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ORIGINAL ARTICLE

The short peritoneal equilibration test in pediatric peritoneal dialysis

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Abstract The peritoneal equilibration test (PET) is the gold standard method for defining peritoneal membrane permeability and for prescribing peritoneal dialysis (PD) therapy on an individual basis. However, it is laborious, consumes nursing time, and requires many hours to be performed. Therefore, several authors have attempted to validate a short PET protocol, with controversial results. To evaluate the concordance between the 2-h (short) and 4-h (classical) peritoneal equilibrium test, a prospective observational protocol was applied in three PD centers (Mexico, Chile, and Uruguay) between July 1, 2008 and July 31 2009. PET protocol: the night prior to the test, each patient received five exchanges, 1 h each, at the same glucose concentration as previously used. Afterwards, a 2.5% glucose dialysis solution was used for a dwell time of 4 h. Exchange fill volume was 1,100 ml/m^2 body surface area. The next morning, the 4-h dwell was drained, and Dianeal 2.5% was infused. Three dialysate samples at 0, 2, and 4 h were obtained. A single blood sample was obtained at 120 min. Creatinine D/P and glucose D/D_0 ratios were calculated at hours 0, 2, and 4. Patients were categorized as low, low average, high average, or high transporters according creat D/P and gluc D/D_0 results. Pearson and Kappa test were used for numerical and categorical correlations, respectively, and $p<0.05$ was considered significant. Eighty-seven PET studies were evaluated in 74 patients, 33 males, age 11.1±5.05 years old. A positive linear correlation of 92% between 2 and 4-h creat D/P and 80% between 2 and 4-h gluc D/D_0 ($p<0.001$) was founded. The Kappa test showed a significant concordance between creat D/P and gluc D/D_0 categories at 2 and 4 h ($p<0.001$). When analyzing cut-off-value categories, creat D/P was founded to be lower and gluc D/D_0 higher than other experiences. This multicentric prospective study strongly suggests that PET obtained at 2 h and 4 h, based on either creatinine or glucose transport, provides identical characterization of peritoneal membrane transport capacity in PD children.

Keywords Peritoneal equilibration test (PET) · Short PET · Transport · Ultrafiltration · Peritoneal dialysis

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Introduction

Determining an appropriate prescription for patients on peritoneal dialysis (PD) requires an exact evaluation of the peritoneal membrane transport characteristics. The peritoneal equilibration test (PET) has been used as the "gold

standard" to define peritoneal membrane permeability and to prescribe peritoneal dialysis therapy on an individual basis. Currently, this test is widely used in adults and children with chronic PD [1–5].

Twardowski introduced this test in clinical practice more than 20 years ago [6, 7], and later it was evaluated in children by Warady et al. [8]. The classical PET is performed during a 4-h dwell with a 2.5% dextrose dialysis solution in order to measure peritoneal solute transport capacity through dialysate/plasma creatinine (creatinine D/P) and dialysate/dialysate glucose (glucose D/D_0) concentration. According to the 4-h dialysate/plasma creatinine and dialysate/dialysate glucose results, patients can be categorized into high, high average, low average, and low transporter, and dialysis should be adjusted to the individual peritoneal characteristics [7–12].

However, despite its critical value, the PET is not used in all dialysis centers according to KDOQI recommendations [12] because it is a time-consuming procedure, requires staff support, and several dialysate samples. In order to move to a more friendly procedure, Twardowski first proposed the fast PET [13] and later in 2003 [14] they set the basis for the currently known "short PET". The PET abbreviated version was also retrospectively evaluated in children by Warady et al. in 20 dialyzed children [15]. These authors concluded that short PET was sufficiently reliable to replace the 4-h version, without meaning a change in the depuration or ultrafiltration category of the patient. Later on, we published a retrospective PET experience in 81 patients, showing a weak concordance between the 2 and 4-h PET results [16]. Therefore, current recommendations are based on retrospective experiences with controversial results.

Our objective was to evaluate the concordance between the 2-h (short) and 4-h (classical) peritoneal equilibrium test in children under chronic peritoneal dialysis therapy.

Patients and methods

A prospective observational protocol was applied in three dialysis centers between July 1, 2008, and July 31, 2009. The Luis Calvo Mackenna Children's Hospital, Santiago, Chile; the Pediatric Hospital, National Medical Center Century XXI, Mexico City, Mexico; and the SENNIAD Medical Center, Montevideo, Uruguay, were the participating dialysis centers.

PET studies were performed according to a common protocol. Inclusion criteria were clinically stable patients with more than 2 months in PD. Exclusion criteria were patients not evaluated if they had a peritonitis episode up to 2 months previous to the entrance, or an active nephrotic syndrome condition. Informed consent was obtained from each participant in each PD Center and the local ethics committee approved the study before the protocol was started.

The PET protocol

A 4-h PET was performed on each patient. During the night prior to the test, each patient received five exchanges of 1-h each at the same glucose concentration as previously used. Afterwards, a 2.5% glucose dialysis solution was used for a dwell time of 4 h. The exchange fill volume was 1,100 ml/m^2 body surface area (BSA), and the dialysate solution was Dianeal® (Baxter Healthcare, USA). The next morning, the last 4-h dwell was drained, and a transfer Y-type set Dianeal PD solution (Ultrabag) was installed. Dianeal 2.5% was infused over 15 min with the patient remaining in the supine position, rolling side to side during the infusion to obtain an optimal mixing of the intraperitoneal solution. As published, three dialysate samples were taken from the patient after infusing the initial exchange solution: a first sample (0 h), at 120 (2 h) and 240 min (4 h) of dwell time. A single blood sample was obtained at 120 min (2 h) of the test. All the samples obtained under non-compliance conditions were discarded. In each study, dialysate creatinine concentration was corrected for the presence of glucose, which interferes with creatinine when Jaffe's reaction is used [12]. Biochemical data were as follows: serum creatinine (Jaffe reaction), electrolytes, blood urea nitrogen (enzyme assay), calcium, phosphate, parathyroid hormone (PTH) (Advantage® Nichols Intact PTH Assay), serum albumin and protein (turbidimetric assay). The dialysate/plasma ratio for creatinine and the glucose ratio in dialysate at hours 0, 2, and 4 divided by dialysate at time 0 were calculated. The PET calculator of the International Pediatric Peritoneal Dialysis Network (www.pedpd.org) was used for mathematical calculations.

Patients were categorized as low, low average, high average, or high transporters according to creatinine (creat) D/P and glucose (gluc) D/D_0 results.

A low transport state was diagnosed when the creatinine D/P ratio was below −1 standard deviation (SD) and glucose D/D_0 ratio was above +1 SD of the mean value; a low average transport corresponding to a creatinine D/P ratio between the mean and −1 SD and a glucose D/D_0 ratio between the mean and +1 SD; a high average transport was diagnosed when the creatinine D/P ratio was between the mean and +1 SD and glucose D/D_0 between the mean and −1 SD; and a high transporter corresponding to a creatinine D/P ratio more than +1 SD and a glucose D/D_0 ratio less than −1 SD.

Statistical analysis

Simple statistics for frequencies and statistics of central tendency were calculated for all variables. Association

Table 1 General characteristics of the study population

Country	*n* (%)	Age (years)	Gender Male (*n*)	Weight (kg)	Height (cm)	BSA (m^2)	Months in PD	Serum creatinine (mg/dl)	Serum phosphorus (mg/dl)	Serum calcium (mg/dl)	Hb (g/dl)
Mexico	47 (63)	12.9±3.6	21	37.2±15.9	137.9±24.6	1.2±0.3	10.7±9.8	10.1±4.6	5.2±1.4	9.3±0.8	10.7±2.4
Chile	21 (29)	7.7±4.5	16	23.5±15.8	112.0±27.2	0.9±0.4	18.1±12.8	6.3±3.8	5.4±1.1	9.8±0.7	11.4±1.3
Uruguay	6 (8)	10.1±6.9	3	27.5±15.8	117.5±29.5	0.9±0.3	23±8.8	8.6±2	5.5±0.9	10.1±0.6	11.7±1.2
Total	74	11.1±5.05	33	32.3±16.7	128.7±27.7	1.1±0.4	14.4±11.6	8.6±4.5	5.2±1.4	9.5±0.8	10.9±2.1

BSA Body surface area; *Hb* Hemoglobin

between the 2-h and 4-h creatinine D/P and glucose D/D_0 with one, two, and three measurements were calculated with ANOVA test, previous confirmation of a normal distribution for variables. The same measurements expressed as continuous variables were assessed by Pearson correlation analysis and linear regression analysis. The concordance between the 2-h and 4-h creat D/P and gluc D/D_0 as categorical variables were calculated with Kappa test (contingency table). A p value$\leq$0.05 was considered statistically significant. Analysis was performed using SPSS version 15.0 (Chicago, IL, USA).

Results

Eighty-nine PET studies were performed in 76 patients, 33 males, mean age 11.1±5.05 years old. Forty-seven patients were from Mexico, eight patients were from Uruguay, and 21 patients were from Chile. Two patients were discarded because non-reliable samples were suspected. Therefore the analysis was performed for 87 equilibration tests and 74 patients (Table 1). Mean time on PD was 14.4±11.7 months (range 2–46 months). All patients were under automated PD with a prescription of 6–12 nightly exchanges, 1,100 ml/m^2 BSA each exchange.

Sixty-four children had one PET, seven patients had two studies, and three patients had three PET studies for analysis. To evaluate if results were influenced by the number of PET studies in each patient, ANOVA test was performed comparing glucose D/D_0 mean values at 2 and 4 h for the groups with one, two, and three measurements. Mean glucose D/D_0 ratio at 2 h was 0.71±0.11, 0.74±0.11 and 0.73±0.05 for groups with one, two, and three PET studies, respectively p= not significant (n.s.), and 0.47±0.13, 0.50±0.09, and 0.58±0.04 at 4 h for the same groups (p=n.s.), without significant differences for intergroup and intragroup comparisons.

Relation between 2 and 4-h PET as numerical variables

Characterization of the peritoneal membrane transport capacity based on the 2-h and 4-h creatinine D/P and the 2-h and 4-h glucose D/D_0 ratios is described in Table 2. The mean 2-h and 4-h creat D/P was 0.38±0.11 and 0.57±0.14, respectively. Pearson test showed a positive linear correlation of 92% between 2-h and 4-h creat D/P (p<0.001), (Fig. 1). The mean 2-h and 4-h gluc D/D_0 was 0.72±0.11 and 0.49±0.12, respectively. Pearson test showed a positive linear correlation of 80% between 2-h and 4-h gluc D/D_0 (p<0.001) (Fig. 2). The separate analysis of patients from Mexico did not show statistically significant differences with the two other countries.

Concordance between 2-h and 4-h PET as categorical variables

Based on the 4-h creatinine D/P data, the percentage of patients within each transport category was as follows: high, 16.1; high average, 32.2; low average, 35.6; low, 16.1. The Kappa test showed a significant concordance between categories at 2 h and 4 h (0.61, p<0.001) (Table 3).

According to the 4-h glucose D/D_0 results, the percentage of patients within each transport category was as follows: high, 16.1; high average, 35.6; low average, 32.2; low, 16.1. The Kappa test showed a significant concordance between categories at 2 h and 4 h (0.31, p<0.001) (Table 3). The 4-h creatinine D/P and glucose D/D cut-off values for each category are shown in Tables 4 and 5.

Table 2 Characterization of the peritoneal membrane transport and ultrafiltration capacity based on the 2-h and 4-h creatinine D/P and 2-h and 4-h glucose D/D_0

Category	2-h creat DIP	4-h creat DIP	2-h gluc D/D_0	4-h gluc D/D_0
Low (< −1 SD)	<0.26	<0.43	>0.83	>0.61
Low average (mean to −1 SD)	0.26–0.38	0.43–0.57	0.73–0.83	0.50–0.61
High average (mean to +1 SD)	0.39–0.5	0.58–0.71	0.61–0.72	0.37–0.49
High (> 1 SD)	>0.5	>0.71	<0.61	<0.37

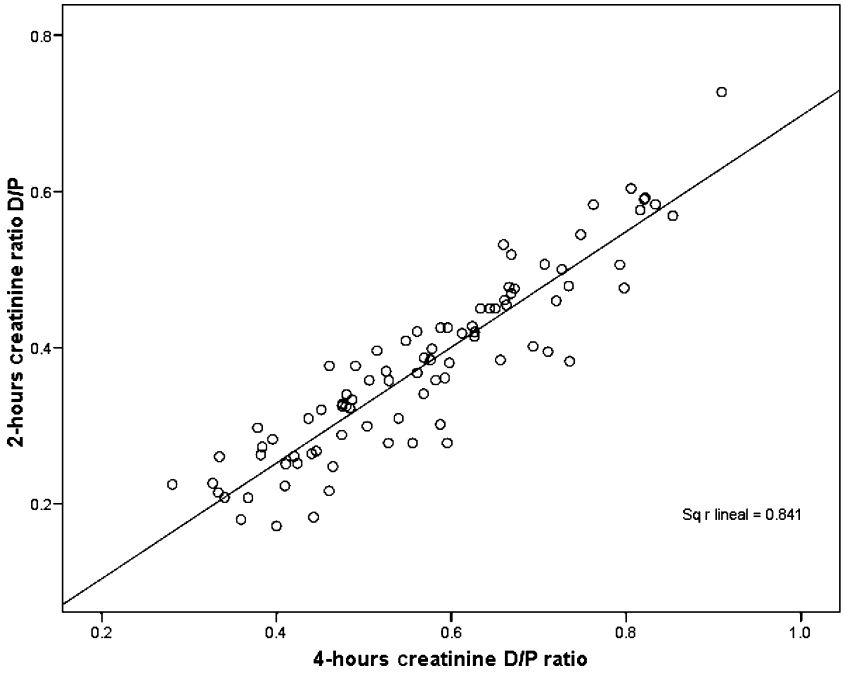

Fig. 1 Correlation between 2-h and 4-h creatinine D/P ratio

Discussion

The peritoneal equilibration test is a widely used method for classifying peritoneal transport characteristics in PD patients [1–5, 8, 12]. Establishing a personal transport peritoneal category not only allows the prescription of the best dialysis modality but also it has been shown to have a major impact on clinical outcome. The Mid European Pediatric Peritoneal Dialysis Study Group evaluated 51 PD children followed for 18 months and showed that a high transport state was negatively correlated with longitudinal growth [17]. In dialyzed adult patients, a higher morbidity has been communicated for a high transporter state [18]. Because peritoneal transport characteristics change with time, repeated equilibration tests are required to optimize dialysis therapy in PD children.

However, the classical PET protocol has several drawbacks: it is laborious, it consumes nursing time, it requires 5–6 h to be correctly performed, and several samples need to be sent for laboratory analysis. Therefore, several authors have attempted to validate a short PET protocol, with controversial results. In 1990, Twardowski described the

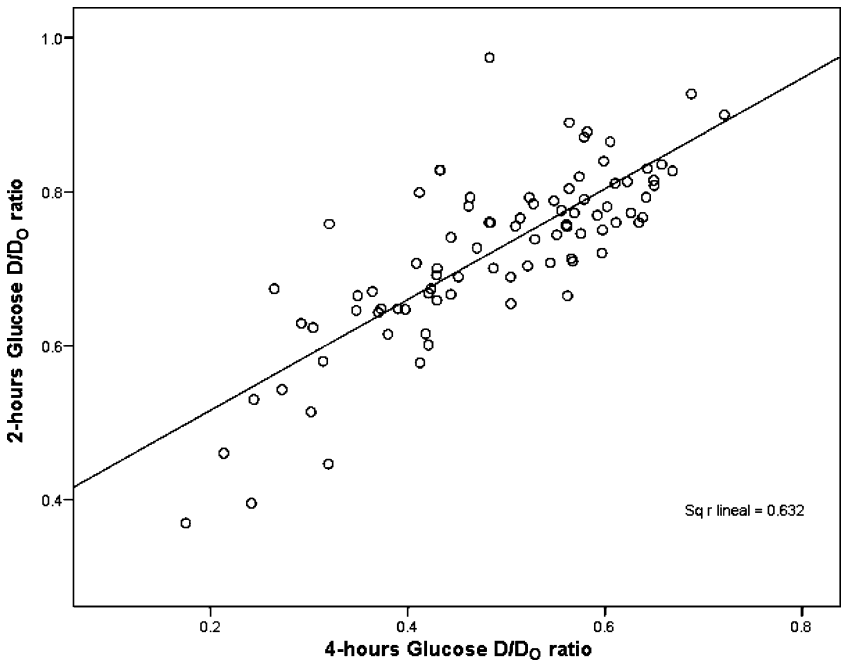

Fig. 2 Correlation between 2-h and 4-h glucose D/D_0 ratio

Table 3 Correlation between 2-h and 4-h PET by frequency of categories

Category	2-h creat D/P* *n* (%)	4-h creat D/P* *n* (%)	2-h gluc D/D_0** *n* (%)	4-h gluc D/D_0** *n* (%)
Low	13 (14.9%)	14 (16.1%)	10 (11.5%)	14 (16.1%)
Low average	32 (36.8%)	31 (35.6%)	29 (33.3%)	28 (32.2%)
High average	29 (33.3%)	28 (32.2%)	39 (44.8%)	31 (35.6%)
High	13 (14.9%)	14 (16.1%)	9 (10.3%)	14 (16.1%)

* Kappa 0.613 ($p<0.001$)

** Kappa 0.308 ($p<0,001$)

Fast PET [13], which requires a single sample of dialysate and blood 4 h after the infusion of the test exchange volume. A few years later, in 2003, the same authors proposed the short PET [14], which requires determination of creat D/P and gluc D/D_0 ratios after a 2-h equilibration time, in contrast to the standard 4-h time period. The short protocol has recently been evaluated for pediatric population by Warady et al., who retrospectively reviewed PET results in 20 patients on automated PD [15]. The authors found that in all patients, the peritoneal transport categories were the same using PET values at 2 and 4 h of the procedure. Later on, in 2007, we conducted another retrospective evaluation of the short PET in 81 patients from two different local medical centers [16] and found no significant correlation between values at 2 and 4 h, suggesting that the use of the short test was not reliable enough to estimate the transport capacity of the peritoneal membrane in a pediatric population.

However, retrospective analysis often lacks the accuracy that procedures like peritoneal equilibration tests require. A uniform procedure for the nightly exchanges before the test, the Dianeal glucose concentration prior to the test, and the dialysis solution used for the 4-h dwell time are all better controlled when the study is designed before the data is collected.

In this protocol, we analyzed results from a numerical and categorical point of view. Pearson analysis showed a strong correlation between 2-h and 4-h results for both variables, creatinine D/P and glucose D/D_0. In the categorical analysis, the Kappa test confirms the same high correlation. Of particular interest, cut-off values for categories were found to be different than those in previously published data. Four-hour creat D/P was found to be lower for all solute transport categories, and glucose D/D_0 categories were observed to be higher than the data of Twardowski and Warady. However, the range of each category between limits is almost the same in the three compared protocols, and patients do not change their transport category more than 1 SD, diminishing the clinical significance of this difference. Age, dialysate volume, and Dianeal concentration have been communicated as potential factors affecting PET results in children [2, 7, 14, 19–21], and they should be analyzed in order to explain differences in the cut-off levels of peritoneal transport in dialyzed populations. A dialysate fill volume of 0.9–1.1 l/m^2 BSA has been suggested to be the "leveling off" volume in order to minimize the variability of the test [22].

When cut-off limits for categories were analyzed as a secondary endpoint, considering only 1 PET by patient ($n=74$), including only the first study in those children with more than one PET, the mean creat D/P and the mean gluc D/D_0 did not show statistically significant differences compared to the 87 PET results, 0.58±0.14 and 0.47± 0.13, respectively ($p>0.05$).

Because our objective was not to characterize the peritoneal membrane in terms of transport category, but to establish the relationship between PET measurements at 2 and 4 h, the main target variable was the test (PET) and not the number of patients. A detailed analysis was done aiming to observe if repeated PET studies in a subgroup of children could represent a bias in our results. Among the 74 children, seven patients were evaluated with two PET studies and three patients had three PET studies. An ANOVA test was performed comparing mean gluc D/D_0 values at hours 2 and 4 for the groups with one, two, and three measurements. Mean glucose D/D_0 ratio at hour 2 was similar for groups with one, two, and three PET studies, respectively, and the same non-significant difference was found at hour 4 between groups, concluding that repeated PET measurements did not influence the final results.

Table 4 Categories of solute transport based on 4-h creatinine D/P ratio

Category	Twardowski	Warady	Protocol
High	>0.81	>0.77	>0.71
High average	0.65–0.81	0.64–0.77	0.58–0.71
Low average	0.50–0.64	0.51–0.63	0.43–0.57
Low	<0.50	<0.51	<0.43

Table 5 Categories of solute transport based on 4-h glucose D/D_0 ratio

Category	Twardowski	Warady	Protocol
High	<0.26	<0.23	<0.37
High average	0.26–0.38	0.23–0.33	0.37–0.49
Low average	0.39–0.49	0.34–0.43	0.50–0.61
Low	>0.49	>0.43	>0.61

Conclusions

This multicentric prospective study strongly suggests that the peritoneal equilibration test obtained at 2 h and 4 h, based on either creatinine or glucose transport, provides identical characterization of peritoneal membrane transport capacity in PD children. Another interesting observation is the fact that cut-off limits used to define the four categories of peritoneal permeability could change from one population to another. Multicentric prospective studies with a higher number of centers are needed to address this point.

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