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Original article

Long-term outcomes of peritoneal dialysis started in infants below 6 months of age: An experience from two tertiary centres

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ABSTRACT

Background. – Little data are available for infants who started renal replacement therapy before 6 months of age. Because of extra-renal comorbidities and uncertain outcomes, whether renal replacement therapy in neonates is justified remains debatable.
Methods. – We performed a retrospective analysis of all patients who began chronic peritoneal dialysis below 6 months between 2007 and 2017 in two tertiary centres. Results are presented as median (min;max).
Results. – Seventeen patients (10 boys) were included (8 prenatal diagnoses, 6 premies), with the following diagnoses: congenital anomalies of kidney and urinary tract ($n = 9$), oxalosis ($n = 5$), congenital nephrotic syndrome ($n = 2$) and renal vein thrombosis ($n = 1$). Five patients had associated comorbidities. At peritoneal dialysis initiation, age was 2.6 (0.1;5.9) months, height-standard deviation score (SDS) −1.3 (−5.7;1.6) and weight-SDS −1.4 (−3.6;0.6). Peritoneal dialysis duration was 12 (2;32) months, and at peritoneal dialysis discontinuation height-SDS was −1.0 (−4.3;0.7) weight-SDS −0.7 (−3.2;0.2), parathyroid hormone 123 (44;1540) ng/L, and hemoglobin 110 (73;174) g/L. During the first 6 months of peritoneal dialysis, the median time of hospitalisation stay was 69 (15;182) days. Ten patients presented a total of 27 peritonitis episodes. Reasons for peritoneal dialysis discontinuation were switch to hemodialysis ($n = 6$), transplantation ($n = 6$), recovery of renal function ($n = 2$) and death ($n = 1$). After a follow-up of 4.3 (1.7;10.3) years, 12 patients were transplanted, 2 patients were still on peritoneal dialysis, 2 patients were dialysis free with severe chronic kidney disease and 1 patient had died. Seven patients displayed neurodevelopmental delay, of whom five needed special schooling.
Conclusion. – We confirm that most infants starting peritoneal dialysis before 6 months of age will be successfully transplanted and will have a favourable growth outcome. Their quality of life will be impacted by recurrent hospitalisations and neurodevelopmental delay is frequent.

Abbreviations: BMI, Body Mass Index; CAKUT, Congenital anomalies of kidney and urinary tract; CKD, Chronic kidney disease; CKD-MBD, Chronic kidney disease–Mineral bone disorder; DP, Dialyse péritonéale; eGFR, Estimated glomerular filtration rate; EPO, Erythropoietin; ESI, Exit site infection; ESRD, End-stage renal disease; GH, Growth hormone; HTN, Hypertension; IRC, Insuffisance rénale chronique; ISPD, International Society for Peritoneal Dialysis; LVH, Left ventricular hypertrophy; PD, Peritoneal dialysis; PTH, Parathyroid hormone; rhGH, Recombinant human growth hormone; RRT, Renal replacement therapy; SDS, Standard deviation score.

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1. Introduction

Little information is available for infants who started chronic PD before 6 months of age. Children who start RRT within the first months of life have more clinical complications, an increased risk of peritonitis and more technical failure of dialysis compared to children who start RRT later [1–5]. Besides, comorbidities are more prevalent in this population with coexisting extrarenal involvement due to primary disease, making prenatal counselling more complicated [1–11]. As summarised in Table 1, long-term data outcomes are scarce, raising the ethical issues whether PD in neonates is justified and leading to different managements between centres [12]. The objective of this retrospective study was to report the experience of two French tertiary pediatric nephrology centres on 17 infants who began chronic PD before 6 months of age, on a 10-year period, to provide additional evidence for the discussion.

2. Patients and methods

We performed a retrospective analysis of all patients followed in two tertiary centres (Lyon and Besançon) who began chronic PD below 6 months of age between January 2007 and January 2017.

The following clinical data were recorded: term of the pregnancy, biometric data (height, body weight, head circumference) at birth, PD initiation, 15 days after PD initiation, every 3 months during the first year of PD, and every 6 months until 3 years or until the last follow-up on PD. Biometrical parameters were normalised as SDS according to chronological age and gender according to French growth reference charts [13]. The surgical procedure for PD catheter insertion was described: catheter placement, associated omentectomy. The primary diagnosis and the presence of a prenatal diagnosis were also recorded. Dialysis was initiated on manual mode (initial volume of 10 mL/kg), with progressive increase until 80 to 100 mL. This volume enabled the use of an automated cycler (Sleep Safe cycler, Fresenius Medical Care AG & Co., Bad Homburg vor der Höhe, Germany). Cycle volume was gradually increased to 800 mL/m^2 before 2 years of age and 1400 mL/m^2 after 2 years of age, with 5 to 15 cycles per night and daytime dwell if needed. PD fluid used for night-time cycles was biocompatible with a neutral pH, bicarbonate buffer, and low levels of glucose degradation products (Bicavera or Balance, Fresenius Medical Care AG & Co., Bad Homburg vor der Höhe, Germany); for daytime cycles icodextrine (Extraneal, Baxter Healthcare LTD, Norfolk, England) was used.

Hemoglobin and PTH status before PD start, 3 months after the beginning of PD, after one year and at last PD follow-up, were registered. In the absence of other formula in this age group, the 2009 Schwartz formula was used to evaluate the eGFR at the beginning of PD [14].

Treatment in terms of active vitamin D doses (μg/kg/d), phosphate binders use and type, EPO week dose (IU/kg/week) and GH treatment if present (mg/kg/week) were recorded before the beginning of PD, at 3 and 6 months after the PD start, at the end of PD and at the end of the follow-up.

Complications assessment includes incidence and characteristics of peritonitis, catheter complications (exit site infection ESI, obstruction, leaks and cuff extrusion). Consequences were reflected by the hospitalisation rate (the number of hospitalisation and cumulative duration at 6 months and 12 months after PD initiation). Peritonitis was defined according to ISPD recommendations [15]: signs and symptoms of peritoneal irritation, peritoneal cellularity in cloudy effluent $>$ 100 cells/mm^3 or a positive culture. Catheter ESI was defined as the presence of purulent discharge from the catheter or marked peri-catheter swelling, redness, tenderness with or without pathogenic germs cultured.

If available, data on cardiological ultra-sounds were recorded. LVH was defined as a left ventricular mass index $>$ 38 g/m^{2,7} according to the definition of the International Pediatric Peritoneal Dialysis Network [16]. We used the International Pediatric Peritoneal Dialysis Network calculator to define the left ventricular mass index according to height, left ventricular end-diastolic diameter, posterior wall thickness and intraventricular septal diastolic thickness (www.pedpd.org). HTN was defined as blood pressure $\geq$ 95th percentile for age and height according to the TASK Force on Blood Pressure Control in Children [17].

Final outcomes were defined as transplantation, hemodialysis switch, PD arrest and/or death. Time before transplantation, height and weight at the time of transplantation and type of donor were reported. Graft survival and causes of graft loss were also collected. Neurodevelopmental outcomes were determined by the clinical status of patients at the end of the follow-up (whether he was presenting developmental delay or not) and the type of schooling (normal schooling or special education).

Statistical analyses were mainly descriptive, and results are presented as median (range). Paired tests were used to compare the evolution of the different parameters at the different time points. Spearman bivariate analyses were performed. A *P*-value below 0.05 was considered statistically significant. This retrospective study was approved by the local IRB (Comité d'éthique des hospices civils de Lyon, session June 7th 2018). By French law, retrospective studies do not require a written consent from the patients/parents but an oral information.

3. Results

3.1. Clinical characteristics

A total of 17 patients (10 boys) began chronic PD before 6 months of age. Their characteristics are reported in Table 2. Median age at PD start was 2.6 (0.1;5.9) months with 11 infants starting dialysis between 0–3 months.

Median PD duration was 12 (2;32) months and follow-up was 4.3 (0.7;10.3) years. Residual diuresis was observed during PD in 11 patients, whilst 4 patients were completely anuric at PD start, and data were missing for 2 patients. The eGFR at PD start was 5 (2;17) mL/min per 1.73 m^2.

Five out of the 17 patients were moderate to late pre-term and one was very pre-term (30 weeks of gestation). Eight out of 12 children had a prenatal diagnosis; medical abortion was refused by parents in 2 cases, and antenatal data were missing for the last 5 cases. The primary diagnosis was: CAKUT (n = 9), oxalosis (n = 5), congenital nephrotic syndrome (n = 2) and renal vein thrombosis (n = 1).

Five patients presented at least one associated comorbidity: lungs hypoplasia in two babies, neurological comorbidities resulting from perinatal asphyxia in two and Prune-Belly-like syndrome in one.

3.2. Growth

Median birth weight and height were 3071 (1570;3870) grams and 48.5 (41.5;51.5) cm, respectively. The median body weight at PD start was of 4.6 (1.5;5.8) kg and −1.4 (−3.6;0.6) SDS. The median SDS for weight at PD discontinuation was −0.7 (−3.2;0.2) (P = NS from PD initiation), with a median delta SDS for weight between the beginning of PD and the end of PD of −0.6 (−2.4;1.7). Median height SDS was −1.3 (−5.7;1.6) at the start of PD and −1.0 (−4.3;0.7) at the end of PD treatment (P = NS). Median delta SDS for

Table 1
Publications on PD in children less than 2 years of age.

Author	Ledermann et al. [8]	Vidal et al. [1]	Chan et al. [10]	Van Stralen et al. [4]	Hogan et al. [20]	Sanderson et al. [5]
Study type	Single centre retrospective	Multi-centre registry	Single centre retrospective	Multi-centre registry	Multi-centre registry	Multi-centre registry
Centres	Greet Ormond Street Hospital (London)	Italian registry of pediatric chronic dialysis	Princess Margaret Hospital (Hong Kong)	ESPN/ERA-EDTA, IPPN, Australian (ANZDATA) and Japanese RRT registries	National Renal Epidemiology an Information Network (REIN)	United States Data Systems (USRDS)
Year of publication	1999	2012	2016	2014	2018	2019
Period	1986–1998	1995–2007	1995–2013	2000–2011	1992–2012	1990–1999 and 2000–2014
Number of children included	20	84	9	264	224	1723
Age	<1 year	<1 year	<2 years	<31 days	<2 years	<1 year
Median age at start of DP	4.1 months	6.9 months	4.7 months	7 days	10.4 months	1990–1999: 2.2 months 2000–2014: 2.5 months
Median follow-up	NS	19 months	NS	29 months	78 months	NS
Death	4 (20%)	8 (10%)	1 (11%)	45 (17%)	29 (13%)	360 (21%)
Transplantation	11 (55%)	33 (39%)	4 (44%)	53 (20%)	171 (76%)	1060 (61.5%)
Shift to dialysis modality	4 (20%)	18 (21%)	6 (67%)	69 (26%)	NS	NS
Catch-up growth	100% Weight SDS −1.6 at PD start and 0.3 at 2 years Height SDS−1.8 at PD start and −0.8 at 2 years	23/47 (49%) Weight SDS−2.3 at PD start and −1.9 at 2 years Height SDS−1.6 at PD start and −1.5 at 2 years	No Weight SDS−1.32 at PD start and −1.3 at 2 years but Height SDS− 0.7 at PD start and −1.45 at 2 years	166 (63%)	NS	NS
Normal neurodevelopment	14/16 (87%)	NS	4/8 (50%)	NS	NS	NS

NS: non-specified.

height between the beginning of PD and the end of PD was 0.2 (−3.9;4.8). Median SDS BMI was at the beginning of PD −3.3 (−4.3;−1.0) and −1.7 (−3.3;1.0) at the end of PD ($P = 0.005$).

Sixteen patients required enteral feeding, 11 by gastrostomy and 5 by nasogastric tube. Gastrostomy were surgically placed at 3.3 (1.4;12.1) months of age, 14 (10;22) days before PD start for 9 patients; it is noteworthy that two patients had a gastrostomy placed after the beginning of PD (respectively 296 and 465 days after). One patient had no enteral feeding at all, but also demonstrated catch-up growth. Three infants received rhGH because of severe growth retardation.

3.3. Peritoneal access and PD complications

Twenty-nine PD catheters were surgically placed in 17 patients, with associated omentectomy in 10 infants. Data about omentectomy were missing for 7 patients. The time between catheter placement and the beginning of PD was 4 (0;22) days.

Six patients required 11 catheter replacements because of catheter obstruction ($n = 3$), dysfunction ($n = 4$), infections ($n = 2$) and leakage ($n = 2$). Of those, one patient needed replacement of the peritoneal access twice, two patients needed three different replacements and three patients needed only one catheter replacement. Nine catheter obstructions occurred in four patients, resolving after urokinase treatment in eight cases, and surgical procedure in one case. Four catheter leakages occur in three infants. Cuff extrusion occurred only once in one patient.

Twenty-seven episodes of peritonitis occurred in 10 infants. Eight infants were affected by ≥ two episodes, two patients underwent a single peritonitis episode and seven patients did not present any peritonitis. One peritonitis episode occurred every 7.6 months–patient. Most frequent organisms were Gram-positive cocci ($n = 13$; *Staphylococcus aureus* $n = 7$; coagulase-negative *Staphylococcus* $n = 5$; *Streptococcus* $n = 1$), followed by Gram-negative bacillus ($n = 9$, *Escherichia Coli* $n = 4$, *Pseudomonas* $n = 2$, *Klebsiella* $n = 3$). One patient had a peritonitis episode with multiple bacteria. Three patients had clinical signs and symptoms of peritonitis with a cloudy effluent and increased effluent cellularity but a negative culture. In one patient, no data were found on the involved organism. ESI were found in two patients, who presented associated peritonitis.

During the first six months of PD, the median number of hospitalisations was 3 (1;10). Six patients were hospitalised only once during this time and all the others underwent two to ten hospitalisations. The total duration of hospitalisation stays was 69 (15;182) days. Most of the reasons for hospital stays were dialysis initiation with education of parents ($n = 7$) and infections ($n = 10$). Between the 6th and 12th months on PD, the number of hospitalisations was 3 (1;11) with a total duration of hospitalisation stays of 25 (1;186) days. The most common cause of hospitalisation during this period was infections ($n = 12$) and clinical complications (dehydration, vomiting, $n = 4$).

3.4. Anemia and CKD-MBD

The biochemical evolution of patients is summarised in Table 3. Before PD, median PTH levels were 212 (6;799) ng/L, decreasing to 130 (23;732) ng/L 3 months after the beginning of PD, and reaching 123 (44;1540) ng/L at the end of PD (P = NS between PD initiation and the end of PD). Phosphate binders were prescribed in five patients before the start of PD, data for 3 patients were missing. Only three patients still received phosphate binders at the end of PD, three data were missing. The most frequent type of phosphate binders remained calcium carbonate. One patient with severe hyperparathyroidism required calcium carbonate and sevelamer. Seven patients received active vitamin D analogs at the start of PD with a median daily dose of alfacalcidol of 0.06 (0.02;0.30) μg/kg. Six patients were still treated at the end of the PD with a median daily dose of 0.07 (0.02;0.20) μg/kg.

Table 2
Clinical characteristics of the 17 patients enrolled in the study.

Infant	Sex	Antenatal diagnosis	Birth (wk)	Primary renal disease	Comorbidities	Enteral feeding	Residual diuresis	Age at PD initiation (months)	Weight (g) at PD initiation	Duration of PD (months)	Outcomes	Follow-up (years)	Time before Tx (months)	Age at Tx (months)	Weight at Tx (kg)	Graft losses	Peritonitis episodes	Catheter related complications	Developmental delay	Age (end of follow-up) non-transplanted	Weight (end of follow-up) (SDS)	Height (end of follow-up) (SDS)
1	F	NO	34.2	CNS	NO	Gastrostomy	YES	5.9	5800	21.8	Tx R	2.9	21.7	27.7	11		3	NO	YES		−0.6	0.1
2	F	NO	36	CNS	Neurological	NG	NO	5.4	5656	10.0	Tx R	8.4	11	15	9.2		0	Obstruction	YES		0	−0.4
3	M	YES	40	CAKUT	NO	NG	YES	0.9	2600	22.8	Tx R	3.2	22	23	11.2		1	NO	NO		−0.6	0
4	M	NO	39	Oxalosis	NO	NG	NO	3.0	4600	4.4	HD −> Tx R	10.5	27	21	11.8		0	Leakage	YES		−0.9	−2.3
5	F	NO	35	Oxalosis	NO	Gastrostomy		2.2	4250	11.9	HD −> Tx R	4.5	18	42	13		3	NO	NO		−0.8	−2.5
6	M	NO		Oxalosis	NO	Gastrostomy	NO	2.7	4450	8.2	HD −> Tx R	5.4	26	30	11.5		0	Obstruction	NO		−1.1	−1.2
7	M	YES	38.6	CAKUT	NO	NG	YES	2.2	4900	32.0	Tx R	10.1	32	34	13		3	NO	NO		−1.1	−2.7
8	F	NO	Term	Oxalosis	NO	Gastrostomy	YES	3.6	5735	4.4	HD −> Tx R	9.3	9	12	11	YES	0	NO	NO		−0.8	−1.9
9	M	NO	40	CAKUT	NO	Gastrostomy	YES	4.1	5500	29.9	PD	2.5					3	Leakage	NO	2 years 7 months	−2	−0.3
10	M	YES	38.3	CAKUT	Dysplasia/ hypoplastic lungs	Gastrostomy	YES	2.7	4300	2.2	Recovery	6.9					0	NO	YES	6 years 11 months	−1.7	−1.6
11	M	YES	39	CAKUT	NO	Gastrostomy	YES	1.7	4930	16.0	HD −> Tx R	4.3	32	33	13.3		2	Leakage/cuff extrusion	YES		−0.3	0
12	F	YES	39.4	CAKUT	Dysplasia/ hypoplastic lungs	NO	YES	0.5	2200	23.1	Tx R	3.1	23	23	9.5	YES	1	NO	No		−1.1	−2.2
13	M	YES	36.6	CAKUT	NO	Gastrostomy	YES	0.2	3100	7.6	Recovery	4.2					0	NO	NO	4 years 2 months	1	−0.2
14	M	NO	37	Oxalosis	NO	Gastrostomy	YES	3.5	5700	12.0	Died	2.5					0	NO	Unknown (died)	2 years 5 months	−0.9	−3.9
15	M	YES	30	Prune Belly	NO	Gastrostomy	YES	5.9	4865	12	HD −> Tx R	8.9	21	13	12.5		3	Obstruction	YES		−1.4	−2.2
16	F	YES	35	CAKUT	NO	Gastrostomy		0.1	2570	30	Tx R	2.9	8	30	8.6		4	Obstruction	NO		−2.4	−1.8
17	F	NO	37	Renal vein thrombosis	Neurological	NG	NO	0.1	1570	20	PD	1.7					4	Dysfunction	YES	1 year 8 months	−3.4	−2.7

F: female M: male; m: months; Wk: week; NG: Nasogastric tube; HD: haemodialysis; Tx R: renal transplantation; Recovery: renal recovery; PD: peritoneal dialysis; CNS: congenital nephrotic syndrome; CAKUT: congenital abnormalities of kidney and urinary tract.

Median hemoglobin levels at PD start were 94 (60;191) g/L, and 110 (73;174) g/L at the end of PD (P = NS). Before PD, 12 patients were receiving EPO, with a median of 369 (179;1235) UI/kg per week. One patient was not receiving EPO and data were not available for 4 patients. At the end of PD, EPO median dose was 333 (163;1250) UI/kg per week (12 treated patients, 2 non-treated patients and 3 missing data).

3.5. Cardiovascular impact

At the beginning of PD, 6 patients had an echocardiography. Of those, five patients demonstrated LVH with a median left ventricular mass index of 55 (34;63) g/m$^{2.7}$. Three over 5 patients with LVH received anti-hypertensive therapies (one missing data) and one patient displayed HTN. After 3 months on PD, 8/11 patients assessed for cardiovascular function displayed LVH with a median left ventricular mass index of 66 (34;108) g/m$^{2.7}$. Four over 8 patients had anti-hypertensive therapy and one patient had HTN. After one year on PD, 10/13 patients who had cardiovascular evaluation displayed LVH and a median left ventricular mass index of 59 (37;94) g/m$^{2.7}$ with associated HTN for 7/10 patients and anti-hypertensive treatment in 5/10 patients (one missing data). At the end of PD, among the 11 patients who underwent an echocardiography, ten still had LVH with a median left ventricular mass index of 72 (35;170) g/m$^{2.7}$, 5/10 having HTN and 2/10 receiving anti-hypertensive therapies (one missing data).

3.6. Neurodevelopmental outcomes

Data concerning the head circumference SDS at PD start were collected in 11 patients with a head circumference SDS of −1.0 (−4.9;1.3), decreasing at −1.1 (−5.0;0.4) after 6 months of PD to −1.2 (−3.6;0.7) one year after PD start (P = NS) between PD initiation and one year after PD initiation. Data were insufficient to assess the cranial perimeter at the end of PD and beyond this date.

Neurological status of the 16 surviving patients was reviewed. After a follow-up of 4.3 (1.7;10.3) years, seven patients displayed neurodevelopmental delay with five patients needing special schooling. Among those seven patients, four presented with severe extra-renal comorbidities, and notably two had perinatal asphyxia with hypoxia. One perinatal asphyxia occurred in a context of congenital nephrotic syndrome with neonatal vascular stroke resulting in right hemiplegia. One patient presented pulmonary hypoplasia and one patient presented a Prune-Belly-like syndrome. The last three patients with neurodevelopmental delay had no associated extra-renal comorbidities.

3.7. Long-term outcomes

The causes of PD discontinuation were the following:

- switch to hemodialysis (n = 6);
- transplantation (n = 6);
- recovery of renal function (n = 2);
- death (n = 1).

Reasons for hemodialysis shift were oxalosis (n = 4), catheter dysfunction (n = 1) and recurrent peritonitis and pleural effusion (n = 1). Oxalosis patients (n = 5) underwent simultaneous hemodialysis and PD during 8.2 (4.4;11.9) months after 7.6 (4.4;10.7) months on PD. Two patients with primary hyperoxaluria were transplanted while they were still on simultaneous hemodialysis and PD, as previously reported [18].

After a follow-up of 4.3 (1.7;10.3) years, 12 patients had received a kidney transplant, 2 patients were still on PD, 2 patients had spontaneous recovery of renal function (after 2.2 and

Table 3
Biochemical evolution of patients during PD treatment.

	PD initiation	M3	M12	PD withdrawal	End of follow-up
Serum PTH (ng/L)	212 (6;799)	130 (23;732)	163 (18;957)	123 (44;1540)	91 (32;378)
Hemoglobin (g/L)	94 (60;191)	107 (70;136)	121 (88;150)	110 (73;174)	114 (84;147)
Serum phosphate (mmol/L)	2.36 (0.64;4,06)	1.86 (1.30;2.71)	1.70 (1.02;2.43)	1.65 (0.66;2.33)	1.34 (0.59;1,51)
Serum phosphate SDS for age	1.5 (−11.0;13.9)	0.3 (−6.2;4.5)	0.4 (−4.0;3.1)	−0.8 (−9.3;2.6)	−1.6 (−6.0;−1.0)
EPO (UI/kg per week)	369 (0;1235)	355 (0;643)	350 (0;659)	333 (0;1250)	293 (0;400)
Number of GH treated patients	0	0	0	2	3
Number of patients receiving phosphate binder					
Sevelamer	0	1	1	1	1
Calcium carbonate	5	4	5	3	1
Total treated patients	5	4	5	3	1

EPO: erythropoietin.

Table 4
Flow chart: long-term outcomes.

Outcome	Ongoing PD	Switch to HD	Transplantation	Renal function recovery	Death
Number of patients	2	6	6	2	1
Median follow-up (years)	2.0 (1.7;2.3)	6.8 (4.3;10.3)	3.0 (2.8;10.1)	4.4 (2.2;6.7)	2.2
Height SDS	−1.5 (−2.8;−0.3)	−2.0 (−2.5;−0,0)	−1.1 (−2.7;0.1)	−0.9 (−1.6;−0.2)	−3.9
Neurodevelopmental outcome	1 developmental delay 2 normal schooling (one child with developmental delay attend normal school)	3 developmental delay 3 normal schooling 3 special schooling	2 developmental delay 5 normal schooling 1 special schooling	1 developmental delay 1 normal schooling 1 special schooling	
6 transplanted					
Evolution		With 1 graft loss (early thrombosis)	1 graft loss	2 CKD cases	

7.6 months of PD with respectively eGFR 45 mL/min per 1.73 m^2 one month post-discontinuation and 23 mL/min per 1.73 m^2 four months after discontinuation). One patient died after 12 months on PD and 2.1 years of follow-up, shortly after central venous catheter positioning because of *Staphylococcus* sepsis.

Median time between PD start and transplantation was 22 (8;32) months and median age at first transplantation was 25 (12;42) months with a median body weight of 11.3 (8.6;13.3) kg and a median height of 83 (72.5;87) cm. All kidney transplants were coming from deceased donors. Two patients lost their graft because of venous graft thrombosis, as previously reported [19]. Long-term outcomes are summarised in Table 4.

4. Discussion

Even if the incidence of ESRD in children less than 4 years is low (5.2 per million age-related inhabitants in France) [20], the initiation of chronic PD in infants below 6 months represents a challenge and dialysis in neonates is still debated [21]. In a recent study, which focused on maintenance dialysis that was started before one year of age, a younger age at RRT start was found to be a significant risk factor for death. This risk fell by 5% for each month that the infants aged [22]. Ethical issues related to the high morbidity rate, the increased risk of peritonitis and the overall fragility of infants starting RRT at a young age need to be weighed against the important progress made in this field over the past years, allowing better chances of survival. In our centre, the decision process from whether or not to start dialysis is mainly based on family information and multi-professional team ethical discussions about the main factors affecting the expected quality of life, such as extra-renal comorbidities and/or anuria [9,12,21].

The majority of patients in our study were successfully transplanted, with favourable growth. This is consistent with the results found by others, which confirmed the good outcomes of children starting RRT before 2 years of age [1,8,20]. In terms of growth, our report shows a slight increase of median height SDS during PD. This is consistent with the data published by others [1,4,6,8,10]. In contrast, a Chinese cohort of nine children starting RRT below 2 years of age showed a satisfactory weight gain but a decline in height SDS from −0.7 SDS at PD initiation to −1.4 SDS at the end of follow-up [10]. Only three patients were treated by rGH at the end of PD in our cohort; we believe that optimisation of nutritional status is most of the time sufficient to ensure growth catch-up in this age group [8]. However, some children will have to be treated with rGH if the nutritional management is insufficient, as recently reviewed in the European guidelines on the use of rhGH in pediatric CKD [23]. In a randomised study collecting 16 patients less than 24 months of age with severe CKD stage 3–4, seven patients were enterally fed and 80% of them had recommended daily calories, GH treated patients showed significantly higher length gains (14.5 versus 9.5 cm/year with mean height SDS +1.43 versus −0.11) [24]. Concerning weight gain, we found a steady increase in weight parameters during the time on PD. In our cohort, 11/17 patients were fed enterally by gastrostomy, which appeared to be the best way of enteral feeding in young children on chronic PD [25]. Only one patient had no enteral feeding at all (refused by parents), despite severe initial intra-uterine growth retardation, but growth was relatively correct provided a very intensive nutritional care (mean height SDS −5.7 at the start of PD to −1.8 after 23 months on PD; mean weight SDS −3.4 at the start of PD to −1.7 at the end of the 23 months on PD). However, this child displayed uncontrolled severe secondary hyperparathyroidism and severe orality troubles.

A significant increase in BMI was found in our study from −3.3 SDS at PD beginning to −1.7 SDS at the end of PD. None of the patients had a BMI > 2 SDS. In Brady's study evaluating carotid intima-media thickness of 101 children aged 2–18 years with mild to moderate CKD during 12 months of follow-up, dyslipidemia was an important cardiovascular risk factor significantly associated

with increased intima-media thickness, although no direct correlation was found between BMI and increased carotid intima-media thickness [26]. According to the study of Bonthuis and al., who evaluated the prevalence of obesity and underweight among 4474 patients less than 16 years on RRT in 25 European countries, the prevalence of underweight was 3.5%, whereas 12.5% were obese [27]. As obesity seems more prevalent than underweight in European children on RRT, it seems necessary to avoid a too important catch-up weight gain in these youngest children, so as to avoid to worsen the cardiovascular risk in the long term [27]. Indeed, a significant proportion of our patients on PD already displayed LVH, and previous works have shown that the control of arterial hypertension in children on PD is far from optimal [4,6].

As it was previously reported, we found an increased risk of peritonitis and PD catheter complication in infants [1,6,8,28]. Compared to previous reports on the subject, our series has an important proportion of patients with hyperoxaluria (our unit is a reference centre for this disease), these patients are known to display severe growth retardation, malnutrition and systemic disease [29]. Oxalosis ($n = 4$) was the major cause of PD discontinuation, followed by catheter dysfunction ($n = 1$) and recurrent peritonitis ($n = 1$).

As described in the two large studies evaluating survival among infants less than 1 year of age, who initiated chronic PD [6,30], most of the infants terminated dialysis for transplantation. This is consistent with the results of the Italian, the French and the GOSH series [1,8,20]. However, they reported a 4-fold greater mortality than in older children and mortality rates were 2-fold higher in infants who had at least one medical comorbidity such as prematurity, hypoxic-ischemic encephalopathy, Wilm's tumour, pulmonary hypoplasia [1]. Interestingly, Sanderson found no significant difference in the risk of mortality based on age of dialysis initiation in the USA [30], as opposed to Vidal who found a 5% lower risk of death per month of later initiation [1]. Nevertheless, in both studies, infectious complications remain the main cause of death in younger children on PD [1,31,32]. In our cohort, one patient with hyperoxaluria died from an infectious complication.

Concerning neurodevelopmental outcomes, a Chinese cohort of nine children starting RRT below 2 years of age showed a developmental delay in 44% of children [10]. In our study, 7/16 patients displayed neurodevelopmental delay with five patients needing special schooling. Of those, four patients had associated comorbidities, which are known to be strongly associated with poor neurodevelopmental outcomes [15]. A positive neurodevelopmental outcome after prolonged period on PD is however frequently observed as reported by Lederman [8], who showed normal developmental scores 1 and 4 years after PD start in 34 infants who started PD before 3 months of age: in this series, 79% of the school-aged children attended normal school. Obviously, a longer follow-up and an evaluation in early adulthood would be crucial, but data are missing, and in the course of CKD in infancy, many events may occur between the first year of age and late teenage, all being able to further compromise developmental outcomes.

We found no significant differences in outcomes for growth, neurological development, infections, catheter-related complications, extra-renal comorbidities and kidney transplant between anuric infants ($n = 4$) compared to those with residual diuresis.

We have to acknowledge some limitations to this study, mainly inherent to the retrospective design in a small population concerning extra-rare conditions. However, the design allowed us to have detailed data on these 17 patients, which represent one of the largest series ever published on the topic (excepting registry data that usually include high numbers of patients with a relative scarcity of data).

5. Conclusion

We focused our study on the outcomes of infants starting PD before 6 months of age and aimed to provide new data in this specific population. Our study suggests that with an intensive management, and close nutritional support, PD in infants can provide a favourable outcome concerning growth, development and transplantation [8]. However, those youngest infants are at increased risk of PD catheter complication and peritonitis with prolonged hospitalisations, having a direct impact on their quality of life. Extra-renal comorbidities remain predictive factor of poor prognosis and need to be considered when counselling parents.

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Author contribution

Angélique Dachy contributed to the writing and original draft preparation, investigation, visualisation, and validation of final draft; Justine Bacchetta, to the conceptualisation, methodology, validation, formal analysis, writing – review and editing, supervision, project administration, and validation of the final draft; Anne-Laure Sellier-Leclerc, Aurélia Bertholet-Thomas, Delphine Demède, Pierre Cochat, and François Nobili, to the resources and validation of the final draft. Bruno Ranchin was responsible for the conceptualisation, methodology, validation, writing – review and editing, supervision, project administration, and validation of the final draft.

Human and animal rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed consent and patient details

The authors declare that this report does not contain any personal information that could lead to the identification of the patient(s) and/or volunteers.

Disclosure of interest

The authors declare that they have no competing interest.

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