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Original Article

The Factors Affecting The Efficiency of Continuous Ambulatory Peritoneal Dialysis in Children

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ABSTRACT

Objective: *Peritoneal dialysis is a complex and variable process. Many factors can affect efficiency of dialysis, and relevant mortality and morbidity rates. Efficient dialysis is important in improving quality of life as well as reducing the morbidity and mortality rates. Dialysis fill volume, intraperitoneal pressure and ultrafiltration (UF) are important variables that determine dialysis efficiency. We aimed to investigate the factors affecting dialysis efficiency and to determine necessities to develop a more effective dialysis program.*
Methods: *Sixteen continuous ambulatory peritoneal dialysis (CAPD) patients between the ages of 7 and 19 years who were followed up in the Pediatric Nephrology Department were included in the study. Patients who had peritonitis, surgical or medical complications in the last 6 months were excluded from the study. Demographic data, duration of dialysis, hemogram, urea, creatinine, albumin, glucose levels, intraperitoneal pressures, peritoneal equilibration test (PET) and Kt/Vurea test results were recorded.*
Results: *Mean Kt /Vurea, dialysis fill volume, UF, intraperitoneal pressure, Hb and serum albumin were found as 2.5±0.93 (1.22-4.64), 1123.4±126.86 (875-1360) ml/m2, 600.1±382.15 (85 -1375) ml, 12.9±2.77 (8.5-19) cm/H2O, 9.0±1.54 (6.3-11.8) gr/dl and 3.6±0.61 (2.45-4.8) gr/dl, respectively. A statistically significant relationship was shown between UF and Kt/Vurea (p=0.04). The mean duration of dialysis was 54±36 months. The majority of the cases had high (37.5%) and medium-high (31.25%) peritoneal permeability. High permeability was found to have a significant relationship with the duration of dialysis (p=0.04).*
Conclusion: *Efficient peritoneal dialysis depends on preserved ultrafiltration. Therefore, the dialysate volume should be calculated according to the intraperitoneal pressure and dialysis should be adjusted according to the permeability properties of the peritoneal membrane.*

INTRODUCTION

The first application of dialysis in humans was carried out by the German scientist Genter in 1923.[1] Peritoneal dialysis (PD) was first performed on children in 1978 by Oreopulos et al. and started to be used in the treatment of chronic renal failure (CRF).[2]

Peritoneal dialysis is the most common, and increasingly used renal replacement therapy in the world for children with CRF until the introduction of renal transplantation procedure.[3] This method of treatment is increasingly used in the world and in Turkey.[4,5] The principle of peritoneal dialysis is based on the fact that the peritoneum is a semipermeable membrane similar to the hemodialysis filter. This method is based on the passage of toxic substances into the fluid delivered into the peritoneal cavity and then evacuation of this fluid.[6]

Peritoneal dialysis is a complex and variable process. Many factors can affect efficiency of dialysis, and related mortality, and morbidity rates. Studies have pointed out that intraperitoneal pressure can affect dialysis adequacy and ultrafiltration. Intraperitoneal pressure measurement is a valuable parameter in determining the optimal fill volume, which is very important for peritoneal dialysis adequacy.[7] Based on this, our study aimed to investigate the factors affecting intraperitoneal pressure, the effects of ultrafiltration, residual renal functions and type of peritoneal permeability on dialysis adequacy, and what should be done to prescribe more effective dialysis.

MATERIAL and METHOD

Sixteen continuous ambulatory peritoneal dialysis (CAPD) patients between the ages of 7 and 19 years who were followed up in the Pediatric Nephrology Department were included in the study. Local ethics committee approval was obtained. Patients who had peritonitis, surgical or medical complications in the last 6 months were excluded from the study. Demographic data, drugs used, primary diagnoses and dwell times of dialysis of the patients were recorded. Hemogram, urea, creatinine, albumin and glucose values were recorded. Peritoneal equilibration (PET) and Kt/Vurea screening tests were used in first month, then every 6 months. Measurements of intraperitoneal pressure, PET and Kt/Vurea were performed, and the results were described in detail

Intraperitoneal pressure measurement: Patients are placed on their back after their bladder is emptied. The peritoneal dialysis system is connected, all fluid is drained and the specified volume of peritoneal dialysis fluid is given. Peritoneal dialysis tube is fixed in an upright position. The ruled column is held so that the zero point is on the mid-axillary line, at the center of the abdominal cavity. The connection path to the patient is opened. The height of the column where the dialysis fluid is located is measured in centimeters during inspiration and expiration, and its arithmetic average is calculated.[7,8] It has been shown that the intraperitoneal pressure measured through the intravesical catheter is equivalent to the pressure measured through the peritoneal catheter while the patient is lying supine.[9] In our study, measurement procedures were done by the same team each time, using the same ruler.

PET test: The patient comes to the hospital 8-12 hours before peritoneal dialysis without emptying the dialysate. In the sitting position, the dialysate is evacuated for 20 minutes and its volume is recorded. With the patient lying supine, 2.27% dialysis solution at a dose of 1100 ml/m^2 is delivered into the peritoneal cavity within 10 minutes. Meanwhile, the patient is turned to his/her right and then left side every 2 minutes to mix the infused solution with the residual dialysate. Immediately after the infusion is completed, 200 ml of dialysate is drained. After a 10 ml sample is taken, the rest is returned to the peritoneal cavity. During the test, the patient walks around. After waiting for 2 hours, 200 ml of dialysate is poured out again and after 10 ml of sample is taken, the remainder is infused into the peritoneum. At the same time 2-3 ml of blood sample is obtained. At the fourth hour, the whole dialysate is emptied in 20 minutes with the patient is in the sitting position. The bag is mixed thoroughly and a final sample of 10 ml is taken. The drainage volume is measured and the sample fluids (30 ml) taken are added to the drainage volume. Creatinine and glucose concentrations in blood and dialysate samples are measured. The ratio between dialysate and plasma creatinine concentrations (D/P creatinine) at the 4th hour of dialysis, and dialysate glucose concentrations between the 4th hour, and beginning of the dialysis (D4/D0 glucose) were calculated.

Peritoneal permeability is considered low if D/P creatinine <0.50, low-medium if 0.50-0.65, high-medium if 0.66-0.81 and highly permeable if >0.81.[10]

Performing the Kt/Vurea test: For the calculation of Kt/V urea, which is the fractional urea clearance standardized according to the urea distribution volume, 24-hour dialysate and 24-hour urine (if not less than 100 ml/day) are collected. After measuring the urea concentrations in blood, dialysate and urine, the Kt/Vurea is calculated using the following formulas.[11]

Dialytic Kt/Vurea= [(D/P urea) x Dialysate discharge volume (L)]/Total body water Renal Kt/Vurea= [(U/P urea) x Urine Volume (L)/Total body water

Weekly total Kt/Vurea=(Dialytic Kt/Vurea + Renal Kt/Vurea) x 7

D: Dialysate urea concentration, P: Plasma urea concentration, U: Urinary urea concentration

Total body water (TBW) was calculated using the Watson formulas:

In males, TBW=(0.3362 x weight) + (0.1074 x height)

+ (0.09516 x age) + 2.447 In females, TBW=(0.2466 x weight) + (0.1069 x height) – 2.097

The parameter of Kt/Vurea was taken as the basis for the dialysis adequacy . Mathematical calculations of Kt/Vurea and PET were made using computer application of "Renal Soft" program.

Statistical Analysis

The analysis of the data was done in SPSS for Windows 15 package program. Shapiro -Wilk test was used to investigate whether the distribution of continuous variables was normal. Descriptive statistics were presented as mean±standard deviation or median (25-75) percentiles for continuous variables, and as number of cases and percentages (%) for categorical variables Whether clinical and laboratory measurements changed significantly over time was examined using the dependent t-test or the Wilcoxon sign test. A significant association (if any) between continuous variables was evaluated with Spearman's correlation analysis. Whether the average change in pressure showed a significant difference according to gender was investigated by Student's t test. The results were considered statistically significant if $p<0.05$.

RESULTS

A total of 16 patients with chronic kidney failure including 9 boys and 7 girls, followed in the CAPD program were included in this study. The mean age of the patients was 14.2±3.7 (7-19) years, and the mean dwell time of dialysis was 54±42 (2-168) months.

Dialysis fill volumes, mean intraperitoneal pressure (IPP), PET and dialysis adequacy parameters of the patients are shown in Table 1.

Mean dialysate volume used for the patients was 1123.4±126.86 ml/m^2 (860-1360 ml/m^2), while the dialysate volume was below 1000 ml/m^2 in 4, and over 1200 ml/m^2 in 3 patients. Mean intraperitoneal pressure was 12.9±2.77 cm/H_2O (8.5-19 cm/H_2O), but it was above 18 cm/H_2O in only one patient. No relationship was found between intraperitoneal pressure and age and sex in the evaluation made considering filling volume ($p=0.187$, $p=0.745$). The mean Kt/Vurea value was 2.5±0.93 (range 1.22 to 4.64). Seven patients had Kt/Vurea values below 2. Four of these patients had no urine output. The mean values and distribution ranges in intraperitoneal pressure, dialysate volume, Kt/Vurea, Uf, Hb, albumin levels of the patients are shown in Table 2.

No relationship was found between intraperitoneal pressure, dialysate volume and dialysis adequacy ($p>0.05$). A statistically significant relationship was found between ultrafiltration and dialysis adequacy

Table 1. Dialysis fill volumes, intraperitoneal pressure and dialysis adequacy parameters of patients

Patients	Duration of dalysis (Month)	PET 1/2*	Volume of dyalisate ml/m^2 1 / 2*	IPP cm/H_2O 1 / 2	Kt/Vur 1 / 2*	Urine volume ml/m^2 day 1 / 2*	UF (ml/day) 1 / 2*	Hemoglobin gr/dl 1 / 2*	Albumin gr/dl 1 / 2*
1.	84	ML/ML	1320/1320	13/17	2.3/2.25	750/500	441/735	7.6 /9.7	3.8/3.89
2.	48	MH/H	1034/1000	10/ 13.5	1.73/1.95	0/0	690/980	8 /10.2	4.1/3.19
3.	60	L/ML	1190/1360	19/ 13.75	1.69/1.75	0/0	675/740	10.6 /6.3	3.8/4.1
4.	36	MH/MH	1000/1000	13/ 14.5	4.55/2.82	2400/2000	1375/425	7/10.7	3.4/3.34
5.	96	H /H	1190/1190	12.5/ 8.5	2.43/2.47	0/0	590/1175	7.9 /11.6	2.9/3.34
6.	24	ML/ML	1200/1170	10.5/10.25	2.41/2.34	300/750	605/450	11.8/11.1	4.8/4.54
7.	72	ML/MH	1150/1000	13.5/11	2.85/1.91	0/0	1150/800	11/7.8	4/3.9
8.	30	MH/H	1300/1100	11.5/12	2.58/2.33	0/0	200/0	8.1/8.3	3.55/3.74
9.	48	H/H	1000/1000	9.75/11.75	3.48/3.0	700/900	500/935	9.3/8.7	2.6/3.0
10.	168	MH/MH	1000/1000	13/13	1.94/1.84	250/300	250/300	9.4/9.1	3.2/3.4
11.	72	H/MH	975/1100	16.5/10.5	1.22/1.79	0/0	125/200	8.5/9.4	3.4/3.1
12.	84	H/(-)	1315/(-)	12.5/(-)	1.23/(-)	0/(-)	260/(-)	6.9/(-)	2.7/(-)
13.	12	H/(-)	860/(-)	11/(-)	3.03/(-)	950/(-)	85/(-)	8.3/(-)	3.4/(-)
14.	1,5	MH/(-)	1078/(-)	12.25/(-)	1.99/(-)	850/(-)	50/(-)	9.4/(-)	2.45/(-)
15.	12	H/(-)	970/(-)	15.25/(-)	4.64/(-)	2500/(-)	0/(-)	10.7/(-)	3.6/(-)
16.	12	ML/ (-)	837/ (-)	12/ (-)	1.83/ (-)	2000/(-)	170/ (-)	10.6/ (-)	3.5/ (-)

** The initial values of the patients and the control values after 6 months were reported as 1/2, respectively.*
H: High, MH: Medium high, ML: Medium low, L: Low, IPP: intraperitoneal pressure, PET: peritoneal equilibration test, Uf: ultrafiltration

Table 2. Dialysate volume, intraperitoneal pressure, dialysis adequacy, ultrafiltration, hemoglobin and albumin levels of the patients

Variables	Mean ± SD
Dialysate volume	1123.4±126.86 (875-1360) ml/m²
Intraperitoneal pressure	12.9±2.77 (8.5-19) cm/H_2O
Kt/Vurea	2.5±0.93 (1.22-4.64)
Ultrafiltration (ml/day)	600.1±382.15 (-85-1375) ml
Hemoglobin (gr/dl)	9.0±1.54 (6.3-11.8) gr/dl
Albumin (gr/dl)	3.6±0.61 (2.45-4.8) gr/dl

Table 3. PET test results of the patients at baseline and after 6 months

PET test	Beginning n (%)	6th month n (%)
High	6 (37.5%)	3 (%27.2%)
Medium high	5 (31.25%)	5 (%45.6%)
Medium low	4 (25.0%)	3 (%27.2%)
Low	1 (6.25%)	-

(p=0.04). While there was no correlation between intraperitoneal pressure and Kt/Vurea values of dialysate volume used (p=0.670, p=0.121, respectively), a significant change was found between ultrafiltration and Kt/Vurea (p=0.04). No relationship was found between hemoglobin and albumin and dialysis adequacy (p>0.05).

The first and second PET results of the patients who underwent peritoneal dialysis are shown in Table 3.

In the control PET test performed six months later, 8 patients had high and moderate-high, 3 patients had low and moderate-low peritoneal permeability. The second PET test could not be performed in five patients for various reasons. It was found that the peritoneal permeability of one of the patients changed from low to medium-high. The mean dwell times of peritoneal dialysis of the patients with high and moderate-high PET were 62 months, and 36 months for those with low and moderate-low peritoneal permeability. It was found that as the duration of peritoneal dialysis increased, peritoneal permeability was more likely to be high and moderate-high (p=0.04).

Nine of 16 patients had a urine output of 100 ml or more. Kt/Vurea values of 4 patients without urine output were below 2. It was found that the mean duration of dialysis was 44 months for patients with and 66 months for those without urine output. There was no statistically significant relationship between duration of dialysis and urine output (p=0.09).

Dialysate volumes, IPP and dialysis adequacy parameters were evaluated for the second time in 11 patients after 6 months. It was found that there was no change in volume of dialysate used in 5 patients, while it decreased in 3, and increased in other 3 patients (Table 4). When the initial and 6th month dialysis parameters were compared, no statistically significant difference was found between dialysate volumes, IPP, Kt/Vurea, and Uf (p>0.05).

Table 4. The initial and 6th month UF, IPP, dialysis proficiency parameters of the patients

Patients	Initial dialysate volume (ml/m²)	6th month dialysate volume (ml/m²)	Initial Intraperitoneal pressure (cm/H_2O)	6th month Intraperitoneal pressure (cm/H_2O)	Initial ultrafiltration	6th month ultrafiltration	Initial Kt/Vur	6th month Kt/Vur
1.	1320	1320	13	17	440	735	2.3	2.3
2.	1035	1000	10	13	690	980	1.73	1.73
3.	1190	1360	19	13.25	675	740	1.69	1.69
4.	1000	1000	13	14.5	1375	425	4.55	4.55
5.	1190	1190	12.5	8.5	590	1175	2.43	2.43
6.	1200	1175	10.5	10.25	605	450	2.41	2.41
7.	1150	1000	13.5	11	1150	800	2.85	2.85
8.	1100	1300	11.5	12	200	0	2.58	2.58
9.	1000	1000	9.75	11.75	500	935	3.48	3.48
10.	1000	1000	13	13	250	300	1.94	1.94
11.	975	1100	16.5	10.5	125	200	1.22	1.22

DISCUSSION

The appropriate dialysis method in children is chosen considering the age, psychosocial status, and the cause of kidney failure.[3] CAPD is the first option in the treatment of CRF due to the technical difficulties of hemodialysis in infants and young children. Peritoneal dialysis fill volume, number of cycles, dialysis fluid content, peritoneal membrane permeability are important factors that determine CAPD adequacy. Therefore, peritoneal dialysis prescriptions should be determined according to the individual parameters of each patient and tried to be optimized.[12,13]

Kt/Vurea is an important criterion in evaluating dialysis adequacy in peritoneal dialysis patients. Although the ideal Kt/Vurea is above 2, it is recommended in the DOQI guideline to keep the weekly total Kt/Vurea value above 1.7, regardless of the peritoneal dialysis method.[14-16] In addition, the definition of dialysis adequacy parameters based on the removal of solutes such as Kt/Vurea is questioned. Although the urea dialysis dose was increased by 30% with this approach, there was no decrease in the morbidity and mortality rates of adult patients using chronic peritoneal dialysis.[17,18] In our study, the Kt/Vurea values of the patients were found to be within normal limits (mean Kt/Vurea. 2.5±0.93). In the initial measurement, Kt/Vurea values of 4 patients were found to be below 1.7. It was observed that by increasing the dialysate volume of two of these patients, the Kt/Vurea values increased above 1.7 in the second measurement without any change in the dialysate volume of the others. There was no change in the Kt/Vurea values of the other patients.

The appropriateness of the peritoneal dialysis fill volume is very important for dialysis adequacy.[19,20] It has been shown that intraperitoneal pressure is an objective criterion reflecting the fill volume. Normal reference ranges for fill volume (1200-1500 ml/m^2), and intraperitoneal pressure (15-18 cm/H_2O) are also specified.[21] Ideal fill volume is 1000-1200 ml/m^2 (7-15 cm/H_2O of intraperitoneal pressure).[21] While low dialysis fill volume causes hyperperfusion, its excessive amount damages the peritoneal membrane and may negatively affect dialysis adequacy. It has been shown that there is an increase of 4 cm/H_2O in intraperitoneal pressure for every 1-liter increase in dialysate volume.[22] In our study, no statistically significant difference was found between the mean fill volume and mean intraperitoneal pressure, and between these parameters and Kt/Vurea. An increase in intraperitoneal pressure above 18 cm/H_2O almost always causes pain.[23] In our study, intraperitoneal pressures were found to be 8.5-19 cm/H_2O at the first measurement. The patient whose fill volume was measured as 1190 ml/m^2 and intraperitoneal pressure as 19 cm/H_2O was found to have no abdominal pain. The intraperitoneal pressure was measured as 13.25 cmH_2O 6 months after the dialysis fill volume of this patient was increased to 1360 ml/m^2 due to dialysis insufficiency. It was found that the intraperitoneal pressure of 3 patients, whose fill volumes were higher than the recommended amount due to insufficient ultrafiltration and dialysis were less than 5 cmH_2O. It has been reported that when the dialysate volume is increased, the intraperitoneal pressure, which is high in the early period, may return to normal over time and the peritoneal membrane will get used to this new condition.[21] In the second evaluation performed 6 months later in our study, it was observed that the intraperitoneal pressure of the patients whose dialysate volumes changed did not change significantly (p=0.247).

Intraperitoneal pressure can be affected by many factors other than dialysate volume such as age, sex, body surface area, body mass index, posture, tolerance acquired over time, constipation, and peritoneal dialysis fluid content. In some studies performed with adults, increased intraperitoneal pressure was found to be associated with complications such as hernia, gastroesophageal reflux, etc.[24], but no complications were detected in our patients. Intraperitoneal pressure is lower in infants compared to adults. Because of higher abdominal tonicity in men, intraperitoneal pressure may be higher.[19,25-28] In our study, no relation was found between intraperitoneal pressure and age or gender of the patients.

In our study, it was determined that the most important factor affecting dialysis adequacy was ultrafiltration. Although the dialysis volume was not increased, an increase was detected in the ultrafiltration of 3 patients whose intraperitoneal pressures increased. The osmotic pressure difference between the peritoneal capillary blood and the hypertonic dialysate solution creates ultrafiltration, and waste products such as urea and creatinine are removed from the body. Ultrafiltration is one of the important determinants of dialysis adequacy.[21,29] In addition to studies showing that ultrafiltration increases with increasing peritoneal dialysis fill volume,[30-32] there are also studies reporting ultrafiltration was caused by increased lymphatic reflux and therefore decreasing dialysis adequacy. Some of them have reported an increase in mortality and morbidity rates by triggering peritoneal fibrosis in the long term associated with an increase fill volume.[21,33,34] It has been reported that increasing intraperitoneal pressure without an increase in dialysis volume will decrease ultrafiltration and adversely affect dialysis adequacy.[22]

In our study, we found that as the dialysis dwell time increased, PET shifted to the higher side (p=0.04), but ultrafiltration did not decrease (p=0.117). In patients with high permeability, the continuation of ultrafiltration was ensured by switching to instrumental peritoneal dialysis and using dialysis fluid with a higher glucose concentration and isodextrin. The solute transport properties of the peritoneal membrane differ from patient to patient, and this leads to a change in water and solute clearance over time affecting dialysis adequacy. In patients with poor dialysis adequacy parameters, it is recommended to determine a dialysis program while taking into account the peritoneal permeability tests. High permeability of the peritoneal membrane is a poor prognostic indicator.[35] In those with medium-high and high PET values, ultrafiltration also decreases due to the faster loss of the osmotic gradient.

Residual renal function is one of the important parameters that determine the patient's quality of life, and the duration and adequacy of dialysis. However, after starting dialysis, the amount of urine gradually decreases, and if there is an ultrafiltration insufficiency, the volume control of the patient becomes difficult, and the number of antihypertensive drugs used increases. In our study, when the patients were evaluated individually, it was seen that residual renal function was one of the important determinants of dialysis adequacy. The Kt/Vurea values of 9 patients whose daily urine output was 100 ml and above were found to be between 1.9 and 4.6. It was determined that three of the 4 patients with Kt/Vurea values below 1.7 had dialysate volumes of 1000-1365 ml/m^2, and one had a Kt/Vurea value of 975 ml/m^2. All of these patients had no urine output. In 3 patients whose dialysate volumes were below 1000 ml/m^2, but their Kt/Vurea values were above 1.7. It was observed that the daily urine output varied between 950-1000 ml. Statistical evaluation could not be made due to the small number of patients.

With peritoneal dialysis, albumin and protein are lost.[36,37] Albumin level is an important parameter showing dialysis adequacy. In our study, no statistically significant relationship was found between albumin levels and parameters of dialysis adequacy. Like albumin, anemia is an indicator of dialysis adequacy. Anemia may adversely affect hemodynamics in CRF patients and thus impair dialysis adequacy.[36,37] In our study, no statistically significant relationship was found between hemoglobin levels and dialysis adequacy.

Our study, like other studies on this subject, was conducted with a small number of patients. Therefore, some of our results are not compatible with the literature. Another problem is that peritoneal dialysis adequacy is affected by many factors and includes multiple variables.

In conclusion, for adequate peritoneal dialysis, ultrafiltration should be preserved. Therefore, the dialysate volume should be calculated taking into account the intraperitoneal pressure, and dialysis should be prescribed according to the permeability properties of the peritoneal membrane. Further studies with larger case series are required on this subject.

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