

*Original Article***Automated peritoneal dialysis: a Spanish multicentre study**

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**Abstract**

**Background.** A prospective sequential study on continuous ambulatory peritoneal dialysis (CAPD) and three techniques of automated peritoneal dialysis (APD) was conducted to assess peritoneal clearances, the influence of peritoneal permeability on nocturnal APD clearances and the suitability of the peritoneal equilibration test (PET) for predicting clearances on APD.

**Methods.** After performing a PET, a series of clinical, biochemical and dialysis adequacy markers were evaluated after 2 months on CAPD, continuous cycling peritoneal dialysis (CCPD) and tidal volume peritoneal dialysis (TPD) with 50% and 25% tidal volumes. Forty five patients participated and 33 completed the study.

**Results.** Serum urea and creatinine decreased significantly whereas haemoglobin and glucose increased. Mean peritoneal urea clearance (l/week) was  $55.40 \pm 8.76$  on CAPD,  $74.82 \pm 12.62$  on CCPD,  $69.20 \pm 14.63$  on TPD (tidal 50%) and  $66.89 \pm 13.23$  on TPD (tidal 25%); mean creatinine clearance (l/week/1.73 m<sup>2</sup>) was  $42.80 \pm 9.95$ ,  $52.19 \pm 11.11$ ,  $51.31 \pm 13.3$  and  $49.17 \pm 11.83$ , respectively. Both clearances were significantly lower on CAPD than on APD ( $P < 0.001$ ). CCPD was the automated technique that provided the best nocturnal urea clearance ( $P < 0.01$ ). Nocturnal creatinine clearance did not show significant differences between CCPD and TPD (tidal 50%), being better with both techniques than with TPD (tidal 25%). There were statistically significant differences between nocturnal dialysate to plasma (D/P) ratios and those corresponding to the nearest times in the PET. The urea D/P ratio at 180 min and the creatinine D/P ratio

at 240 min of the PET were the parameters that better estimated nocturnal clearances on APD.

**Conclusions.** This study confirms that TPD does not improve the results of CCPD. Significant differences between D/P ratios during actual nocturnal cycles and PETs were observed.

**Key words:** automated peritoneal dialysis; CAPD; clearances; PET

**Introduction**

Automated peritoneal dialysis (APD) recently has become an established mode of renal replacement therapy for end-stage renal disease. Continuous cycling peritoneal dialysis (CCPD) and tidal volume peritoneal dialysis (TPD) are the most frequently used modalities [1–5]. However, despite the accumulated experience, there are no precise rules concerning the definition of objectives in ADP adequacy or choosing the best technique to adopt for each individual patient [6–11].

A number of studies have dealt with mathematical models to predict night time peritoneal clearances according to dialysate/plasma (D/P) ratios in the peritoneal equilibration test (PET) for orientating the prescription of APD [12–16]. Although in most studies D/P values predicted from PET results are assumed, these theoretical predictions need clinical confirmation. For that purpose, since June 1994, nine services of nephrology in different hospitals in Spain participated in a prospective study which was conducted (i) to compare peritoneal clearances of three APD modalities and continuous ambulatory peritoneal dialysis (CAPD), (ii) to determine the suitability of PET for predicting night time peritoneal clearances in APD and

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(iii) to evaluate the influence of peritoneal permeability in the clearances obtained in APD.

## Subjects and methods

### Patients

Between January 1994 and December 1996, 45 patients (31 men, 14 women) with a mean ( $\pm$ SD) age of  $52 \pm 13.7$  years were included in the study. Fifteen (33.3%) patients had diabetes mellitus. For 25 patients, CAPD was the initial peritoneal dialysis (PD) modality, six patients were treated initially with APD but switched to CAPD, three patients were on PD after failed transplant, two were transferred from haemodialysis, and the remaining nine patients entered the study when they initiated dialysis.

### Design

A prospective sequential study was carried out in which the following therapeutic modalities were instituted for a period of 2 months: CAPD, CCPD, TPD with 50% exchange volume (tidal 50%) and TPD with 25% exchange volume (tidal 25%). At the end of each 2 month period, the patient's clinical condition was assessed and blood samples for haematological parameters (Coulter counter SKR analyser), urea nitrogen (urease kinetic test), creatinine (Jaffe reaction), calcium (*o*-cresolphthalein complexone), phosphate (molybdate reaction), glucose (hexokinase method), total protein (biuret method) and albumin (nephelometry) were drawn. Urine and dialysate total protein content (turbidimetry), and urea and creatinine levels were also measured. Dialysate creatinine measurement was corrected for glucose interference using a correction factor determined at each clinical laboratory. Residual renal function was calculated in 24 h urine samples. Peritoneal urea and creatinine clearances were measured in 24 h dialysate volumes in patients on CAPD and in day and night time dialysate volumes in patients on APD. Body surface was calculated by the formula of Du Bois and Du Bois [17], and urea distribution volume by the formula of Watson *et al.* [18].

At the end of the 2 month period on the CAPD regimen and before receiving APD, a PET was performed as described by Twardowsky *et al.* [19]. The mass transfer area coefficient (MTAC) was determined by the model of Garred *et al.* [20]. Peritoneal solute transport was characterized as either high, high-average, low-average or low.

PD regimens were prescribed according to the patients' body weight. Patients on CAPD followed a schedule with  $8.9 \pm 0.7$  l per day and, in APD, total nightly infused dialysate and volume exchange were kept unchanged throughout the study and proportionally adjusted to the body weight. An exchange volume of 35–40 ml/kg was established, and 1 h was determined as the time on CCPD (e.g. 15 l and 2500 ml/exchange for a standard weight of 70 kg). Schedules involved 9–9.5 h of treatment overnight. Glucose concentration was adjusted to attain the mean ultrafiltration rate desired for each patient. In all three APD regimens, diurnal volumes were 25–30 ml/kg, with glucose concentrations between 1.36 and 2.27%.

### Statistical analysis

The statistical data are expressed as mean  $\pm$  SD.

In order to assess the effect of the modality of peritoneal dialysis delivered and the peritoneal permeability, and the

effects of their interactions on blood, urine and dialysate parameters, urea peritoneal clearance, creatinine peritoneal clearance and  $Kt/V$ , an analysis of variance (ANOVA) model was applied as follows:

$$Y_{ijk} = \mu + (\text{Peritoneum})_i + (\text{Ind})_{j(i)} + (\text{Technique})_k + (\text{Inter})_{ik} + e_{ijk}$$

where  $Y_{ijk}$  represents each of the measurements in the  $j$ -th patient with a  $j$ -th type of peritoneal permeability after a dialysis modality delivered by the  $k$  technique;  $\mu$ , the overall mean;  $(\text{Peritoneum})_i$ , the main effect of type  $i$  peritoneal permeability;  $(\text{Ind})_{j(i)}$ , the random effect of the  $j$ -th patient tested in type  $i$  peritoneal permeability;  $(\text{Technique})_k$ , the fixed effect of the  $k$ -th technique; and  $e_{ijk}$ , the random error. It was assumed that random errors were independent with a common  $N$  distribution ( $\theta\rho$ ).

The  $F$  test statistic was used to assess equal effects of the type of peritoneal permeability and treatment modality, as well as the presence of interactions. Differences between peritoneal permeabilities and dialysis techniques were evaluated by means of linear  $F$  tests.

The set of variables corresponding to D/P ratios during PET and MTAC of urea and creatinine that best predicted nocturnal peritoneal clearances on APD were determined by means of a stepwise multiple linear regression analysis and the coefficient of multiple determination ( $R^2$ ).

The SAS (Statistical Analysis Systems, version 6.04) statistical software package was used for the analysis of data [21].

## Results

Peritoneal solute transport was low in eight patients, low-average in 16, high-average in 16, and high in five. Mean D/P concentration ratios at 240 min of PET were  $0.87 \pm 0.7$  and  $0.62 \pm 0.16$  for urea and creatinine, respectively. A total of 161 studies of dialysis adequacy were made [45 on CAPD, 42 on CCPD, 41 on TPD (tidal 50%) and 33 on TPD (tidal 25%)]. The study could not be completed in 12 patients because of renal transplantation ( $n=3$ ), peritonitis and switch to haemodialysis ( $n=3$ ), poor compliance ( $n=2$ ) and death ( $n=4$ ).

Table 1 details the characteristics of the therapy and the mean values of haematological and biochemical parameters during the four study periods. Mean glucose concentration in the dialysate was significantly lower in APD (CCPD  $1.81 \pm 0.31\%$ , tidal 50%  $1.82 \pm 0.34\%$ , tidal 25%  $1.73 \pm 0.28\%$ ) than in CAPD ( $2.01 \pm 0.29\%$ ) ( $P < 0.01$ ). Significant changes in the amount of ultrafiltration (ml/24 h) in the different periods were not observed (CAPD  $1066 \pm 626$ , CCPD  $939 \pm 713$ , tidal 50%  $700 \pm 718$ , tidal 25%  $790 \pm 637$ ). There were no statistically significant changes in body weight, white blood cell count, serum albumin, total protein, calcium, phosphate and dialysate protein content. Serum haemoglobin concentration increased significantly on CCPD ( $1.6 \pm 0.30$  mmol/l) as compared with CAPD ( $1.49 \pm 0.24$  mmol/l) ( $P < 0.01$ ). Serum glucose levels showed a significant increase with all of the APD techniques in comparison with CAPD ( $P < 0.01$ ) (Table 1). Increased glucose levels were found in both diabetic and non-diabetic patients when switched from CAPD to CCPD ( $6.99 \pm 3.24$  vs

**Table 1.** Demographic, dialytic, haematological and biochemical parameters

	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
No. of studies	45	42	41	33
Weight (kg)	70.3 ± 11	70.5 ± 11	70.4 ± 12	71.9 ± 12
Night time volume (ml)		14 347 ± 2211	14 276 ± 2091	14 490 ± 2986
Exchange volume (ml)	2000	2436 ± 324	2434 ± 332	2464 ± 317
Tidal volume (ml)			1197 ± 158	625.7 ± 90.3
Time by exchange (min)		59.3 ± 9.5	37.8 ± 6.9	19 ± 5.7
Day time volume (ml)		1878 ± 206	1893 ± 200	1914 ± 180
Haemoglobin (mmol/l)	1.49 ± 0.24	1.60 ± 0.30	1.55 ± 0.26	1.57 ± 0.20
Leukocytes (mm <sup>3</sup> )	7337 ± 2062	7482 ± 2492	7771 ± 2140	7542 ± 2411
Lymphocytes (%)	24.5 ± 7.57	26.8 ± 6.93	24.7 ± 6.97	24.6 ± 7.76
Urea (mmol/l)	25.19 ± 8.69	19.13 ± 7.24	19.99 ± 6.97	19.79 ± 6.12
Creatinine (μmol/l)	918.15 ± 326.55	836.53 ± 296.55	852.19 ± 298.95	843.68 ± 299.81
Glucose (mmol/l)	5.93 ± 2.54	7.97 ± 6.17	7.65 ± 4.51	7.63 ± 2.93
Total protein (g/l)	65.26 ± 7.5	64.15 ± 7.25	65.5 ± 7.3	64.69 ± 6.9
Albumin (g/l)	35.91 ± 5.5	34.69 ± 5.8	34.39 ± 8.4	35.12 ± 5.3
Calcium (mmol/l)	2.4 ± 0.2	2.5 ± 0.2	2.3 ± 0.3	2.4 ± 0.3
Phosphate (mmol/l)	1.8 ± 0.4	1.8 ± 0.4	1.8 ± 0.5	1.8 ± 0.5
Dialysate protein content (g/24 h)	6.5 ± 3.5	6.5 ± 5	5.7 ± 3.8	6.5 ± 3.5

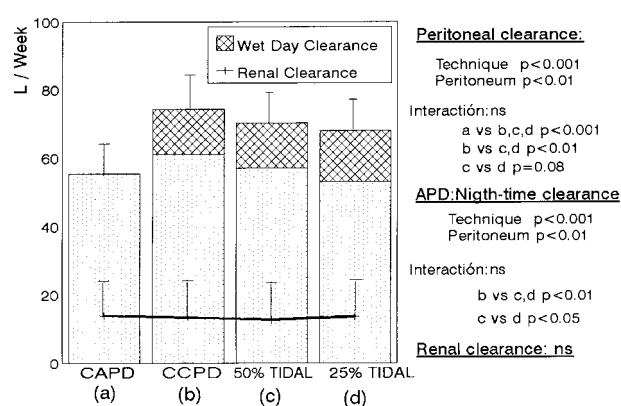
**Table 2.** Dialysate to plasma ratios (D/P) for urea and creatinine during night time dialysis on APD and at 30 and 60 min of the peritoneal equilibration test (PET)

	D/P urea	D/P creatinine
Night time APD		
CCPD	0.57 ± 0.09 <sup>a</sup>	0.39 ± 0.11
TPD (tidal 50%)	0.53 ± 0.09	0.39 ± 0.13
TPD (tidal 25%)	0.49 ± 0.09 <sup>b</sup>	0.36 ± 0.11
PET		
30 min	0.37 ± 0.12	0.24 ± 0.11
60 min	0.52 ± 0.13	0.34 ± 0.13

avs b,  $P < 0.01$ .

10.44 ± 8.2 mmol/l and 5.43 ± 2.02 vs 6.74 ± 4.51 mmol/l, respectively). There were statistically significant decreases in serum concentrations of urea ( $P < 0.001$ ) and creatinine ( $P < 0.01$ ) on any automated technique as compared with CAPD (Table 1).

D/P ratios for urea and creatinine during the night time period for the three APD procedures and at 30 and 60 min of the PET are shown in Table 2. At 30 min of PET, D/P ratios for urea and creatinine were significantly lower ( $P < 0.01$ ) than those obtained during the night time period in the three automated dialysis methods. At 60 min of PET, the D/P ratio for urea was significantly lower than that on CCPD ( $P < 0.01$ ) and higher than on TPD (tidal 50%) ( $P < 0.05$ ), whereas the D/P ratio for creatinine was significantly lower than that on CCPD and TPD (tidal 50%) ( $P < 0.05$ ). Correlations between D/P ratios for urea and creatinine at different times of PET and night time peritoneal clearances for all three APD procedures were statistically significant. Results of regression analysis showed that the D/P ratio for urea at 180 min ( $R^2 = 0.38$ ,  $P < 0.001$ ) and for creatinine at 240 min ( $R^2 = 0.50$ ,  $P < 0.001$ ) were the best predictors of night time clearances on APD.

**Fig. 1.** Peritoneal urea clearance (l/week) on CAPD, CCPD, TPD (tidal 50%) and TPD (tidal 25%) and renal urea clearance (l/week) throughout the study.

Peritoneal urea clearance and Kt/V studies showed statistically significant increases with APD techniques ( $P < 0.001$ ), in particular with CCPD ( $P < 0.01$ ) as compared with CAPD (Table 3, Figure 1). When the Kt/V values of patients on CAPD and CCPD were compared, a statistically significant reduction in the percentage of patients with values  $< 2.1$  (93% vs 59%) and  $< 1.7$  (75% vs 17%) was found. Peritoneal creatinine clearance also improved significantly with APD techniques in comparison with CAPD ( $P < 0.001$ ) (Table 4, Figure 2). There was a statistically significant increase in the percentage of patients with peritoneal creatinine clearance between 50 and 70 l/week/1.73 m<sup>2</sup> on CCPD as compared with CAPD (55% vs 22%,  $P < 0.01$ ).

Peritoneal clearances of urea and creatinine in relation to solute transport categories showed statistically significant effects of the transport category and the modality of dialysis (Tables 3 and 4). However, no interaction between these effects was found.

**Table 3.** Peritoneal urea clearance (l/week) in relation to the transport category

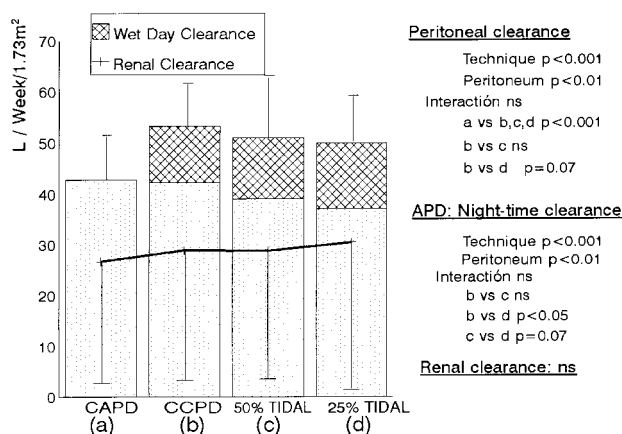
	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	55.40 ± 8.76	74.82 ± 12.62	69.20 ± 14.63	66.89 ± 13.23
Kt/V	1.51 ± 0.32	2.03 ± 0.39	1.88 ± 0.35	1.80 ± 0.40
At night time		61.38 ± 12.2	56.45 ± 13.53	53.19 ± 11.33
Transport category				
High	60.58 ± 3.51	84.51 ± 10.43	80.04 ± 13.02	68.78 ± 20.26
High-average	55.12 ± 10.7	75.78 ± 14.27	71.58 ± 20.20	69.39 ± 15.02
Low-average	53.78 ± 8.29	71.55 ± 10.79	67.40 ± 9.34	72.07 ± 5.52
Low	56.28 ± 7.32	73.01 ± 12.59	65.36 ± 14.26	64.85 ± 7.01

High vs low-average,  $P < 0.001$ ; high vs low,  $P < 0.01$ ; high-average vs low-average,  $P < 0.05$ .

**Table 4.** Peritoneal creatinine clearance (l/week/1.73 m<sup>2</sup>) in relation to the transport category

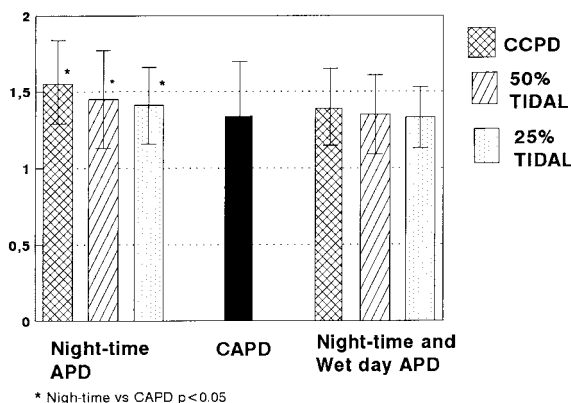
	CAPD	CCPD	TPD (tidal 50%)	TPD (tidal 25%)
All patients	42.80 ± 9.95	52.19 ± 11.11	51.31 ± 13.35	49.17 ± 11.83
At night time		40.80 ± 11.09	39.94 ± 12.88	37.22 ± 10.57
Transport category				
High	61.53 ± 4.04	66.44 ± 8.35	69.09 ± 20.98	66.75 ± 22.46
High-average	45.35 ± 10.71	53.71 ± 9.67	53.69 ± 7.05	51.08 ± 6.7
Low-average	43.77 ± 5.9	50.37 ± 10.32	49.54 ± 9.66	48.13 ± 10.53
Low	32.77 ± 9.16	44.67 ± 8.49	40.31 ± 10.11	41.37 ± 7.94

High vs other categories,  $P < 0.001$ ; high-average vs low-average,  $P < 0.05$ ; high-average vs low,  $P < 0.001$ ; low-average vs low,  $P < 0.001$ .

**Fig. 2** Peritoneal creatinine clearance (l/week per 1.73 m<sup>2</sup>) on CAPD, CCPD, TPD (tidal 50%) and TPD (tidal 25%) and renal creatinine clearance (l/week per 1.73 m<sup>2</sup>) throughout the study.

When the quotient between renal clearances of urea and creatinine on CAPD and on APD techniques was calculated, the relationship was greater in APD techniques than in CAPD only if night time values were considered (Figure 3). Nocturnal peritoneal urea clearance was significantly higher on CCPD than on TPD (tidal 50%) ( $P < 0.01$ ) and in TPD (tidal 25%) ( $P < 0.001$ ), as well as higher on TPD (tidal 50%) than on TPD (tidal 25%) ( $P < 0.05$ ) (Table 3). On the other hand, nocturnal peritoneal creatinine clearance was significantly higher on CCPD and TPD (tidal 50%) than on TPD (tidal 25%) ( $P < 0.05$ ).

The contributions of day time clearance and residual renal function to peritoneal clearance of urea and

**Fig. 3** Quotient between renal clearances of urea and creatinine clearances on CAPD and APD techniques.

creatinine are illustrated in Figures 1 and 2. Residual urea renal clearances accounted for 19 and 16% of total renal urea clearance, and renal creatinine clearances accounted for 38.4 and 36.5% on CAPD and APD respectively. Residual renal function did not change significantly in the 23 patients in whom some degree of renal function was present at the start of the study (mean  $2.5 \pm 2$  ml/min on CAPD and  $3.01 \pm 3.0$  ml/min after 6 months on APD).

## Discussion

APD progressively is becoming a popular alternative for renal substitution therapy in patients with end-stage renal disease. The relationship between dialytic

doses and clinical outcome in CAPD has been assessed in a number of studies [23–27]. Data from the CANUSA multicentre study [27] have established a weekly Kt/V >2.1 and creatinine clearance >70 l/week per 1.73 m<sup>2</sup> as optimal targets of adequacy in patients dialysed by the CAPD method. However, the relative importance of urea and creatinine as markers of dialysis adequacy and mortality in CAPD is still unknown. With regard to APD, the situation is more complex and has been studied to a lesser extent.

On the one hand, there is general agreement that objectives of dialysis adequacy should be greater but, on the other hand, much work is needed before weekly clearance targets are clearly defined as accurate and prognosticators of clinical outcome [5–11,28–30]. Moreover, the shorter time required for the exchanges may cause a dissociation between urea and creatinine clearances, usually favouring the former, thus increasing difficulties in establishing targets for these molecules [10].

In the design of this study, exchange volume and total night time volume were calculated according to the patients' body weight, with the aim of optimizing peritoneal efficiency in APD using the largest intraperitoneal volume tolerated in the decubitus position. As compared with CAPD, patients on CCPD showed increases of 34% in Kt/V and 24% in peritoneal creatinine clearance. If data derived from the CANUSA study [27] were applicable to our study, these increases would be associated with an expected 2 year survival improvement of ~12%.

We believe that the increase in the fill volume resulted in an improvement in clearances on APD as compared with CAPD, in which obviously there is a lower exchange volume, although exchange volume was significantly correlated with urea and not with creatinine clearance in patients on APD. According to these findings, we consider that the proportional increases in urea and creatinine clearances in this study are related to the diurnal period in APD, since over the night time period there is a proportionally higher increase in urea clearance, and only when diurnal and nocturnal periods are analysed together are quotients between both clearances on CAPD and APD similar.

Patients in the low and low-average category—a group in which objectives of dialysis adequacy are rarely accomplished—peritoneal Kt/V increased from  $1.54 \pm 0.31$  on CAPD to  $2.01 \pm 0.45$  on CCPD, and creatinine clearance increased from  $39.6 \pm 8.9$  to  $48.11 \pm 9.8$  l/week per 1.73 m<sup>2</sup>. Accordingly, the percentage of patients in whom creatinine clearances of >50 l/week per 1.73 m<sup>2</sup> were achieved increased from 12.5% on CAPD to 40% on CCPD, and patients with peritoneal Kt/V >1.7 increased from 25% on CAPD to 78% on CCPD ( $P < 0.001$ ). In our opinion, this is a considerable increment that depends mainly on the type of dialysis given as, in the analysis of clearances, an interaction between peritoneal permeability and dialysis technique was not found. In addition, according to the data of our study, it can be estimated that an intermediate 2 l exchange during the day time would

be followed by increases in Kt/V urea up to 2.34 and in creatinine clearance up to 54 l/week per 1.73 m<sup>2</sup>, moving nearer to reasonable definitions of dialysis adequacy.

It has been suggested that residual renal function decreases rapidly on APD. It should be noted that in our study no significant changes were observed during the 6-month follow-up period in patients on APD. This finding, that might be related to the use of day time period, is encouraging given that residual renal function constitutes an important aid for patients on PD, especially those patients with low transport characteristics [31,32].

Since the initial description of TPD by Twardowsky [33], it has already been established that this technique offers superior peritoneal clearances, especially for urea, to intermittent nocturnal PD due to the use of a greater volume of dialysate, although the proportion which is affected by the patient's peritoneal permeability was unknown [33]. The present study was designed in an attempt to obtain a maximum homogeneity of total nocturnal volume and intraperitoneal volumes on APD in order to determine the influence of peritoneal permeability on the nocturnal clearances obtained.

Urea clearance on CCPD has been significantly better than on TPD, whereas creatinine clearance has been lower in TPD (tidal 25%) than on CCPD and TPD (tidal 50%). In this study, there is evidence that peritoneal permeability does not influence the differences among clearances found on APD therapies and it can therefore be stated that CCPD was more efficient than TPD for any type of transport category with respect to the clearance of urea, and CCPD and TPD (tidal 50%) were equivalent in reference to the clearance of creatinine.

Durand *et al.* [34] studied only six patients in whom night time volume was increased from 15 to 35 l. Maximal clearance of creatinine is attained in a patient with a D/P ratio for creatinine of 0.78 at 240 min using 35 l [34]. The creatinine clearance obtained in these patients was similar to that achieved in the five high transporters in our study in whom an average of  $16\,000 \pm 1457$  ml in the night time and  $1923 \pm 183$  ml in the day time was employed. It is likely that the higher efficiency of creatinine clearance in our patients may be attributed to the use of the diurnal period and to the attempt at taking maximal advantage of the peritoneal capacity in the decubitus position. Thus, it was estimated that in order to increase the clearance of creatinine it is not strictly necessary to use high nocturnal flows, but to increase exchange volumes up to the maximal volume tolerated by each patient.

This hypothesis is supported further by results of the quotient between D/P ratios of urea and creatinine at different times of the PET and in the night time period of ADP. The quotient between nocturnal D/P ratios of urea and creatinine (which is equivalent to the relationship between their clearances) is similar to the quotient of D/P ratios at 120–180 min of PET, and this occurred despite clearly shorter times per exchange.

Finally, in relation to the usefulness of the PET for predicting nocturnal clearances on APD, we found that although it allowed a reasonable estimation of peritoneal urea and creatinine clearances, a more reliable estimation was obtained by means of D/P ratios than with the use of MTAC. D/P ratios at 180 and 240 min were the best predictors of nocturnal clearances of urea and creatinine, respectively, in patients on APD therapy. Nevertheless, significant differences between D/P ratios of urea and creatinine on APD and those corresponding to the nearest times in the PET were observed. It may thus be anticipated that estimations made by interchanging these parameters would contain significant errors.

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