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Original article

Residual renal function in children on haemodialysis and peritoneal dialysis therapy

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Abstract. Residual renal function was studied in 28 haemodialysis (HD) and 31 peritoneal dialysis (PD) patients aged 1–20 years observed over 6–43 (median 19) months. After the start of dialysis urine volume (UV) decreased to 57%, 46% and 26% of initial mean values in HD patients after 6, 12 and 24 months, respectively. In PD patients the corresponding figures were 57%, 69% and 62%. Mean UV calculated from all individual mean UV measurements observed was higher in PD than HD patients (954 vs. 537 ml/m^2 per 24 h, $P < 0.01$). A better conservation of diuresis in PD patients was also suggested by a significantly longer persistence of a UV greater than 500 ml/m^2 per 24 h compared with HD patients. Cox proportional hazard analysis identified dialysis modality and pre-dialysis UV of less than 1,000 ml/m^2 per 24 h as the only significant risk factors for UV survival. However, the decline of UV per time was similar in both modes of treatment. No significant changes of glomerular filtration rate were observed during both HD and PD treatment.

Key words: Residual renal function – Haemodialysis – Peritoneal dialysis – Glomerular filtration rate – Urine volume

Introduction

The term residual renal function (RRF) in patients on renal replacement therapy (RRT) has been used differently in the literature. Usually it is defined as urinary volume (UV) or as endogenous creatinine clearance (C_{Cr}) or both, without considering other excretory or endocrine functions of the failing kidney. The clinical impact of RRF is considerable because very small changes in glomerular filtration rate (GFR), in the order of 1–2 ml/min, may account for major differences in quality of life and dialysis requirements [1–3]. A number of complications observed on RRT, such as overhydration, hypertension, anaemia, osteodystrophy, polyneuritis and malnutrition, are dependent on the amount of RRF [4–6]. Some of these complications may be partially explained by the inadequate excretion of potentially toxic uraemic products, such as middle molecules or organic acids. For at least two toxic products, the direct influence of RRF was demonstrated [7, 8]. RRF has also been characterized as an important determinant for dialysis prescription, as demonstrated by a good correlation with the Kt/V index [9]. In some cases, preserved RRF may be a prerequisite for recovery of renal function [3]. A sufficient residual urine output is especially important in small children and infants because of the frequent compliance problems with regard to fluid restriction in this age group.

Reports in adult patients have demonstrated that RRF is better maintained during treatment by peritoneal dialysis (PD) than by haemodialysis (HD) [10–13]. Comparable data are not available in children. The aim of our study was therefore to compare the course of RRF in a cohort of paediatric patients with end-stage renal disease undergoing HD and PD over long periods. The use and influence of drug therapy was also investigated.

Patients and methods

Medical records were reviewed from 91 paediatric patients who started RRT at the University Children's Hospital Heidelberg between January 1982 and December 1992. The starting point of the investigation was chosen because it corresponds to the start of our PD programme in children [14]. Patients were included in the study if they had the same modality of initial dialysis treatment with RRF data at least for the initial 6 months. Twenty-eight patients were treated by HD and 31 by PD, i.e. by continuous ambulatory (CAPD) or continuous cycling PD. The dialysis modality was chosen after repeated discussion with the patient and his parents on feasibility, advantages and disadvantages of each procedure. Analysis was performed up to the time of a change in RRT. Thirty-two patients were not included in the study because of an

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Table 1. Clinical and laboratory data of haemodialysis (HD) and peritoneal dialysis (PD) patients

	HD	PD	*P* value
No. of patients	28	31	
Males : females	11 : 17	21 : 10	0.038*
Age (years)[a] mean ± SD	13.9 ± 2.8	9.8 ± 5.4	0.0006**
median (range)	14.0 (8.6–20.5)	9.4 (1.2–18.5)	
Weight SDS median (range)	–0.99 (–3.42 to +2.09)	–1.52 (–3.56 to +1.15)	0.03
Height SDS median (range)	0.74 (–4.23 to +1.54)	–1.26 (–5.07 to +2.21)	NS
Primary renal disorder:			
glomerulonephritis	14	11	
malformation of urinary tract	5	7	
renal hypoplasia	6	3	
cystinosis	1	4	
cystic kidney disease	0	4	
interstitial nephritis	2	0	
nephrocalcinosis	0	1	
unknown	0	1	
acquired : congenital	13 : 15	11 : 20	NS
Serum creatinine[a] (mg/dl):			
mean ± SD	9.4 ± 3.2	8.3 ± 2.5	NS
median (range)	8.7 (5.3–20.7)	7.9 (3.1–13.6)	

SDS, Standard deviation score; NS, not significant
* Chi-squared test; ** Wilcoxon rank sum test
[a] At the start of dialysis

early change in RRT, bilateral nephrectomy, death or insufficient RRF data, i.e. less than six determinations of UV. None of the children studied recovered renal function to a degree that RRT was unnecessary.

Clinical data are summarized in Table 1. The proportion of acquired to congenital disorders was not significantly different in the HD and the PD groups. Patients undergoing HD were usually dialysed three times per week for 3–4 h, using plate dialysers before 1985 and hollow-fibre dialysers since. In PD patients, the number of bag exchanges varied between four and six per day, with exchange volumes adapted to body size.

Weight, height and serum creatinine (SCr) levels were recorded at the time of each assessment of RRF and before the start of a dialysis session in HD patients. RRF was evaluated from measurements of UV (expressed as ml/m^2 per 24 h) and by GFR, calculated from SCr taken before HD sessions and body height, using the formula of Schwartz et al. [15] with a K factor of 0.55. Information was obtained about the use of frusemide and anti-hypertensive drugs throughout the whole observation period.

We defined pre-dialysis RRF using the most recently available SCr and UV data obtained within 1–54 (median 4) days of initiation of HD and within 1–35 (median 2) days of the start of PD. Further data on RRF were collected weekly during the 1st month of dialysis, at the end of the 2nd and 3rd month and every 3 months thereafter, until a change in the dialysis modality or until the patient received a transplant, died or was lost to follow-up.

The mean (± SD) period of observation was 694 ± 349 days (median 614, range 180–1,275 days) in HD patients and 612 ± 327 days (median 547, range 201–1,341 days) in PD patients. The number of observations of RRF per patient was similar in both groups: 7–20 (median 12) in HD patients and 6–21 (median 10) in PD patients.

In each patient we determined the time from the first dialysis until UV had dropped for the first time below 500 ml/m^2 per 24 h followed by a second UV in the same range and the time until UV less than 50 ml/m^2 per 24 h (defined as anuria) was recorded for the first time. Patients with an initial UV less than 500 ml/m^2 per 24 h were not included in this UV survival analysis.

Medication. The proportion of patients treated with frusemide, angiotensin converting enzyme (ACE) inhibitors and erythropoeitin at different time intervals after initiation of dialysis was not significantly different in the two treatment groups, with two exceptions: (1) HD patients were treated more frequently with frusemide than PD patients at 3 months (15/28 vs. 8/31 patients) and 6 months after the start of dialysis (14/28 vs. 7/31, respectively) with $P < 0.05$ for both; (2) more children on PD received ACE inhibitors compared with HD patients at 3 (7/31 vs. 1/28), 12 (9/25 vs. 1/22) and 18 months (6/18 vs. 0/17) of dialysis ($P < 0.05$ for all). The number of patients without any anti-hypertensive therapy was higher in PD than in HD patients at all time intervals.

Statistical analysis. The proportion of congenital and acquired renal disease and the number of anuric patients after 12 months on RRT were compared in the two patient groups by the chi-squared test. The Wilcoxon rank sum test was applied to compare mean SCr, calculated C_{Cr} and UV values before initiation of dialysis therapy. The same test was used to compare percentage mean UV in the two dialysis groups calculated from individual patients at defined time intervals. Mean UV values were derived from all UV measurements after the start of dialysis in each patient in order to calculate the overall mean UV values in the HD and PD groups. The decline of UV was determined from individual differences between the initial value and the last UV measurement on dialysis divided by the corresponding observation time; the mean value obtained for each dialysis group was then calculated and compared by the Wilcoxon test.

Kaplan-Meier survival analysis was used to construct UV survival curves. Risk factors assumed to be associated with UV survival analysis were evaluated using the Cox proportional hazard regression model. A simple regression analysis was performed in each HD and PD patient on log-transformed calculated GFR values from the start of dialysis until the last observation or until 24 months at maximum. The mean intercept and slope values were then used to represent the regression coefficients in each dialysis group and compared by means of the Wilcoxon test. A P value < 0.05 was accepted as statistically significant.

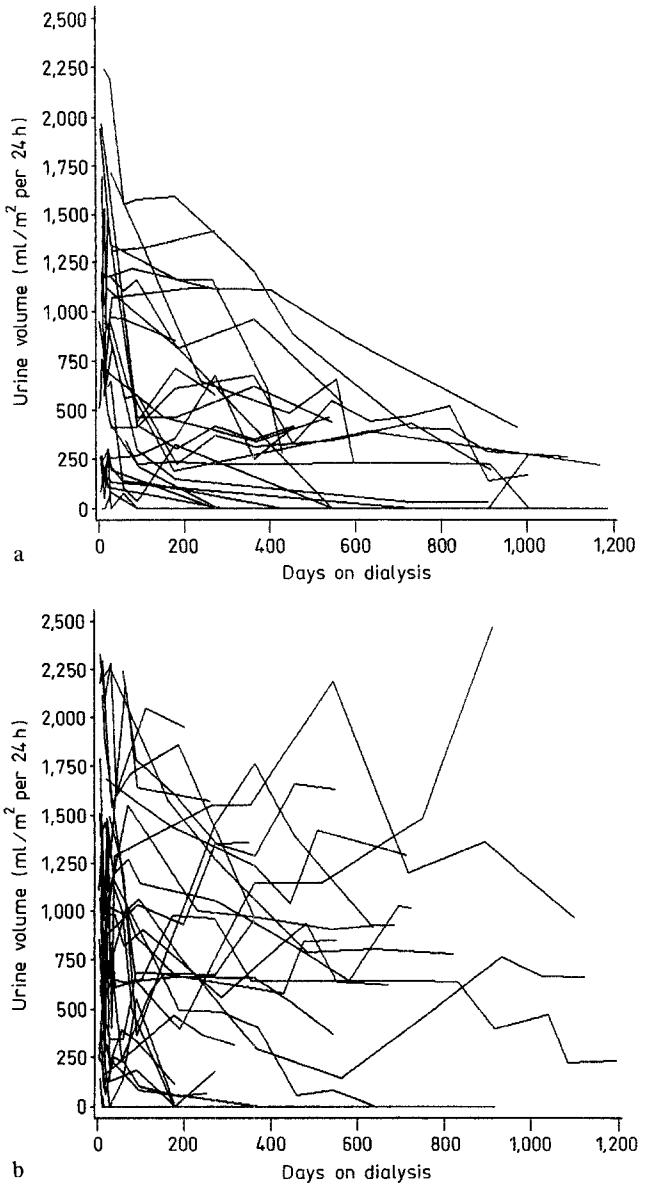

Fig. 1. Individual courses of urine volume in **a** haemodialysis (HD) and **b** peritoneal dialysis (PD) patients

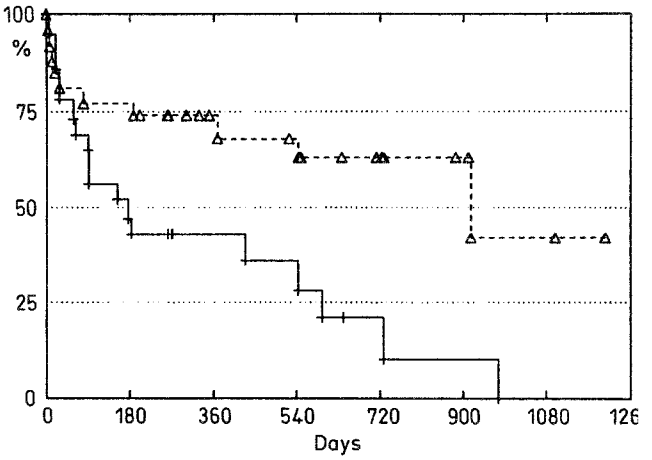

Fig. 2. Urine volume survival analysis (Kaplan-Meier). +, HD patients; △, PD patients; $P = 0.006$

Table 2. Urine volume in HD and PD patients at different time intervals after onset of dialysis therapy*

Time of measurement	No. of urine volume measurements		Urine volume (ml/m² per day), mean ± SD (median)	
	HD	PD	HD	PD
Before dialysis	20	27	1,047±783 (918)	1,249±773 (1023)
6 months after	19	23	547±430 (462)	801±764 (669)
12 months after	15	18	444±406 (341)	823±556 (958)
18 months after	11	13	371±288 (439)	740±672 (638)
24 months after	8	10	196±214 (130)	797±501 (861)

* Differences between HD and PD are not significant

Results

Urine volume

Table 2 shows the changes in UV with time in the two dialysis groups. The initial UV was not significantly different in HD and PD patients. The figures suggest a decreasing urinary output with time on dialysis, but a better preservation of UV in PD compared with HD patients. The comparison of Fig. 1a with Fig. 1b confirms this suggestion and demonstrates wide individual variations, with a transient increase of UV in some patients.

When the change in diuresis was calculated from the individual changes in percentage of the initial value, we obtained a mean drop of UV to 57% after 6 months in both dialysis groups, followed by a more pronounced decrease down to 46% at 12 months in HD patients, whilst in PD patients UV stabilized at 69%. At 18 and 24 months, HD patients conserved only 44% and 26% of their initial UV compared with 58% and 62% respectively in PD patients. However, these differences were not significant. The drop in UV as a percentage of initial diuresis was less in congenital than in acquired disorders, irrespective of the type of dialysis, but the numbers of patients are too small for a valid separate analysis. Anuria was reached after 1 year of dialysis therapy in 4 of 15 (27%) HD patients compared with 3 of 18 (17%) PD patients; these figures increased only slightly after 24 months (37% vs. 20%, respectively, NS).

Mean (± SD) UV derived from all individual mean UV measurements during the whole period of dialysis was significantly lower in HD (537±404 ml/m² per day, median 530, range 16–1,346) than PD patients (954±701 ml/m² per day, median 742, range 5–3,007, $P = 0.014$). However, the decrease in UV with time, from the initial value to the last measurement on dialysis, was almost the same: HD patients 26±52 ml/week (median 7, range 0–264), PD patients 26±59 ml/week (median 9, range 0–312). When this analysis was performed after exclusion of patients receiving frusemide therapy at the time of at least 2 UV measurements in the first 6 months of dialysis, 10 HD patients had a mean (± SD) decline in UV of 50±82 ml/week (median 10, range 0–264) compared with 31±70 ml/week (median 8, range 11–312) in 22 PD patients (NS). No significant difference in UV decline was

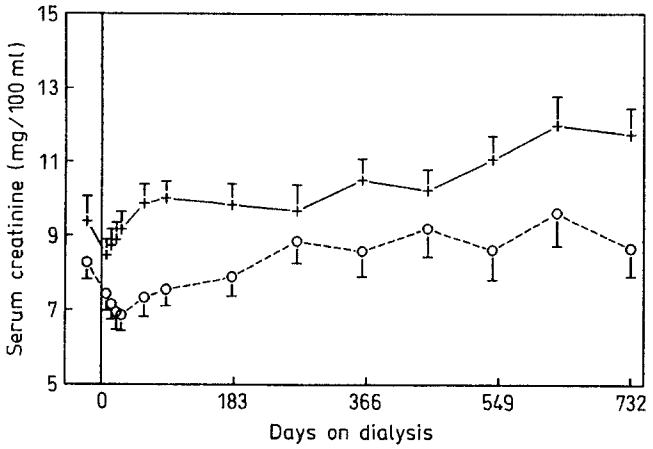

Fig. 3. Serum creatinine levels during dialysis treatment (means ± SEM), +, HD patients; ○, PD patients

noted between HD and PD patients who were not treated with ACE inhibitors during the first 6 months of dialysis.

By applying the Kaplan-Meier survival analysis we noted that a minimal UV of more than 500 ml/m² per day was conserved for a significantly longer period in PD compared with HD patients (Fig. 2). UV values less than 500 ml/m² per day were reached in 50% of patients within 176 days of the start of HD compared with 916 days of the start of PD (log-rank test, $P = 0.006$). This difference was independent of age, sex, primary renal disease and the calender year at start of dialysis, but was significantly influenced by the initial diuresis (Table 3): as expected a UV greater than 1,000 ml/m² per day before institution of dialysis was associated with a lower risk of developing a UV less than 500 ml/m² per day later.

The mean survival time until anuria was not significantly different between HD and PD patients (876 days for 50% of HD patients vs. 584 days in PD patients), but with acquired kidney diseases the risk of developing anuria was higher (×6.19) compared with congenital disorders ($P < 0.05$)

Glomerular filtration rate

Mean (± SD) SCr levels immediately before the start of dialysis were similar in HD and PD patients (Table 1). The further course of SCr is shown in Fig. 3. The median calculated C_{Cr} dropped only slightly from 8.8 (range 3.5–13.4) ml/min per 1.73 m² before dialysis to 7.8 (range 5.8–13.2) ml/min per 1.73 m² after 12 months and 7.2 (range 6.0–9.7) ml/min per 1.73 m² after 24 months in HD patients. This drop was even less marked in PD patients: 8.2 (range 5.2–12.7) initially, 8.7 (range 5.6–16.8) at 12 months and 7.6 (range 5.9–12.3) at 24 months.

The mean (± SD) slope estimates of log-transformed C_{Cr} obtained from each patient"s regression curve were not significantly different between HD and PD patients: 0.005 ± 0.018 and -0.015 ± 0.022, respectively (NS). No difference was found in the intercept values of calculated GFR at the start of dialysis in both groups: 9.3 ± 1.2 ml/min per 1.73 m² in HD versus 9.9 ± 1.2 ml/min per 1.73 m² in PD patients.

Table 3. Cox regression analysis of possible risk factors for urine volume decreasing to less than 500 ml/m² per 24 h during dialysis treatment

Factors	Parameter estimate	Standard error	Chi-squared	*P* value	Risk ratio
HD	1.44	0.61	5.58	<0.02	4.24
Age <8 years	0.90	0.74	1.49	0.22	2.46
Males	0.27	0.51	0.28	0.59	1.31
Acquired disease	0.60	0.44	1.84	0.17	1.82
Year of dialysis before 1985	0.56	0.50	1.23	0.27	1.75
Initial urine volume <1,000 ml/m² per 24 h	1.74	0.52	11.39	<0.01	5.72

Discussion

Changes in RRF after the start of HD and PD have been compared in three previous studies of adult patients. Rottembourg et al. [10] found that in two matched groups of 25 adult HD and PD patients, each followed over a period of 18 months, the mean urine output declined to 26% of predialysis values in HD patients compared with 91% in CAPD patients. At the same time the mean 24-h C_{Cr} fell from 4.3 to 1.3 ml/min in HD patients and from 4.4 to 4.0 ml/min in PD patients. Cancarini et al. [11] observed a decline of UV per 24 h to 35% of initial values in HD compared with 61% in CAPD patients within a mean observation period of 2.1 years. These authors noted a concomitant decrease of C_{Cr} from 5.8 to 1.3 ml/min in HD patients and from 6.4 to 3.9 ml/min in PD patients. This drop of UV and C_{Cr} was significant only for patients with nephroangiosclerosis and interstitial nephropathy, but not for patients with glomerulopathies.

Recently, Lysaght et al. [12] retrospectively studied residual C_{Cr} in 57 HD and 55 CAPD patients and found an exponential decrease with both modes of treatment. The rate of decline in HD patients was twice that in the CAPD group (5.8% vs. 2.9% per month); however this difference was significant only for patients with diabetic and glomerular nephropathies. Preliminary data from a prospective multicentre study in Australia (applying ^{51}chromium-EDTA clearance) seem to confirm the more rapid decline of GFR in HD patients [13]. The relatively good preservation of RRF with long-term CAPD is in agreement with two multicentre investigations [16, 17].

Our study demonstrates that also in paediatric patients RRF is preserved better with PD than HD. Although we failed to find a significant difference in the rate of decline of UV between the two forms of dialysis, the UV calculated from all mean values recorded over the whole period of dialysis was significantly higher in the PD patients, despite a similar initial UV as in the HD patients. In addition, a fall of UV to less than 500 ml/m² per day occurred much earlier in the HD than in the PD group. Finally, the proportion of paediatric patients becoming anuric was lower with PD than HD, although this difference was not significant and

less than in adult patients, where a diuresis of less than 100 ml/day occurred after a mean observation period of 2.2 years in 57% of HD patients compared with 7% of PD patients [11]. The generally better preservation of diuresis in our paediatric population might be related to the younger age or to the higher proportion of congenital and hereditary nephropathies, which are known to often have a polyuric pre-terminal phase. However, we were not able to identify age or primary renal disease as risk factors associated with a decrease of UV to less than 500 ml/m^2 per day.

Numerous studies have pointed out the difficulties of evaluating GFR in advanced renal failure. The problem with using C_{Cr} as an indicator of GFR in dialysed patients is perhaps best demonstrated by the discrepancy between a 35% fall in inulin clearance subsequent to a HD session in the absence of a concomitant change in C_{Cr}, suggesting tubular creatinine secretion [18]. Other authors believe that C_{Cr} is a suitable marker of GFR in dialysed patients under given conditions [3, 19]. Only a few authors have applied generally recognized precise methods to measure GFR in these patients [13, 20].

By applying reciprocal SCr values related to body height, we found a stable GFR during the whole observation period of HD and PD treatment. This is in contrast to reports from adult nephrology units, where a decrease of GFR with time was found [10–13, 21], with larger changes in HD than in PD patients. Renal function also declined with time in adult HD patients when reciprocal SCr was taken as a parameter [22]. Our observation suggests that GFR on dialysis treatment might be preserved for a longer period in children than in adults, irrespective of the mode of treatment.

The mechanisms for a better preservation of RRF in PD than in HD patients are unclear [3, 12]. It has been speculated that HD per se may be nephrotoxic by exposing the kidney transiently to inflammatory mediators generated by the extracorporeal circulation. In addition, rapid changes of plasma osmolality and volume associated with hypotensive episodes during HD sessions may induce renal ischaemia and reduce excretion of osmotically active substances and water, which is regularly observed after a HD session [20].

In conclusion, our study suggests that the urinary output over time is better preserved in children treated by PD than by HD, whilst the GFR appears to remain stable with both modes of treatments. Since RRF has been recognized as a main determinant for dialysis prescription [9], prospective studies applying more precise markers of glomerular and tubular functions in children with end-stage renal disease seem to be indicated.

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