Risk Factors of Infectious Peritonitis of CAPD Patients in Rajavithi Hospital

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Objective: *Continuous ambulatory peritoneal dialysis (CAPD) is a renal replacement therapy for end stage renal disease (ESRD) patients. Peritoneal infection, peritonitis is a major cause of death and technical failure in ESRD patients receiving CAPD treatment. Previous studies demonstrated that lower serum albumin, higher body mass index, and diabetic kidney disease were associated with increase in incidence of peritonitis. However, the demographics of the patients in the Rajavithi hospital such as race, gender, age, socioeconomic status and various other factors were different from the patients in the previous studies. The present study was conducted to investigate the risk factors of peritonitis, causative organisms, and route of infection among CAPD patients in Rajavithi Hospital.*

Material and Method: *This is a retrospective descriptive study. All patients in the present study are ESRD patients who received CAPD treatment during March 2009 to February 2011 and adhered with the treatment for at least 1 year. The patients were divided into two groups 1) the patients who got infectious peritonitis within 1 year after catheter implantation and 2) the patients who did not get or got infectious peritonitis after 1 years. The medical records were reviewed and the data were analyzed to identify the risk factors of peritonitis, frequency of causative organisms, and the route of infection.*

Results: *Of 27 patients, 16 patients (59.3%) had peritonitis within the first year, and 11 patients (40.7%) had no peritonitis or had peritonitis after the first year. The risk factors associated with peritonitis were diabetes (62.5 % in patients with peritonitis within first year vs. 18.2% in the patients who had no peritonitis or had peritonitis after the first year, p = 0.047) and higher blood sugar level (139.5 $\pm$ 34.6 mg/dl in patients with peritonitis within first year vs. 115.9 $\pm$ 23.4 mg/dl 18.2% in the patients who had no peritonitis or had peritonitis after the first year, p = 0.011). Transluminal peritoneal catheter route was the route of infection in every subject in the present study. The major causative agents were gram-positive bacteria.*

Conclusion: *Diabetic kidney disease and high fasting blood sugar were the risk factors of peritonitis and trans-luminal peritoneal catheter are the major route of infection in the present study. Therefore, good blood sugar control and strict adherence with sterile technique for peritoneal dialysis would decrease the incidence of peritonitis in CAPD patients.*

Keywords*: Continuous ambulatory peritoneal dialysis, CAPD, Infectious peritonitis, Risk factor*

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Peritoneal dialysis (PD) is a renal replacement therapy for the patients with end stage renal disease (ESRD) and continuous ambulatory peritoneal dialysis (CAPD) is the most popular method of peritoneal dialysis in Thailand especially after launching of the "PD First" policy. This method is a patient-based therapy because the patients have to run the treatment by themselves. One of the major causes of deadth and technical failure in the patients with CAPD is infectious peritonitis[1-3]. The majority of the patients with infectious peritonitis presented with local symptoms such as abdominal pain (67-97%), cloudy effluent (98-100%), volume overload due to ultrafiltration failure, or the symptoms of the organs that are the origin of peritonitis. Only three-thirds of patients presented with systemic symptoms such as fever with or without chill[4,5].

Previous studies have shown that lower serum albumin[2,6-8], higher body mass index (BMI)[2], lower hematocrit level[6], and diabetes kidney disease[2,9] are associated with peritonitis. However, there are many

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differences between the CAPD patients in Rajavithi Hospital and the patients who were enrolled in the previous studies including race, underlying diseases of ESRD, comorbid diseases, socioeconomic and educational status. In addition, the selection bias effect of the "PD First" policy that may force the patients who are not perfectly suitable with CAPD treatment, for example they may have some socioeconomic problems to attend to this treatment program. The objective of the present study is to evaluate the risk factors of intraperitoneal infection in the CAPD patients in Rajavithi Hospital.

Material and Method

The institutional ethical committee approved the present study and all patients gave written informed consent after reviewing a written summary of the study plan. The authors retrospectively reviewed charts of the CAPD patients who were being treated at Rajavithi Hospital during March 2009 to February 2011 and the CAPD patients who got intraperitoneal infection within a month after PD catheter implantation were excluded. The patients were divided into 2 groups: 1) the patients who got infectious peritonitis within the first year after catheter implantation and 2) the patients who did not get or got infectious peritonitis after 1 year. Two out of three of the following criteria are needed for the diagnosis of peritonitis. 1) Symptom of peritoneal inflammation including abdominal pain, abdominal tenderness or rebound tenderness. 2) Cloudy effluent which contains white blood cells (WBC) more than 100/microliter (after a dwell time of at least 2 hours), with at least 50% polymorphonuclear cells. 3) Positive Gram stain or positive effluent culture result. Then, the authors compared demographic, socioeconomic, clinical and biochemical factors which might affect intraperitoneal infection between the 2 studied groups. The authors also explored the frequency of causative organisms, and the route of infection.

Statistical analysis

All analyses were performed using the SPSS statistical package, version 17.0 (SPSS Inc, Chicago, Illinois, USA). Variables normally distributed were expressed as mean $\pm$ SD and the group comparisons were assessed by independent sample t-test. Variables not normally distributed were expressed as median (Min, Max) and the group comparisons were assessed by the Mann-Whitney U test and Chi-square test. Values of $p < 0.05$ were considered statistically significant.

Results

Twenty-seven CAPD patients were enrolled. There were 16 patients who got one infectious peritonitis in the first year and 11 patients who have never infected or infected after one year (59.3% and 40.7% respectively).

The patient demographics of 27 cases were shown in Table 1. The mean age was 59.7 $\pm$ 14.5 years (28-85 years), and 59% were male. Most of the patients had hypertension and about half of the patients had diabetes. Other comorbid diseases included coronary heart disease and dyslipidemia. The comparisons of demographics and socioeconomic status between the 2 groups were illustrated in Table 2. There were no significant differences between these 2 groups, except there were more diabetes in the group with infectious peritonitis in the first year (62% vs. 18%, $p = 0.047$).

The clinical data obtained from physical examination including exit site grading, body mass index (BMI), systolic and diastolic blood pressure during the follow-up were detailed in Table 3. The mean BMI and systolic and diastolic blood pressure of the patients with infectious peritonitis in the first year were slightly, but not significantly, higher than the other group. Of note, the mean BMI of the patients with infectious peritonitis in the first year was classified as pre-obese stage.

The biochemistry findings were demonstrated in Table 4. The mean fasting blood sugar of the patients with intraperitoneal infection in the first year was significantly higher than the other group (139.5 $\pm$ 34.6 vs. 115.9 $\pm$ 23.4 mg/dl, $p = 0.011$). Therefore, this finding

Table 1. Demographics of 27 patients

Patient demographics	n (%)/mean $\pm$ SD
gender	
Male	16 (59%)
Female	11 (51%)
Ages (year)	59.7 $\pm$ 14.5
Comorbid diseases	
Diabetes	12 (44%)
Hypertension	26 (96%)
Hyperlipidemia	14 (51%)
Coronary artery heart disease	2 (7%)
Causes of chronic kidney failure	
Unknown cause	17 (62%)
Diabetes	7 (25%)
Hypertension	2 (7%)
Lupus nephritis	1 (5%)

Table 2. The comparisons of demographics and socioeconomic status between the patients with infectious peritonitis in the first year and the patients with no or with infectious peritonitis after one year

Demographic and socioeconomic status	With infectious peritonitis in the first year (n = 16)	No or with infectious peritonitis after one year (n = 11)	p-value
Gender			0.710
Male	10 (62.5%)	6 (54.5%)	
Female	6 (37.5%)	5 (45.5%)	
Ages (year)	59.3 ± 14.6	60.4 ± 15.1	0.849
Comorbid diseases			
Diabetes	10 (62.5%)	2 (18.2%)	0.047
Hypertension	15 (93.8%)	11 (100%)	1.000
Hyperlipidemia	9 (56.3%)	5 (45.5%)	0.704
Coronary artery heart disease	1 (6.3%)	2 (18.2%)	0.549
Education			0.471
No	0 (0%)	1 (9.1%)	
Primary	5 (31.3%)	5 (45.5%)	
Secondary	5 (31.3%)	1 (9.1%)	
Secondary (end)	1 (6.3%)	2 (18.2%)	
High career certificate	3 (18.8%)	1 (9.1%)	
Graduate	2 (12.5%)	1 (9.1%)	
Performed CAPD by themselves.			1.00
Yes	5 (31.3%)	3 (27.3%)	
No	11 (68.8%)	8 (72.7%)	
Family monthly income			0.431
No	4 (25.0%)	0 (0%)	
< 5,000	5 (31.3%)	3 (27.3%)	
5,000-< 20,000	4 (25.0%)	5 (45.5%)	
20,000-< 50,000	2 (12.5%)	2 (18.2%)	
≥ 50,000	1 (6.3%)	1 (9.1%)	

Table 3. Comparisons of physical examination findings between the patients with intraperitoneal infection in the first year and the patient with no or with intraperitoneal infection after one year

Physical examination findings	With infectious peritonitis in the first year (n = 16)	No or with infectious peritonitis after one year (n = 11)	p-value
Exit site grading			0.124
Excellent	6 (37.5%)	2 (18.2%)	
Good	9 (56.3%)	7 (63.6%)	
Equivocal	0 (0%)	2 (18.2%)	
Chronic infection	1 (6.3%)	0 (0%)	
Body mass index (Kg/m^2)	25.4 ± 6.5	22.5 ± 8.1	0.315
Systolic blood pressure (mmHg)	122.6 ± 39.0	92.3 ± 60.5	0.125
Diastolic blood pressure (mmHg)	66.6 ± 22.0	51.4 ± 35.0	0.177

was in agreement with the higher prevalence of diabetes. The patients with intraperitoneal infection in the first year trended to have lower residue renal function than the other group although the statistical significance was not attained (8.3 ± 4.2 vs. 5.6 ± 3.4 ml/min/1.73 m^2, 0.056).

The most common causative organism of infectious peritonitis in the present study was *Acinetobacter buamanii*. However, this organism was not exclusively predominant. The ratio of gram positive bacterial peritonitis was slightly higher than gram negative bacteria (Table 5). The culture negative

Table 4. Comparisons of biochemistry findings between the patients with intraperitoneal infection in the first year and the patient with no or with intraperitoneal infection after one year

Biochemistry findings	With infectious peritonitis in the first year (n = 16)	No or with infectious peritonitis after one year (n = 11)	p-value
Residual glomerular filtration rate (ml/min/1.73m^2)	8.3 ± 4.2	5.6 ± 3.4	0.056
Hemoglobin (g/dl)	10.1 ± 1.3	9.3 ± 2.0	0.190
Hematocrit (%)	30.6 ± 4.2	27.9 ± 6.2	0.174
Serum sodium (mEq/L)	138.2 ± 2.0	137.6 ± 3.6	0.554
Serum potassium (mEq/L)	3.8 ± 0.4	3.7 ± 0.2	0.543
Serum total calcium (mg/dl)	8.7 ± 0.8	9.1 ± 0.6	0.218
Serum phosphate (mg/dl)	4.5 ± 1.2	4.3 ± 0.8	0.665
Fasting blood sugar (mg/dl)	139.5 ± 34.6	115.9 ± 23.4	0.011
LDL (mg/dl)	113.3 ± 59.8	106.8 ± 35.4	0.746
Serum albumin (g/dl)	3.3 ± 0.5	3.0 ± 1.1	0.345

Table 5. Causative organisms of intraperitoneal infection

Type of disease	n (%)
Culture negative	5 (29%)
Acinetobacter buamanii	3 (17%)
Coagulase negative Staphylococcus	2 (12%)
Enterobacter cloace	2 (12%)
Escherrichia coli	1 (6%)
Staphylococcus aureus	1 (6%)
Pseudomonas aeruginosa	1 (6%)
Streptococcal group D	1 (6%)
Streptococcal epidermidis	1 (6%)

peritonitis in the present study was 29% and there was no fungal peritonitis.

Of 27 cases, only 1 patient got exit site infection. The examination revealed only chronic infection of exit site and the culture obtained from the exit site revealed the positive result of *Stahylococcus aureus*. Moreover, the exit site infection occurred 39 days prior to peritonitis and the effluent culture was positive for *Acinetobacter buamanii*. The authors could not find the tunnel infection or any infections in other parts of the authors patients at the same time with peritoneal infection. As such, the authors concluded that the route of peritonitis in the present study is only transluminal route.

Discussion

In the present study, the risk factors that were significantly associated with peritonitis were diabetes and higher fasting blood sugar (Table 1). Lower residual renal function showed only borderline impact on the incidence of peritonitis. *Acinetobacter buamanii* was the most common causative organism of peritonitis but not exclusively predominant (Table 5) and the frequency of gram positive bacterial peritonitis is only slightly higher than gram negative bacteria. The incidence of culture negative peritonitis in the present study is high. The only route of infection was assumed to be transluminal pathway.

The present study confirms the finding from most of the previous studies that diabetes patients appear to have more frequent peritonitis than those without diabetes[2,6]. It could be explained by immunocompromising effect of diabetics with hyperglycemia including neutrophil chemotaxis and adherence to vascular endothelium, phagocytosis, intracellular bactericidal activity, opsonization, and cell-mediated immunity impairment[10-12]. Diabetes could also be the cause of autonomic neuropathy and intestinal dysmotility involving in bacteria over growth. Moreover, the patients with diabetes particularly those who inject insulin daily, often have asymptomatic nasal and skin colonization with *Staphylococcus aureus* that serves as the source of infection[13]. *In vitro* studies suggested that glucose degradation products (GDPs) accelerate neutrophil apoptosis in a caspase-dependent manner. As a consequence, the antibacterial function of these cells decreases[14]. GDPs also injure peritoneal mesothelial cells, causing increased secretion of cytokines, chemokines, and growth factors, and to express several adhesion molecules[15]. In order to induce cytotoxicity, However, the concentration of

these GDPs has to be at least three times, and in most cases more than 10 times, higher than those actually found in the PD fluids[16].

The lower residual renal function trends to be associated with higher frequency of peritonitis. The authors could not explain the direct effect of residual renal function on peritonitis rate. It is probably associated with lower immune function or malnutrition, but the authors do not have sufficient evidence to confirm this hypothesis.

The present study could not demonstrate the associations between higher BMI and peritonitis as were demonstrated in the present studies from the western countries[2]. It could be explained by over a half of people in western country have BMI more than 25kg/m^2, in contrast to Asian people that the prevalence of obesity is much lower. This negative result is also agreed with the studies from another Thai group[6] and Chinese group[8]. The author also could not demonstrate the associations between lower serum albumin and peritonitis, probably because the number of the patients in the present study is limited.

The transluminal route is the most common pathway of peritonitis in Rajavithi Hospital. The cause would be touch contamination. By observation, it is more likely to occur with the patients who do not adhere with sterile technique, or with the patients who are physically or mentally incapable of performing PD and do not have suitable assistants or frequently change their assistants.

The incidence of culture negative peritonitis in Rajavithi Hospital is higher than the recommendation of ISPD guideline 2010[17] (less than 20% vs. 29% in Rajavithi Hospital) even the authors used the standard culture technique as ISPD recommendation. The explanation for this result might be that some patients had already received the antibiotic before the cultures were obtained. However, most of the patients responded well with standard empiric antibiotics such as cefazolin and ceftazidime or amikacin.

Some limitations of the present study should be mentioned. First, the present study had small sample size performed as retrospective design. Secondly, several factors that may have some impacts on peritonitis such as nutritional assessment scoring, assessment of physical or mental handicap, the details of the assistants as well as nasal and skin colonization were not included in the present study.

In conclusion, diabetic kidney disease and high fasting blood sugar were the risk factors of peritonitis and transluminal peritoneal catheter is the major route of infection in the present study. Therefore, good blood sugar control and strict adherence with sterile technique for peritoneal dialysis fluid exchanging would decrease the incidence of peritonitis in CAPD patients.

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Potential conflicts of interest

None.

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ความเสี่ยงการติดเชื้อที่เยื่อบุผนังช่องท้องของผู้ป่วยที่ได้รับการล้างไตทางช่องท้องอย่างต่อเนื่องในโรงพยาบาลราชวิถี

สกานต์ บุนนาค, ประเสริฐ ธนกิจจารุ, อุดม ไกรฤทธิชัย, บุญธรรม จิระจันทร์, วรรณิยา มีนุ่น, ชุลีกร กาญจนพันธุ์

วัตถุประสงค์: *การล้างไตทางช่องท้องอย่างต่อเนื่องหรือซีเอพีดีเป็นการรักษาผู้ป่วยไตวายเรื้อรังระยะสุดท้ายวิธีหนึ่ง ซึ่งมีภาวะแทรกซ้อนที่สำคัญพบบ่อยและรุนแรง คือภาวะการติดเชื้อที่เยื่อบุช่องท้อง โดยเป็นสาเหตุอันดับต้นของการตายและการสิ้นสุดการล้างไตทางช่องท้อง จากการศึกษาก่อนหน้านี้พบว่าปัจจัยที่มีผลต่อการเกิดภาวะติดเชื้อที่เยื่อบุผนังช่องท้องคือ ระดับอัลบูมินในเลือดต่ำ ดัชนีมวลกายสูง และภาวะไตวายจากเบาหวาน อย่างไรก็ตามลักษณะของผู้ป่วยในโรงพยาบาลราชวิถี มีความแตกต่างจากผู้ป่วยในการศึกษาที่ผ่านมาทั้ง เชื้อชาติ เพศ อายุ การดำเนินชีวิต เศรษฐฐานะ และปัจจัยอื่นๆ ซึ่งอาจมีผลต่อการเกิดภาวะติดเชื้อที่เยื่อบุช่องท้อง ทำการศึกษานี้เพื่อศึกษาปัจจัยที่มีผลต่อการเกิดภาวะติดเชื้อที่เยื่อบุผนังช่องท้องในผู้ป่วยที่รับการล้างไตทางช่องท้องในโรงพยาบาลราชวิถี*

วัสดุและวิธีการ: *เป็นการศึกษาเชิงพรรณนาย้อนหลัง โดยกลุ่มผู้ป่วยที่เข้าร่วมในการศึกษาทุกรายเป็นผู้ป่วยไตวายเรื้อรังระยะสุดท้ายที่ทำการล้างไตทางช่องท้อง ตั้งแต่มีนาคม พ.ศ. 2552 จนถึงกุมภาพันธ์ พ.ศ. 2554 และมีการติดตามการรักษาอย่างน้อย 1 ปี โดยการสืบทบทวนจากรายงานเวชระเบียน เพื่อหาปัจจัยเสี่ยงต่อการติดเชื้อที่ผนังเยื่อบุช่องท้อง เชื้อที่เป็นสาเหตุ และช่องทางการติดเชื้อ โดยการวิเคราะห์เปรียบเทียบปัจจัยต่างๆ ในผู้ป่วย 2 กลุ่ม คือกลุ่มตัวอย่างผู้ป่วยที่เกิดการติดเชื้อภายใน 1 ปี และกลุ่มตัวอย่างผู้ป่วยที่ไม่เคยเกิดการติดเชื้อหรือติดเชื้อหลัง 1 ปี*

ผลการศึกษา: *จากข้อมูลตัวอย่าง 27 ราย คือกลุ่มตัวอย่างผู้ป่วยที่เกิดการติดเชื้อภายใน 1 ปี และกลุ่มตัวอย่างผู้ป่วยที่ไม่เคยเกิดการติดเชื้อหรือติดเชื้อหลัง 1 ปีจำนวน 16 และ 11 ราย หรือคิดเป็นร้อยละ 59.3 และ 40.7 ตามลำดับ พบว่าปัจจัยเสี่ยงของการติดเชื้อได้แก่โรคร่วมประจำตัวกลุ่มเบาหวาน (มีผู้ป่วยเป็นเบาหวานร้อยละ 62.5 ในกลุ่มตัวอย่างผู้ป่วยที่เกิดการติดเชื้อภายใน 1 ปี และร้อยละ 18.2 ในกลุ่มตัวอย่างผู้ป่วยที่ไม่เคยเกิดการติดเชื้อหรือเกิดการติดเชื้อภายหลัง 1 ปี $p = 0.047$) และค่าระดับน้ำตาลในเลือดหลังอดอาหาร (139.5 ± 34.6 ในกลุ่มตัวอย่างผู้ป่วยที่เกิดการติดเชื้อภายใน 1 ปี และ 115.9 ± 23.4 ในกลุ่มตัวอย่างผู้ป่วยที่ไม่เคยเกิดการติดเชื้อ หรือเกิดการติดเชื้อภายหลัง 1 ปี $p = 0.011$) เกิดการติดเชื้อทั้งหมดผ่านทางภายในท่อส่งน้ำยา เชื้อที่เป็นสาเหตุ ส่วนใหญ่เกิดจากพบเชื้อแบคทีเรียกรัมบวก*

สรุป: *โรคประจำตัวเบาหวาน และระดับน้ำตาลในเลือดมีผลต่อการติดเชื้อเยื่อบุช่องท้องในผู้ป่วยล้างไตทางช่องท้อง และช่องทางของการติดเชื้อทั้งหมดในการศึกษานี้เป็นการติดเชื้อผ่านทางภายในท่อส่งน้ำยา ดังนั้นการควบคุมระดับน้ำตาลในเลือด การเฝ้าระวังการติดเชื้อ การให้คำแนะนำดูแลการล้างไตทางช่องท้อง และการเข้มงวดในขั้นตอนการปฏิบัติในการเปลี่ยนน้ำยาจะช่วยลดภาวะแทรกซ้อนนี้ได้*