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ORIGINAL ARTICLE

Is peritoneal dialysis still an equal option? Results of the Berlin pediatric nocturnal dialysis program

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Abstract
Background Peritoneal dialysis (PD) or conventional hemodialysis (HD) are considered to be equally efficient dialysis methods in children and adolescents. The aim of our study was to analyze whether an intensified, nocturnal HD program (NHD) is superior to PD in an adolescent cohort.
Methods Thirteen patients were prospectively enrolled in a NHD program. We measured uremia-associated parameters, parameters for nutrition, medication and blood pressure and analyzed the data. These data were compared to those of 13 PD controls, matched for gender, age and weight at the beginning the respective dialysis program and after 6 months of treatment.
Results Serum phosphate levels decreased significantly in the NHD group and remained unchanged in the PD group. Arterial blood pressure in the NHD was significantly lower despite the reduction of antihypertensive treatment, whereas blood pressure levels remained unchanged in the PD controls. Preexisting left ventricular hypertrophy resolved and albumin levels improved with NHD. Dietary restrictions could be lifted for those on NHD, whereas they remained in place for the patients on PD treatment. Residual diuresis remained unchanged after 6 months of either NHD or PD. NHD patients experienced fewer days of hospitalization than the PD controls.
Conclusions Based on our results, NHD results in significantly improved parameters of uremia and nutrition. If individually and logistically possible, NHD should be the treatment modality of preference for older children and adolescents.

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Introduction

Renal transplantation is the therapy of choice for end-stage renal disease (ESRD) in children and adolescents. However, due to the shortage of organs, and often the lack of preemptive possibilities, time to transplantation must be bridged with either peritoneal dialysis (PD) or hemodialysis (HD). Both procedures are well established in these patients, and both forms are considered as being in general an equal option for children and adolescents with ESRD, with the natural restriction that in newborns and toddlers, preference is given to PD.

Innovative and successful variants of PD have been developed for the delivery of optimal dialysis dosage, treatment of complications, peritoneal access and composition of solutions [1–4]. Many of these achievements are due to the establishment of a unique worldwide registry for children and adolescents on PD [5]. A similar improvement has not been achieved for HD; only little, if any, progress has been made, such as the introduction of high-flux membranes and the use of hemodiafiltration [6–8]. Therefore, based on clinical experience in adult patients, programs have been initiated for children and adolescents extending the time on dialysis ('intensified dialysis'), thus increasing the dialysis dose delivered [9–11]. The combination of intensified dialysis with hemofiltration has also investigated [12, 13]. Such programs offer a tremendous benefit to the patient, leading us to hypothesize that these beneficial effects, at least for some patients, are superior to those obtained on current PD programs. Therefore, we designed a case–control study in which we compared data collected on adolescents who were

prospectively enrolled in our intensified nocturnal HD (NHD) program (cases) with data collected from a matched PD cohort (controls).

Subjects and methods

Thirteen patients were prospectively enrolled in our NHD program (Table 1). Patients were only included in the NHD program upon their expressed wish and only after being enrolled for at least 2 months in the regular HD program (3×5 h per week, daytime). Written consent from patients and parents or caregivers was obtained; the program itself was approved by the ethical committee of the Charité. NHD was performed overnight for 3×8 h per week. Either Fresenius model 4008H or 5008H (Fresenius SE & Co. KGaA, Bad Homburg, Germany) or Gambro AK 200 (Gambro Group, Stockholm, Sweden) dialysis machines were used. Blood flow was set to the maximal possible (4–7 ml/kg/min), and dialysate flow was set at 500 ml/min. Dialysis fluids were adapted (Na^+, K^+, bicarbonate) to each individual patient. Anticoagulation was realized in all patients with unfractionated heparin and monitored by activated clotting time (ACT) (150–180 s). For all patients, dialysate Ca^{2+} was set at 1.75 mmol/l and adjusted if necessary [14].

Thirteen controls retrospectively matched for age, weight and gender were selected for the PD program (Table 2). In these patients either the Baxter HomeChoice (Baxter International, Deerfield, IL) or the Fresenius SleepSafe machines were used. For both systems, biocompatible solutions were used, either Physioneal or BicaVera, with glucose concentrations ranging from 1.36 to 2.3 %, respectively. Dialysis dosage was set initially according to internal guidelines, but at 3 months after treatment initiation we performed a peritoneal equilibration test and, based on the results and if applicable, adjusted the dialysis dosage [15, 16]. Data collected on both cohorts were compared at the beginning of renal replacement therapy and 6 months after start of NHD or PD, respectively.

Table 1 Characterization of the nocturnal hemodialysis cohort

Patient	Age (years. months)	Gender	Underlying disorder[a]	Weight (kg)
1	16.3	Female	D+HUS	45.3
2	12.7	Male	NPH	49.2
3	17.4	Male	NPH	54.5
4	17.5	Male	Alport's Syndrome	62.2
5	11.9	Male	ARPKD	56.5
6	12.3	Female	aHUS	33.7
7	16.5	Male	CAKUT	57.2
8	14.5	Male	CAKUT	73.6
9	14.8	Male	D+HUS	55.2
10	14.5	Female	CyA Tox after HTx	49.6
11	17.5	Female	Wegeners Granulomatosis	53.9
12	16.3	Male	ARPKD	74.5
13	13.5	Male	FSGS	53.2

[a] D+HUS:,Diarrhea-associated hemolytic uremic syndrome; NPH, nephronophthisis; ARPKD, autosomal recessive polycystic kidney disease; aHUS: atypical HUS; CAKUT, congenital abnormalities of the kidney and urinary tract; CyA tox, cyclosporine A toxicity; HTX, heart transplantation; FSGS, focal segmental glomerulosclerosis

Table 2 Characterization of the peritoneal dialysis cohort

Patient	Age (years. months)	Gender	Underlying disorder[a]	Weight (kg)
1	15.9	Female	ARPKD	52.3
2	13,1	Male	Alport's Syndrome	45.7
3	16,4	Male	MPGN II	55.4
4	17.2	Male	CAKUT	59.9
5	12.2	Male	ARPKD	59.3
6	13.1	Female	ARPKD	41.5
7	15.9	Male	FSGS	55.3
8	16.0	Male	CAKUT	65.3
9	15.1	Male	SLE	54.3
10	15.3	Female	Alport's Syndrome	56.3
11	16.3	Female	NPH	56.6
12	16.9	Male	NPH	69.3
13	14.0	Male	FSGS	59.3

[a] MPGN II, Membranoproliferative glomerulonephritis type II; SLE, systemic lupus erythematodes; for other abbreviations, see footnote to Table 1

Serum parameters

Phosphate, albumin and cholesterol levels were determined in both cohorts in a central laboratory, always before a dialysis session: in the late afternoon for PD or in the evening for NHD.

Kt/V

The Kt/V was either calculated using the internal algorithm (eKt/V) of the machines (NHD) using, if applicable, the Mellits–Cheek formula to determine urea distribution volume (V), or calculated according a standard formula (PD) [17]. For both cohorts, residual kidney Kt/V was not included in the calculation.

Blood pressure and end organ damage

Mean arterial blood pressure (MAP) was monitored, either before NHD at the center, or at home, before starting PD. Blood pressure monitors used at home were compared regularly with the monitors used in-center and if there was a >5 %

difference, the home monitor was replaced. The presence of left ventricular hypertrophy (LVH) was documented by echocardiogram before and 6 months after the initiation of NHD or PD [18]. Retinal changes, if any, were documented in all patients every 6 months.

Residual diuresis

Residual diuresis was determined by 24-h urine collection before and 6 months after enrolment in each program.

Medication, dietary and fluid restrictions

In all patients, medication intake was registered and grouped by antihypertensives, phosphate binders and potassium binders. In all patients, dietary restrictions (potassium and phosphate) were noted as well as fluid restrictions at the beginning of the respective treatment and after 6 months either NHD or PD (Table 3).

Hospitalization days

The number of hospitalization days of patients in each treatment group was registered within the 6-month study period; in-hospital days during the initiation of either NHD or PD (especially catheter placement) were not included since initiation of PD requires in general more in-center time than that of HD/NHD and, since patients enrolled in the NHD program already had vascular access, either via fistula or by central venous line.

Statistical analysis

The impact of different medical treatments with respect to the measured quantity y (e.g. phosphate) was analyzed separately for each quantity using a random intercept model that considers individual baselines for each subject. An excellent overview of the theoretical background and the applicability of such models to the investigation at hand can be found in the publication of Pinheiro and Bates [19]. All statistical analyses were performed using the R statistical software (version 3.0.1) [20]. The models were fitted using the nlme package [21]. Afterwards, a hypothesis system considering the differences between the control and treatment (case) group before dialysis and the differences within the two groups due to dialysis was composed. The three null hypotheses that the differences are zero were tested family-wise using the multcomp package [22]. The two quantities for which no pre-treatment data are available (Kt/V and hospitalization days) were analyzed as follows: the significance of the differences between NHD and PD group was assessed by the statistics of a t test with the null hypothesis that both treatments are identical [20]. The applicability of the t test, namely the normality of the observed values, was assured given the insignificant statistics of a Shapiro–Wilk test.

Table 3 Medication and dietary restrictions of the cohorts

Medication and dietary restrictions	Peritoneal dialysis (n=13)		Nocturnal hemodialysis (n=13)	
	Treatment initiation	After 6 months	Treatment initiation	After 6 months
Potassium binders	7	8	10	1
Phosphate binders	12	12	11	1
Antihypertensive drugs	11	10	11	3
Dietary restrictions	13	13	13	0
Fluid restrictions	9	10	7	0

Results

Epidemiology

Both groups contained four female and nine male patients. The median age of patients included in the NHD and PD groups was 14.8 (range 11.9–17.5) and 15.9 (range 12.2–16.9) years, respectively. The median weight of patients in the NHD and PD groups was 55.3 (range 33.7–74.5) and 56.3 (range 41.5-69.3) kg, respectively (Tables 1, 2).

Kt/V and residual diuresis

The Kt/V in NHD patients was significantly higher than that in the PD patients (2.7 vs. 2.1, respectively; $p<0.001$) (Fig. 1a). Residual diuresis was equal in both groups before and after 6 months of dialysis. Before starting dialysis, residual diuresis was 0.19 ml/kg/h in patients in the NHD group and 0.17 ml/kg/h in patients in the PD group ($p=0.99$). After 6 months of dialysis, residual diuresis was 0.22 ml/kg/h urine in the NHD patients ($p=0.2$), and 0.15 ml/kg/h in the PD patients ($p=0.4$) (Fig. 2a).

Blood pressure and cardiovascular parameters

The MAP in both patient groups before starting dialysis was equal [80 (NHD group) vs. 83 mmHg (PD group); $p=0.59$]. After 6 months of the respective dialysis treatment, the MAP had fallen significantly in NHD patients (−6 mmHg; $p<0.001$), but had remained stable in PD patients (+1 mmHg; $p=1$) (Fig. 2b). Ten patients in the PD group needed antihypertensive treatment, whereas only three patients receiving NHD needed antihypertensive medication (Table 3). After 6 months of dialysis, none of the NHD patients showed LVH (3 preexisting cases before entering the program), while

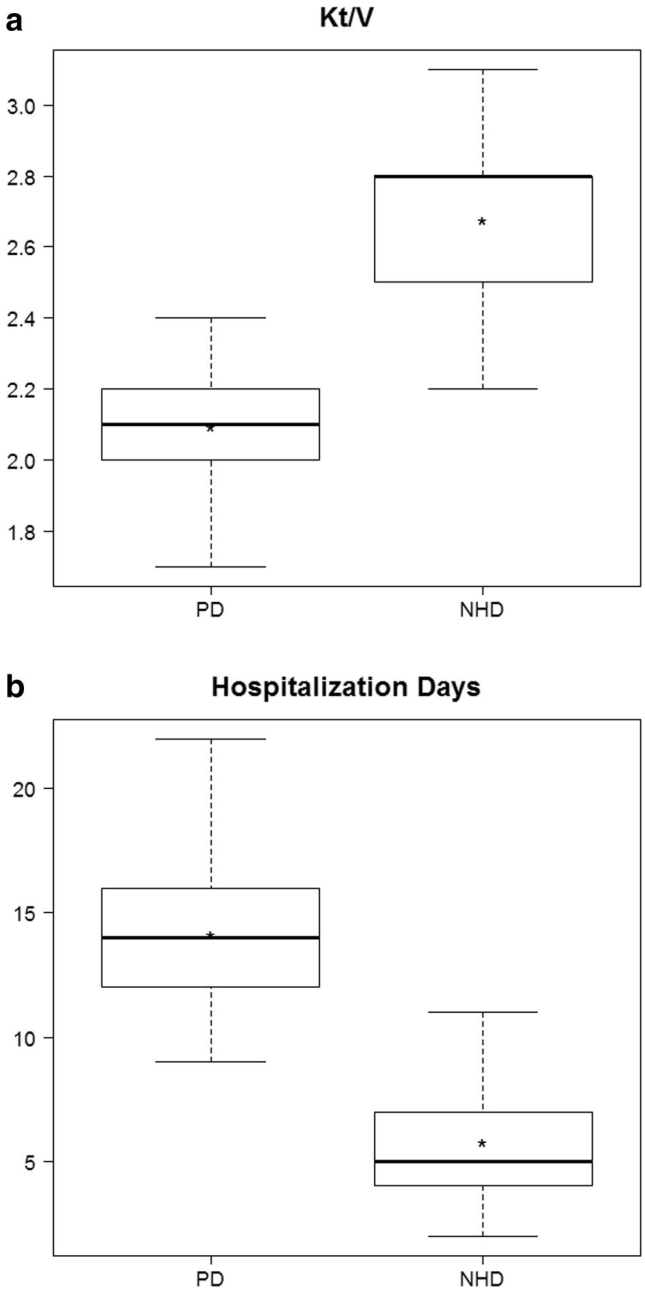

Fig. 1 Observed differences in Kt/V (**a**) and number of hospitalization days (**b**) between the peritoneal dialysis (*PD*) and nocturnal hemodialysis (*NHD*) cohorts. The corresponding *boxplots*, including median (*thick, black horizontal line in boxes*) and mean (*asterisk*), are shown. The *whiskers* represent 1.5 times the interquartile range above the upper quartile and below the lower quartile. The differences between the distributions for the two groups were tested via a *t* test and are significant at $p<0.001$)

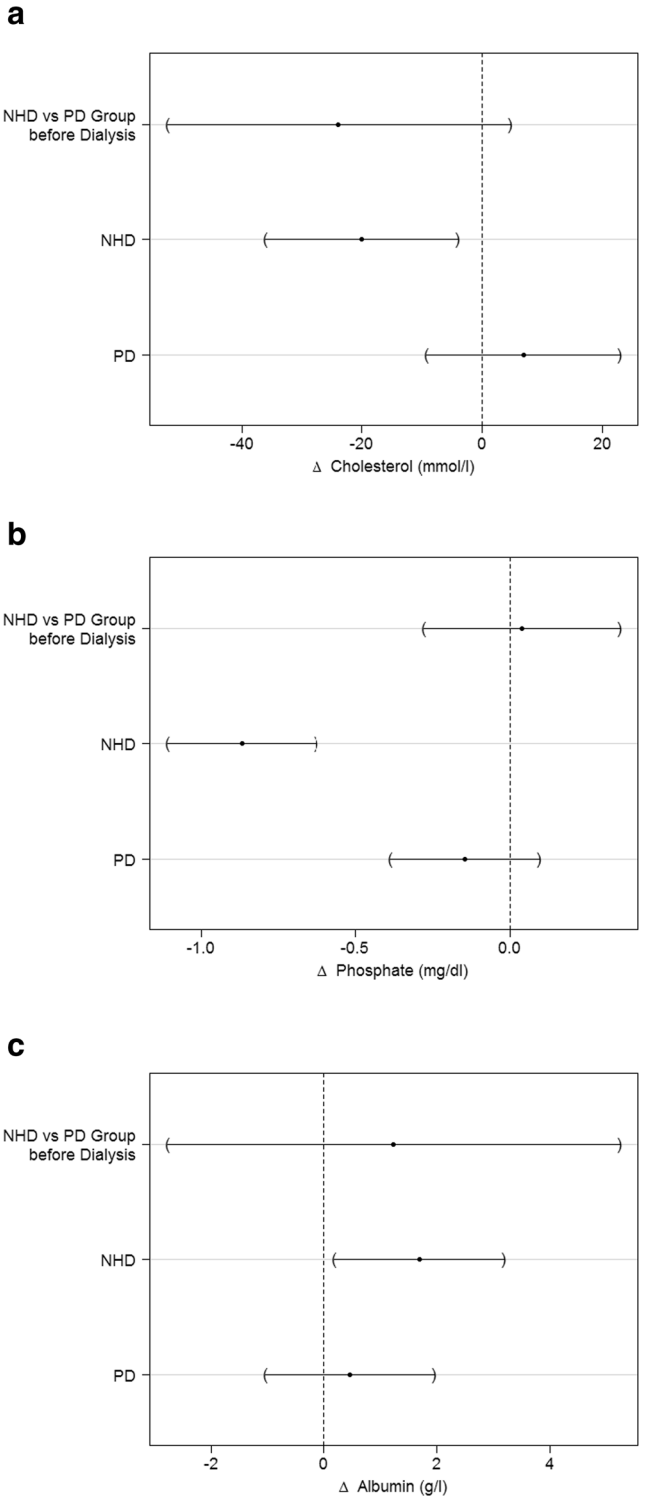

Fig. 2 Observed laboratory differences for cholesterol (**a**), phosphate (**b**) and albumin (**c**) between the peritoneal dialysis (*PD*) and nocturnal peritoneal dialysis (*NHD*) cohorts. **a**–**c** *Top row* Difference between the NHD and the PD group before starting dialysis, *middle row* difference between 6 months of NHD and initiation of NHD, *bottom row* difference between 6 months of PD and initiation of PD. The significance of each of these differences is tested simultaneously and the corresponding 95% CI are shown

five patients of the PD cohort had LVH (4 preexisting, 1 new). None of the patients in either treatment group suffered retinal damage at any time point.

Cholesterol levels in both groups before starting dialysis were equal [171 (NHD group) vs. 195 mmol/l (PD group); $p=0.13$]. After 6 months of dialysis, cholesterol levels in NHD patients had fallen significantly (136 mmol/l; $p<0.01$),

whereas those in PD patients remained high (202 mmol/l; $p=0.66$) (Fig. 3a). Phosphate levels before dialysis fell within the same range in both groups (2.3 mmol/l; $p=0.99$). After 6 months of dialysis, phosphate levels were significantly lower in NHD patients (1.5 mmol/l; $p<0.001$), whereas in PD patients phosphate levels remained high (2.2 mmol/l; $p=0.36$) (Fig. 3b). One patient in the NHD cohort and 12 patients in the PD group required phosphate binders (Table 3).

Nutritional status and dietary restrictions

Serum albumin concentration did not differ between both groups at the beginning of the dialysis treatment [40 (NHD group) vs. 38 g/l (PD group); $p=0.84$] (Fig. 3c). After 6 months of dialysis, albumin levels in NHD patients improved (+1.7 g/l; $p=0.02$), whereas albumin levels in PD patients remained stable (+0.5 g/l; $p=0.84$). Ten PD patients had fluid restrictions. All PD patients had dietary restrictions regarding potassium and phosphate intake, while none of the patients on NHD had any fluid or dietary restrictions (Table 3).

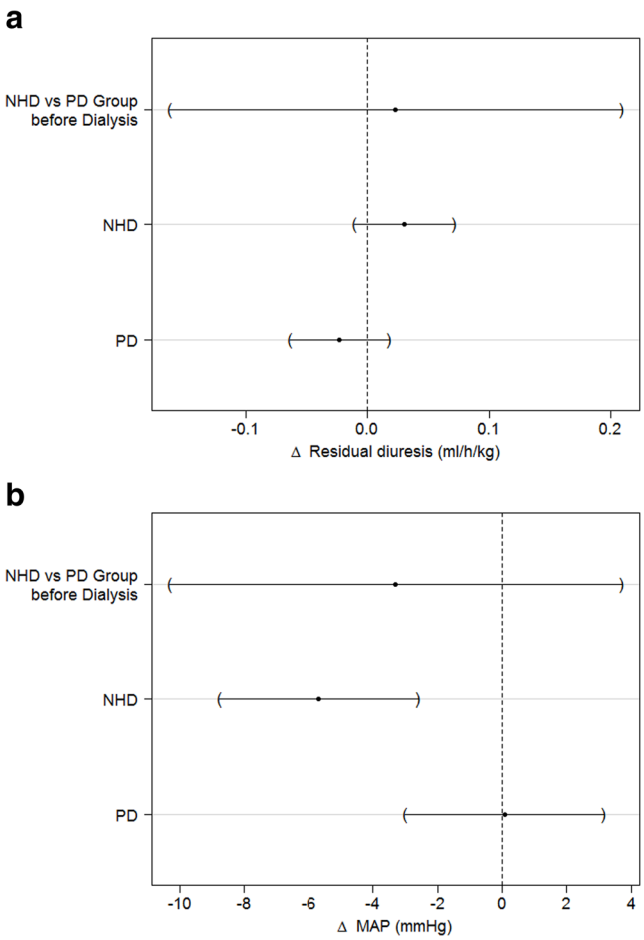

Fig. 3 Observed differences in residual diuresis (**a**) and mean arterial pressure (*MAP*; **b**) between the peritoneal dialysis (*PD*) and nocturnal hemodialysis (*NHD*) cohorts. **a**, **b** *Top row* Difference between the NHD and the PD group before starting dialysis, *middle row* difference between 6 months of NHD and initiation of NHD, *bottom row* difference between 6 months of PD and initiation of PD. The significance of these differences are tested simultaneously and the corresponding 95% confidence intervals (CI) are shown

Social rehabilitation

During the 6-month study period, patients receiving NHD stayed 6 days in the hospital, whereas PD patients were hospitalized for 14 days ($p<0.001$) (Fig. 1b).

Discussion

The results of our study demonstrate that, at least for the cohorts and time span investigated here, several uremia-associated parameters, as well as indicators of quality of life, significantly improved in patients in a NHD program when compared to matched patients in a PD program.

Among our study subjects, NHD patients displayed a significantly higher Kt/V than patients on PD. Whereas a small increase of Kt/V did not influence mortality in adults, the use of an intensified program generating a Kt/V that is two to threefold higher has been associated with improved survival [23, 24]. Thus, we conclude that intensified dialysis programs could improve long-term outcome also in children and adolescents. Given the shortage of organs worldwide and the restricted life-time of an organ, it can be anticipated that children with ESRD will have a significant life-time on dialysis.

The NHD cohort also showed significantly lower MAP despite a reduction of antihypertensive medication and free access to fluids. As cardiovascular morbidity and mortality is excessively high in patients with ESRD, NHD seems to be the method that provides a better outcome [25–27]. Additionally, NHD eliminates phosphate more efficiently than PD. As phosphate has been identified as one of the major factors triggering uremic vasculopathy, it can be speculated that the superior removal of this compound results in a better cardiovascular risk profile [28–30]. This hypothesis is further supported by our finding that none of our NHD patients showed LVH 6 months after starting the program. Finally, cholesterol, which also contributes to vascular disease, was significantly lowered in patients on NHD, whereas the cholesterol levels of our patients on PD remained high.

Interestingly, residual diuresis was not reduced after 6 months in either the NHD or the PD patients. This finding in particular has often been used as an argument for PD rather than for HD, as conserved residual diuresis has been associated with morbidity and mortality improvement [31, 32]. Our study shows that this argument does not hold true for the comparison of PD and NHD; moreover, conserved residual diuresis might even contribute to the significantly better

results of NHD. Residual diuresis may be more conserved in patients on NHD because of better volume and blood pressure control.

In addition to these uremia-associated factors, the quality of life was markedly improved in NHD patients. First, the amount of medication prescribed could be significantly reduced (antihypertensives, phosphate and potassium binders). Second, patients on NHD had neither dietary nor fluid restrictions. Third, and probably most important, patients were hospitalized less than patients on PD. In particular, the occurrence of catheter dysfunction and peritonitis contributed to the inferior result of the PD cohort in terms of number of days hospitalized. That our patients on NHD were able to attend school with few disruptions than those on PD implies that they might, in the future, due to a better education and grades, contribute to social welfare systems rather than becoming dependent for life on such systems.

Our study has a number of limitations. The study design with retrospectively matched PD controls is not optimal. PD patients visited the dialysis center every 4 weeks, whereas NHD patients were visited weekly by a pediatric nephrologist. The number of patients in each group is quite small. All of these factors could confound the results. Prospective studies with more patients are needed to clarify our results.

In summary, if intensified programs are logistically and individually feasible, NHD should be given preference over PD for older children and adolescents. Moreover, although the setting of a nocturnal dialysis program requires a team effort that involves physicians, nurses, social workers, psychologists and dietitians, the unprecedented beneficial effects of intensified programs (including short daily dialysis) pose the question of whether such programs should become the standard and not the exception of HD.

Conflict of Interest None.

References

1. Schmitt CP, Nau B, Gemulla G, Bonzel KE, Hölttä T, Testa S, Fischbach M, John U, Kemper MJ, Sander A, Arbeiter K, Schaefer F (2013) Effect of the dialysis fluid buffer on peritoneal membrane function in children. Clin J Am Soc Nephrol 8:108–115
2. Schmitt CP, Haraldsson B, Doetschmann R, Zimmering M, Greiner C, Böswald M, Klaus G, Passlick-Deetjen J, Schaefer F (2002) Effects of pH-neutral, bicarbonate-buffered dialysis fluid on peritoneal transport kinetics in children. Kidney Int 61:1527–1536
3. Borzych-Duzalka D, Bilginer Y, Ha IS, Bak M, Rees L, Cano F, Munarriz RL, Chua A, Pesle S, Emre S, Urzykowska A, Quiroz L, Ruscasso JD, White C, Pape L, Ramela V, Printza N, Vogel A, Kuzmanovska D, Simkova E, Müller-Wiefel DE, Sander A, Warady BA, Schaefer F, International Pediatric Peritoneal Dialysis Network (IPPN) Registry (2013) Management of anemia in children receiving chronic peritoneal dialysis. J Am Soc Nephrol 24:665–676
4. Fischbach M, Zaloszyc A, Schaefer B, Schmitt CP (2014) Optimizing peritoneal dialysis prescription for volume control: the importance of varying dwell time and dwell volume. Pediatr Nephrol 29:1321–1327
5. Schaefer F, Warady BA (2011) Peritoneal dialysis in children with end-stage renal disease. Nat Rev Nephrol 7:659–668
6. Locatelli F, Altieri P, Andrulli S, Bolasco P, Sau G, Pedrini LA, Basile C, David S, Feriani M, Montagna G, Di Iorio BR, Memoli B, Cravero R, Battaglia G, Zoccali C (2010) Hemofiltration and hemodiafiltration reduce intradialytic hypotension in ESRD. J Am Soc Nephrol 21: 1798–1807
7. Maduell F, Moreso F, Pons M, Ramos R, Mora-Macià J, Carreras J, Soler J, Torres F, Campistol JM, Martinez-Castelao A, ESHOL Study Group (2013) High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. J Am Soc Nephrol 24:487–497
8. Locatelli F, Martin-Malo A, Hannedouche T, Loureiro A, Papadimitriou M, Wizemann V, Jacobson SH, Czekalski S, Ronco C, Vanholder R, Membrane Permeability Outcome (MPO) Study Group (2009) Effect of membrane permeability on survival of hemodialysis patients. J Am Soc Nephrol 20:645–654
9. Hoppe A, von Puttkamer C, Linke U, Kahler C, Booss M, Braunauer-Kolberg R, Hofmann K, Joachimsky P, Hirte I, Schley S, Utsch B, Thumfart J, Briese S, Gellermann J, Zimmering M, Querfeld U, Müller D (2011) A hospital-based intermittent nocturnal hemodialysis program for children and adolescents. J Pediatr 158:95–99
10. Geary DF, Piva E, Tyrrell J, Gajaria MJ, Picone G, Keating LE, Harvey EA (2005) Home nocturnal hemodialysis in children. J Pediatr 147:383–387
11. De Camargo MFC, Henriques CL, Vieira S, Komi S, Leão ER, Nogueira PCK (2014) Growth of children with end-stage renal disease undergoing daily hemodialysis. Pediatr Nephrol 29:439–444
12. Fischbach M, Terzic J, Laugel V, Dheu C, Menouer S, Helms P, Livolsi A (2004) Daily on-line haemodiafiltration: a pilot trial in children. Nephrol Dial Transplant 19:2360–2367
13. Thumfart J, Puttkamer CV, Wagner S, Querfeld U, Müller D (2014) Hemodiafiltration in a pediatric nocturnal dialysis program. Pediatr Nephrol 29:1411–1416
14. Thumfart J, Müller D (2014) Nocturnal intermittent hemodialysis. Pediatr Nephrol 29:1411–1416
15. Fischbach M, Desprez P, Terzic J, Lahlou A, Mengus L, Geisert J (1996) Use of intraperitoneal pressure, ultrafiltration and purification dwell times for individual peritoneal dialysis prescription in children. Clin Nephrol 46:14–16
16. Schaefer F, Langenbeck D, Heckert KH, Schärer K, Mehls O (1992) Evaluation of peritoneal solute transfer by the peritoneal equilibration test in children. Adv Perit Dial 8:410–415
17. Mellits ED, Cheek DB (1970) The assessment of body water and fatness from infancy to adulthood. Monogr Soc Res Child Dev 35: 12–26
18. Kampmann C, Wiethoff CM, Wenzel A, Stolz G, Betancor M, Wippermann CF, Huth RG, Habermehl P, Knuf M, Emschermann T, Stopfkuchen H (2000) Normal values of M mode echocardiographic measurements of more than 2000 healthy infants and children in central Europe. Heart 83:667–672
19. Pinheiro JC, Bates DM (2009) Mixed effects models in S and S-Plus, 2nd edn. Springer SBM, New York
20. R Core Team (2013): R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna. URL http://www.R-project.org
21. Pinheiro JC, Bates DM, DebRoy S (2013) nlme: linear and nonlinear mixed effects models, R package version 3.1-109
22. Hothorn T, Bretz F, Westfall P (2008) Simultaneous inference in general parametric models. Biom J 50:346–363
23. Lacson E Jr, Wang W, Lester K, Ofsthun N, Lazarus JM, Hakim RM (2010) Outcomes associated with in-center nocturnal hemodialysis from a large multicenter program. Clin J Am Soc Nephrol 5:220–226

24. Nesrallah GE, Lindsay RM, Cuerden MS, Garg AX, Port F, Austin PC, Moist LM, Pierratos A, Chan CT, Zimmerman D, Lockridge RS, Couchoud C, Chazot C, Ofsthun N, Levin A, Copland M, Courtney M, Steele A, McFarlane PA, Geary DF, Pauly RP, Komenda P, Suri RS (2012) Intensive hemodialysis associates with improved survival compared with conventional hemodialysis. J Am Soc Nephrol 23:696–705
25. Mitsnefes M, Flynn J, Cohn S, Samuels J, Blydt-Hansen T, Saland J, Kimball T, Furth S, Warady B, CKiD Study Group (2010) Masked hypertension associates with left ventricular hypertrophy in children with CKD. J Am Soc Nephrol 21:137–144
26. Mitsnefes MM (2012) Cardiovascular disease in children with chronic kidney disease. J Am Soc Nephrol 23:578–585
27. Shroff R, Weaver DJ Jr, Mitsnefes MM (2011) Cardiovascular complications in children with chronic kidney disease. Nat Rev Nephrol 7:642–649
28. Shroff RC, McNair R, Skepper JN, Figg N, Schurgers LJ, Deanfield J, Rees L, Shanahan CM (2010) Chronic mineral dysregulation promotes vascular smooth muscle cell adaptation and extracellular matrix calcification. J Am Soc Nephrol 21:103–112
29. Shroff RC, McNair R, Figg N, Skepper JN, Schurgers L, Gupta A, Hiorns M, Donald AE, Deanfield J, Rees L, Shanahan CM (2008) Dialysis accelerates medial vascular calcification in part by triggering smooth muscle cell apoptosis. Circulation 118: 1748–1757
30. Shroff R (2013) Phosphate is a vascular toxin. Pediatr Nephrol 28: 583–593
31. Wang AY-M, Lai K-N (2006) The importance of residual renal function in dialysis patients. Kidney Int 69:1726–1732
32. Shafi T, Jaar BG, Plantinga LC, Fink NE, Sadler JH, Parekh RS, Powe NR, Coresh J (2010) Association of residual urine output with mortality, quality of life, and inflammation in incident hemodialysis patients: the Choices for Healthy Outcomes in Caring for End-Stage Renal Disease (CHOICE) Study. Am J Kidney Dis 56:348–358