Relationship between Malnutrition-Inflammation Syndrome and Ultrafiltration Volume in Continuous Ambulatory Peritoneal Dialysis Patients

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Objective*: Malnutrition inflammation syndrome may contribute to a change of peritoneum, leading to high peritoneal membrane transport, peritoneal albumin loss, and increased glucose uptake into systemic circulation and decreased ultrafiltration (UF) volume. Fluid overload is a common problem among CAPD patients which has an effect on morbidity and mortality in these patients. The present study was designed as a pilot to find out a correlation between malnutrition and UF volume in CAPD patients.*

Material and Method: *A cross-sectional study was comducted in 42 stable CAPD cases at CAPD clinic, Maharaj Chiang Mai Hospital. Subjective global assessment score (SGA), malnutrition inflammation score (MIS), and laboratory values were utilized to identify nutritional and inflammatory status. Peritoneal equilibration test (PET) was performed to measure UF volume while bioelectrical impedance assay was determined to measure extracellular fluid volume (ECF), lean body mass (LBM), lean fat mass, and fluid status.*

Results: *Of 42 CAPD patients, 30 subjects were classified to have normal nutritional status while 12 patients were categorized to have malnutrition. Only 1 patient was classified to have malnutrition inflammation syndrome. MIS scores and serum albumin were significantly different between 2 groups ($p < 0.001$). PET-UF volume was significantly decreased in the malnutrition group ($p < 0.05$), especially when serum albumin was less than 3.0 g/dl. PET-UF volume was reduced 137.44 ml for every 1 g/dl of serum albumin below 3.0 g/dl. Residual renal function (RRF) was also significantly reduced in malnutrition group ($p < 0.05$). Malnutrition, decreased RRF, and decreased UF volume led to ECF expansion, hypertension, and fluid overload. Other factors that were correlated with UF volume were ACEI and/or ARB use ($p < 0.05$) and total protein loss per day ($p < 0.05$).*

Conclusion: *There was a significantly positive correlation between malnutrition and reduction of UF volume. Other factors that were correlated with UF volume were ACEI and/or ARBS use and total protein loss per day.*

Keywords: *Continuous ambulatory peritoneal dialysis, Malnutrition- inflammation syndrome, Ultrafiltration volume*

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Fluid control and fluid balance are as important as uremic toxin clearance among continuous ambulatory peritoneal dialysis (CAPD) patients, especially in patients without residual renal function (RRF). It was widely known that ultrafiltration (UF) failure led to technical failure, morbidity, and mortality[1-6]. These patients were at risk of extracellular fluid expansion, fluid overload, worsening hypertension, left ventricular hypertrophy, activations of inflammatory cascade and neurohormonal system atherosclerosis, and cardiovascular disease[7]. To date, it was discovered that malnutrition and fluid overload had a liaison, but their relationship was not well understood. Malnutrition in CAPD patients rose from many causes *i.e.* decreased protein nutritional intake due to anorexia, abdominal discomfort, glucose reuptake from PDF, and increased total energy expenditure from inflammatory processes within the body[7-13].

Explaining from a concept of malnutrition inflammation atherosclerosis (MIA) syndrome, malnutrition caused inflammation, peritoneal vasculopathy, and peritoneal membrane sclerosis. High

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peritoneal membrane transport and decreased UF volume developed as a consequence of the circumstance. Previous studies[14-17] showed that many cytokines and adhesion molecules were increased in response to malnutrition *i.e.* tissue necrosis factor, C-reactive protein, fibrinogen, lipoprotein a, plasminogen activator inhibitor, intracellular adhesion molecules-1, and vascular cell adhesion molecules-1 while nitric oxide was decreased[14-16]. This inflammatory process resulted in peritoneal membrane sclerosis and vasculopathy. There were inflammatory cell infiltration, decreased mesothelial cell population, submesothelial fibrosis, thickening of capillary basement membrane, and peritoneal membrane sclerosis[17,18]. These occurred in association with increased D/Pcreatinine and decreased sodium sieving[7,19-21].

The present study aimed to search for an association between nutritional status and UF volume among CAPD patients. The authors hypothesized that malnourished patients would have lower UF volume.

Material and Method

Patients

This cross-sectional pilot study was conducted to compare the amount of UF volume between well-nourished and malnourished CAPD patients at Maharaj Nakhon Chiangmai Hospital. Patients included in the study had age of more than 15 year-old, initiation of CAPD within one year, using 1.5% or 2.5% Dianeal solution (Baxter®) with good compliance, and were clinically stable for more than 3 months prior to the present study. Patients who were non-compliance, had bacterial or fungal infection in any organ system within 3 months, Child-Pugh class B-C cirrhosis, malignancy, acute decompensated heart failure, mechanical complication of CAPD, and patients who were unable to undergo bioelectrical impedance assay (BIA) were excluded. Forty nine patients were eligible and 42 patients were included in the present study.

Study scheme

First visit (week 0)

Only patients who met inclusion criteria and gave inform-consent were joined the present study. Using subjective global assessment score (SGA) and malnutrition-inflammation score (MIS), nutritional status was evaluated at this time point to categorize all cases into 2 groups. Patients who had SGA A were classified into well-nourished group while those having SGA B and C were allocated into malnourished group. After that, they were advised to record the amount of fluid intake, urine output, and CAPD-UF for 3 consecutive days before the time to the second visit.

The insensible loss via sweating and feces were not taken into account since it was estimated that at the same geographical area and weather, this amount should be similar. In addition, patients were also advised to bring all bags of peritoneal dialysis fluid (PDF) and 24-hr urine on the day before the second visit to the clinic to measure for adequacy and protein nitrogen appearance (PNA).

Second Visit (week 4)

The patients were interviewed to check for the accuracy of their records. After that, physical examination, laboratory test, standard PET test, and BIA were performed. All patients were examined for anthropometric data and nutritional status. A 10 ml blood sample was drawn to determine blood chemistry, nutrition, CA-125, and inflammatory peritoneal transport characteristics. BIA was done to assess fluid as well as body composition status. Standard PET test was performed. The 24-hour PDF and urine volume calculated for total creatinine clearance, total Kt/Vurea, and PNA. Of note, the blood pressure and BIA measurement were evaluated after finishing the standard PET test and the patients had dry empty peritoneal cavity for 15-20 minutes to allow for body fluid redistribution. All patients received standard CAPD care in every visit.

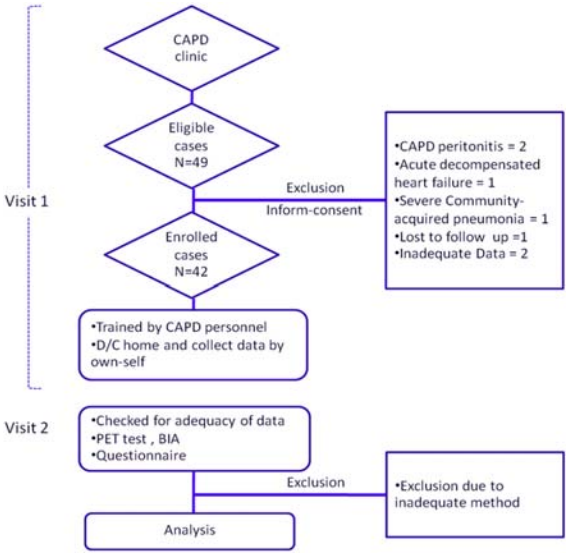

Fig. 1

Statistical analysis

The authors used SPSS version 17.0 to analyze the data. Student t-test and Chi-square were utilized to compare the means for continuous and non-continuous data, respectively. Pearson's Correlation test was used to analyze for the correlation between nutritional status and UF volume.

The authors used UF volume recorded from standard PET test (PET-UF) in the analysis because there was a study showed that PET-UF and CAPD-UF were correlated and the PET-UF was not interfered by sex, age, diabetes, inflammatory status, residual renal function, CAPD prescription, concentration of PDF and body fluid status[22]. Multiple regression analysis was

Table 1. Baseline patient characteristics

	SGA A (n = 30)	SGA B and C (n = 12)	p-value
Sex (Male: Female)	0.7:1	0.5:1	0.551
Age (years)	53.0 ± 11.1	54.1 ± 4.7	0.352
Body weight (kilograms)	57.28 ± 10.28	54.40 ± 12.39	0.457
BMI (kg/m^2)	23.00 ± 3.58	22.88 ± 4.91	0.928
Underlying disease			
Diabetes mellitus	10 (33.3%)	4 (33.3%)	1.00
Hypertension	30 (100%)	11 (91.6%)	0.11
Coronary arterial disease/congestive heart failure	0%	0%	-
Peripheral artery disease	0%	0%	-
Residual renal function (urine output>100ml/day)	21 (70%)	9 (75%)	0.746
Medication			
Any diuretics	10 (56.6%)	4 (75%)	0.269
Beta-blockers	15 (50%)	8 (67.6%)	0.327
ACEI or ARB	17 (83.3%)	9 (91.6%)	0.486
Hemodialysis vintage (months)	4.2 ± 8.8	3.5 ± 1.9	0.759
MIS score	3.30 ± 1.67	6.25 ± 2.49	
MIS 0-2	10 (33.3%)	1 (8.33%)	
MIS 3-4	12 (40%)	1 (8.33%)	
MIS 5-7	8 (26.67%)	6 (50%)	0.000
MIS ≥ 8	0	4 (33.34%)	0.001
Systolic blood pressure (mmHg)	143 ± 21	163 ± 13	0.011
Diastolic blood pressure (mmHg)	82 ± 13	87 ± 11	0.330
Mean arterial blood pressure (mmHg)	104 ± 19	112 ± 12	0.229
Ankle brachial index (ABI)	1.11 ± 0.10	1.15 ± 0.07	0.222

Table 2. CAPD data between 2 groups of patients

	SGA A (n = 30)	SGA B and C (n = 12)	p-value
Amount of PDF use (ml/day)	7,200 ± 1,627	8,100 ± 1,066	0.044
Peritoneal membrane transport type			0.218
High	4 (13.3%)	3 (25%)	
High average	7 (23.3%)	6 (50%)	
Low average	14 (46.6%)	2 (16.6%)	
Low	2 (6.6%)	1 (8.3%)	
Duration of CAPD (months)	15.5 ± 9.8	10.9 ± 7.3	0.149
D/PCr	0.62 ± 0.16	0.66 ± 0.23	0.558
D/D$_0$Glucose	0.41 ± 0.10	0.36 ± 0.11	0.185
Weeklyc total Kt/V urea	6.05 ± 3.87	2.51 ± 1.80	0.005
Weekly total CCr/1.73m^2	180.23 ± 236.88	95.61 ± 147.08	0.258

Table 3. Laboratory data between 2 groups of patients

	SGA A (n = 30)	SGA B and C (n = 12)	p-value
Hemoglobin (gm/dl)	11.7 ± 1.61	11.1 ± 1.3	0.260
Absolute lymphocyte counts (cells/ml)	1,602 ± 826	1,343 ± 523	0.323
Serum BUN (mg/dl)	55.9 ± 19.1	56.3 ± 28.5	0.962
Serum creatinine (mg/dl)	10.5 ± 4.5	15.0 ± 15.3	0.150
Serun sodium (mEq/l)	140.3 ± 3.9	139.3 ±3.8	0.457
Serum potassium (mEq/l)	4.0 ± 0.6	3.4 ± 0.7	0.020
C-P product(mg^2/dl^2)	43.40 ± 14.39	42.78 ± 13.32	0.940
FBS (mg/dl)	114 ± 26	106 ± 21	0.327
Total cholesterol (mg/dl)	193 ± 40	248 ± 96	0.079
Serum TIBC (mg/dl)	270 ± 44	261 ± 31	0.554
CRP	4.6 ± 4.8	4.1 ± 1.7	0.724
CA-125	12.05 ± 4.35	44.22 ± 56.05	0.072
Serum albumin (g/dl)	3.45 ± 0.40 (2.7-4.2)	2.85 ± 0.36 (1.9-3.4)	0.000
Serum albumin < 3.0 (g/dl)	4 (13.3%)	26 (86.67%)	0.001
Serum albumin ≥ 3.0 (g/dl)	8 (66.67%)	4 (33.33%)	
Lean tissue index (%)	14.23 ± 2.23	12.67 ± 3.57	0.102
FTI, fat tissue index (%)	8.12 ± 4.60	9.20 ±6.44	0.551
Total body protein loss (g/day)	5.74 ± 2.47	6.74 ±3.70	0.312
PNA	114 ± 67.8	64.8 ± 47.7	0.026

Table 4. Fluid balance between 2 groups of patients

	SGA A (n = 30)	SGA B and C (n = 12)	p-value
Fluid intake (ml/day)	758 ± 350	559 ± 287	0.090
Urine output (ml/day)	606 ± 582	262 ± 262	0.012
CAPD UF (ml/day)	653 ± 528	617 ± 394	0.830
PET UF (ml)	388 ± 195	308 ± 235	0.264
Extracellular fluid (ECF) volume (L)	14.35 ± 2.98	17.12 ± 6.05	0.154
ECF/height (L/m)	0.09 ± 0.16	0.11 ± 0.34	0.078
Fluid overload (L)	1.40 ± 1.93	4.55 ± 3.73	0.015

used to determine variable that could predict PET-UF volume.

Results

Patients' characteristics (Table 1-4)

Only 42 from 49 eligible cases were included. Seven patients were excluded because two patients had CAPD peritonitis, one patient had acute decompensated heart failure, 2 patients had incomplete data, and 2 patients lost to follow-up for the second visit. Among 42 patients, there were 17 males and 25 females, age of 53.33 ± 9.59 years (21-76), body weight of 56.40 ± 10.85 kg (27.0-84.7). Thirty cases were categorized into well-nourished group while 12 cases (28.57%) were classified as malnourished group. Only one patient had C-reactive protein (CRP) more than 10 mg/L and was classified to have MIA syndrome.

Correlation between nutritional status and ultrafiltration volume

A correlation between nutritional status and UF volume was obriously noted. The more serum albumin decreased, the more UF volume reduced. Every 1.0 g/dl of serum albumin reduction below 3.0 g/dl caused PET-UF volume to reduce 135.44 ml. When other nutritional parameters were utilized for analysis, SGA class and MIS were also slightly but not significantly, correlated with PET-UF volume (Table 5).

Other variables that could predict PET UF volume were also analyzed. By Pearson's correlation test (Table 5). Variables other than hypoalbuminemia that influenced the UF volume were angiotensin

Table 5. Pearson's correlation test between PET UF and nutritional status

	Pearson's correlation test	p-value
SGA	-0.176	0.264
Serum albumin	0.311	0.045*
MIS score	-0.166	0.295
CAPD duration	0.343	0.026*
ACEI/ARB use	0.329	0.033*
Residual renal function	-0.332	0.017*
Total protein loss	-0.424	0.005*
Peritoneal membrane transport	-0.332	0.046*
CA-125	-0.279	0.056

*$p < 0.05$

converting enzyme inhibitor/angiotensin II receptor blocker (ACEI/ARB) use, CA-125, peritoneal transport characteristics, residual renal function, and total protein loss per day. However, when linear regression analysis was utilized, only ACEI/ARB use, residual renal function, and total protein loss per day were statistically significant.

Discussion

As described above, 28.57 percent of the patients in the present study had malnutrition. The authors found that the well-nourished patients had their MIS in the lower 2 quartiles while the malnourished patients had their MIS in the higher 2 quartiles. Peritoneal transport characteristics were not statistically different between 2 groups but the malnourished patients tended to have high-average or high (75%) peritoneal transport. As a result, they had lower UF volume, total weekly Kt/Vurea, and higher amount of extracellular fluid despite they drank less and were prescribed a higher CAPD dose. This data contribute to the hypothesis that malnutrition may contribute to peritoneal vasculopathy, leading to higher peritoneal transport characteristics and lower UF volume. The authors also found that the malnourished patients had higher blood pressure and inflammation that may lead to premature atherosclerosis and cardiovascular disease.

Other variables affecting UF volume were ACEI/ARB use, residual renal function, and total protein loss per day. From a knowledge that peritoneal inflammation from bioincompatibility, higher concentration of PDF and glucose degradation product, PDF acidity and CAPD peritonitis-activated both local and systemic rennin-angiotensin aldosterone system (RAAS)[23,24]. Local RAAS up-regulated TGF-β and VEGF production and played an important role in peritoneal vasculopathy and sclerosis[24]. RAAS blockade by ACEI/ARB was effective to reduce TGF-β and submesothelial fibrosis in rat model[25] and slowed pathologic change of peritoneal transport in CAPD patients[26]. This was also seen in the present study that patients who usedthese drugs tended to have low or low-average peritoneal transport characteristics.

The loss of residual renal function may lead to malnutrition, volume overload, and increasing morbidity and mortality[27-31]. Few studies identified that loss of residual renal function caused a decreased in middle and small uremic toxin clearance, poorer fluid control, and activation of inflammatory cytokines. Anorexia, inflammation, and increased catabolic rate resulted from these situations caused malnutrition and vasculopathy[32,33].

This was only a pilot study which founded a correlation between malnutrition and decreased UF volume. There are limitations of the present study. First, the correlation coefficient from the present study was quite weak and this might be due to quite small sample size. Second, the present study was not designed as a prospective study thus, it is difficult to asses whether malnutrition or peritoneal change is the primary cause of all phenomenon. A larger prospective study is required to confirm the observation and to delineate the relationships among these factors.

In conclusion, malnutrition is associated with decreased ultrafiltration volume and residual renal function, leading to ECF expansion and fluid overload.

Potential conflicts of interest

None.

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ความสัมพันธ์ระหว่างภาวะทุพโภชนาการ การอักเสบและปริมาณการดึงน้ำในผู้ป่วยล้างไตทางหน้าท้อง

นันทวรรณ ถิ่นรุ่งโรจน์, ศุภฤกษ์ จิตติกานนท์, ดุสิต ล้ำเลิศกุล

วัตถุประสงค์*: ภาวะทุพโภชนาการ การอักเสบอาจทำให้เกิดการเปลี่ยนแปลงเยื่อหุ้มช่องท้อง และลดปริมาณการดึงน้ำ ส่งผลให้เกิดภาวะน้ำเกินในผู้ป่วยล้างไตทางหน้าท้อง*

วัสดุและวิธีการ*: ทำการศึกษาแบบตัดขวางในผู้ป่วยล้างไตทางหน้าท้อง 42 ราย ทำการตรวจภาวะทางโภชนาการและการอักเสบ ทำการวัดปริมาณการดึงน้ำ ปริมาณน้ำในส่วนต่างๆ ของร่างกาย*

ผลการศึกษา*: ผู้ป่วย 30 ราย มีโภชนาการปกติ ผู้ป่วย 12 ราย มีภาวะทุพโภชนาการ มีผู้ป่วย 1 ราย ที่มีภาวะทุพโภชนาการการอักเสบ กลุ่มผู้ป่วยภาวะทุพโภชนาการมีปริมาณการดึงน้ำลดลงโดยเฉพาะในกลุ่มที่มีระดับแอลบูมินในเลือดต่ำกว่า 3 กรัม/เดซิลิตร มีค่าการทำงานที่เหลืออยู่ของไตลดลง*

สรุป*: มีความสัมพันธ์เชิงบวกระหว่างภาวะทุพโภชนาการ และปริมาณการดึงน้ำในผู้ป่วยล้างไตทางหน้าท้อง*