytoca* (15%) and *Enterobacter cloacae* (15%). Antibiotic sensitivity of Gram-positive and Gram-negative bacteria is presented in TABLE 2 and TABLE 3, respectively. In 4 cases (20%) it was essential to remove the Tenckhoff catheter because of fungal PDRP (1 case) and *Staphylococcus aureus* PDRP (3 cases). 2 cases of PDRP caused by *Staphylococcus aureus* occurred shortly (approx. 1 week) after catheter implantation and were associated with exit-site and tunnel infection (ESI/TI). In the 3rd case of *Staphylococcus aureus* PDRP, which occurred 18 months after dialysis initiation, the Tenckhoff catheter was found obstructed, which required its immediate removal.

If the dialysate culture was negative, cephazolin and ceftazidime were administered intraperitoneally for 14 days. *Staphylococcus epidermidis* infections were initially treated with cephazolin and ceftazidime, in 2 cases, when antibiogram was determined, vancomycin was introduced intraperitoneally in a dose of 2.0 g twice daily, every 5 days. In 3 cases *Staphylococcus aureus* infections resulted in catheter removal with antibiotic protection provided (cloxacillin and gentamycin, cloxacillin and ceftazidime, cloxacillin and ciprofloxacin). In 1 case infection was successfully treated with cephazolin and ceftazidime administered for 10 days. That resulted from the fact that *Staphylococcus aureus* strain was sensitive to empirical antibiotic therapy. *Staphylococcus haemolyticus* infection was initially treated with ceftazidime, and then intraperitoneally with ciprofloxacin for 14 days, while *Staphylococcus hominis* infection was initially treated with cephazolin and ceftazidime for 6 days, and then a single dose of vancomycin was administered intraperitoneally.

For both *Klebsiella oxytoca* and *Moraxella catarrhalis* infections cephazolin and ceftazidime were used for 14 days, however, in 1 case of *Moraxella catarrhalis* infection intravenous ciprofloxacin was administered for 7 days. *Echerichia coli* infections were treated with cephazolin and ceftazidime for 10 days, while PDRP caused by *Enterobacter cloacae* was initially treated with ceftazidime and, on determining the antibiogram, aminoglycosides, i.e. gentamycin or amikacin, were used for 14 days.

In the case of fungal infection, fluconazole was introduced intravenously and the patient was transferred to a surgical ward to have the Tenckhoff catheter removed.

Neither tuberculosis peritonitis nor PDRP caused by *Pseudomonas aeruginosa* were observed. There were no deaths causally associated with PDRP.

## DISCUSSION

Indications of effectiveness of the peritoneal program related to PDRP prophylaxis are:[1]

**1** not more than 1 PDRP episode for 18 patient-months (0.67 episode/year of treatment)

**2** PDRP proportion with a negative baseline culture of the dialysate below 20% of bacteriological tests in a given center.

In the study group, the incidence of PDRP was 1 episode/32 patient-months, and the PDRP proportion with a negative baseline culture of the dialysate was 10%, what shows the effectiveness of the patient training program on prophylaxis of infectious complications of peritoneal dialysis in the discussed center.

Of note, reducing proportion of PDRP caused by Gram-positive bacteria; the incidence of *Staphylococcus epidermidis* (coagulase-negative staphylococci) infections in numerous centers was 30–40%, while in the described center it was 15% (TABLE 1). Lower incidence of infections caused by skin pathogens indicates, among others, the patients' better hygiene while performing insertion of a new catheter. However, the proportion of PDRP caused by Gram-negative flora

**TABLE 3** Antibiotic sensitivity of Gram-negative bacteria causing peritoneal dialysis-related peritonitis

| | Amicacin | Gentamycin | Netilmicin | First-generation cephalosporins | Third-generation cephalosporins | Fluorochinolones | Co-trimoxazole | Imipenem | Piperacillin/ Tazobactam |
|---|---|---|---|---|---|---|---|---|---|
| *Enterobacter* species (3) | + | + | + | – | + | + | + | 2 strains +<br>1 strain N/A | + |
| *Klebsiella oxytoca* (3) | + | + | + | + | + | + | + | N/A | + |
| *Moraxella catarrhalis* (1) | + | + | + | + | N/A | + | + | N/A | N/A |
| *Escherichia coli* (1) | +/– | – | + | – | + | + | + | + | + |

+ sensitive, – resistant

Abbreviations: N/A – data not available

is on the rise. The proportion of PDRP caused by Gram-negative bacteria in other centers was 20%, as compared to 40% in the Szczecin center (TABLE 1). A similar trend is also detectable in some peritoneal dialysis centers in the world[8,9], although in many others Gram-positive flora is still a predominant one[10-12].

Incidence of peritonitis was influenced by the exchange method applied; PDRP was more commonly reported in CAPD patients (12 patients, 14 cases of PDRP) than in APD patients (6 patients, 6 cases of PDRP), which was in keeping with previous observations.[1]

A high percentage of patients who were successfully treated by standard methods was achieved (80%). In empirical antibiotic therapy, cephazolin and ceftazidime was used intraperitoneally in 1.0 g doses for the long nightly dialysis, with possible modification after obtaining the dialysate culture. A similar proportion of successful therapy has been presented by other investigators.[13-15]

Gram-positive bacteria strains in the study group were resistant to cloxacillin in 44% of cases, to macrolides in 55% of cases, to aminoglycosides and co-trimoxazole in 33%, and resistant to fluorochinolons in approximately. 11% of cases (TABLE 2). Approximately 12% of Gram-negative bacteria strains were resistant to gentamycin (a similar proportion of resistance to aminoglycosides was observed also in other centers)[9]. However, Gram-negative bacteria isolated in the discussed center showed extremely high sensitivity to third-generation cephalosporins, chinolons and co-trimoxazole (TABLE 3), what resulted in successful PDRP therapy in this group of patients.

Catheter removal was caused by fungal infection (*Candida albicans*) in 1 case and by *Staphylococcus aureus* infection in 3 cases (methicillin-resistant *Staphylococcus aureus* strains were not isolated). 1 case of PDRP caused by fungi constituted 5% of all PDRP cases, a proportion similar to those observed in other centers.[16] *Staphylococcus aureus* infection is quite commonly concomitant with the ESI and catheter TI (caused most commonly by that pathogen) and in such cases the therapy is often ineffective. This makes it necessary to remove the Tenckhoff catheter.[17] In the Szczecin center, antibiotic cover is used prior to catheter implantation and in the perioperative period according to the recommendations.[7,18] The antibiotic cover consists in intravenous administration of cefuroxim in 1.5 g doses, with a switch to the oral route for several days (cefuroxim 2 × 250 mg for 3–5 days). Topical mupirocin or gentamycin are also used in selected cases (a reddened ESI, discharge from the ESI area).

In our center, tests for the carrier state of *Staphylococcus aureus* in all peritoneally dialyzed patients are not routinely performed. However, nasopharyngeal swabs were taken from PDRP patients, where *Staphylococcus aureus* (4 cases) was the pathogen causing peritonitis. Only 1 patient was found a carrier and in that case the decision was made to remove the Tenckhoff

catheter and to continue renal replacement therapy in the hemodialysis ward.

In conclusion, a high proportion of successful standard therapy (80%) seems to be achieved, in 20% of PDRP cases removal of the Tenckhoff catheter was necessary. A higher proportion of PDRP, caused by Gram-negative bacteria with high sensitivity of isolated strains to third-generation cephalosporins and chinolons, was observed. The appropriate training program (training lasts at least 5 days and is conducted during hospitalization; in selected cases it is prolonged until both the patient and the training personnel become certain that the exchanges are made properly) contributed to lower incidence of PDRP in the Szczecin center. The dates of replacement of connecting the tube are definitely obeyed. The patients in this center are infrequently carriers of *Staphylococcus aureus*. In the perioperative period (catheter implantation), the antibacterial prophylaxis described here is followed.

A low incidence of PDRP in the Szczecin center and bacteriological profile of strains causing the disease show that patients' qualifications and training quality are appropriate, and insertions of the dialysis catheter are correctly performed.

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