

The Changing Profile of PD-Related Peritonitis in Thailand: A Single Center's Experience

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Objective: The percentage of utilizing peritoneal dialysis (PD) in Thailand was increased dramatically since the implementation of PD-First policy in 2008. However, peritonitis remains a major obstacle to achieve success of this modality. The aim of the present study, was to assess the clinical characteristics of PD peritonitis in the PD-first policy era.

Material and Method: The PD peritonitis patients in Bhumibol Adulyadej Hospital between October 2008 and December 2010 were reviewed. Microbiological diagnosis, treatment responses, technique, and patient survival were analyzed.

Results: Since October 2008, 93 peritoneal dialysis patients were followed-up in Bhumibol Adulyadej Hospital including 75 new cases. During the present study period of 1,560 patient-months, 51 episodes of peritonitis from 33 cases were recorded and analyzed. The mean age of the peritonitis patients was 57.9 ± 16.1 years and 63.6% were females. The most common isolates were gram negative organisms (33.3%) followed by gram positive (17.6%) and fungi (5.9%). Nocardiosis was diagnosed in 1 patient. However, 43.1% of episodes were culture-negative peritonitis. Treatment of peritonitis resulted in a complete cure in 74.5% of patients while 7.8% of patients required catheter removal, and 17.6% died. Event-free survival was better in gram positive organisms (43.3 months) compared with those infected with gram negative (26.8 months) and culture negative peritonitis (16.1 months).

Conclusion: The proportions of peritonitis due to gram negative organisms were increased and associated with less favorable outcome. These findings suggest that it is necessary to prepare the appropriate protocol for prevention and treatment of PD peritonitis under national PD-First policy scheme.

Keywords: Peritonitis, CAPD, Gram negative organisms, PD-First policy.

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Peritonitis is not only a common complication of continuous ambulatory peritoneal dialysis (CAPD) but also a cause of technical failure and patient mortality⁽¹⁻³⁾. Although the improvement in PD systems, especially the disconnected technique, has significantly reduced the overall incidence of peritonitis since 1990⁽⁴⁻¹⁰⁾, it has been shown that the microbiological trends have changed in the past few years with an increased proportion of gram-negative peritonitis^(4,10-12). The changes in character of causative organisms have a great impact upon clinical outcome

such as catheter removal and death^(4,11,13). In Thailand, PD-First policy scheme was introduced in October 2008 and CAPD became the fastest growing mode of renal replacement therapy (RRT) among people under universal coverage (UC) health care⁽¹⁵⁾. Nowadays, there are at least 111 hospitals around the country providing more than 11,000 CAPD cases under this scheme. However, it has been shown from registry data that the outcome of these patients remains less favorable with a first-year drop-out rate of 26.33%⁽¹⁶⁾. Further analysis demonstrated the high rate of peritonitis with mean peritonitis-free time of 23.2 months that could have been a major obstacle for achieving success of CAPD in Thailand⁽¹⁶⁾.

Although some publications have addressed the epidemiology of CAPD peritonitis in Thailand⁽¹⁷⁾, there is still no study about clinical characteristics and

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outcome of these patients after the initiation of PD-First policy scheme. The aim of the present study was to examine microbiological trends and clinical outcomes of PD patients in our hospital during the past 2 years. The results from the present study could provide us with a strategy to improve the authors PD patient outcomes.

Material and Method

Patient selection

From October 1, 2008 to December 31, 2010, 93 patients treated with PD were followed-up at PD clinic in Bhumibol Adulyadej hospital, Bangkok. All of the episodes of PD peritonitis were collected by reviewing the database and hospital records of individual patient by the investigators. The diagnosis of PD peritonitis was based on at least two of the following criteria: (1) presence of clinical symptoms (abdominal pain, fever or cloudy dialysate); (2) presence of leukocytosis (more than 100 leukocytes/mm³) in dialysate, with at least 50% neutrophils; and (3) positive gram stain or culture from dialysate. The episodes of peritonitis within 4 weeks after the previous treatment and episodes of peritonitis within 7 days after catheter placement were excluded.

The peritonitis rate was reported as one episode per number of patient-months of follow-up. The demographic characteristics, causative organisms, pattern of antimicrobial susceptibility, and clinical outcomes (initial cure, catheter removal or death) were analyzed.

Microbiological investigation

Culture of the dialysate has been performed by inoculating 10 ml of dialysate into blood culture media and was changed to concentration method as recommended by the ISPD since June 2010⁽¹⁸⁾. Whole dialysate (50 ml) was concentrated by centrifugation, resuspended in sterile saline, inoculated into blood culture media, and observed for at least 72 hours to document pathogens. Antimicrobial susceptibility was determined by standard disk-diffusion method.

In the present study, the causative organisms were categorized as gram-positive organisms (*Staphylococcus coagulase* positive, *Staphylococcus coagulase* negative, *Streptococcus* and *Enterococcus*), gram-negative organisms (*Escherichia coli*, *Klebsiella spp.*, *Pseudomonas aeruginosa*, other *Pseudomonas spp.*, *Acinetobacter baumannii*, and other gram-negative organism), fungi, *Nocardia spp.*, and culture negative.

Clinical management protocol

When PD peritonitis was diagnosed, the empirical therapy with a combination of cefazolin and ceftazidime (or gentamicin) was initiated by intraperitoneal route. Within 72 hours, the antibiotics were adjusted based on the antimicrobial susceptibility test. In culture-negative peritonitis with clinical improvement, cefazolin was continued to 14 days. The catheter was removed in case of peritonitis with no response to appropriate therapy after 96 hours, fungal peritonitis, and tuberculous peritonitis.

Statistical analysis

Categorical data were summarized using frequency and percentages while continuous data were summarized using mean $\pm$ standard deviations (SD). Peritonitis rate were expressed as one episode per number of patient-months of follow-up. Chi-square tests were used to compare the outcomes (catheter removal rate and death) according to the pathogens. Patient survival analysis was analyzed by using Log Rank test and is presented by a Kaplan Meier curve. Statistical significance was determined as p-value less than 0.05.

Results

From October 1, 2008 to December 31, 2010, 51 PD-related peritonitis episodes were occurred in 33 patients. The overall peritonitis rate was one episode per 30.6 patient-months follow-up.

The demographic data and baseline characteristics were summarized in Table 1. Of 93 patients, 17 patients (18.3%) were using automated peritoneal dialysis (APD). The mean age at the first PD-related peritonitis was 57.9 ± 16.1 years and the mean time to first peritonitis episode was 15.2 ± 21.1 months. When compared between patients with and without peritonitis, there were no significant differences in the baseline characteristics between groups, except the mean duration of dialysis was higher in the PD-related peritonitis group ($p = 0.037$).

Causative organism

The causative organisms of the PD-related peritonitis were illustrated in Table 2. The most common organisms were gram-negative organisms (33.3%) while gram-positive organisms, fungi and, *Nocardia spp.* comprised 17.6, 5.9, and 2.0% respectively. The culture-negative peritonitis accounted for 41.2% of total episodes.

Among gram-negative peritonitis, *Enterobac-*

Table 1. Baseline characteristics of study patients

Baseline characteristics	Patient without peritonitis (n = 60)	Patient with peritonitis (n = 33)	p-value
Age (yr)	60.8 ± 13.6	57.9 ± 16.1	0.381
Female n (%)	36 (60.0)	21 (63.6)	0.525
Reimbursement schemes			0.127
Universal coverage	39 (65.0)	18 (54.5)	
Health care official	21 (35.0)	13 (39.4)	
Social security	0	2 (6.1)	
Duration of dialysis (months)	13.7 ± 15.7	22.3 ± 19.9	0.037*
Mode of dialysis			0.254
APD	13 (21.7)	4 (12.1)	
CAPD	47 (78.3)	29 (87.9)	

Abbreviations: APD, automated peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis

Table 2. Causative organism in 51 episodes of peritonitis

Organisms (n = 51)	n (%)
Gram positive (n = 9)	
<i>Staphylococcus coagulase</i> negative	3 (5.9)
<i>Staphylococcus coagulase</i> positive	2 (3.9)
<i>Streptococcus mitis</i>	1 (2.0)
<i>Streptococcus gallolyticus</i>	2 (3.9)
<i>Enterococcus faecium</i>	1 (2.0)
Gram negative (n = 17)	
<i>Escherichia coli</i>	4 (7.8)
<i>Escherichia coli</i> (ESBL)	2 (3.9)
<i>Klebsiella pneumoniae</i>	2 (3.9)
<i>Enterobacter cloacae</i>	1 (2.0)
<i>Acinetobacter baumannii</i>	1 (2.0)
<i>Aeromonas hydrophila</i>	1 (2.0)
<i>Pseudomonas aeruginosa</i>	2 (3.9)
<i>Pseudomonas stutzeri</i>	2 (3.9)
<i>Stenotrophomonas maltophilia</i>	1 (2.0)
<i>Brevundimonas diminuta</i>	1 (2.0)
Fungi (n = 3)	
<i>Candida parapsilosis</i>	1 (2.0)
<i>Candida tropicalis</i>	2 (3.9)
Nocardia spp.	1 (2.0)
No growth	21 (41.2)

terraceae and non-*Enterobacteriaceae* accounted for 17.6% and 15.7% of total peritonitis, respectively. *Escherichia coli* was the most common causative organism in *Enterobacteriaceae* peritonitis (35.3% of gram-negative peritonitis) while *Pseudomonas aeruginosa* and *Pseudomonas stutzeri* were the common pathogens in non-*Enterobacteriaceae* peritonitis (each 11.7% of gram-negative peritonitis)

Regarding gram-positive peritonitis, *coagulase negative staphylococcus* was the most

common followed by *coagulase positive staphylococcus* and *Streptococcus gallolyticus* (5.9%, 3.9% and 3.9% of total peritonitis, respectively).

Treatment outcomes

Organism-specific outcomes were shown in Table 3. The overall proportions of initial cure rate, catheter removal rate, and death rate were 74.5%, 7.8% and 17.6%, respectively. The initial cure rate in gram-positive peritonitis was better than gram-negative peritonitis and culture-negative peritonitis (88.9% vs. 70.6% vs. 85.7%). Catheter removal was noted in 1 patient with *Escherichia coli* (ESBL), 1 patient with *Candida parapsilosis* and 1 patient with culture-negative peritonitis. The death rate was slightly, but not significantly ($p = 0.45$), higher in gram-negative peritonitis (23.5%) compared with gram-positive peritonitis (11.1%).

Among gram-negative peritonitis, there were no significant differences in organ-specific outcomes but the death rate in *Enterobacteriaceae* group was higher than non-*Enterobacteriaceae* group (33.3% vs. 12.5%). Regarding gram-positive peritonitis, there were also no significant differences in organ-specific outcomes. One case of PD-peritonitis associated with *Enterococcus faecium* was dead in the present study.

Antimicrobial susceptibility

The sensitivity rate of gram-negative organisms to ceftazidime and gentamicin were 82.4% and 100% respectively (Table 4). All of those were susceptible to ciprofloxacin. *Escherichia coli* (ESBL) resisted ceftazidime and gentamicin, but sensed to meropenem. For gram-positive peritonitis, 80% of *Staphylococcal* peritonitis was susceptible to

Table 3. Organism-specific outcomes in PD-related peritonitis patients

Organisms	Treatment outcome			p-value
	Initial cure n (%)	Catheter removal n (%)	Death n (%)	
All episodes	38 (74.5)	3 (5.9)	9 (17.6)	
Gram positive (n = 9)	8 (88.9)	-	1 (11.1)	
<i>Staphylococcus coagulase</i> negative	3 (100.0)	-	-	
<i>Staphylococcus coagulase</i> positive	2 (100.0)	-	-	
<i>Streptococcus mitis</i>	1 (100.0)	-	-	0.061
<i>Streptococcus gallolyticus</i>	2 (100.0)	-	-	
<i>Enterococcus faecium</i>	-	-	1 (100.0)	
Gram negative (n = 17)	12 (70.6)	1 (5.9)	4 (23.5)	
<i>Escherichia coli</i>	4 (100.0)	-	-	
<i>Escherichia coli</i> (ESBL)	-	1 (50)	1 (50.0)	
<i>Klebsiella pneumoniae</i>	-	-	2 (100.0)	
<i>Enterobacter cloacae</i>	1 (100.0)	-	-	
<i>Acinetobacter baumannii</i>	1 (100.0)	-	-	0.549
<i>Aeromonas hydrophila</i>	1 (100.0)	-	-	
<i>Pseudomonas aeruginosa</i>	2 (100.0)	-	-	
<i>Pseudomonas stutzeri</i>	1 (50.0)	-	1 (50.0)	
<i>Stenotrophomonas maltophilia</i>	1 (100.0)	-	-	
<i>Brevundimonas diminuta</i>	1 (100.0)	-	-	
Fungi (n = 2)	-	1 (33.3)	2 (67.7)	
<i>Candida parapsilosis</i>	-	1 (100.0)	-	0.083
<i>Candida tropicalis</i>	-	-	2 (100.0)	
Nocardia (n = 1)	-	-	1 (100.0)	
No growth (n = 21)	18 (85.7)	1 (4.8)	2 (9.5)	

cefazolin. The sensitivity rate to ciprofloxacin was 77.8% (Table 5). *Enterococcus faecium*-related peritonitis resisted to amoxicillin-clavulanic acid and ciprofloxacin, but was susceptible to vancomycin.

Survival analysis

The survival data included patients who initiated PD after October 1, 2008. Patient survival analysis was analyzed by using Log Rank test and is presented by a Kaplan Meier curve. Events were defined either patients died or transferred to hemodialysis. Unit of time was reported in months with standard error (SE). There were no significant differences in survival between patients with and without peritonitis. When explored to the micro-organisms, However, patients who had culture-negative peritonitis has worst outcome with a mean event-free survival of 16.1 months (SE 3.0) followed by gram negative (26.8 months, SE 7.4) and fungus (32.3 months, SE 13.6). Patients who had peritonitis caused by gram positive had longest event-free survival of 43.3 months (SE 14.6) (Fig. 1).

Discussion

Although the overall PD peritonitis rate decreased significantly during the last 20 years, several studies have shown that the incidence of gram-negative peritonitis remained constant^(4,11,12). The benefit of disconnected, double bag system is limited to peritonitis caused by single gram-positive organisms such as *staphylococcus coagulase* negative, the major organism responsible for touch contamination. Gram negative organisms, However, are associated more with patient co-morbidities (*i.e.*, age, diabetes, and malnutrition). Similar to previous studies, the present study showed a high proportion of gram negative as a cause of PD peritonitis during the past 2 years in Bhumibol Adulyadej Hospital. This should underscore the importance of gram negative peritonitis in the PD First policy era because it is associated with decreased technique and patient survival.

The overall peritonitis rate in Bhumibol Adulyadej Hospital was lower than the national average with a mean peritonitis-free time of 30.8 months. Furthermore, when compared with previous

Table 4. Antimicrobial susceptibilities for gram negative microorganisms

Organisms	Isolate (n)	Susceptibility (%)											
		Ceftazidime			Gentamicin			Ciprofloxacin			Cefoperazone/Sulbactam		
		S	R	S	S	R	S	S	R	S	R	S	R
<i>Escherichia coli</i>	4	100.0			100.0			100.0				100.0	
<i>Escherichia coli (ESBL)</i>	2		100.0					100.0			100.0	100.0	
<i>Klebsiella pneumoniae</i>	2	100.0			100.0			100.0			100.0		
<i>Enterobacter cloacae</i>	1	100.0			100.0			100.0			100.0		
<i>Acinetobacter baumannii</i>	1	100.0			100.0			100.0			100.0		
<i>Aeromonas hydrophila</i>	1	100.0			100.0			100.0			100.0		
<i>Pseudomonas aeruginosa</i>	2	100.0			100.0			100.0			50.0	100.0	
<i>Pseudomonas stutzeri</i>	2	100.0			100.0			100.0				100.0	
<i>Stenotrophomonas maltophilia</i>	1		100.0					100.0				100.0	
<i>Brevundimonas diminuta</i>	1	100.0			100.0			100.0			100.0		

Table 5. Antimicrobial susceptibilities for gram positive microorganisms

Organisms	Isolate (n)	Susceptibility (%)											
		Cefazolin			Ampicillin			Amoxicillin/Clavulanic acid			Ciprofloxacin		
		S	R	S	S	R	S	S	R	S	R	S	R
<i>Coagulase negative staphylococcus</i>	3	66.7	33.3			100.0		33.3	66.7	66.7	33.3	66.7	33.3
<i>Coagulase positive staphylococcus</i>	2	100.0						100.0				100.0	
<i>Streptococcus mitis</i>	1			100.0								100.0	
<i>Streptococcus gallolyticus</i>	2			100.0				50.0	50.0	100.0			
<i>Enterococcus faecium</i>	1							100.0	100.0	100.0	100.0		100.0

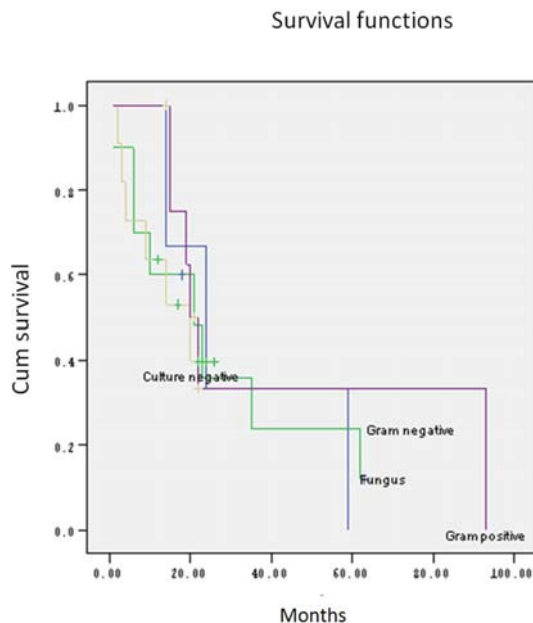


Fig. 1 Kaplan Meier survival curve in PD-related peritonitis patients according to microorganisms (gram negative, gram positive, fungus, and culture negative peritonitis)

unpublished data, the authors peritonitis rate was constantly improved since 2005. Specially trained PD nurses who participated in training new PD patients might contribute to this improvement. Even though the authors have an acceptable peritonitis rate, the outcome of the authors PD-related peritonitis patients is quite poor with the drop-out rate of 25.6% after the peritonitis episode. Thus, the authors still have an area for improvement in the authors' patient care. With the accumulating experience of our PD team, the authors believe that the better patient selection criteria are the most important strategy to a better result.

It is important to note that the authors had a higher proportion of culture-negative peritonitis in the present study than the general accepted rate⁽¹⁸⁾. Moreover, the present study showed the worst outcome with this group. Unidentified organisms caused physicians to choose less appropriate antibiotics, resulting in poor outcomes. Therefore, improvement of laboratory culture technique should be another important strategy to improve outcome of the authors' patients.

The appropriate use of intraperitoneal antibiotic is the most important step in treatment of PD peritonitis. However, epidemiology of peritonitis varies

among centers. Therefore, many investigators suggest that each center should adapt treatment guideline into a "center tailored" treatment protocol⁽¹⁹⁾. The aim of the present study, therefore, was to examine the epidemiology of causative organisms and their antimicrobial susceptibilities. The authors found that susceptibility to initial empirical antibiotics (cefazolin, ceftazidime and gentamicin) was high in most organisms. The exception was extended spectrum beta-lactamase (ESBL) *Escherichia coli* that was only susceptible to meropenem and *Enterococcus* which was only sensitive to vancomycin. However, these organisms only accounted for 5.9% of all episodes. The authors conclude that our current protocol for treatment of PD-related peritonitis is still appropriate in Bhumibol Adulyadej Hospital.

In conclusion, the present study revealed that the proportions of peritonitis due to gram negative organisms were increased and associated with less favorable outcome. Since the number of peritoneal dialysis cases in Thailand continue to increase, it is necessary to prepare the appropriate protocol for prevention and treatment of PD-related peritonitis under national PD-First policy scheme.

Potential conflicts of interest

None.

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การเปลี่ยนแปลงลักษณะทางคลินิกของ PD-Related Peritonitis ในประเทศไทย

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วัตถุประสงค์: ผู้ป่วยที่ได้รับการบำบัดทดแทนไตด้วยวิธีล้างทางหน้าท้องในประเทศไทย มีจำนวนเพิ่มขึ้นอย่างรวดเร็วหลังจากมีการเริ่มใช้ PD-First policy แต่ภาวะติดเชื้อของผนังช่องท้อง (peritonitis) ยังคงเป็นอุปสรรคสำคัญการศึกษานี้มีวัตถุประสงค์ที่จะวิเคราะห์ลักษณะทางคลินิกของผู้ป่วย PD peritonitis ในประเทศไทยในยุคปัจจุบัน

วัสดุและวิธีการ: ทำการศึกษาและวิเคราะห์ข้อมูลทางคลินิกแบบย้อนหลังในผู้ป่วย PD peritonitis ของโรงพยาบาลภูมิพลอดุลยเดชตั้งแต่ช่วงเดือน ตุลาคม พ.ศ. 2551 ถึง ธันวาคม พ.ศ. 2553

ผลการศึกษา: ผู้ป่วยที่เข้าร่วมการศึกษาทั้งสิ้นมีจำนวน 93 คน ตลอดช่วงระยะเวลาของการศึกษามีอุบัติการณ์การเกิด PD peritonitis 51 ครั้ง ในผู้ป่วย 33 คน อายุเฉลี่ยของผู้ป่วยที่เกิด peritonitis เท่ากับ 57.9 ± 16.1 ปี และร้อยละ 63.6 เป็นผู้หญิง เชื้อก่อโรคที่พบบ่อยที่สุดได้แก่ เชื้อกรัมลบ (33.3%) ตามด้วย เชื้อกรัมบวก (17.6%) เชื้อรา (5.9%) และโนคาร์เดีย (2%) แต่พบวาร์รอยละ 43.1 เป็น culture negative peritonitis ผลการรักษา PD peritonitis ในภาพรวมพบว่ารักษาหายร้อยละ 74.5 จำเป็นต้องเอา catheter อกร้อยละ 7.8 และมีอัตราการเสียชีวิตร้อยละ 17.6 การศึกษาแบบวิเคราะห์การอยู่รอดพบว่า กลุ่มเชื้อกรัมบวกมีอัตราการอยู่รอด ดีที่สุด (43.3 เดือน) เมื่อเทียบกับเชื้อกรัมลบ (26.8 เดือน) และกลุ่ม culture negative peritonitis (16.1 เดือน)

สรุป: สัดส่วนของผู้ป่วย PD peritonitis ที่เกิดจากเชื้อกรัมลบมีจำนวนสูงขึ้นกว่าในอดีตและมีผลลัพธ์การรักษาที่ไม่ดี การปรับปรุงแนวทางการป้องกันและรักษาตามข้อมูลที่ได้เป็นปัจจัยสำคัญของความสำเร็จในการดูแลรักษาผู้ป่วย
