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

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### 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.

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<sup>2</sup> 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:  $RWT = (IVED \pm PWED)/LVED$ . 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.

## Results

One hundred and ten patients aged  $13.8 \pm 4.5$  (range 5–22) years, treated with PD for a period of  $31 \pm 27$  (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  $K_t/V_{\text{urea}}$  was  $2.55 \pm 0.85$ , 4-h D/P creatinine was  $0.68 \pm 0.18$  and 4-h D/D0 glucose was  $0.39 \pm 0.12$ .

### *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 ( $r = -0.327$ ,  $P = 0.000$  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  $r = -0.208$ ,  $P = 0.047$ , 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 ( $\beta = -4.806$ ; 95% confidence interval, CI:  $-7.920$ ,  $-1.692$ ;  $P = 0.003$ ) and higher MAP ( $\beta = 0.545$ , 95% CI:  $0.156$ – $0.935$ ,  $P = 0.006$ ) were independent predictors of increased LVMI. Lower residual urine volume ( $\beta = -0.934$ ; 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<sup>a</sup>

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

<sup>a</sup>D/P creatinine at 4 h.

**Table 2.** Biochemical data of the patients in different solute transport categories<sup>a</sup>

	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 <sup>2</sup> /dl <sup>2</sup> )	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 <sup>2</sup> )	10 ± 3	11 ± 4	10 ± 3	NS
Weekly K <sub>t</sub> /V <sub>urea</sub>	2.31 ± 0.91	2.70 ± 0.98	2.64 ± 0.65	NS
PD vintage (months)	32 ± 28	33 ± 26	31 ± 27	NS

<sup>a</sup>D/P creatinine at 4 h. SD, standard deviation.

**Table 3.** Echocardiographic data of the patients in different solute transport categories<sup>a</sup>

	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 <sup>2</sup> )	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 <sup>2</sup> )	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

<sup>a</sup>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<sub>t</sub>/V<sub>urea</sub> (2.75 ± 0.92 vs 2.34 ± 0.73, P = 0.012) and higher DGC (122 ± 44 vs 78 ± 30 g/m<sup>2</sup>/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<sup>2</sup>, 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

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

Type of peritoneal dialysis	High transporter <i>n</i> (%)	High-average transporter <i>n</i> (%)	Low-average/low transporter <i>n</i> (%)	Total <i>n</i>
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) <i>n</i> = 27	High-average transporter (mean ± SD) <i>n</i> = 22	Low-average/low transporter (mean ± SD) <i>n</i> = 31	<i>P</i>
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 <sup>2</sup> )	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  $0.68 \pm 0.18$  and D4/D0 glucose was  $0.39 \pm 0.12$ , which were highly comparable to adult data [1]. We used a test volume of 1100 mL/m<sup>2</sup> 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

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 ( $42 \pm 8$  vs  $39 \pm 9$  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.

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

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### 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  $\geq 10$  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 ( $1.16 \pm 0.25$  *versus*  $0.96 \pm 0.23$  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].