International Urology and Nephrology (2019) 51:723–727
https://doi.org/10.1007/s11255-019-02100-w

NEPHROLOGY - ORIGINAL PAPER

ISPD guideline-driven retraining, exit site care and decreased peritonitis: a single-center experience in Israel

Yael Einbinder[1,3] · Keren Cohen-Hagai[1,3] · Pnina Shitrit[2,3] · Tali Zitman-Gal[1,3] · Daniel Erez[1,3] · Sydney Benchetrit[1,3] · Ze'ev Korzets[1,3] · Andy Kotliroff[1,3]

Received: 16 August 2018 / Accepted: 8 February 2019 / Published online: 5 March 2019

Abstract

Purpose Evaluate the efficacy of retraining and catheter exit site care in reducing peritonitis rates.

Methods This interventional study included all prevalent PD patients from 1/2009 to 12/2017 from a single center. Peritonitis rates and causative organisms were assessed and compared in three periods: (1) Before intervention (01/2009–12/2014), (2) after educational intervention: assessment of training process by infection control nurse and repeat training every 3 months, after each peritonitis episode and after hospitalizations > 2 weeks (01/2015–02/2016), and (3) in addition to the measures in period 2, an exit site care protocol including postoperative care, topical antibacterial therapy and nasal Staph aureus screening and eradication was implemented (03/2016–12/2017).

Results The study included 201 patients (149 men, 52 women), mean age was 65.1 ± 12.6 years. After both interventions, including educational and exit site care strategies, peritonitis decreased significantly from 1.05 episodes per patient-year ($n = 113$) to 0.67 ($n = 54$); $P = 0.017$ between periods 1 and 3. The percentage of peritonitis-free patients increased from 27.4 to 52.4 and 55.6%, respectively ($P = 0.001$ between period 1 vs. 2 and period 1 vs. 3.). Coagulase-negative staph was the most common pathogen, causing 7.56 peritonitis episodes per year, followed by pseudomonas at 4.33 episodes annually and staph aureus at 3.44 episodes per year.

Conclusions Enforcement of an educational program and strict adherence to an exit site care protocol was associated with a significant decrease in peritonitis rates.

Keywords Peritonitis · Peritoneal dialysis · Exit site care · Education and training

Introduction

Over the last few years, the use of peritoneal dialysis (PD) for renal replacement therapy has increased [1]. Peritonitis remains a significant and serious complication of PD and is a major contributing cause of technical failure and permanent transfer to hemodialysis. Furthermore, 16% of deaths among PD patients are related to peritonitis [2, 3]. The risk of death due to infection, cardiovascular complications and dialysis withdrawal is significantly increased within the first month after a single peritonitis episode and remains elevated for up to 6 months [4].

According to the International Society for Peritoneal Dialysis (ISPD) guidelines, several measures are recommended to prevent peritonitis, including systemic prophylactic antibiotics prior to PD catheter insertion, daily application of topical antibiotics to the catheter exit site and a detailed training program [5, 6]. The ISPD guidelines recommend annual monitoring of peritonitis rates in each unit, with a goal of < 0.5 episodes per patient-year [6, 7]. However, large variations in peritonitis rates between countries and between centers within the same country have been documented, with rates as low as 0.196 episodes per patient-year and up to 1.66 episodes per year [8–11]. A recent study found wide variations in adherence to the guidelines [12]. A study in Australia and New Zealand demonstrated a clear

✉ Yael Einbinder
yael.einbinder@clalit.org.il

1 Department of Nephrology and Hypertension, Meir Medical Center, 44281 Kfar Saba, Israel

2 Infection Control Unit, Meir Medical Center, 44281 Kfar Saba, Israel

3 Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel

association between poorer outcomes and deviation from evidence-based recommendations [13].

Only two previous studies have reported peritonitis rates among PD patients in Israel. The first, published in 1989 included 51 patients in a single center with a rate of 1.7 peritonitis episodes per patient year [14]. The second study reported a rate of 1.66 peritonitis episodes per patient-year in a pediatric population [11, 14]. The present study monitored peritonitis rates in a single center in Israel for 8 years. After identifying higher rates than recommended, we report the results of stepwise interventions that were implemented in accordance with ISPD guidelines.

Methods

Patients

The study cohort included all patients who underwent chronic PD (including continuous ambulatory peritoneal dialysis (CAPD) and automated peritoneal dialysis (APD)) for > 3 months in our unit from 01/2009 through 12/2017. The study period was divided into three intervals. Period 1, before the intervention, included 72 months from 01/2009 through 12/2014 and served as the baseline. Period 2, 14 months from 01/2015 through 02/2016 involved an enhanced educational effort consisting of assessment of the ongoing training program by a nurse from the Infectious Disease Unit and correction of faults, as well as patients retraining every 3 months, after each peritonitis episode and after a period of prolonged hospitalization (> 2 weeks). Retraining in all circumstances was uniformly carried out by a dedicated PD nurse and consisted of the following: (i) observance of a dialysis exchange as regularly performed by the person responsible, either the patient, appointed care giver or family member (ii) any inaccuracies found corrected (iii) repeat observance of procedure on a consecutive visit. Period 3 consisted of 22 months from 03/2016 through 12/2017. In addition to the measures practiced in period 2, it was supplemented by strict adherence to exit site care, including: (i) twice weekly postoperative dressing changes performed by the dialysis unit nurse, (ii) daily application of topical gentamycin or mupirocin ointment to the exit site, and (iii) screening for nasal staph aureus colonization at the time of catheter implantation and if positive, eradication with nasal mupirocin as previously recommended [15]. Exit site infection (ESI) was defined as per ISPD guidelines that is, either the presence of a purulent discharge with or without erythema of the surrounding skin or in the absence of a purulent discharge, peri exit site erythema exceeding 1 cm in diameter with localized tenderness and warmth. During period 1, data regarding isolated ESI was unavailable and only ESI concomitant with peritonitis was recorded. Thereafter, during periods 2 and 3, both isolated ESI and that associated with peritonitis were recorded.

Peritonitis was diagnosed when two of the following three criteria were present: (i) Clinical findings consistent with peritonitis, (ii) Dialysis effluent with white cell count of > 100/µl (after a dwell time of > 2 h) with > 50% PMN and (iii) Positive effluent culture. All peritonitis episodes were recorded, including the causative organism and exit site involvement (defined as either concomitant or present up to 1 month prior to peritonitis). Relapsing peritonitis was counted as a single episode.

Statistical analysis

Data are described as mean ± standard deviation for continuous parameters and as numbers and percentage for discrete variables. Peritonitis rates were compared between groups using Chi-Square and Bonferroni Correction or Ratio Test for non-metric data. $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS-25 (IBM, Armonk, NY, USA).

Results

A total of 201 patients (149 men and 52 women) at a mean age (65.1 ± 12.6 years) were included in the study. The mean duration of PD was 14.7 ± 11.5 months (range 3 to 66 months). Demographic data are provided in Table 1. No significant difference was found in patient characteristics between the three periods. Fourteen of 201 (7%) patients were included in all three study periods, 9 out of 142 (6.3%) were included in periods 1 and 2 and 13 of 96 (13.5%) were included in periods 2 and 3. Analyzing the data with or without these patients showed no statistical differences.

Peritonitis rate decreased from 1.05 episodes per patient-year in period 1 to 0.85 and 0.67 in periods 2 and 3, respectively ($P = 0.297$ between period 1 versus 2,

Table 1 Patient characteristics ($N = 201$)

Variable	Value
Sex (M/F)	149/52
Age (years)	65.07 ± 12.6
BMI (kg/m^2)	27.9 ± 4.6
Mean duration of PD (months)	14.7 ± 11.5
Comorbidities: *n* (%)	
Diabetes mellitus	102 (50.7)
Hypertension	145 (72.2)
Ischemic heart disease	98 (48.8)
Congestive heart failure	80 (39.8)
Post CVA/TIA	44 (21.9)

$P = 0.017$ between period 1 vs. 3, and $P = 0.355$ between period 2 vs. 3) (Table 2). The percentage of peritonitis-free patients increased from 27.4% (31/113) in period 1 to 52.4% (22/42) and 55.6% (30/54) in periods 2 and 3, respectively ($P = 0.001$ between period 1 vs. 2 and period 1 vs.3, and $P = 0.757$ between period 2 vs. 3). The percentage of patients with more than 1 peritonitis episode was 46% (52/113) in period 1, decreased to 12% (5/42) and 11% (6/54) in periods 2 and 3, respectively ($P < 0.0001$, period 1 vs. 2 and 1 vs. 3, $P = 1.0$, between period 2 vs. 3). Peritonitis rates were not associated with age, diabetes or BMI.

The microbiologic profile is presented in Fig. 1. A total of 244 peritonitis episodes were documented during the study period. *Staph coagulase negative* (SCN) was the most common pathogen, accounting for 68 peritonitis episodes, 7.56 episodes per year during the study period (7.33, 6 and 9.27 episodes per year in periods 1, 2 and 3, respectively; not statistically significant). *Pseudomonas aeruginosa* was the second most common pathogen, with a total of 39 peritonitis episodes, 4.33 episodes per year (4.67, 6 and 2.18 episodes per year in period 1, 2 and 3, respectively, not statistically significant). This was followed by *Staphylococcus aureus* (SA) with a total of 31 peritonitis episodes, 3.44 episodes per year (3.67, 4.29 and 2.18 episodes per year in periods 1, 2 and 3, respectively; not statistically significant). There were 44 peritonitis episodes (4.4 episodes per year) with other gram-negative bacteria (*Serratia, Neisseria, Citrobacter, Klebsiella, Escherichia coli, Acinetobacter, Enterobacter*

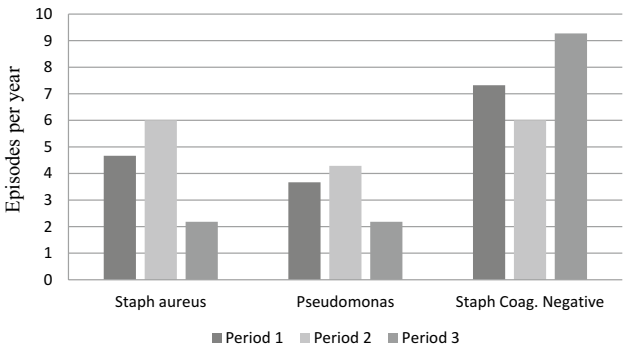

Fig. 1 Microbiologic profile of peritonitis rate (episodes per year) according to three study periods. The prevalence of peritonitis events according to the different pathogens is presented. Difference between the three study periods did not reach statistical significance

and *Morganella*) and 22 peritonitis episodes (2.75 episodes per year) with gram-positive bacteria (Strep sp. *Enterococcus* and *Corynebacterium*). Fungal peritonitis occurred in only five cases (0.625 episodes per year). Of these, four were seen in period 1 and one in period 2. Antifungal prophylaxis was not practiced in our unit during the entire study period. Culture negative peritonitis declined over the study period from 29/183 (15.8%) in period 1 to 2/28 (7%) and 0/33 in periods 2 and 3, respectively ($P = 0.226$ between period 1 vs. 2, $P = 0.014$ between period 1 vs. 3, and $P = 0.118$ between period 2 vs. 3). Peritonitis with documented exit

Table 2 Peritonitis episodes before and after interventions

Variable	Before intervention (Period 1)	After educational intervention (Period 2)	After exit site care intervention (Period 3)	*P* value
Number of patients	113	42	54	
Mean PD months	18.5 ± 13.6	9.4 ± 4.25	10.9 ± 6.5	
Total peritonitis episodes	183	28	33	
Peritonitis rate (episodes/patient-year)	1.05	0.85	0.67	0.297*
				0.017**
				0.355***
Peritonitis-free patients, *n* (%)	31/113 (27.4)	22/42 (52.4)	30/54 (55.6)	0.001*
				< 0.001**
				0.757***
Patients with > 1 peritonitis episode, *n* (%)	52/113 (46)	5/42 (12)	8/54 (11)	< 0.001*
				< 0.001**
				0.99***
Peritonitis with exit site infection, *n* (%)	58/183 (31.7)	17/28 (60.7)	8/33 (25)	0.152*
				0.035**
				0.004***

*Statistical significance between periods 1 and 2, before and after the first intervention

**Statistical significance between periods 1 and 3, before and after the second intervention

***Statistical significance between periods 2 and 3, after the first and second interventions

site infection (ESI) occurred in 58/183 (31.7%) in period 1, 17/28 (60.7%) in period 2 and 8/33 (25%) in period 3 ($P=0.152$ between period 1 vs. 2, $P=0.035$ between period 1 vs. 3, and $P=0.004$ between period 2 vs. 3).

Discussion

Peritonitis represents a major complication of PD, limiting both its utilization and retention as renal replacement therapy. In a survey of Australian pre-dialysis patients, up to 60% were concerned or very concerned about the possibility of PD-related peritonitis [16]. ISPD guidelines for prevention of peritonitis outline the following measures: systemic prophylactic antibiotics prior to catheter insertion (evidence 1A), "Flush before fill" methodology (evidence 1A), dedicated training program for patients and their caregivers (1C), daily application of topical antibiotics to the exit site (evidence 1A), and prompt treatment for ESI (evidence 1C) [6, 7]. However, recent data have demonstrated that adherence to these recommendations varies greatly between centers, resulting in a significant effect on peritonitis rates and patient outcomes [12, 13]. In our PD unit, evidence 1A measures were meticulously practiced except for topical antimicrobial application to the exit site. Of note, this latter recommendation was only upgraded from evidence 1C to 1A in 2017 [7]. Patient training was carried out by an experienced PD nurse for 4 days on average, including a home visit prior to treatment initiation. Despite this, the peritonitis rate (1.05 episodes/patient-year in period 1) was significantly higher than the ISPD guidelines target of <0.5 episodes/patient-year [6]. This led us to reevaluate all aspects of our PD program, focusing on strategies to decrease the peritonitis rate. The high rate of peritonitis in period 1 was due to an increased number of recurrent or repeated peritonitis cases, 46% of patients with more than 1 episode, and a relatively small percentage of peritonitis-free patients (27.4%). We, therefore, initially focused on educational interventions. Unfortunately, a high level of evidence regarding the preferred training method (how, where, when and by whom) is lacking. Our teaching program was in concordance with ISPD guidelines [17]. It was conducted by a dedicated PD nurse, lasted on average for 4 days and included a home visit prior to start of therapy. However, retraining after each peritonitis episode, as well as periodic retraining were not done routinely. Two small, uncontrolled studies have demonstrated the importance of retraining in reducing peritonitis [18, 19]. In conjunction with the Infection Control Unit, our educational intervention measures included assessing the techniques of the ongoing training program, retraining after each peritonitis episode, after hospitalizations longer than 2 weeks, and routinely every 3 months at the unit or at the patient's home. After implementing the enhanced educational efforts, the peritonitis rate decreased to 0.85 episodes/patient-year (period 2). The percentage of peritonitis-free patients increased and occurrence of more than a single peritonitis episode declined, both reaching statistical significance. However, during period 2, we still noted several peritonitis episodes with simultaneous ESI, 31.7% and 60.7% in periods 1 and 2, respectively. The increased rate of coincident peritonitis and ESI during period 2 is probably due to the lack of uniform exit site care practiced in this period. This resulted in a higher rate of SA and Pseudomonas peritonitis, both highly correlated with ESI. In period 3, therefore, attention was directed at exit site care. Early, post-operative exit site care instructions are mainly opinion based and vary greatly between centers [20, 21]. Dressing changes are suggested from 1 to 7 days after implantation. Directions regarding exposing the exit site to water are also vague and not clearly addressed by the guidelines. The only firm recommendation of the ISPD guidelines is daily administration of topical antibacterial ointment to the catheter exit site [5–7].

Screening for nasal SA carriage is graded as 2D recommendation, but once identified eradication with topical nasal mupirocin is strongly recommended (1B) [5, 7]. With strict adherence to the exit site care protocol as detailed before, the peritonitis rate in period 3 further decreased to 0.67 episodes/patient-year. Peritonitis with simultaneous ESI improved significantly.

It might be expected that nasal screening and eradication of SA, as well as improvement of exit site care would lead to a reduction of SA and pseudomonas peritonitis, which typically invade the peritoneum following ES contamination [22–25]. Although, increased rate of Pseudomonas peritonitis has been reported with chronic usage of Mupirocin ointment at the exit site, our data show a trend toward a decrease in SA and Pseudomonas peritonitis between periods 2 and 3. These trends did not, however, reach statistical significance most likely due to the small number of peritonitis episodes involving these pathogens in periods 2 and 3. Mupiracin, in contrast to Gentamycin is not an anti-pseudomonal agent. We have no data as to which ointment was preferentially used in period 3. Thus, contrary to the reported literature, our results of a trend toward a decrease in Pseudomonas peritonitis may be an artifact or perhaps due to the use of Gentamycin rather than Mupiracin at the exit site. There was a trend toward a decrease in SA peritonitis between periods 2 and 3 ($P=0.09$). However, this did not reach statistical significance, most likely because few peritonitis events involved these pathogens in periods 2 and 3.

Although the final peritonitis rate achieved was still higher than that targeted by the ISPD, we are confident that with time it will decline further. It should be borne in mind that other factors such as climate [26], obesity [27, 28], and health system resources (such as assisted peritoneal dialysis)

[29, 30] could impact peritonitis rates in different countries. Tropical climates are associated with higher rates of peritonitis and shorter time to first peritonitis episode [26]. Israel has a humid, sub-tropical climate, which might contribute to higher peritonitis rates. Unfortunately, methods of data collection did not allow us to monitor seasonal variations in peritonitis episodes to support this theory.

The current study emphasizes the importance of retraining, as well as close attention to the exit site care postoperatively, followed by daily application of topical antibacterial cream as per ISPD guidelines to prevent PD-related peritonitis. The study reinforces this practice and demonstrates the importance of each of these factors to achieve a decline in peritonitis.

Compliance with ethical standards

Conflict of interest No conflict exists.

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.

References

1. Mehrotra R, Devuyst O, Davies SJ, Johnson DW (2016) The current state of peritoneal dialysis. J Am Soc Nephrol 27:3238–3252
2. Johnson DW, Dent H, Hawley CM et al (2009) Associations of dialysis modality and infectious mortality in incident dialysis patients in Australia and New Zealand. Am J Kidney Dis 53:290–297
3. Cho Y, Johnson DW (2014) Peritoneal dialysis-related peritonitis: towards improving evidence, practices, and outcomes. Am J Kidney Dis 64:278–289
4. Boudville N, Kemp A, Clayton P et al (2012) Recent peritonitis associates with mortality among patients treated with peritoneal dialysis. J Am Soc Nephrol 23:1398–1405
5. Segal JH, Messana JM (2013) Prevention of peritonitis in peritoneal dialysis. Semin Dial 26:494–502
6. Li PK, Szeto CC, Piraino B et al (2016) ISPD Peritonitis Recommendations: 2016 Update on Prevention and Treatment. Perit Dial Int 36:481–508
7. Szeto CC, Li PK, Johnson DW et al (2017) ISPD catheter-related infection recommendations: 2017 update. Perit Dial Int 37:141–154
8. Hsieh YP, Chang CC, Wen YK, Chiu PF, Yang Y (2014) Predictors of peritonitis and the impact of peritonitis on clinical outcomes of continuous ambulatory peritoneal dialysis patients in Taiwan—10 years' experience in a single center. Perit Dial Int 34:85–94
9. Piraino B, Bernardini J, Brown E et al (2011) ISPD position statement on reducing the risks of peritoneal dialysis-related infections. Perit Dial Int 31:614–630
10. Nessim SJ, Bargman JM, Austin PC, Nisenbaum R, Jassal SV (2009) Predictors of peritonitis in patients on peritoneal dialysis: results of a large, prospective Canadian database. Clin J Am Soc Nephrol 4:1195–1200
11. Cleper R, Davidovits M, Kovalski Y, Samsonov D, Amir J, Krause I (2010) Peritonitis in a pediatric dialysis unit: local profile and implications. Isr Med Assoc J 12:348–352
12. Lanot A, Bechade C, Verger C, Fabre E, Vernier I, Lobbedez T (2017) Clusters of practice in peritoneal dialysis in France: data from the catheter section of the Rdplf. Perit Dial Int 38:89–97
13. Nadeau-Fredette AC, Johnson DW, Hawley CM et al (2016) Center-specific factors associated with peritonitis risk-a multi-center registry analysis. Perit Dial Int 36:509–518
14. Benjamin J, Ben-Ezer Gradus D, Mostoslavski M, Rapoport J, Chaimovitz C (1989) Peritonitis in continuous ambulatory peritoneal dialysis patients in southern Israel. Isr J Med Sci 25:699–702
15. Bending M, Mellotte G (1996) Nasal mupirocin prevents *Staphylococcus aureus* exit-site infection during peritoneal dialysis. Mupirocin Study Group. J Am Soc Nephrol 7: 2403–2408
16. Morton RL, Snelling P, Webster AC et al (2012) Dialysis modality preference of patients with CKD and family caregivers: a discrete-choice study. Am J Kidney Dis 60:102–111
17. Figueiredo AE, Bernardini J, Bowes E et al (2016) A syllabus for teaching peritoneal dialysis to patients and caregivers. Perit Dial Int 36:592–605
18. Russo R, Manili L, Tiraboschi G et al (2006) Patient re-training in peritoneal dialysis: why and when it is needed. Kidney Int 70:S127–132
19. Bordin G, Casati M, Sicolo N, Zuccherato N, Eduati V (2007) Patient education in peritoneal dialysis: an observational study in Italy. J Ren Care 33:165–171
20. Bender FH, Bernardini J, Piraino B (2006) Prevention of infectious complications in peritoneal dialysis: best demonstrated practices. Kidney Int 70:44–54
21. Kopriva-Altfahrt G, Konig P, Mundle M et al (2009) Exit-site care in Austrian peritoneal dialysis centers—a nationwide survey. Perit Dial Int 29:330–339
22. Szeto CC, Chow KM, Kwan BC et al (2007) Staphylococcus aureus peritonitis complicates peritoneal dialysis: review of 245 consecutive cases. Clin J Am Soc Nephrol 2:245–251
23. Govindarajulu S, Hawley CM, McDonald SP et al (2010) Staphylococcus aureus peritonitis in Australian peritoneal dialysis patients: predictors, treatment, and outcomes in 503 cases. Perit Dial Int 30:311–319
24. Siva B, Hawley CM, McDonald SP et al (2009) Pseudomonas peritonitis in Australia: predictors, treatment, and outcomes in 191 cases. Clin J Am Soc Nephrol 4:957–964
25. Mehrotra R, Singh H (2013) Peritoneal dialysis-associated peritonitis with simultaneous exit-site infection. Clin J Am Soc Nephrol 8:126–129 discussion 129–130
26. Cho Y, Badve SV, Hawley CM et al (2013) Effects of climatic region on peritonitis risk, microbiology, treatment, and outcomes: a multicenter registry study. Perit Dial Int 33:75–85
27. Lim WH, Johnson DW, McDonald SP (2005) Higher rate and earlier peritonitis in Aboriginal patients compared to non-Aboriginal patients with end-stage renal failure maintained on peritoneal dialysis in Australia: analysis of ANZDATA. Nephrology (Carlton) 10:192–197
28. McDonald SP, Collins JF, Rumpsfeld M, Johnson DW (2004) Obesity is a risk factor for peritonitis in the Australian and New Zealand peritoneal dialysis patient populations. Perit Dial Int 24:340–346
29. Benabed A, Bechade C, Ficheux M, Verger C, Lobbedez T (2016) Effect of assistance on peritonitis risk in diabetic patients treated by peritoneal dialysis: report from the French Language Peritoneal Dialysis Registry. Nephrol Dial Transplant 31:656–662
30. Bevilacqua MU, Turnbull L, Saunders S et al (2017) Evaluation of a 12-month pilot of long-term and temporary assisted peritoneal dialysis. Perit Dial Int 37:307–313