



Current epidemiology and practice patterns in prevention and treatment of PD-related infections in Poland

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Abstract

Background Peritoneal dialysis (PD) related infections are associated with technique failure and mortality. The aim of this multicentre study was to examine epidemiology, treatment and outcomes of PD-related infections in Poland as well as practice patterns for prevention of these complications in the context of current ISPD recommendations.

Methods A survey on PD practices in relation to infectious complications was conducted in 11 large Polish PD centres. Epidemiology of peritonitis and exit-site infections (ESI) was examined in all patients treated in these units over a 2 year period.

Results The study included data on 559 PD patients with 62.4% on CAPD. Practice patterns for prevention of infectious complications are presented. The rate of peritonitis was 0.29 episodes per year at risk, with Gram positive microorganisms responsible for more than 50% of infections and 85.8% effectively treated. Diagnosis and treatment followed ISPD guidelines however most units did not provide an anti-fungal prophylaxis. Although neither of the centres reported routine topical mupirocin on catheter exit-site, the rate of ESI was low (0.1 episodes per year at risk), with *Staphylococcus aureus* as most common pathogen and full recovery in 78.3% of cases.

Conclusion The study shows rewarding outcomes in prevention and treatment of PD-associated infections, mainly due to a thorough compliance with the current ISPD guidelines, although some deviations from the recommendations in terms of practice patterns have been observed. More studies are needed in large numbers of patients to differentiate the importance of specific recommendations and further support the guidelines.

Keywords Peritoneal dialysis · Infection · Peritonitis

Introduction

Infectious complications of peritoneal dialysis (PD) remain a significant cause of morbidity and mortality in PD patients [1]. In addition, they may result in a loss of peritoneal membrane anatomical and functional capacity. Updated guidelines of the International Society for Peritoneal Dialysis (ISPD) on peritonitis and catheter-related infections aim at reducing these complications and provide specific recommendations of variable strength depending on the supporting evidence [1, 2].

Given the high variability of infection rates and outcomes among PD centres, it appears that there may be different practice patterns for preventing and tackling PD-associated infections. Moreover, the predominant flora of causative microorganisms may be different influencing local treatment protocols. There is a need to investigate to what extent the current recommendations are implemented and how they impact the outcomes. In the present paper, we report the rates, microbiology and data on practice patterns for prevention, treatment and outcomes of infective complications in major PD centres in Poland.

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Methods

This is a retrospective analysis of all the PD-related infections reported for the years 2014 and 2015 by 11 PD centres willing to participate in this initiative under the auspices of the PD Working Group of the Polish Society of Nephrology. The reported data included clinical information on all the PD patients treated in the centres during this period, i.e. age, gender, primary kidney disease, co-morbidities, dialysis vintage, dialysis type, fluids utilized. The data on the patterns of training for PD, as well as on the policies for exit-site care were gathered. Variables that might influence the susceptibility to PD-related infections were also analysed, and included: *Staphylococcus aureus* colonization, presence of intestinal diverticula and the use of steroids. Furthermore, information on the policy for the empirical treatment of peritonitis episodes and of exit-site infections (ESI) was collected. Analysis of PD-related infections consisted of: the type of infection, the pathogen responsible, antibiotics used and the outcome. Apart from the data on individual patients, information was gathered on the centre-specific policies on prophylaxis and treatment of PD-related infections.

Results are expressed as mean and standard deviation, median and interquartile range or percentages, as appropriate. The assumption of normality was verified with the Kolmogorov–Smirnov test. A p -value < 0.05 was considered to be statistically significant. To assess the potential impact of consecutive variables on outcome, relative risk (RR) was calculated. Independent associations among variables were assessed with multiple regression analysis. Statistical processing of the results was performed with the use of the statistical software STATISTICA PL v 13.0 (Statsoft, Kraków, Poland).

Results

The study included data on 559 PD patients (283 women, 276 men), treated in 11 centres across Poland during the years 2014 and 2015. The basic characteristics are presented in Table 1. The data on PD treatment are demonstrated in Table 2. The overall number of patients treated with PD in Poland equals ca 1100. Given the incidence of PD, as well as the patient drop-out due to mortality, transplantations or transfer to HD, an approximate number of 2000 patients have been treated with PD within two years (time of data collection). This means, that the studied group constituted about a quarter of the whole PD population during this period.

Table 3 shows the dialysis training patterns in the PD centres taking part in the survey. The training was conducted by a nurse as an in-patient training in all the

Table 1 Basic characteristics of the studied group; GN-glomerulonephritis, ADPKD-autosomal dominant polycystic kidney disease

Number	559 patients (283 women)
Age (years)	57 (43–69)
Dialysis vintage (days)	729 (517–1766)
Days in observation (2014–2015)	530 (220–730)
Nephropathy N (%)	
Primary GN	156 (27.8)
Diabetic nephropathy	115 (20.6)
Hypertensive nephropathy	75 (13.5)
ADPKD	37 (6.7)
Other	111 (19.9)
Unknown	65 (11.5)
Co-morbidities N (%)	193 (34.5)
Diabetes mellitus	
Heart failure	185 (33.1)

Table 2 Basic characteristics of the PD treatment status; CAPD-continuous ambulatory peritoneal dialysis, APD-automatic peritoneal dialysis

Presence of intestinal diverticula N (%)	
Yes	44 (7.8)
No	354 (63.3)
Not known	161 (28.9)
PD therapy N (%)	
CAPD	349 (62.4)
APD	210 (37.6)
Biocompatible fluids N (%)	
Balance®	357 (63.9)
Physioneal®	17 (3.0)
Icodextrin N (%)	123 (22.0)
<i>S. aureus</i> carrier status N (%)	
No	289 (51.6)
Yes	78 (14.0)
Not known	192 (34.4)
Assisted PD N (%)	66 (11.8)

centres, and comprised of a planned education programme with a written test and a practical assessment at the end. Routine retraining was performed in most centres, and an additional one was mandatory following a peritonitis episode. In majority of centres, the incidence of peritonitis was monitored on a yearly basis.

The catheter exit-site care policy is demonstrated in Table 4. It needs to be underlined that none of the examined centres used mupirocin routinely on the exit-site. The dressing was changed every second, or every third day, and included a thorough disinfection with an antiseptic solution, povidone-iodine or octenidine dihydrochloride/phenoxyethanol in most cases. The description of the change

Table 3 Dialysis training patterns in the 11 PD centres

Duration	Average 5–12 days Minimum 3–7 days
Place	Ward
Person responsible	Nurse
One person responsible for the training <i>N</i> (%)	8 (73)
Mandatory training for the family <i>N</i> (%)	8 (73)
Planned education programme with written test and practical assessment in the end <i>N</i> (%)	11 (100)
Retraining after peritonitis <i>N</i> (%)	11 (100)
Retraining routinely every 6 months <i>N</i> (%)	9 (82)
Monitoring the incidence of peritonitis <i>N</i> (%)	9 (82)

Table 4 Exit-site care in the 11 PD centres

Change of dressing <i>N</i> (%)	
Every other day	8 (73)
Every 2–3 days	3 (27)
Mupirocin on exit-site <i>N</i> (%)	
No	11 (100)
Examining for <i>S. aureus</i> carrier status <i>N</i> (%)	
Before catheter placement	5 (45)
Every 6 months	3 (27)
Following SA peritonitis	3 (27)

of the dressing was meticulous and, in principle, similar in every centre.

In Table 5, the PD centres' policies for peritonitis episodes are shown. In all the centres, there was a practice for patients to come to the unit or the adjacent ward once a cloudy dialysate had been spotted. There was a good cooperation between the PD units and microbiology departments and all dialysates were cultured via inoculation to blood-culture media either directly in the ward or sent immediately to the bacteriology laboratory where after centrifuging, the resuspended pellet was cultured with a similar technique to blood. There was a low percentage of negative cultures – 10.7%. In most patients, empirical therapy comprised of cefazolin and ceftazidime given intraperitoneally. The duration of antibiotic therapy for peritonitis episodes ranged from two–three weeks, depending on the microorganism cultured, following the ISPD recommendations.

The PD centres' policies for ESI are demonstrated in Table 6. The empirical therapy varied considerably among centres, with no antibiotic being significantly more prevalent.

The follow-up median equalled 530 days (220–730 days). During this time, 183 episodes of dialysis related peritonitis were reported. This resulted in an incident rate of peritonitis episodes of 1 per 41 patient-months (0.29 episodes per year at risk). Table 7 shows the major pathogens responsible for peritonitis episodes.

Table 5 The PD centres' policies for peritonitis episodes

Empiric antibiotics <i>N</i> (%)	
Cefazolin + ceftazidime i.p.	(73)
Vanco i.p. + ciprofloxacin p.o.	2 (18)
Cefazolin + ceftriaxon i.p.	(9)
Routine anti-fungal prophylaxis <i>N</i> (%)	3 (27)
Urokinase in relapsing peritonitis <i>N</i> (%)	2 (18)
Simultaneous removal and insertion of PD catheter in relapsing peritonitis <i>N</i> (%)	5 (45)
Temporary shift from APD to CAPD during peritonitis <i>N</i> (%)	9 (82)
Antibiotic prophylaxis prior to PD catheter insertion <i>N</i> (%) and endoscopic procedures <i>N</i> (%)	11 (100) 8 (73)

Table 6 The PD centres' policies for exit-site infections

Routine ultrasound when suspected <i>N</i> (%)	2 (18)
Swab when redness <i>N</i> (%)	7 (64)
Swab when exudate <i>N</i> (%)	11 (100)
Oral empirical antibiotic when redness <i>N</i> (%)	1 (9)
Oral empirical antibiotic when exudate <i>N</i> (%)	10 (91)
Mupirocin on site when redness <i>N</i> (%)	6 (54)
Duration of oral antibiotic therapy	7–14 days
External cuff removal in resistant infection <i>N</i> (%)	6 (54)

The risk of peritonitis was increased by an advanced age (RR 1.73; $p < 0.01$, for patients aged over 60), the presence of diabetes mellitus (RR 1.36; $p < 0.05$), heart failure (RR = 1.96; $p < 0.01$), diverticula (RR 2.48; $p < 0.01$) and *S. aureus* carriage (RR 1.30; $p < 0.05$). Meanwhile, gender, the type of dialysis (CAPD – 0.31 episodes per year at risk vs. APD – 0.26 episodes per year at risk), fluids (icodextrin, biocompatible solutions) or assisted PD did not show significant associations with the risk of a peritonitis episode. In multiple regression analysis, only age, heart failure and diverticula remained as independent predictors of peritonitis.

In four cases (2.2%), peritonitis led to patient's death, in 22 (12.0%) transfer to haemodialysis was needed, the remainder (85.8%) was effectively treated.

Neither of the centres reported routine topical mupirocin on catheter exit-site. Nevertheless, the combined number of all ESI equalled 69, which resulted in an incidence of exit-site/tunnel infections to be only 1/121 months (0.1 episodes per year at risk). The most common pathogen responsible was methicillin-sensitive *S. aureus* (MSSA, 49% of cases), followed by *Pseudomonas aeruginosa* (15%) and methicillin-resistant *Staphylococcus epidermidis* (MRSE, 11%). Treatment included topical antibiotic (mupirocin or gentamycin) in six centres, and in case of exudate from exit-site, bacterial swab followed by empirical oral antibiotic in all

Table 7 The major pathogens responsible for peritonitis episodes (%)

Coagulase-negative <i>Staphylococci</i>	29.2
<i>S. aureus</i>	15.5
<i>Streptococci</i>	11.9
<i>Enterococci</i>	3.6
<i>Enterobacteriaceae</i>	10.1
Non-fermenting	5.4
Multiple pathogens	6.0
Negative culture	10.7
Other	7.6

centres. The median duration of therapy equalled 14 days, and resulted in full recovery in 78.3% of cases, with more than half of the centres performing external cuff removal in case of resistant infection.

Discussion

This is a multicentre retrospective study presenting data on PD centre policies towards prophylaxis and treatment of PD-associated infective complications, as well as on the epidemiology of peritonitis and ESI in a cohort of patients treated in 11 major PD units in Poland, over a 2 year period. It was conducted to evaluate how the current ISPD recommendations were followed, and what were the specific factors affecting outcomes of infective complications in this part of Europe.

According to the current recommendations of ISPD as of 2016 and 2017 on peritonitis and catheter-related infections, the overall peritonitis rate should not exceed 0.5 episodes per patient per year. While the studied population seemed typical in terms of age, dialysis vintage, primary diagnosis and co-morbidities, such as diabetes and heart failure, the incidence of peritonitis was low (0.29 episodes per year at risk). In addition, although there is no minimum target for the rate of ESI and tunnel infections, it appeared to be low as well (0.1 episodes per year at risk).

Numerous studies showed various modifiable and non-modifiable patient-related factors contributing to the risk of PD-associated peritonitis. In a study of Chow et al. [3], it was shown that age did not appear to be a risk factor for PD-related infections. In contrast, an early Italian and a more recent Brazilian study did document an age-related risk [4, 5]. This association is understandable, taking into account potentially impaired sight and manual precision of older patients, as well as their weakened immunological capacity. However, we believe that with an appropriate pre-dialysis assessment, meticulous training and, in particular cases, assisted treatment, the risk of PD-related infections associated with age can be

minimized. Nevertheless, in our study the risk of peritonitis was increased in patients over 60 years of age, and in multiple regression analysis, it remained as independent predictor of peritonitis.

Whereas the risk of infections associated with progressive age is likely true, relations between gender and peritonitis/ESI, documented by some authors, are much more difficult to explain [6]. In our study, gender did not show any associations with the risk of infections, similarly to the results from large national databases in the United States of America, Australia and New Zealand [7, 8].

Presence of co-morbidities, as diabetes mellitus, predisposes to infectious complications, mainly through impairing immunological defence capacity. This is currently well-acknowledged in the general population [9], and probably similarly holds true in PD patients [10, 11]. We also found that the risk of peritonitis was associated with the presence of diabetes mellitus (RR = 1.36), but this association did not remain as an independent factor in multiple regression analysis. In addition, we showed an increased independent risk of peritonitis in patients with heart failure (RR = 1.96), a finding previously demonstrated by other authors [7].

In the examined population, presence of intestinal diverticula was as independent predictor of peritonitis. There are inconsistent data on associations between diverticulosis and PD-related infections. It appears that while silent disease is not a contraindication for PD, repeated symptoms of diverticulitis might pose a risk for enteric peritonitis [12, 13].

One of the most critical factors for achieving peritonitis-free PD is appropriate training [14]. It appears that Polish PD centres are successful in following the ISPD guidelines from 2006 to 2011 related to patient training [15, 16]. All the centres had a planned and structured education programme which was performed on an in-hospital basis by the same nurse throughout the education time. There was a 1:1 nurse to patient ratio, time of training was individualized according to patient's needs, and at the end of the training, all the patients underwent a practical and a written test to assess patient's knowledge of PD theory and safety of performing exchanges. In addition, most centres provided retraining routinely every 6 months and all the patients were trained again after a peritonitis episode. This policy appears to be important in decreasing peritonitis rates, especially in view of studies of Dong et al. [17] demonstrating that after 6 months of PD treatment, nearly half of the patients does not wash their hands or check the bag for an expiry date or leaks, and 10% does not wear their cap or face mask. Although, in addition to appropriate training, home visits were reported to be important for the identification of problems and compliance, they are typically not performed in Poland due to logistic and financial reasons [18].

One of the strategies important for reducing infectious complications in PD is administering prophylactic antibiotics prior to catheter implantation. A systematic review of studies evaluating this issue was the basis for the ISPD recommendations to use antibiotic prophylaxis peri-operatively as a routine action [2, 19]. All the centres in the present study followed this recommendation administering cephalosporins routinely before the procedure.

Bacteriology of the PD-associated peritonitis was typical, with Gram positive cocci being most prevalent (more than 50%), similarly to results reported by others [20]. Polymicrobial episodes were less frequent in our study, in comparison to reports from large Australian and Canadian databases (6%, 11%, 15%, respectively) [21, 22]. There was no peritonitis of fungal aetiology among the reported episodes. In accordance with the ISPD 2016 recommendations, most centres monitored the incidence of peritonitis episodes on a yearly basis [1].

As well as the low incidence of peritonitis episodes, the study also showed excellent outcomes of treating this complication. This may be partly due to immediate patients' reaction, showing-up in the unit or adjacent ward once a cloudy dialysate was observed. Laboratory and microbiology diagnostic procedures were performed according to the recommendations, and the percentage of negative cultures was low. All patients with diagnosed peritonitis were hospitalized and treated with various antibiotic protocols. Most units transferred patients from APD to CAPD during the treatment which could also have impacted the outcome. On the other hand, most units did not provide an anti-fungal prophylaxis. Campbell et al. [23] also reported that this ISPD recommendation, which was based on two randomized controlled trials and a systematic review, has not been followed routinely. In fact, some observational studies showed no benefit associated with anti-fungal prophylaxis [24]. The potential side-effects, drug interactions and a very low incidence rate of fungal peritonitis in Poland were probably the main reasons for not following this guideline.

As far as the exit-site care was concerned, all the centres had written meticulous description of the dressing change procedure. *S. aureus* nasal carrier status was examined in most centres, and, when positive, treated with mupirocin according to a typical protocol. None of the PD units used mupirocin routinely on the exit -site. This deviation from the guidelines has also been reported in an Australia/New Zealand survey [23] and in the PDOPPS study [25]. In fact, a recent study on a topical use of mupirocin and chlorhexidine cream on the exit site did not show any significant differences in the ESI rates [26]. It has to be acknowledged that there is a lot of concern associated with applying antibiotic on a daily basis, as it might result in antibiotic resistance and breaching the host–microbe equilibrium. On the other hand, however, there are studies documenting decrease in both ESI

and peritonitis rates following routine use of mupirocin [27, 28].

The ESI were infrequent in the studied patients, with about half of the cultured strains being *S. aureus* and about 80% resulting in recovery. Ultrasound was used rarely but exudate was always cultured. More than half of the units used mupirocin on exit-site when redness and performed an external cuff removal in case of prolonged infection. Extensive analysis of exit-site care and anti-infection practices in Austrian PD centres revealed a greater variety in the strategies and a more frequent rate of infections [29].

It has been suggested that specific centre-level characteristics might be associated with the variation in the risk of infectious complications. French Language Peritoneal Registry study showed that presence of a trained PD nurse and home visits may decrease the risk of peritonitis [30]. On the other hand, retrospective data from Australia /New Zealand Registry revealed somewhat controversial centre-level predictors of lower peritonitis rates, like smaller centre size, while low or high use of anti-fungal prophylaxis at the time of peritonitis was associated with a higher peritonitis rate [31, 32]. PDOPPS is yet another initiative that aims at looking at centre and patient – specific effects of treatment across different countries [33]. In the present study, the centre-effect was not examined in details because of a relatively small number of participating units. There appeared to be no differences among centres in terms of the size, presence of a well-established PD programme and experience of the personnel. It has to be added that essentially, the training programme, exchange procedures, exit-site care policy were similar in all the centres. This is, most probably, due to the fact that almost all PD physicians and PD nurses are being trained in a sole country reference centre.

The limitations of the study include its retrospective character. The analysis of a 2 year quasi-registry data from large PD centres that have been willing to participate might, obviously, bias the obtained results. However, in the absence of a country registry, this was the only possibility to access the data. Overall, surveys on practice patterns may be of limited quality, but in this study, the questionnaires were filled either by the centre leading nephrologist or a PD head-nurse. The strength of the study is that in the presence of the recent PD infection guidelines, it shows how actually the recommendations are followed. Controversially, it appeared that although some guidelines were not strictly implemented, the outcomes were good. This may be due to the fact that other recommendations, which were thoroughly applied and followed across the centres, were of greater importance in achieving satisfying results. In addition, to our knowledge, this is the first multicentre study from a Central/Eastern European country that reports extensively on PD-related infections and centre strategies to decrease them.

In conclusion, the study shows rewarding outcomes in prevention and treatment of PD-associated infections, mainly due to a thorough compliance with the current ISPD guidelines, although some deviations from the recommendations in terms of practice patterns have been observed. More studies are needed in large numbers of patients across the world and various populations to differentiate the importance of specific recommendations and further support the guidelines.

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Compliance with ethical standards

Conflict of interest MLN, JMR, EG, BS, MG, PJ - Speaker's honoraria from Fresenius Medical Care, MLN, MC, BN, EG, BS, EW, ES, MG, RK - Speaker's honoraria from Baxter, BN, BS - Speaker's honoraria from MSD, BN - Speaker's honoraria from Amgen, JMR, BN, BS - Speaker's honoraria from Roche, BS - Speaker's honoraria from Servier, MLN, BN, JMR, EG, ES, BS, MG - Travel sponsorship from Fresenius Medical Care, BS - Travel sponsorship from Servier, MLN, PJ, BM, MA, KK, RK, KC - employees of Fresenius Nephrocare Dialysis Units, MB declares that he has no conflict of interest

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study contains retrospective observational data. For this type of study formal consent is not required. Protocol of the study received approval from the Local Bioethics Committee.

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