**Free Water Transport Measured by Double
Mini-PET May Be Increased by
Higher Glucose Exposure in
Peritoneal Dialysis**

Peritoneal ultrafiltration (UF) during peritoneal dialysis (PD) is recognized to be one of the main predictors of mortality and drop-out in PD patients (1). The “three-pore” model has been used to describe solute and water transport across the peritoneum (2). Ultrasmall pores are

transcellular channels that allow for free water transport (FWT); they have been identified as the aquaporin (AQP) channels (3). The effectiveness of the osmotic pressure exerted by glucose to generate UF is called the “osmotic conductance to glucose” (OCG) of the peritoneal membrane (4).

The recently published advice of the European Renal Best Practice working group on the evaluation of the peritoneal membrane suggests use of the double mini peritoneal equilibration test (mini-PET)—a simple, accurate, and easily reproducible method—to determine OCG and FWT in standard clinical practice (5,6).

The aim of the present study was to analyze, in patients on chronic PD without UF failure (UFF), changes in water transport and OCG, and in their determinants.

METHODS

The study included all prevalent patients on chronic PD for at least 6 months referring to a single center. Patients with UFF or with an acute illness, including peritonitis, in the preceding 3 months were excluded. The resulting 14 patients (10 men, 4 women; mean age: 65.1 ± 9.2 years) underwent both a standard PET (7,8) with hypertonic solution (3.86% glucose) and a double mini-PET (6) on separate days. In all patients, a glucose-based solution was used for the overnight exchange preceding the tests.

The double mini-PET consists of two consecutive 1-hour PETs: the first is performed with a 1.36% glucose solution, and the second, with a 3.86% glucose solution. Using formulas validated by La Milia and colleagues (6), UF through the small pores (UFSP), FWT, and OCG are calculated using the results of the double mini-PET.

From the records of the study patients, we obtained demographic data, dialysis parameters (time on dialysis, Kt/V, PD solution, cumulative glucose exposure, mean daily glucose exposure, diuresis, residual renal function, previous peritonitis), main comorbidities, and drug therapies.

Pearson linear correlation analysis was used to investigate the possible relationships between all clinical parameters, OCG, and double mini-PET parameters (total UF, UFSP, FWT, sodium sieving).

RESULTS

Table 1 shows the main clinical and PET characteristics. Table 2 shows the main parameters obtained from the double mini-PET, particularly the 1-hour UF with hypertonic solution (542 ± 121 mL), of which 228 ± 66 mL was the FWT (FWT / UF ratio: $43.2\% \pm 12.2\%$), and 315 ± 119 mL, the UFSP. The mean decline in sodium concentration was 11.5 ± 3.1 mmol/L, corresponding to sodium sieving (dialysate Na / serum Na) of 0.889 ± 0.043 . The

OCG was normally distributed, the mean value being 3.947 ± 1.437 $\mu\text{L}/\text{min}/\text{mmHg}$.

Among the main double mini-PET parameters, we observed a negative correlation between sodium sieving and FWT / UF ratio ($r = -0.721$, $p = 0.004$). The OCG was strongly correlated with total UF volume ($r = 0.751$, $p = 0.002$) and with UFSP ($r = 0.806$, $p < 0.001$). Although the correlation between OCG and UFSP was stronger than

TABLE 1
Clinical and Dialysis Characteristics of the Study Patients

Parameter	Value
Sex, men/women [<i>n</i> (%)]	10/4 (71/29)
Mean age (years)	65.1 ± 9.2
Mean daily diuresis (mL)	1000 ± 500
Mean RRF (mL/min) ^a	3.6 ± 4.1
Mean PD vintage (months)	31.5 ± 17.8
Weekly total Kt/V	1.87 ± 0.23
Daily glucose exposure (g)	109 ± 69
Cumulative glucose exposure (kg)	100 ± 76
Peritonitis rate (ep/pt-mo)	$1/22.1$
Mean D/P creatinine	0.67 ± 0.10
Mean D/D ₀ glucose	0.27 ± 0.06
Mean PET ultrafiltration (mL)	681 ± 227

RRF = residual renal function; PD = peritoneal dialysis; ep/pt-mo = episodes per patient-month; D/P = dialysate-to-plasma ratio; D/D₀ = end-to-initial dialysate ratio; PET = peritoneal equilibration test.

^a Mean of urinary creatinine and urea clearances.

TABLE 2
Results and Parameters Derived from the Double Mini-Peritoneal Equilibration Test

Parameter	Value	Range
UF isotonic ^a (mL)	94 ± 114	-100 to 300
UF hypertonic ^b (mL)	542 ± 121	350 to 700
Small-pore UF (mL)	315 ± 119	173 to 552
FWT (mL)	228 ± 66	132 to 345
FWT/UF (%)	43.2 ± 12.2	21 to 63
OCG ($\mu\text{L}/\text{min}/\text{mmHg}$)	3.95 ± 1.44	1.50 to 6.50
ΔNa (mmol/L)	11.2 ± 2.8	5.5 to 17.4
D/P Na	0.891 ± 0.041	0.82 to 0.99

UF = ultrafiltration; FWT = free water transport; OCG = osmotic conductance to glucose; ΔNa = reduction of the sodium concentration in the dialysate after the hypertonic dwell; D/P Na = sodium sieving at hour 1 of the hypertonic dwell.

^a Standard 1.36% glucose PD solution.

^b Standard 3.86% glucose PD solution.

expected, there was no evidence that this relation was the result of mathematical coupling or systematic bias. No other dialysis and clinical variables were found to be correlated with OCG.

Figure 1 shows correlations for total UF, FWT, and UFSP with time on dialysis and cumulative glucose exposure. The total UF showed a negative trend with respect to time on dialysis ($r = -0.479$, $p = 0.083$) and no correlation

Figure 1 — Correlations between time on dialysis (months) and (a) total ultrafiltration (UF tot), (b) free water transport (FWT), and (c) ultrafiltration through the small pores (UFSP); and correlations between cumulative glucose exposure (kg) and (d) UF tot, (e) FWT, and (f) UFSP.

with prior cumulative glucose exposure ($r = -0.068$, $p = 0.817$). However, the UFSP was related both to time on dialysis ($r = -0.589$, $p = 0.0267$) and to glucose exposure ($r = -0.482$, $p = 0.081$). The FWT did not seem to be affected by time on dialysis ($r = 0.115$, $p = 0.696$), but it was positively correlated with higher glucose exposure ($r = 0.679$, $p = 0.0076$). No other dialysis and clinical variables were found to be correlated with FWT or UFSP.

DISCUSSION

Estimation of the characteristics of water transport through the peritoneal membrane could be a useful tool for exploring that membrane's complex physiology. However, the clinical significance of OCG and FWT in patients without UFF is still uncertain (9).

Our study is limited by its lack of power and its cross-sectional design. The small number of patients is itself the main limitation, and the conclusions drawn may therefore be weak. The cross-sectional design makes it impossible for the current report to determine whether the correlations found are causal or reflect a selection or competition bias.

The results obtained in the present work accord with results from previous studies. In the study that first proposed the double mini-PET, patients had an OCG of 3.28 ± 1.46 $\mu\text{L}/\text{min}/\text{mmHg}$, and the UFSP and FWT were 251 ± 133 mL and 243 ± 79 mL respectively (6). In a study that used dextran 70 in PD solution to evaluate transperitoneal fluid kinetics in patients without UFF (10), the OCG was 4.7 $\mu\text{L}/\text{min}/\text{mmHg}$ (range: $2.9 - 13.4$ $\mu\text{L}/\text{min}/\text{mmHg}$); the FWT, 168 mL (range: $48 - 375$ mL); and the UFSP, 268 mL (range: $71 - 605$ mL). More recently, in 10 stable patients on PD without UFF, Cnossen *et al.* (11) tested a new method of conducting the standard PET, with temporary drainage after the first hour. Those authors found 164 ± 74 mL of FWT and 204 ± 181 mL of UFSP.

Our study showed some unexpected correlations. The FWT showed no correlation with time on dialysis, but a positive correlation with glucose exposure. That finding is unexpected because we assumed that, as the total UF declined, the UFSP and the FWT would both decline. However, in the study by La Milia *et al.* (6), which compared patients with and without UFF, patients without UFF had a mean UFSP that was greater than the FWT (267 ± 126 mL vs 254 ± 70 mL), but patients with UFF had a mean UFSP that was smaller than the FWT (68 ± 48 mL vs 112 ± 69 mL). That relationship accords with experimental *in vitro* studies that show overexpression of AQP in cells exposed to glucose-based PD solutions (12). Furthermore, the FWT, as calculated in a double

mini-PET, correlated with vascular AQP1 expression (13). Our unexpected correlation between FWT and glucose exposure might therefore reflect wider neoangiogenesis and increased AQP1 expression (14).

Moreover, our data generate some interesting hypotheses. First, it may be that patients who maintain good water transport are less likely to be dropped from PD, whereas patients starting dialysis with lower water transport are more likely to develop UFF and so be shifted to hemodialysis. Another hypothesis is that patients without UFF have conserved water transport and that only just before UFF develops does a significant change occur in both OCG and FWT. If this latter hypothesis were to be confirmed in longitudinal studies, FWT could be an interesting predictor of UFF.

DISCLOSURES

None of the authors has a financial conflict of interest to declare.

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