Reduced residual renal function is a risk of peritonitis in continuous ambulatory peritoneal dialysis patients

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Abstract

Background. Loss of residual renal function (RRF) contributes to anaemia, inflammation and malnutrition and is also a strong predictor of mortality in continuous ambulatory peritoneal dialysis (CAPD) patients. However, the role of RRF on peritonitis is not yet clearly established. This study aimed to evaluate the effect of RRF on the development of peritonitis.

Methods. Study subjects were 204 end-stage renal disease (ESRD) patients who started PD from January 2000 to December 2005. Biochemical and clinical data within 1 month of PD commencement were considered as baseline. To determine risk factors for peritonitis, multivariate Cox regression was performed. Kaplan–Meier analysis and log-rank test were used to examine the difference of peritonitis-free period according to the presence of diabetes and RRF.

Results. On univariate analysis based on baseline data in first peritonitis, diabetes was less prevalent and RRF (6.7 ± 2.6 vs 4.0 ± 2.3 ml/min/1.73 m², P < 0.01), haemoglobin (10.9 ± 1.2 vs 10.6 ± 1.2 g/dl, P < 0.05) and serum albumin level (3.6 ± 0.4 vs 3.4 ± 0.4 g/dl, P < 0.01) were significantly higher in the peritonitis-free group. Kaplan–Meier analysis showed that time to first PD peritonitis episode was significantly longer in the non-diabetic patients (P < 0.001) and in patients with higher residual GFR (P < 0.001). Multivariate analysis showed that diabetes [hazard ratio(HR) 1.64, P < 0.05] and RRF (per 1 ml/min/1.73 m² increase, HR 0.81, P < 0.01) were independent risk factors.

Conclusion. Our study revealed that RRF and diabetes were risk factors for peritonitis. These results suggest that preservation of RRF should be viewed as a protective strategy to reduce peritonitis.

Keywords: peritonitis; residual renal function; diabetes

Introduction

Continuous ambulatory peritoneal dialysis (CAPD) is an established treatment modality in end-stage renal disease (ESRD) patients and ~150 000 patients are being maintained on CAPD worldwide [1]. Although the incidence of peritonitis has decreased significantly since the introduction of the (53) Y-set system [2,3], PD peritonitis still remains as the leading cause of technique failure in CAPD patients. Factors related to PD peritonitis include diabetes, hypoalbuminaemia, catheter connection technique, age, PD modality, positive staphylococcal nasal carrier status, etc. [3–7].

For the last decade, the importance of residual renal function (RRF) has become evident in CAPD patients [8,9].Decline of RRF is associated with fluid overload [10], anaemia [11], inflammation [12], malnutrition [13] and mortality [14–15]. However, a role of RRF on the development of peritonitis is not yet established. We undertook this study to investigate risk factors for PD peritonitis and elucidate the effect of RRF on the development of peritonitis.

Patients and methods

Patient selection and data collection

This is a single-centre study with retrospective data collection. Study subjects were 240 ESRD patients who started CAPD from January 2000 to December 2005 and had urea kinetic studies including measurements of RRF within
3 months of CAPD initiation. Sixteen patients who had been undergoing haemodialysis prior to CAPD initiation were excluded because most of these subjects were anuric. Also, eight patients who received kidney transplantation before CAPD were also excluded due to long-term use of an immunosuppressive agent. Twelve patients whose medical records were not available or data were not eligible were also excluded. Therefore, 204 patients were included in this study. All procedures of CAPD catheter insertion were performed by nephrologists. On the day of surgery, a prophylactic antibiotic (cefazolin sodium 1.0g) was administered intravenously 2 h before catheter insertion. The twin-bag system was employed in all patients and different kinds of PD fluid (Baxter Healthcare, Deerfield, Illinois, USA, Fresenius Medical Care, Deutschland GmbH, Germany and Gambro, Lund, Sweden) were used.

The management of PD peritonitis was followed by International Society for Peritoneal Dialysis (ISPD) committee guidelines [16,17].

Demographic and clinical data were collected based on retrospective review of patient records; sex, age, body mass index (BMI) calculated as weight/(height)², primary renal disease, duration of dialysis, time to first peritonitis episode, exit site infection (ESI), use of biocompatible PD solution, and use of automated PD (APD). The following laboratory data obtained within 1 month after CAPD commencement were considered as baseline; haemoglobin, BUN, creatinine, albumin, total cholesterol, ferritin, ESR, CRP, residual GFR, Kt/V urea, normalized protein catabolic rate (nPCR) and percentage of lean body mass (%LBM) [18]. Residual GFR was calculated as an average of urea and creatinine clearance from a 24 h urine collection [19].

Statistical analysis

Statistical analysis was performed using SPSS for Windows software, version 12.0 (SPSS Inc., Chicago, IL, USA). All data were expressed as mean ± SD. To compare the difference between peritonitis group and peritonitis-free group, Student’s t-test was used for continuous variables and chi-square test was used for categorical variables. To determine risk factors for peritonitis, multivariate Cox regression was performed. Kaplan–Meier analysis and log-rank test were used to examine the difference of peritonitis-free period according to the presence of diabetes and RRF. Data were defined as censored if death and transfer to haemodialysis or renal allograft occurred. All probabilities were two-tailed and the level of significance was set at 0.05.

Results

Demographic and clinical data

Table 1 details baseline characteristics of 204 patients. Mean age of patients was 54 years and 57% were males. Diabetes was the most common cause of ESRD in this study (34.8%). All diabetic patients had type 2 diabetes. Baseline mean concentrations of haemoglobin and serum albumin were 10.7 ± 1.2 g/dl (107 ± 12 g/l), and 3.5 ± 0.4 g/dl (35 ± 4 g/l), respectively. Baseline residual glomerular filtration rate (GFR) was 5.2 ± 2.8 ml/min/1.73 m². A total of 195 episodes of PD peritonitis were observed in 110 patients during the follow-up period (total 650.2 patient-years). Mean peritonitis rate was 0.30 per patient-year. Staphylococcus coagulase negative (21.0%) was the most common causative organism (Table 2).

Analysis of risk factors for peritonitis

Patients were classified as peritonitis-free (n = 94) and peritonitis group (n = 110). Table 3 presents the differences between these two groups. In the peritonitis-free group, diabetes was less prevalent and residual GFR and levels of haemoglobin and serum albumin at baseline were significantly higher than those observed in the peritonitis group (Table 3).
Multivariate Cox regression showed that diabetes and RRF were independent risk factors for first PD peritonitis when adjusted for age, haemoglobin, serum albumin and exit site infection (Table 4). When residual GFR was not considered in the multivariate model, hypoalbuminaemia was a significant determinant for peritonitis (Table 4, model 1). Kaplan–Meier analysis showed that time to first PD peritonitis episode was significantly longer in non-diabetic patients (Figure 1, \( P < 0.001 \)) and in patients with higher residual GFR (Figure 2, \( P < 0.001 \)).

Discussion

In the present study, we found that reduced RRF and diabetic status were independent risk factors for peritonitis in CAPD patients. An important finding
Table 5. Comparison of peritonitis rate and other parameters according to the baseline GFR

<table>
<thead>
<tr>
<th>Parameter</th>
<th>&gt;5 ml/min/1.73 m²</th>
<th>≤5 ml/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>55.4 ± 9.8</td>
<td>52.5 ± 13.0</td>
</tr>
<tr>
<td>Gender (male: female)</td>
<td>65: 42</td>
<td>52: 45</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>23.2 ± 3.4</td>
<td>21.6 ± 2.7</td>
</tr>
<tr>
<td>DM</td>
<td>37 (34.6%)</td>
<td>34 (35.1%)</td>
</tr>
<tr>
<td>Residual GFR (ml/min/1.73 m²)</td>
<td>7.3 ± 2.2</td>
<td>3.0 ± 1.2*</td>
</tr>
<tr>
<td>Peritonitis rate (episodes per patient-year)</td>
<td>0.24</td>
<td>0.57*</td>
</tr>
<tr>
<td>Time to first peritonitis (months)</td>
<td>28.5 ± 22.7</td>
<td>20.7 ± 15.3*</td>
</tr>
<tr>
<td>Haemoglobin (g/dl)</td>
<td>10.8 ± 1.2</td>
<td>10.6 ± 1.3</td>
</tr>
<tr>
<td>BUN (mg/dl)</td>
<td>54.5 ± 18.4</td>
<td>60.3 ± 20.6*</td>
</tr>
<tr>
<td>Creatinine (mg/dl)</td>
<td>8.2 ± 2.6</td>
<td>9.8 ± 2.5*</td>
</tr>
<tr>
<td>Albumin (g/dl)</td>
<td>3.7 ± 0.5</td>
<td>3.4 ± 0.4*</td>
</tr>
<tr>
<td>Total cholesterol (mg/dl)</td>
<td>179 ± 37.7</td>
<td>176 ± 39.4</td>
</tr>
<tr>
<td>Kt/V urea</td>
<td>2.4 ± 0.5</td>
<td>2.2 ± 0.4*</td>
</tr>
<tr>
<td>Lean body mass (% body weight)</td>
<td>74.2 ± 13.3</td>
<td>70.6 ± 12.1</td>
</tr>
<tr>
<td>nPCR (g/kg/day)</td>
<td>1.01 ± 0.22</td>
<td>0.98 ± 0.19</td>
</tr>
</tbody>
</table>

*P < 0.01, *P < 0.05 vs patients with residual GFR >5 ml/min/1.73 m².

Also, nutritional status was reported as a significant predictor for PD peritonitis [29,30]. In our study, serum albumin level which might reflect nutritional status was significantly higher in patients with residual GFR >5 ml/min/1.73 m² compared with those with GFR <5 ml/min/1.73 m². Other nutritional markers such as BMI and %LBM were also higher in the former group, although the differences were not statistically significant (Table 5). Based on these findings, it is tempting to postulate that the preventive effect of RRF on peritonitis is mediated, at least partially, by the better preserved nutritional status. However, other unidentified mechanisms may also play a role and this remains to be explored.

Contrary to our results, previous studies reported that baseline serum albumin level was a significant determinant for PD peritonitis [24,28,29]. One possible explanation for this is that residual GFR was not considered for the risk analysis in the previous reports. It should be noted that lower albumin level was also identified as an independent risk factor when baseline data were analysed excluding RRF in the present study (Table 4, model 1). To further ascertain the role of hypoalbuminaemia on peritonitis, we conducted a risk analysis of second peritonitis (recurrence), in those patients who experienced the first peritonitis. The effects of RRF were hardly expected as mean residual GFR was <1.5 ml/min/1.73 m² in recurrence and recurrence-free groups. In this analysis, hypoalbuminaemia was a significant determinant of second peritonitis along with the diabetic status (data not shown). These findings together suggest that lower albumin level contributes to the development of peritonitis.

The fact that hypoalbuminaemia became insignificant when RRF was considered in the multivariate model suggests that there might be an interaction between RRF and albumin level. To examine this possibility, we then tested the interaction term of RRF and serum albumin using a Cox proportional hazard model. When the interaction term was included in a multivariate model, there was a significant interaction between the two variables (P < 0.01, data not shown). This finding implies that serum albumin level is significantly affected by RRF.

of our study is the fact that baseline RRF was identified as a risk factor for PD peritonitis. There have been numerous reports indicating poor clinical outcome in CAPD patients with lower residual GFR [10–15]. Recently, RRF has been studied in relationship to outcome of peritonitis. [20–22]. An observational study of Szeto et al. [21] reported that adult CAPD patients with better RRF experienced fewer peritonitis episodes, although this study was not aimed at examining the risk factors of PD peritonitis. Perez Fontan et al. [22] reported that lower residual GFR was an independent risk factor for at least one episode of peritonitis and its related mortality. Liu et al. [23] reported that loss of RRF was the most significant factor in predicting poor outcome in CAPD patients with fungal peritonitis. Our results clearly indicate that time to first peritonitis episode was significantly longer and peritonitis rate was significantly lower in patients with residual GFR >5 ml/min/1.73 m² compared with those with GFR <5 ml/min/1.73 m² (Figure 2, 0.24 vs 0.57 episodes per patient-year, P < 0.001). Also, patients with residual GFR between 2 and 5 ml/min/1.73 m² experienced less peritonitis compared with those patients with residual GFR <2 ml/min/1.73 m² (0.49 vs 0.68 episodes per patient-year, P < 0.05). Underlying mechanisms for this preventive effect of RRF on PD peritonitis are unclear. It is possible that patients with better preserved RRF might have better immune defense mechanisms along with a better preserved nutritional status. Actually, it has been reported that RRF independently affects the nutritional status of CAPD patients [13,21].
Risk factors for PD peritonitis

dialysate could be a route for peritonitis in diabetic patients. However, we do not recommend such a treatment to avoid a risk of peritonitis, thus all patients were treated with oral hypoglycaemic agents or subcutaneous insulin. Therefore, increased episodes of peritonitis in diabetic patients were unlikely to be caused by insulin mixed to dialysate. Also, the effect of diabetes on the development of peritonitis appears to be independent of RRF or albumin level since these variables were not different between diabetic and non-diabetic patients (data not shown).

Other factors previously reported as potential risk factors for PD peritonitis were age [5], dialysis modality [6], anaemia [31], economic status [32] and exit site infection [33]. However, the results of studies on these factors were controversial. De Vecchi et al. [5] reported that the peritonitis rate was higher in the elderly patients. On the contrary, Holley et al. [4] reported that older age per se was not associated with higher peritonitis rates. In our study, age was not found to be a risk factor for PD peritonitis. Only 10 patients using APD were included in this study and their mean peritonitis rate was 0.32 episodes per patient-year, which was not different from the non-APD patients (0.30 episodes per patient-year, P = 0.92).

There are several limitations in the present study. This is an observational study based on retrospective data collection with relatively small sample size. Hence, the causality of our findings needs further confirmation. Also, other potential risk factors such as socioeconomic status or personal hygiene were not considered in the analysis. We have not included other relevant data representing overall nutritional status such as subjective global assessment (SGA) to fully assess the impact of nutritional status. High incidence of culture-negative peritonitis was another drawback. Despite these limitations, it should be noted that RRF was identified as an independent risk factor for peritonitis in this study. There have been few studies in the past documenting the importance of RRF in association with peritonitis development in PD patients. A prospective study with a large number of patients is needed to verify risk factors identified in this study.

In conclusion, this study shows that RRF and diabetes are independent risk factors for PD peritonitis. After a decline or loss of RRF, lower serum albumin level appeared to play a significant role in the development of peritonitis. These results suggest that preservation of RRF should be viewed as a protective strategy to reduce peritonitis.

Conflict of interest statement. None declared.

References


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