21. Williams JD, Topley N, Craig JK *et al*. The Euro-Balance Trial: the effect of a new biocompatible peritoneal dialysis fluid (balance) on the peritoneal membrane. *Kidney Int* 2004; 66: 408–418
22. Fan SLS, Pile T, Raftery MJ *et al*. Randomized controlled study of biocompatible peritoneal dialysis solutions: effect on residual renal function. *Kidney Int* 2008; 73: 200–206
23. Locatelli F, La Milia V. Preservation of residual renal function in peritoneal dialysis patients: still a dream? *Kidney Int* 2008; 73: 143–145
24. Rippe B, Simonsen O, Heimbürger O *et al*. Long-term clinical effects of a peritoneal dialysis fluid with less glucose degradation products. *Kidney Int* 2001; 59: 348–357
25. Breborowicz A, Pawlaczyk K, Polubinska A *et al*. Effect of peritoneal dialysis on renal morphology and function. *Nephrol Dial Transplant* 2006; 21: 3539–3544
26. Uribarri J, Tuttle KR. Advanced glycation end products and nephrotoxicity of high-protein diets. *Clin J Am Soc Nephrol* 2006; 1: 1293–1299
27. Cheng LT, Chen W, Tang W *et al*. Residual renal function and volume control in peritoneal dialysis patients. *Nephron Clin Pract* 2006; 104: c47–c54
28. Konings CJAM, Kooman JP, Schonck M *et al*. Fluid status in CAPD patients is related to peritoneal transport and residual renal function: evidence from a longitudinal study. *Nephrol Dial Transplant* 2003; 18: 797–803
29. Jean G, Chazot C, Charra B. Hyperphosphataemia and related mortality. *Nephrol Dial Transpant* 2006; 21: 273–280
30. Wang AYM, Woo J, Sea M *et al*. Hyperphosphatemia in Chinese peritoneal dialysis patients with and without residual renal function: what are the implications? *Am J Kidney Dis* 2004; 43: 712–720
31. Schwenger V, Morath C, Salava A *et al*. Damage to the peritoneal membrane by glucose degradation products is mediated by the receptor for advanced glycation end-products. *J Am Soc Nephrol* 2006; 17: 199–207
32. Visser CE, Brouwer-Steenbergen JJE, Betjes MGH *et al*. Cancer antigen 125: a bulk marker for the mesothelial mass in stable peritoneal dialysis patients. *Nephrol Dial Transplant* 1995; 10: 64–69
33. Fang W, Mullan R, Shah H *et al*. Comparison between bicarbonate lactate and standard lactate dialysis solution in peritoneal transport and ultrafiltration: a prospective, crossover single-dwell study. *Perit Dial Int* 2008; 28: 35–43
34. Ahmad S, Sehmi JS, Ahmad-Zakhi KH *et al*. Impact of new dialysis solutions on peritonitis rates. *Kidney Int* 2006; 70: S63–S66
35. Lee HY, Park HC, Seo BJ *et al*. Superior patient survival for continuous ambulatory peritoneal dialysis patients treated with a peritoneal dialysis fluid with neutral pH and low glucose degradation product concentration (Balance). *Perit Dial Int* 2005; 25: 248–255
36. Lee HY, Choi HY, Park HC *et al*. Changing prescribing practice in CAPD patients in Korea: increased utilization of low GDP solutions improves patient outcome. *Nephrol Dial Transplant* 2006; 21: 2893–2899

Received for publication: 24.6.08; Accepted in revised form: 2.2.10

Nephrol Dial Transplant (2010) 25: 2296–2303
doi: 10.1093/ndt/gfq027
Advance Access publication 4 February 2010

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

Impact of peritoneal transport characteristics on cardiac function in Paediatric peritoneal dialysis patients: a Turkish Pediatric Peritoneal Dialysis Study Group (TUPEPD) report

Sevcan A. Bakkaloglu[1], Arda Saygili[2], Lale Sever[3], Nejat Aksu[4], Aytul Noyan[5], Sema Akman[6], Mesiha Ekim[7], Beyza Doganay[8], Nurdan Yildiz[9], Figen Akalin[10], Salim Caliskan[3], Orhan D. Kara[4], Ali Duzova[11], Alper Soylu[12] and Semra Atalay[13]

[1]Deparment of Pediatric Nephrology, Gazi University, Ankara, Turkey, [2]Department of Pediatric Cardiology, Acibadem University, Istanbul, Turkey, [3]Department of Pediatric Nephrology, Istanbul University, Istanbul, Turkey, [4]Division of Pediatric Nephrology, Tepecik Teaching Hospital, Izmir, Turkey, [5]Deparment of Pediatric Nephrology, Cukurova University, Adana, Turkey, [6]Department of Pediatric Nephrology, Akdeniz University, Antalya, Turkey, [7]Deparment of Pediatric Nephrology, Ankara University, Ankara, Turkey, [8]Department of Biostatistics, Ankara University, Ankara, Turkey, [9]Division of Pediatric Nephrology, Goztepe Teaching Hospital, Istanbul, Turkey, [10]Deparment of Pediatric Cardiology, Marmara University, Istanbul, Turkey, [11]Deparment of Pediatric Nephrology, Hacettepe University, Ankara, Turkey, [12]Deparment of Pediatric Nephrology, Dokuz Eylül University, Ankara, Turkey and [13]Deparment of Pediatric Cardiology, Ankara University, Ankara, Turkey

Correspondence and offprint requests to: Sevcan A. Bakkaloglu; E-mail: sevcan@gazi.edu.tr

Abstract

Background. The peritoneal equilibration test (PET) is recommended in paediatric peritoneal dialysis (PD) patients to assist prescription management. Despite contradictory reports, high transporter status is associated with reduced survival rate in adults. Since cardiac disease is one of the main causes of mortality in paediatric PD patients, we aimed to evaluate whether transport features have any effect on biochemical data and cardiac function in this group.

Methods. One hundred and ten PD patients (13 ± 5 years, PD vintage: 31 ± 27 months) were enrolled into the study.

© The Author 2010. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.
For Permissions, please e-mail: journals.permissions@oxfordjournals.org

Four-hour dialysate/plasma creatinine ratio was used for differentiating PET groups. Thirty-eight patients were high transporters, 29 were high-average transporters and 43 were low-average/low transporters. Echocardiography was performed in all subjects.

Results. Age, PD vintage, dialysate glucose concentration, ultrafiltration volume, urine volume and blood pressure levels were similar in all PET groups. No biochemical or echocardiographic data (ejection fraction, fractional shortening, left ventricular mass index, myocardial performance index, power Doppler E/tissue Doppler E ratio reflecting diastolic function) were different among PET groups except lower albumin ($P = 0.025$) levels in high transporters and higher high-sensitivity C-reactive protein ($P = 0.026$) levels in high and high-average transporters compared to other transport groups.

Conclusions. Cardiac structural and functional abnormalities are highly prevalent among paediatric PD patients. Transport rates did not have a significant effect on biochemical parameters or cardiac structural/functional parameters. It might be suggested that being a high transporter does not provide a disadvantage in terms of atherogenic tendency and cardiac disease in paediatric PD patients. Oligoanuria, anaemia and hypertension were independent predictors of cardiac disease.

Keywords: cardiac function; children; echocardiography; peritoneal dialysis; peritoneal equilibration test

Introduction

Solute transport and ultrafiltration (UF) rates vary largely in patients undergoing peritoneal dialysis (PD). With the use of the peritoneal equilibration test (PET), peritoneal membranes can be classified into four main types: high (H), high-average (HA), low-average (LA) and low (L) [1]. Peritoneal membrane solute transport characteristics (PMTC) of children in terms of 4-h dialysate-to-plasma (D/P) creatinine and D/D0 glucose ratios are markedly similar to data obtained in adults and have been used to assist the development of an individualized PD prescription [2].

The relationship between PMTC and the outcomes of patients receiving PD has been the subject of several studies [3–8]. Despite contradictory reports [4,5], H transport status was associated with a higher mortality risk and a trend to higher technique failure in recent studies [6,7]. It has been associated with several poor outcome parameters like hypoalbuminaemia [9], poor nutrition [10], elevated inflammatory markers [11] and cardiovascular disease (CVD) [11,12] in adults.

The paediatric PET has been proven to be remarkably sensitive in demonstrating changes in peritoneal transport [2] and their relationship to PD outcomes [8]. Although the low morbidity and mortality rates in children, the relatively short dialysis periods and the small patient numbers in each paediatric centre render an assessment of PD outcome in children difficult, and growth, nutritional parameters and physical/cognitive performance had been proposed as important possible end points of treatment outcome [8], CVD is increasingly being recognized as one of the most important outcome variables in paediatric end-stage renal disease (ESRD) patients [13–15]. Children with ESRD have an increased risk for death, particularly from CVD [13,14]. CVD is more common in H transporters than in other transport groups in adult studies [11,12]. To our knowledge, cardiac structural and functional parameters have not been studied in paediatric PD patients with different PMTC.

The study was designed to determine if PMTC assessed by the PET are associated with cardiac structural and functional abnormalities evaluated by echocardiography [M-mode, pulsed wave Doppler (PWD) and tissue Doppler imaging (TDI)] in a large group of paediatric maintenance PD patients.

Methods

One hundred and ten patients and 124 control subjects were enrolled in this study. The patients on PD <3 months and having an acute infection during the last 3 months were excluded from the study.

A 4-h paediatric PET was conducted on each patient. The test exchange fill volume was 1100 mL/m^2 and dialysate (D) was 2.27% Dianeal (Baxter Healthcare, Deerfield, IL, USA). D samples were taken at 0, 2 and 4 h of dwell. Blood (P) samples were obtained at 0 and 4 h. All D and P samples were analysed for creatinine and glucose. D/P creatinine ratios were calculated by using dialysate creatinine concentrations at 2 and 4 h of the PET divided by the average of the two plasma creatinine concentrations. The D/D0 ratios for glucose were calculated by dividing the dialysate glucose concentration (DGC) at 2 and 4 h by the initial DGC.

To characterize peritoneal membrane transport capacity, the results of the PET assessment (D/P creatinine and D/D0 glucose) were plotted on the reference curves published by Warady *et al.* [2]. Patients were categorized as H, HA, LA or L transporters according to the D/P creatinine ratios at 4 h. Due to the small number of patients, L and LA patients were pooled into the same group: H transporters ($n = 38$), HA ($n = 29$) and LA/L transporters ($n = 43$).

Routine blood tests as well as high-sensitivity C-reactive protein (HS-CRP) levels were studied in patients. M-mode, PWD and TDI echocardiography was performed in both groups (Vivid 7 Pro, GE Medical Systems, Vingmed Ultrasound AS, N-3190 Horten, Norway) by experienced paediatric cardiologists in each centre by following the same protocols that were given in detail in our previous study [15]. Left ventricular mass (LVM) was calculated using the Devereux formula [16], and LVM index (LVMI; mass divided by height raised to a power of 2.7) was used to evaluate left ventricular hypertrophy (LVH) [17]. LVH was defined as LVMI greater than the 95th percentile for age and gender in normal children and adolescents [18]. The relative wall thickness (RWT) was calculated as an index of the LV geometric pattern: RWT = (IVED ± PWED)/LVED. Concentric LVH was defined as increased LVMI and RWT greater than the 95th percentile of paediatric patients, eccentric LVH was defined as elevated LVMI with normal RWT and concentric remodelling was defined as normal LVMI but elevated RWT [19].

Statistical analysis

Differences between the two and three groups for continuous variables were evaluated by using Student's *t*- or Mann–Whitney *U* test and Kruskal–Wallis or ANOVA test, respectively, where applicable. Correlations between variables were evaluated by using Pearson and Spearman correlations, where applicable. Regression analysis was performed to determine the variables that significantly affect LVMI as a measure of structural cardiac abnormality and PWD E/TDI E ratio as a measure of diastolic dysfunction. Stepwise elimination was used for selection of covariates in regression models. SPSS version 15.0 was used (SPSS, Chicago, IL, USA). Local ethical committee approval was obtained.

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

Results

One hundred and ten patients aged 13.8 ± 4.5 (range 5–22) years, treated with PD for a period of 31 ± 27 (3–108) months in 11 paediatric CPD centres, and 124 sex- and body mass index (BMI)-matched healthy subjects as a control group were enrolled in this study.

Aetiologic causes of ESRD and frequencies of cardiovascular risk factors in the patients

It was observed that 34.5% (n = 38) of the patients had urological problems/tubulointerstitial diseases. The second most common group was primary glomerulonephritides (29%, n = 32), as reported in our national registry [20]. Other diagnoses were hereditary/metabolic disorders in 9% (n = 10) of the patients (n = 10), hypo-/dysplasia in 6.4% (n = 7), cystic renal disease in 3.6% (n = 4), unknown aetiology in 13% (n = 14) and miscellaneous in 4.5% (n = 5). There were no diabetic patients. None of the patients had a previous transplant and were on steroids or other immunosuppressives. Fifty-five patients were oligoanuric. Haemoglobin levels were <11 g/dL in 73% of the subjects. None of the patients had serum albumin levels <2.5 g/dL; however, approximately one-third of patients had hypoalbuminaemia as well as dyslipidaemia.

Systolic/diastolic blood pressure (BP) levels were within the normal limits in 60 patients compared to the BP nomograms of Turkish children [21]. Fifty-five patients (50%) were on antihypertensives (44 of 55 patients were on a single drug and 46 patients were on angiotensin-converting enzyme inhibitors). Seventeen patients were on lipid-lowering drugs. Lipid profile, uric acid levels and calcium–phosphorus product were found within acceptable limits. Half of the patients had increased HS-CRP levels. Parathormone (PTH) levels were <200 pg/mL in 34.5% of the patients, between 200 and 300 in 14% and >300 in 51.5%. The mean weekly K_t/V_{urea} was 2.55 ± 0.85, 4-h D/P creatinine was 0.68 ± 0.18 and 4-h D/D0 glucose was 0.39 ± 0.12.

Comparisons of echocardiographic data between the patients and control subjects

LVMI, RWT and PWD E/TDI E ratio were significantly higher, while ejection fraction (EF) and fractional shortening (FS) were lower in patients on PD compared to controls. LVH was prevalent in 72.7% of the patients (50% concentric, 22.7% eccentric). Moreover, 11.8% of the patients had concentric remodelling and 15.5% of the patients had normal cardiac structure.

LVMI as well as PWD E/TDI E ratio was positively correlated with mean arterial pressure (MAP; r = 0.306, P = 0.001 and r = 0.264, P = 0.004, respectively), while it was negatively correlated with Hb (r = −327, P = 0.000 and r = −0.354, P = 0.001, respectively), residual diuresis (r = −0.202, P = 0.035 and r = −0.306, P = 0.003, respectively) and albumin levels (r = −0.198, P = 0.038 and r = −208, P = 0.047, respectively).

DGC was positively correlated with PWD E/TDI E ratio (r = 0.241, P = 0.004), while it was negatively correlated with residual diuresis (r = −0.264, P = 0.006). There were no correlations between LVMI and PET data, HS-CRP levels, lipid parameters, calcium–phosphorus product or PTH levels. Lower Hb (β = −4.806; 95% confidence interval, CI: −7.920, −1.692; P = 003) and higher MAP (β = 0.545, 95% CI: 0.156–0.935, P = 0.006) were independent predictors of increased LVMI. Lower residual urine volume (β = −0.934; 95% CI: −1.693, −0.176; P = 0.016) was an independent predictor of increased PWD E/TDI E ratio.

Comparisons among patients with different solute transport features

The patients were divided into three groups by using 4-h D/P creatinine: H (n = 38), HA (n = 29) and LA/L transporters (n = 43). Age, sex distribution, anthropometric measures, PD vintage, urine output, UF volume, DGC, BP, Hb and PTH levels were similar in each PET group (Tables 1 and 2). No biochemical and echocardiographic data were different among PET groups, except slightly lower serum

Table 1. Descriptive features of the patients in different solute transport categories[a]

	High transporter (mean ± SD)	High-average transporter (mean ± SD)	Low-average/low transporter (mean ± SD)	*P*
Age (years)	13.0 ± 4.6	14.8 ± 4.2	13.7 ± 4.7	NS
Sex (M/F)	17/21	14/15	17/26	NS
Body weight (kg)	33 ± 18	36 ± 13	34 ± 13	NS
Height (cm)	132 ± 23	139 ± 20	135 ± 21	NS
BMI (g/m^2)	17.6 ± 4.4	18.2 ± 3.2	18.0 ± 3.6	NS
Time on PD (months)	32 ± 29	32 ± 25	31 ± 27	NS
Daily urine output (ml/kg/h)	0.8 ± 1.0	0.9 ± 1.1	0.7 ± 1.0	NS
Daily ultrafiltration (ml/m^2)	556 ± 418	607 ± 408	633 ± 453	NS
Dialysate glucose concentration (g/m^2/day)	91 ± 38	99 ± 43	110 ± 47	NS
Systolic blood pressure (mmHg)	120 ± 18	119 ± 17	115 ± 15	NS
Diastolic blood pressure (mmHg)	77 ± 13	79 ± 14	76 ± 15	NS
MAP (mmHg)	92 ± 14	93 ± 15	91 ± 14	NS

[a]D/P creatinine at 4 h.

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

Table 2. Biochemical data of the patients in different solute transport categories[a]

	High transporter (mean ± SD)	High-average transporter (mean ± SD)	Low-average/low transporter (mean ± SD)	*P*
Blood urea nitrogen (mg/dl)	74 ± 39	57 ± 22	68 ± 36	NS
Creatinine (mg/dl)	7.6 ± 2.3	7.7 ± 2.4	8.1 ± 2.4	NS
Uric acid (mg/dl)	5.4 ± 1.0	5.7 ± 1.2	5.9 ± 1.4	NS
Albumin (g/dl)	3.5 ± 0.5	3.7 ± 0.6	3.8 ± 0.5	0.025
Triglyceride (mg/dl)	154 ± 64	143 ± 81	170 ± 114	NS
Cholesterol (mg/dl)	200 ± 41	176 ± 44	199 ± 49	NS
High-density lipoprotein cholesterol (mg/dl)	47 ± 16	42 ± 8	49 ± 12	NS
Low-density lipoprotein cholesterol (mg/dl)	120 ± 38	105 ± 36	119 ± 43	NS
Very-low-density lipoprotein cholesterol (mg/dl)	31 ± 13	29 ± 16	34 ± 23	NS
Calcium (mg/dl)	8.8 ± 0.9	9.4 ± 0.9	9.4 ± 1.4	0.038
Phosphorus (mg/dl)	5.4 ± 1.7	5.4 ± 1.4	5.8 ± 1.6	NS
Calcium phosphorus product (mg^2/dl^2)	48 ± 16	51 ± 14	55 ± 15	NS
Alkaline phosphatase (U/l)	505 ± 446	618 ± 706	431 ± 415	NS
Parathormone (pg/ml) (*N*: 12–72)	402 ± 489	511 ± 478	509 ± 478	NS
Haemoglobin (g/dl)	9.3 ± 1.5	9.9 ± 1.9	9.9 ± 1.9	NS
Ferritin (ng/ml)	365 ± 416	272 ± 267	416 ± 560	NS
HS-CRP (mg/l) (*N*: 0–0.3)	1.3 ± 2.1	1.2 ± 1.5	0.7 ± 1.5	0.026
Creatinine clearance (ml/min/1.73 m^2)	10 ± 3	11 ± 4	10 ± 3	NS
Weekly K_t/V_{urea}	2.31 ± 0.91	2.70 ± 0.98	2.64 ± 0.65	NS
PD vintage (months)	32 ± 28	33 ± 26	31 ± 27	NS

[a]D/P creatinine at 4 h. SD, standard deviation.

Table 3. Echocardiographic data of the patients in different solute transport categories[a]

	High transporter (mean ± SD)	High-average transporter (mean ± SD)	Low-average/low transporter (mean ± SD)	*P*
EF (%)	63 ± 10	65 ± 13	63 ± 11	NS
FS (%)	37 ± 6	37 ± 8	34 ± 7	NS
LVMI (g/m^2)	68 ± 34	57 ± 28	56 ± 32	NS
RWT (cm)	0.47 ± 0.12	0.45 ± 0.13	0.42 ± 0.10	NS
WS (g/cm^2)	57 ± 22	61 ± 25	61 ± 24	NS
PWD E/A ratio	1.40 ± 0.39	1.47 ± 0.37	1.45 ± 0.37	NS
IVRT (ms)	76 ± 33	76 ± 23	73 ± 25	NS
DT (ms)	143 ± 42	158 ± 41	154 ± 40	NS
Myocardial performance index	0.54 ± 0.26	0.59 ± 0.25	0.51 ± 0.21	NS
TDI lateral mitral annulus E/A ratio	1.78 ± 0.48	1.71 ± 0.72	1.56 ± 0.57	NS
PWD E/TDI E ratio	9.1 ± 3.1	8.4 ± 3.6	8.3 ± 3.3	NS

[a]D/P creatinine at 4 h.

albumin levels in H transporters compared to the other groups (3.5 ± 0.5 vs 3.7 ± 0.6 and 3.8 ± 0.5 g/dL, respectively, P = 0.023) and higher HS-CRP levels in HA and H transporters compared to LA/L transporters (1.3 ± 2.1 and 1.2 ± 1.5 vs 0.7 ± 1.5 mg/L, respectively, P = 0.026; Tables 2 and 3). High transporters tended to have a lower UF, higher LVMI and a higher PWD E/TDI E ratio compared to the other transport groups, although it did not reach statistical significance (Table 3).

The effect of PD modality on clinical and laboratory data

Fifty-five patients were on continuous ambulatory peritoneal dialysis (CAPD) and 55 on ambulatory peritoneal dialysis (APD; Table 4). There were no significant differences in demographic, biochemical or echocardiographic data between patients on CAPD or APD, except longer PD vintage (39 ± 30 vs 25 ± 22 months, P = 0.000), lower diastolic BP (80 ± 13 vs 74 ± 14 mmHg, P = 0.020), higher K_t/V_{urea} (2.75 ± 0.92 vs 2.34 ± 0.73, P = 0.012) and higher DGC (122 ± 44 vs 78 ± 30 g/m^2/day, P = 0.006) in APD patients. Fifty-one patients were not on an appropriate PD regimen. Twenty-three (62%) H transporters were on CAPD and 28 L transporters were on APD, while 59 patients were on appropriate PD modality. Compared to these two groups of patients, there were no differences in blood pressure, UF and urine volumes, and biochemical parameters. LVMI was found to be significantly increased in these 51 patients compared to the remaining 59 patients (LVMI: 65 ± 31 vs 56 ± 30 g/m^2, P = 0.051), as was PWD E/TDI E ratio (9.0 ± 3.5 vs 7.7 ±3.2, P = 0.026).

Four-hour D/D0 glucose values were available in 80 subjects. Discrepancies in the results existed in 40 cases

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

Table 4. Type of dialysis and solute transport status of the patients

Type of peritoneal dialysis	High transporter *n* (%)	High-average transporter *n* (%)	Low-average/low transporter *n* (%)	Total *n*
APD	14 (38%)	13 (42%)	28 (33%)	55
CAPD	23 (62%)	18 (58%)	14 (67%)	55
Total	37 (100%)	31 (100%)	42 (100)	110

Table 5. Laboratory data by transport features based on 4-h D/D0 glucose

	High transporter (mean ± SD) *n* = 27	High-average transporter (mean ± SD) *n* = 22	Low-average/low transporter (mean ± SD) *n* = 31	*P*
Haemoglobin (g/dl)	9.2 ± 1.5	9.9 ± 1.6	10.4 ± 2.0	0.041
Albumin (g/dl)	3.4 ± 0.6	3.8 ± 0.4	3.9 ± 0.5	0.002
PWD E/TDI E ratio	9.8 ± 3.3	7.9 ± 3.8	6.9 ± 2.7	0.012
LVMI (g/m^2)	62 ± 40	53 ± 25	55 ± 28	NS

when comparing creatinine- and glucose-based data. In 30 of the 40 cases, the discrepancies were of a single transport category. When transport groups were defined based on 4-h D/D0 glucose data, there were significant differences only in Hb, serum albumin and PWD E/TDI E ratio. H transporters had lower Hb and albumin levels and higher PWD E/TDI E ratio as well as relatively higher LVMI compared to the other groups (Table 5).

Discussion

This study showed a high prevalence of cardiac functional and structural abnormalities, which was significantly affected by well-known CV risk factors, mainly anaemia, hypertension and residual diuresis as well as hypoalbuminaemia and microinflammation rather than PMTC in paediatric PD patients. Since CVD is increasingly being recognized as one of the leading causes of death among adult and paediatric ESRD patients [13,14,22] and the prevalence of CVD is more common in H transporters than other transport groups in adult studies [11,12], cardiac function and structure were selected as our outcome of interest. To the best of our knowledge, this is the first study evaluating the effect of PMTC on cardiac function in a large paediatric patient group on maintenance PD. However, we did not find any significant impact of being an H transporter on structural and functional cardiac parameters by using 4-h D/P creatinine data to characterize PMTC. This can result from comparable fluid removal in H transporters with other transport groups characterized by equal UF and residual urine volume. However, in fact, H transporters tended to have a lower UF but a higher residual urine output. Since residual diuresis has been shown to have a significant impact on structural and/or functional cardiac abnormalities rather than UF in the present and previous studies [15,23], one can understand the similar clinical volume status and echocardiographic parameters in H transporters and other transport groups. Use of icodextrin in H transporters may provide further benefit with an additional UF capacity [24,25].

There was a common belief supported by several studies that paediatric patients, particularly infants, are high transporters [26–28]. However, subsequent studies showed that standard PET results in children were not essentially different from results obtained in adult patients [29–32]. No influence of age, dialysis vintage or dialysate composition (conventional or biocompatible) on the fluid kinetic parameters was also demonstrated in some paediatric studies [31,33,34]. An important factor affecting PET results was instilled test volume [2,31]. If PET was performed with a test volume in millilitres per kilogram, its expression as square metre gives a relatively low volume, especially in small children, and thus an apparently more rapid equilibration of solutes resulting in higher D/P ratios [35]. Based on 110 paediatric patients in our study, the mean D/P creatinine at 4 h was 0.68 ± 0.18 and D4/D0 glucose was 0.39 ± 0.12, which were highly comparable to adult data [1]. We used a test volume of 1100 mL/m^2 and did not have any patients <5 years. On the other hand, the frequency of being an H transporter is highly variable in paediatric studies from different parts of the world. Thirty-five percent of our patients were H transporters, while it was 12, 15 and 60% in recent studies from Chile, USA and China, respectively [29,30,36]. The variation mainly results from instilled test volume, and possibly ethnical differences and previous peritonitis episodes are suggested as an important factor for higher peritoneal permeability [37], although not acknowledged in all studies [31,38]. Our patients did not have a peritonitis episode during the 3 months before the study entry. However, we do not have data about previous peritonitis experiences. This is one of the limitations of our study. Additionally, dialysis vintage had no effect on PMTC in our study despite contradictory paediatric reports [32,36].

In a recent paediatric study, PMTC based on glucose and creatinine kinetics provided discrepant results in 14

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

of 20 cases [29]. However, in only one case was the discrepancy of more than a single transport category. Our data showed discrepant results in 50% of the cases. In 12% of the cases, the discrepancies were of more than a single transport category. In addition to creatinine-based data, we categorized patients based on their glucose absorption rate as H, HA and LA/L transporters. Data were available in 80 patients and all descriptive, biochemical and cardiac variables were compared among the three groups. There were lower Hb and albumin levels and higher PWD E/TDI E ratio, reflecting diastolic dysfunction in H transporters compared to the other groups, as was relatively higher LVMI. Also, higher glucose transport rates were associated with diastolic dysfunction. Since creatinine transport rates tend to demonstrate the best correlation with adult patients' clinical response to PD, consideration has been given to the preferential use of D/P creatinine data. However, our data suggested that glucose-based data and its clinical implications may deserve further attention and should be investigated in longitudinal studies in larger groups.

A recent meta-analysis and a large registry demonstrated that a higher peritoneal membrane solute transport rate is associated with a higher mortality risk and a trend to higher technique failure in adults [6,7]. The mechanisms responsible for the problem status of H transporters are diverse. They have enhanced clearance of small solutes, while greater peritoneal loss of proteins may contribute to hypoalbuminaemia and malnutrition [39,40]. The concomitant increase in glucose transport results not only in UF failure leading to fluid overload [41], which is one of the driving forces for LVH and hypertension [11,12], but also in anorexia [42] and increased atherogenesis [43]. All these factors cause an increased cardiovascular risk in H transporters. However, it is unclear whether being an H transporter is the cause of this increased morbidity and mortality *per se* or whether comorbid conditions play a major role. This is because hypoalbuminaemia, CVD, inflammation, oligoanuria and malnutrition are known risk factors for mortality on PD [3,4,13,23,38]. To clarify this issue, 918 haemodialysis (HD) patients switched from PD were evaluated. Survival disadvantage conferred by being a high transporter during PD treatment was not found to be a risk factor after transfer to HD [44]. Some studies showed that PMTC are not associated with patient survival [4,5,45,46]. Despite more convincing data on survival advantage of being a non-high transporter, there is still a debate. Furthermore, due to the scant paediatric data on the effect of PMTC on clinical condition and outcome [8], it is hard to make clear conclusions in our patient population. No difference was found among transport groups with regard to cardiac and biochemical data, except lower albumin levels in H transporters and higher HS-CRP levels in H and HA transporters. These data support the notion that H transporters have a tendency toward malnutrition and inflammation, which may contribute to the poor outcome of the patients [11,38]. Adult data showed that inflammation and residual diuresis were indicated as predictors of mortality in PD patients rather than H transport rate [4] as was volume status [6]. We have not evaluated volume status, which is another limitation of our study. However, the impact of residual diuresis, inflammation, anaemia and hypertension on CVD was well demonstrated in the present and previous studies of our group [15].

High transporter status was suggested as a predictor of mortality in patients receiving CAPD but not APD [7]. APD may be more appropriate for patients with a higher membrane solute transport rate and provides better fluid removal [25,48]. Dialysis modalities facilitating intravascular volume control may mitigate the adverse prognosis of H transporters. As such, the poor prognosis associated with H transport status may relate more to the use of a therapy that is disadvantageous in this particular group rather than to comorbidities and genetic factors [44]. Our data showed that 51 patients were not on appropriate PD regimen according to their PET category, and these patients had a higher LVMI and PWD E/TDI E ratio, a measure of diastolic dysfunction, compared to those on appropriate PD modality. This may be partly due to a relatively higher pulse pressure (42 ± 8 vs 39 ± 9 mmHg, $P = 0.075$) levels in these patients. Twenty-three patients on CAPD should be on APD and 28 patients on APD must be on CAPD. It is our belief that if we take into account their PMTC and put them on appropriate PD modality, their cardiac morbidity might decrease. Compared to CAPD patients, APD patients had higher K_t/V_{urea} and lower MAP levels, which were previously shown to be negatively associated with CVD in children on PD [15]. On the other hand, significantly higher dialysate volume and glucose exposure in APD patients without having a better fluid removal as well as the inverse correlation between DGC and residual urine volume, both of which had a significant impact on cardiac disease, deserves further attention. Icodextrin use may be a reasonable option for these patients by providing a better fluid removal without an increased glucose exposure. Compared with glucose-based solution, 7.5% icodextrin was shown to significantly improve UF and small solute clearance even in patients with low-average peritoneal transport [49].

In conclusion, this study has shown that the majority of paediatric patients on maintenance PD were high/high-average transporters. LVH and diastolic dysfunction are highly prevalent and tightly related to anaemia, hypertension and lower residual diuresis rather than being a high transporter. On the other hand, tendency toward hypoalbuminaemia and inflammatory state in high transporters can contribute to cardiac morbidity. Therefore, for decreasing CVD, in addition to optimal control of BP and volume status, optimal correction of anaemia, better preservation of residual diuresis and management of inflammation and individualized PD prescription with optimal PD modality based on patients' clinical status combined with PET results are of particular significance.

Acknowledgement. Part of this study was presented at the 12th ISPD Meeting, 21–24 June 2008, Istanbul, Turkey (Travel Grant) and at the 10th National Congress of Hypertension and Kidney Diseases, 21–25 May 2008, Antalya, Turkey (Oral Communication Award-4).

Conflict of interest statement. None declared.

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

References

1. Twardowski ZJ. Clinical value of standardized equilibration tests in CAPD patients. *Blood Purif* 1989; 7: 95–108
2. Warady BA, Alexander SR, Hossli S *et al*. Peritoneal membrane transport function in children receiving long-term dialysis. *J Am Soc Nephrol* 1996; 7: 2385–2391
3. Churchill DN, Thorpe KE, Nolph KD *et al*. Increased peritoneal membrane transport is associated with decreased patient and technique survival for continuous peritoneal dialysis patients. The Canada–USA (CANUSA) Peritoneal Dialysis Study Group. *J Am Soc Nephrol* 1998; 9: 1285–1292
4. Chung SH, Heimburger O, Stenvinkel P *et al*. Association between residual renal function, inflammation and patient survival in new peritoneal dialysis patients. *Nephrol Dial Transplant* 2003; 18: 590–597
5. Park HC, Kang SW, Choi KH *et al*. Clinical outcome in continuous ambulatory peritoneal dialysis patients is not influenced by high peritoneal transport status. *Perit Dial Int* 2001; 21: S80–S85
6. Brimble KS, Walker M, Margetts PJ *et al*. Meta-analysis: peritoneal membrane transport, mortality, and technique failure in peritoneal dialysis. *J Am Soc Nephrol* 2006; 17: 2591–2598
7. Rumpsfeld M, McDonald SP, Johnson DW. Higher peritoneal transport status is associated with higher mortality and technique failure in the Australian and New Zealand peritoneal dialysis patient populations. *J Am Soc Nephrol* 2006; 17: 271–278
8. Schaefer F, Klaus G, Mehls O. Peritoneal transport properties and dialysis dose affect growth and nutritional status in children on chronic peritoneal dialysis. Mid-European Pediatric Peritoneal Dialysis Study Group. *J Am Soc Nephrol* 1999; 10: 1786–1792
9. Margetts PJ, McMullin JP, Rabbat CG *et al*. Peritoneal membrane transport and hypoalbuminemia: cause or effect? *Perit Dial Int* 2000; 20: 14–18
10. Kang DH, Yoon KI, Choi KB *et al*. Relationship of peritoneal membrane transport characteristics to the nutritional status in CAPD patients. *Nephrol Dial Transplant* 1999; 14: 1715–1722
11. Sezer S, Tutal E, Arat Z *et al*. Peritoneal transport status influence on atherosclerosis/inflammation in CAPD patients. *J Ren Nutr* 2005; 15: 427–434
12. Tonbul Z, Altintepe L, Sozlu C *et al*. The association of peritoneal transport properties with 24-hour blood pressure levels in CAPD patients. *Perit Dial Int* 2003; 23: 46–52
13. Mitsnefes MM. CV complications of pediatric chronic kidney disease. *Pediatr Nephrol* 2008; 23: 27–39
14. Chavers BM, Li S, Collins AJ *et al*. CV disease in pediatric chronic dialysis patients. *Kidney Int* 2002; 62: 648–653
15. Bakkaloglu SA, Saygili A, Sever L *et al*. Assessment of cardiovascular risk in paediatric peritoneal dialysis patients: a Turkish Pediatric Peritoneal Dialysis Study Group (TUPEPD) report. *Nephrol Dial Transplant* 2009; 24: 3525–3532
16. Devereux RB, Reichec N. Echocardiographic determination of left ventricular mass in man: anatomic validation of the method. *Circulation* 1977; 55: 613–618
17. De Simone G, Daniels SR, Devereux RB *et al*. Left ventricular mass and body size in normotensive children and adults: assessment of allometric relations and impact of overweight. *J Am Coll Cardiol* 1992; 20: 1251–1260
18. Khoury PR, Mitsnefes M, Daniels SR *et al*. Age-specific reference intervals for indexed left ventricular mass in children. *J Am Soc Echocardiogr* 2009; 22: 709–714
19. Daniels SR, Loggie JMH, Khoury P *et al*. Left ventricular geometry and severe left ventricular hypertrophy in children and adolescents with essential hypertension. *Circulation* 1998; 97: 1907–1911
20. Bakkaloglu SA, Ekim M, Sever L *et al*. Chronic peritoneal dialysis in Turkish children: a multicenter study. *Pediatr Nephrol* 2005; 20: 644–651
21. Tumer N, Yalcinkaya F, Ince E *et al*. BP nomograms for children and adolescents in Turkey. *Pediatr Nephrol* 1999; 13: 438–443
22. USRDS United States Renal Data System 2008 Annual Report. http://www.usrds.org/2008/pdf/V2_06_2008.pdf
23. Wang AY, Wang M, Woo J *et al*. Inflammation, residual kidney function, and cardiac hypertrophy are interrelated and combine adversely to enhance mortality and cardiovascular death risk of peritoneal dialysis patients. *J Am Soc Nephrol* 2004; 15: 2186–2194
24. Chung SH, Heimbürger O, Lindholm B. Poor outcomes for fast transporters on PD: the rise and fall of a clinical concern. *Semin Dial* 2008; 21: 7–10
25. Davies SJ. Mitigating peritoneal membrane characteristics in modern peritoneal dialysis therapy. *Kidney Int* 2006; 103: S76–S83
26. Mendley SR, Majkowski N. Peritoneal equilibration test results are different in infants, children, and adults. *J Am Soc Nephrol* 1995; 6: 1309–1312
27. Edefonti A, Picca M, Galato R *et al*. Evaluation of the peritoneal equilibration test in children on chronic pentoneal dialysis. *Peritoneal Dial Int* 1993; l3: S260–S262
28. Geary DF, Harvey EA, MacMillan JH *et al*. The peritoneal equilibration test in children. *Kidney Int* 1992; 42: 102–105
29. Warady BA, Jennings J. Short PET in pediatrics. *Perit Dial Int* 2007; 27: 441–445
30. Cuevas M, Zambrano P, Dinamarca H *et al*. Short PET in pediatric peritoneal dialysis. *Pediatr Nephrol* 2008; 23: 1853–1858
31. Bouts AH, Davin JC, Groothoff JW *et al*. Standard peritoneal permeability analysis in children. *J Am Soc Nephrol* 2000; 11: 943–950
32. Kaku Y, Honda M, Japanese Study Group of Pediatric Peritoneal Dialysis. Standardized peritoneal equilibration test in Japanese children and the influence of long-term peritoneal dialysis. *Perit Dial Int* 2008; 28: S150–S152
33. Schmitt CP, Haraldsson B, Doetschmann R *et al*. Effects of pH-neutral, bicarbonate-buffered dialysis fluid on peritoneal transport in children. *Kidney Int* 2002; 61: 1527–1536
34. Fischbach M, Terzic J, Chauve S *et al*. Effect of peritoneal dialysis fluid composition on peritoneal area available for exchange in children. *Nephrol Dial Transplant* 2004; 19: 925–932
35. Warady BA, Alexander S, Hossli S *et al*. The relationship between intraperitoneal volume and solute transport in pediatric patients. *J Am Soc Nephrol* 1995; 5: 1935–1939
36. Yao Y, Chen Y, Yang JY *et al*. Peritoneal equilibration test and results analysis in children undergoing chronic peritoneal dialysis. *Zhonghua Er Ke Za Zhi* 2007; 45: 189–193
37. Andreoli SP, Leiser J, Warady BA *et al*. Adverse effect of peritonitis on peritoneal membrane function in children on dialysis. *Pediatr Nephrol* 1999; 13: 1–6
38. Davies SJ, Phillips L, Russell GI. Peritoneal solute transport predicts survival on CAPD independently of residual renal function. *Nephrol Dial Transplant* 1998; 13: 962–968
39. Cueto-Manzano AM, Gamba G, Correa-Rotter R. Peritoneal protein loss in patients with high peritoneal permeability. Comparison between continuous ambulatory peritoneal dialysis and daytime intermittent dialysis. *Arch Med Res* 2001; 32: 197–201
40. Kagan A, Bar-Khayim Y, Schafer Z *et al*. Heterogeneity in peritoneal transport during continuous ambulatory peritoneal dialysis and its impact on ultrafiltration, loss of macromolecules and plasma level of proteins, lipids and lipoproteins. *Nephron* 1993; 63: 32–43
41. Ateş K, Nergizoglu G, Keven K *et al*. Effect of fluid and sodium removal on mortality in peritoneal dialysis patients. *Kidney Int* 2001; 60: 767–776
42. Bergstrom J. Why are dialysis patients malnourished?. *Am J Kidney Dis* 1995; 26: 229–241
43. Kreisberg RA. Diabetic dyslipidemia. *Am J Cardiol* 1998; 82: 67U–73U
44. Wiggins KJ, McDonald SP, Brown FG *et al*. High membrane transport status on peritoneal dialysis is not associated with reduced survival following transfer to haemodialysis. *Nephrol Dial Transplant* 2007; 22: 3005–3012
45. Brown EA, Davies SJ, Rutherford P *et al*. Survival of functionally anuric patients on automated peritoneal dialysis: the European APD Outcome Study. *J Am Soc Nephrol* 2003; 14: 2948–2957

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

46. Fernandez-Reyes MJ, Bajo MA, Hevia C *et al*. Inherent high peritoneal transport and ultrafiltration deficiency: their mid-term clinical relevance. *Nephrol Dial Transplant* 2007; 22: 218–223
47. Perl J, Huckvale K, Chellar M *et al*. Peritoneal protein clearance and not peritoneal membrane transport status predicts survival in a contemporary cohort of peritoneal dialysis patients. *Clin J Am Soc Nephrol* 2009; 4: 1201–1206
48. Churchill DN. Patient selection for automated peritoneal dialysis on the basis of peritoneal transport characteristics. *Contrib Nephrol* 1999; 129: 69–74
49. Lin A, Qian J, Li X *et al*. Randomized controlled trial of icodextrin versus glucose containing peritoneal dialysis fluid. *Clin J Am Soc Nephrol* 2009; 4: 1799–1804

Received for publication: 24.9.09; Accepted in revised form: 13.1.10

Nephrol Dial Transplant (2010) 25: 2303–2309
doi: 10.1093/ndt/gfq094
Advance Access publication 24 February 2010

Downloaded from https://academic.oup.com/ndt/article/25/7/2296/1868850 by ANKARA UNIVERSITY user on 11 December 2021

Extra-high-dose hepatitis B vaccination does not confer longer serological protection in peritoneal dialysis patients: a randomized controlled trial

Kai Ming Chow[1], Stanley Hok King Lo[2], Cheuk Chun Szeto[1], Sze Kit Yuen[3], Kin Shing Wong[2], Bonnie Ching Ha Kwan[1], Chi Bon Leung[1] and Philip Kam-Tao Li[1]

[1]Department of Medicine and Therapeutics, Prince of Wales Hospital, The Chinese University of Hong Kong, Shatin, Hong Kong, China, [2]Department of Medicine, Pamela Youde Nethersole Eastern Hospital, Chai Wan, Hong Kong, China and [3]Department of Medicine and Geriatrics, Caritas Medical Centre, Kowloon, Hong Kong, China

Correspondence and offprint requests to: Kai Ming Chow; E-mail: Chow_Kai_Ming@alumni.cuhk.net

Abstract

Background. The response to recombinant hepatitis B vaccine remains suboptimal among the dialysis population.
Methods. In this multi-centre randomized controlled trial, we studied the factors that modify the response to intramuscular Engerix-B vaccination in patients on peritoneal dialysis. The primary aim was to study if a three-dose schedule of extra-high dose (80 μg) of Engerix-B would offer better primary seroconversion and more persistent serological protection than the conventional 40-μg dose.
Results. Forty-two peritoneal dialysis patients were randomized to receive the conventional 40-μg Engerix-B dose and 45 patients to 80-μg dose. Seroconversion [hepatitis B surface antibody (anti-HBs) level ≥10 IU/l 3 months after completion of the third dose] occurred in 78.6% of patients after 40-μg Engerix-B dosage treatment *versus* 62.2% for those receiving 80-μg Engerix-B treatment ($P = 0.11$). After 12 months, the persistence of protective anti-HBs also did not differ between 40- (45.2%) and 80-μg (51.1%) treatment groups ($P = 0.67$). In contrast, patients with seroconversion 3 months after the third dose of Engerix-B had a higher normalized protein nitrogen appearance (nPNA) than patients without seroconversion (1.16 ± 0.25 *versus* 0.96 ± 0.23 g/kg/day, $P = 0.001$).
Conclusions. We found no evidence of a worthwhile clinical benefit from increasing the three-dose intramuscular Engerix-B vaccine from 40- to 80-μg dose. An unplanned analysis suggested a role of improved protein intake to improve the immune response to hepatitis B vaccine in peritoneal dialysis patients.

Keywords: end-stage renal disease; Engerix-B; hepatitis B; peritoneal dialysis; protein nitrogen appearance

Introduction

Viral hepatitis B infection remains a major health hazard for end-stage renal disease patients on dialysis. The direct costs of hepatitis B infection and their long-term impact on patient morbidity and mortality are substantial among patients receiving dialysis [1] as well as subsequent renal transplantation [2]. Ten-year graft and patient survival was observed to be significantly lower in hepatitis B surface antigen positive than seronegative renal transplant recipients [3], and further confirmed in a meta-analysis [4]. Apart from the devastating consequences of hepatitis B infection on end-stage renal disease patients on dialysis or after transplantation, the infected patients are potential reservoirs for outbreaks in health-care setting, infecting other patients and staff [5,6].

© The Author 2010. Published by Oxford University Press on behalf of ERA-EDTA. All rights reserved.
For Permissions, please e-mail: journals.permissions@oxfordjournals.org