Longitudinal Change in Peritoneal Membrane Function with Continuous Ambulatory Peritoneal Dialysis (CAPD) after Peritonitis Episodes

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Background: To assess changes in the peritoneal membrane after peritonitis episodes in patients undergoing continuous ambulatory peritoneal dialysis (CAPD).

Methods: From 1989 to 2002, CAPD patients who had peritonitis episodes were enrolled. We used the peritoneal equilibration test (PET) and measured plasma creatinine (Cr) levels at 2 hours, and dialysate Cr and glucose levels at 0, 2, and 4 hours. In addition, the dialysate-to-plasma ratio of Cr (D/PCr) at 0, 2, and 4 hours, the ratio of glucose levels in the dialysate effluent and infused dialysate ((D/D0)G), the drained ultrafiltration (UF) volume at 4 hours, and the mass transfer area coefficient of Cr (MTAC) normalized for the body surface area were also calculated. D/PCr, (D/D0)G, UF volume, and MTAC were measured at the baseline and after 2 years, and the results were analyzed and compared.

Results: Totally 27 patients were enrolled in the peritonitis group, including 17 males and 10 females. They had received CAPD for 71.23±28.13 months. Forty-nine peritonitis episodes were noted during the study period. Twenty-four patients were enrolled as controls, including 9 males and 15 females. They had undergone CAPD for 55.83±25.94 months. The baseline and 2-year levels of D/PCr (0.66±0.11 vs. 0.62±0.10, $p<0.05$), (D/D0)G (0.37±8.45vs. 0.43±7.71, $p<0.05$), and MTAC (9.36±3.53 vs. 8.08±3.41, $p<0.05$) showed significant changes, but UF volume (253.70±224.43 vs. 311.54±186.71 ml, $p>0.05$) showed no significant change. In the control group, there were no significant changes in D/PCr, (D/D0)G, MTAC, or UF volume.

Conclusion: Peritonitis episodes affect the peritoneal membrane solute transport function in CAPD patients.

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Key words: **continuous ambulatory peritoneal dialysis, peritonitis.**

The main complication resulting from long-term continuous ambulatory peritoneal dialysis (CAPD) is peritonitis. It has been shown that peritonitis might result in morphological and functional

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changes to the peritoneal membrane.[1-5] Sequelae of CAPD-related peritonitis include decreased ultrafiltration (UF) volume and an immediate increase in solute transport.[3] These peritoneal membrane changes may reverse themselves within a few weeks.[6-8] However, the long-term effects of peritonitis on peritoneal membrane function are still controversial. Some studies have shown increased creatinine transport in patients with frequent episodes of peritonitis,[9,10] whereas another study showed no significant changes.[11] Moreover, some studies found a high cumulative peritonitis rate to be a risk factor for UF failure.[12,13] In a single episode of peritonitis, previous studies demonstrated increased solute transport or no change.[10,14,15] Thus, it appears that not all peritonitis episodes are equivalent in terms of their effect on peritoneal transport. In the present study, we used CAPD patients with successful treatment of peritonitis episodes and analyzed their 2-year longitudinal changes in peritoneal solute transport and UF volume.

METHODS

From 1989 to 2002, CAPD patients with peritonitis episodes were enrolled in this study. The diagnosis of peritonitis was made using conventional criteria.[10] Patients were excluded if peritonitis episodes developed within 2 months after commencing CAPD. Another 24 patients without peritonitis episodes or a diabetes history were enrolled as a control group. Patients were followed for at least 2 years while undergoing maintenance CAPD, during which time peritoneal transport was measured by the standard peritoneal equilibration test (PET).[16] An initial PET was performed 2 months after patients had commenced CAPD, and then it was repeated once per year. When a peritonitis episode occurred, PET was followed up at least 2 months after the peritonitis episode had subsided. Patients were excluded if the peritonitis resulted in removal of the peritoneal catheter or termination of CAPD, or in the event of patient mortality.

We measured plasma glucose and creatinine levels at 2 hours, and dialysate glucose and creatinine levels at 0, 2, and 4 hours. The dialysate-to-plasma (D/P) ratio of creatinine at 0, 2, and 4 hours, the ratio between the glucose level in the dialysate effluent and that in the infused dialysate ((D/D0)G), and UF volume at 4 hours were also calculated. Creatinine concentration in the dialysate was corrected for glucose interference. The mass transfer area coefficient of creatinine (MTAC), normalized for body surface area, was calculated using the formula described by Krediet et al.[17] Body surface area was determined by a monogram based on body weight and height.[18] D/PCr, (D/D0)G, UF volume at 4 hours, and MTAC were measured at the baseline and again after 2 years, and results were analyzed. Serum albumin level, weekly dialysate Kt/V, creatinine clearance (Ccr), and residual renal function (RRF) were also recorded.

All data are expressed as the mean±SD. Statistical analysis was performed using chi-square test and repeated-measures ANOVA followed by multiple comparisons. Correlations were made using the Pearson correlation test. A p value of less than 0.05 was considered statistically significant.

RESULTS

In total, 27 patients were enrolled in the peritonitis group, including 17 males and 10 females. They had received maintenance CAPD for 71.23±28.13 months. The etiologies of their end-stage renal disease (ESRD) were chronic glomerulonephritis (CGN), diabetes mellitus, lupus nephritis, hypertensive nephropathy, IgA nephropathy, and obstructive nephropathy. The control group included 9 male and 15 female patients. They had received maintenance CAPD for 55.83±25.94 months. The etiologies of their ESRD were CGN, adult polycystic kidney disease, reflux nephropathy, lupus nephritis, and unknown (Table 1).

Totally 49 peritonitis episodes were noted during the study period. The numbers of peritonitis episodes were distributed in patients as follows: one (12/27), 2 (8/27), 3 (2/27), 4 (4/27), and 5 (1/27). The peritoneal membrane categories at the baseline were high (2/27), high average (12/27), low average (12/27), and low (1/27); and at the 2-year measurement, they were high average (5/27), low average (20/27), and low (2/27). The organisms of peritonitis are shown in Table 2, the majority being gram-positive Staphylococcus epidermidis and gram-negative Escherichia coli. The longitudinal values of D/PCr at 4 hours and MTAC at 2 years had declined when compared to the baseline, but (D/D0)G at 2 years had

increased when compared to the baseline (Table 3). UF volume showed no significant changes in the 2-year period. In the control group, no significant changes were seen in D/PCr, (D/D0)G, MTAC, or UF volume in the 2-year period. Correlations of longitudinal values of D/PCr at 4 hours, (D/D0)G, MTAC, and UF volume with peritonitis episodes (r = -0.2694 - 0.2831), organisms (r = -0.5408 - 0.4567), serum albumin level (r = -0.460-0.2633), weekly Kt/V (r = -0.3381 - 0.2764), Ccr (r = -0.5506 - 0.5841), and RRF (r = -0.2038 - 0.0379) were not statistically significant.

Table 1. Demographic Data of Study Patients

	Peritonitis (N = 27)	Without peritonitis (N = 24)	*p*
Gender (male: female)	17:10	9:15	0.0461
Age (years)	46.38±17.52	43.92±11.09	0.7292
Duration of dialysis (months)	71.23±28.13	55.83±25.94	0.0533
Etiologies of ESRD			
CGN	20 (74%)	17 (71%)	
DM	2 (7%)		
Lupus nephritis	2 (7%)	1 (4%)	
Hypertensive nephropathy	1 (4%)		
IgA nephropathy	1 (4%)		
Obstructive nephropathy	1 (4%)		
PKD		2 (8%)	
Reflux nephropathy		1 (4%)	
Unknown		3 (13%)	

Abbreviations: ESRD, end-stage renal disease; CGN, chronic glomerulonephritis; PKD, polycystic kidney disease.

Table 2. Infectious Organisms in CAPD-related Peritonitis

	Episodes
Gram positive	No. of episodes
Staphylococcus epidermidis	10
Streptococcus viridans	7
Staphylococcus aureus	5
Enterococcus sp.	1
Gram negative	
Escherichia coli	10
Neisseria sp.	3
Pseudomonas aeruginosa	2
Klebsiella pneumonia	2
Citrobacter freundii	1
Acinetobacter sp.	1
Aeromonas hydrophila	1
No growth	5

Table 3. Longitudinal Changes in Peritoneal Parameters

	At the baseline	At 1 year	At 2 years
D/PCr			
peritonitis	0.66±0.11	0.65±0.13	0.62±0.10a
without peritonitis	0.63±9.35	0.60±8.60	0.59±0.11
(D/Do)G			
peritonitis	0.37±8.45	0.40±9.03	0.43±7.71b
without peritonitis	0.40±7.67	0.43±5.84	0.43±9.39
MTAC			
peritonitis	9.36±3.53	8.93±4.58	8.08±3.41c
without peritonitis	8.80±2.42	8.54±2.60	7.90±3.17
UF			
peritonitis	253.70±224.43	296.30±135.82	311.54±186.71
without peritonitis	307.50±131.22	345.83±136.67	368.26±146.99

Abbreviations: D/PCr, dialysate-to-plasma ratio of creatinine at 4 hours; (D/D0)G, ratio between the glucose level in the dialysate effluent and that in the infused dialysate; MTAC, mass transfer area coefficient of creatinine; UF, ultrafiltration.
a: $p = 0.0060$, b: $p = 0.0034$, c: $p = 0.0178$, for baseline values vs. 2-year values.

DISCUSSION

Well-established peritonitis may injure the peritoneal membrane in CAPD patients. Changes in solute transport and UF volume can be observed clinically in these patients. Changes in solute transport may be due to increases in the effective peritoneal surface area and intrinsic permeability.[19] A change in the UF volume is probably due to impairment of transcellular water transport. In previous studies, the intensity of peritoneal inflammation and the number of peritonitis episodes were important factors in changes of solute transport and UF volume. Davies et al. showed that recurrences or clusters of infection caused an increase in D/P creatinine and a reduction in UF volume, whereas single peritonitis episodes had no significant effect on D/P creatinine and UF volume.[10] Ates et al. further observed that the increased transport of low-, middle-, and high-molecular-weight solutes returned to the baseline at the end of the 2nd to 4th weeks, although net UF did not completely recover.[20] Hung et al. demonstrated increased solute transport during 17.4 months of follow-up in culture-positive peritonitis.[14] Wong et al. showed that peritonitis episodes did not change values of solute transport after 2 years, but that severe peritonitis patients had higher solute transport than patients who experienced no severe peritonitis.[11] Davies et al. demonstrated

significant correlations between the cumulative dialysate leukocyte count and changes in both D/P creatinine and UF volume.[10] But they also observed some patients with cluster infection who had no significant changes in D/P creatinine or UF volume. Therefore, the severity of peritonitis may affect the outcomes of peritoneal solute transport and UF capacity, although some patients show a heterogeneous distribution.

During the 2-year observation period, it appeared that peritonitis episodes affected longitudinal solute transport in our study. Although dialysate leukocyte counts were not recorded, it seemed that the bacterial category had no significant effect on the solute transport or UF volume changes. Culture-negative peritonitis episodes did not seem to result in any more-favorable changes in solute transport or UF volume compared to culture-positive peritonitis episodes. The effects of the frequency of peritonitis on solute transport and UF volume changes were also analyzed, revealing that single or multiple episodes of peritonitis showed no significant effects on solute transport or UF volume changes. These results are in accordance with some studies cited above, except that solute transport declined over the 2 years. Rafael et al. showed that there was no significant difference in MTAC after 5 to 11 years of CAPD.[13] Because our observation period was less than 10 years, we supposed that a longer CAPD duration in the peritonitis group would not have affected the final outcome regarding solute transport. This study differs from previous studies in that we excluded cases of technical failure and cases of mortality, therefore avoiding bias from the heterogeneous distribution of cohort patients. But enrolled patients did not have severe disease, so the longitudinal decline in solute transport may reflect intrinsic peritoneal membrane changes in CAPD patients. However, the study was retrospective in design and had a relatively small number of patients and only a 2-year observation period, thus warranting further study. In conclusion, peritonitis episodes which have been cured do not appear to affect UF capacity, but may cause a decline in solute transport function in CAPD patients.

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連續可活動性腹膜透析病人腹膜炎後腹膜功能的變化

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背 景： 評估連續可活動性腹膜透析病人腹膜炎後，腹膜功能的變化。

方 法： 1989年至2002年，於高雄長庚醫院接受連續可活動性腹膜透析而發生腹膜炎的病人納入分析研究，我們使用腹膜平衡試驗，測量第2小時血漿肌酐酸值，第0, 2, 4小時透析液肌酐酸和葡萄糖值，並且計算第0, 2, 4小時透析液與血漿肌酐酸比值，第4小時與第0小時透析液葡萄糖濃度比值，第4小時水份過濾量及肌酐酸質量移轉面積係數(mass transfer area coefficient)，分析統計上述數據的基本值及2年後數值的變化。

結 果： 腹膜炎的病人總共27個，17位男性，10位女性，平均接受腹膜透析治療71.23±28.13月，研究期間總共有49次的腹膜炎發生，對照組有24個病人，9位男性，15位女性，平均接受腹膜透析治療55.83±25.94月。基本值及2年後的數值變化分別如下：第4小時透析液與血漿肌酐酸比值：0.66±0.11對0.62±0.10，$p<0.05$，第4小時與第0小時透析液葡萄糖濃度比值：0.37±8.45對0.43±7.71，$p<0.05$，肌酐酸質量移轉面積係數：9.36±3.53對8.08±3.41，$p<0.05$，但是水分過濾量：253.70±224.43對311.54±186.71毫升，沒有有意義的變化。對照組第4小時透析液與血漿肌酐酸比值，第4小時與第0小時透析液葡萄糖濃度比值，肌酐酸質量移轉面積係數，水分過濾量，沒有有意義的變化。

結 論： 腹膜透析病人若發生腹膜炎，溶質運送的腹膜功能會受影響。
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關鍵字： 連續可活動性腹膜透析，腹膜炎。

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