Successes and pitfalls of chronic peritoneal dialysis in infants – a Polish nationwide outcome study

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Abstract

Introduction: Peritoneal dialysis (PD) is a preferred method of renal replacement therapy for end-stage renal disease in children. Recent advances have allowed chronic PD to be provided to children of all ages and sizes.
Material and methods: The study was designed as a national (10 dialysis centres), multicentre retrospective analysis of the medical history of 33 children who started chronic peritoneal dialysis in their infancy between 1993 and 2005, with a follow-up period of at least 24 months.
Results: The nutritional status of the infants was unsatisfactory. The mean SDS of body weight at the start was –2.0, at 1 year of age –1.7. Only 40% of infants were adequately nourished at 1 year of age. Long-term follow-up analysis showed that 12 children received a kidney transplant, 13 were still on dialysis (4 changed method) and 6 died (mortality rate in the first year of life of 9%). In 2 children we observed an improvement of renal function. We observed a relatively high (1/8.8 patient-months) peritonitis rate in the analysed children when compared to 1 : 22 patient-months in all children undergoing PD in Poland.
Conclusions: The results of our survey have shown that the management of dialysed infants is still a challenge for the medical team and families, but long-term results of the therapy are encouraging.

Key words: infant, chronic dialysis, peritoneal dialysis, outcome, children.

Introduction

Peritoneal dialysis (PD) is a method of choice for renal replacement therapy for end-stage renal disease (ESRD) in children. Advanced dialysis technology has allowed chronic PD to be provided to children of all ages and sizes. Among them, special attention should be given to infants, in whom excessive mortality, infections and poor growth remain the major medical problems [1-7].

Infants require a multidisciplinary approach, intensified nutrition, and adequate control of uraemia focused on appropriate physical, neurological

and social development [1, 2, 8, 9]. Continuous peritoneal dialysis (CPD), introduced in children in the early 1970s, has been widely applied in the childhood population for the last 30 years [10]. In Poland, children have been offered peritoneal dialysis since the late 1970s. Nowadays, the population of dialysed children comprises about 170 subjects, in whom over 70% are dialysed peritoneally [11]. Despite this, there have been only scarce data published on the long-term outcome, survival and nutrition in infants treated with PD, and analysed groups were very small [4, 7, 10, 12]. In our opinion, exchange of experience between investigators and clinicians dealing with PD in children should result in an improvement in the care of the dialysis patients. Therefore, the aim of the study was to analyse chronic PD in infancy, accompanied by further evaluation of long-term follow-up of 24 months.

Material and methods

Study design

The study was designed as a retrospective analysis of the medical history of children who started chronic peritoneal dialysis in their infancy (below 1 years of life) between 1993 and 2005 with a follow-up period of at least 24 months. The data were acquired by completion of a questionnaire addressed to medical staff of all paediatric peritoneal dialysis units in Poland (10 centres – the whole population of dialysed children in Poland). The response rate was 100%. The form included questions concerning the origin of the CKD, clinical status (nutrition – body weight, psychomotor development – assessed by treating physician) and basic laboratory measures (kidney function, calcium-phosphate balance, parathormone, haemoglobin concentration). The data were collected anonymously. The form was constructed so as to contain all the data in one sheet. The respondents additionally reported the 2-year outcome as separate information.

The data were gathered at the beginning of PD and at 3, 6, 9 and 12 months of life. Episodes of exit site infection (ESI) and peritonitis were counted and related to the duration of PD. These entities were diagnosed by commonly accepted guidelines [13, 14]. Factors responsible for and the number of Tenckhoff catheter reimplantations were assessed. Based on anthropometric measures and available normal values of the Polish population, standard deviation scores (SDS) were calculated from the formula (observed value – 50^{th} percentile value)/(0.5 × (value of 50 percentile – value of 3^{rd} percentile)) [15]. Additional information on the overall outcome (transplantation, change in renal replacement therapy, renal function improvement, death) was assessed in a long-term observation at the age of 3 years.

Statistical analysis

Statistica 6.0 PL software (StatSoft Inc, Tulsa, USA) was used for statistical analysis. The distribution of the data was checked by the Kolmogorov-Smirnov one sample test for normality. Mann-Whitney two-sample rank test or Kruskal-Wallis ANOVA was used for between-group statistical analysis. Spearman rank correlation coefficient was calculated to assess relations between variables. Values of p of less than 0.05 were considered significant. All non-normally distributed variables are presented as median and 25-75% interquartile range.

Results

The data of 33 infants (26 male, 7 female) from the participating centres were gathered and analysed. The mean age was 4.5 ±3.5 months (range 0-11 m), and the mean body weight 5.4 ±2.5 kg (range 2.5-10.0 kg) at the start of dialysis. Fifteen of them started PD before 3 months, 9 at 3-6 months and 9 over 6 months of life. Mean time of dialysis under 1 years of life was 6.4 ±3.9 months, adding up to 210 peritoneal dialysis months. Continuous

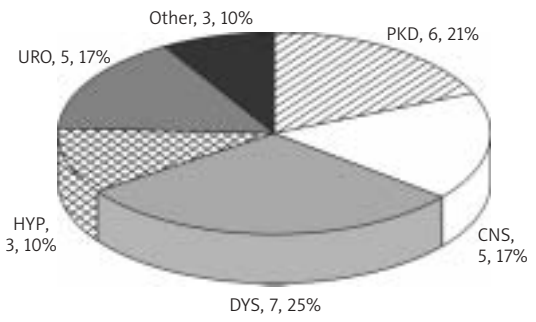

Figure 1. Primary kidney disease in the study group *PKD – polycystic kidney disease, CNS – congenital nephrotic syndrome, DYS – dysplastic kidneys, HYP – hypoplastic kidneys, URO – uropathies*

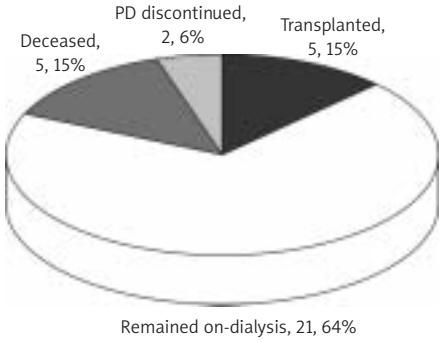

Figure 2. Three-year follow-up of children who started PD in infancy

Table I. Selected biochemical data in the study group at the start of PD. Data are presented as median value and 25-75% interquartile range

	Initiation of PD
Number of patients	33
Serum creatinine [µmol/l]	310 (278-395)
Haemoglobin concentration [g/l]	100 (90-112)
Serum calcium [mmol/l]	2.2 (1.9-2.4)
Serum phosphate [mmol/l]	2.3 (1.7-3.5)
PTH [pg/ml]	309 (170-614)
Body weight [kg]	4.7 (3.0-6.9)
SDS for body weight	–2.0 (–2.5 - –0.9)
Urine output [ml/kg/day]	48* (16-65)

**4 children were anuric*

ambulatory peritoneal dialysis (CAPD) was chosen as the first method of treatment in 73% of infants, whereas at the age of 1 years the percentage decreased to 57% due to the transfer to automated peritoneal dialysis. The most frequent kidney diseases that led to ESRD were renal dysplasia (25%) and polycystic kidney disease (21%) (Figure 1). In 18 patients (54%) other co-morbid conditions were present (congenital heart disease, hypoplastic lungs, hypothyroidism, cerebral palsy, hepatitis or liver cirrhosis). Data on pregnancy or birth weight were unavailable for analysis in most patients.

At the start of PD, infants had anaemia, acidosis, hyperphosphataemia with secondary hyperparathyroidism (results presented in Table I). Twenty patients (61%) were malnourished (below –1.65 SDS for body weight). Overall SDS for body weight was –2.0.

In the analysis undertaken according to the protocol at 3 m, 6 m, 9 m, 12 m of life, we observed that the haemoglobin concentration and phosphate concentration increased, and PTH concentration increased with no significant tendency or change at all time points. The infants had SDS at 3 m of –2.2 for body weight without further increase at 1 years (–1.7). At the age of 1 y. the body weight was over –1.65 of SDS in only 12 children (40%). KT/V data were absent in over 75% of patients. The detailed biochemical characteristics at 3, 6, 9 and 12 months of life are given in Table II.

Peritonitis (24 episodes) occurred with the frequency of 1.34 episodes/patient/years (1 per 8.8 patient-months) while ESI occurred with the frequency of 0.63 episodes/patient/years (1 per 19 patient-months). Gram positive pathogens were the major causative agents (61%). Ten infants (30%) required surgical hernia repairs. Three patients (9%) died in infancy due to cardiac arrest (1), sepsis (1) and dialysis withdrawal (1). No infant was kidney transplanted below 1 year of age. Three other patients died later in childhood (due to sepsis $n = 2$, abdominal catastrophe $n = 1$), which led to overall mortality of 18.2%.

Long-term follow-up analysis showed that 5 children were transplanted before 3 years (7 patients later in life), 21 were still on dialysis (1 was transferred to haemodialysis) and 2 more died (1 later in life). In 2 children dialysis was withdrawn due to kidney function improvement. For 12 children who were transplanted the mean age of surgery was 58 months, with the body weight over 12 kg. They have been waiting for a renal graft from 24 to 104 months from the initiation of PD. Out of 22 infants (available data) neurological assessment

Table II. Selected clinical and biochemical data in the study group in the first year of life (in 3-month intervals). Data are presented as median value and 25-75% interquartile range

	3 months of life	6 months of life	9 months of life	12 months of life
Number of patients	15	20	26	30
Serum creatinine [µmol/l]	292 (248-392)	292 (258-317)	270 (172-318)	327 (283-424)
Haemoglobin concentration [g/l]	103 (96-119)	109 (95-120)	110 (93-123)	109 (95-118)
Serum calcium [mmol/l]	2.3 (2.0-2.6)	2.3 (2.1-2.4)	2.2 (2.0-2.4)	2.4 (2.1-2.5)
Serum phosphate [mmol/l]	1.9 (1.4-2.3)	2.2 (1.5-2.9)	2.2 (1.3-2.5)	1.9 (1.7-2.3)
PTH [pg/ml]	312 (221-393)	384 (127-540)	214 (118-513)	454 (152-596)
Body weight [kg]	4.3 (4.1-4.8)	5.2 (4.7-6.5)	6.7 (5.7-7.6)	7.8 (7.0-8.6)
SDS for body weight	–2.0 (–3.3 - –1.6)	–1.9 (–3.0 - –1.1)	–1.9 (–2.6 - –1.5)	–1.7 (–2.2 - –1.1)
Urine output [ml/kg]	50 (50.3-60.0)	48 (24-64)	49 (13-71)	55* (37-71)

**10 children were anuric*

Table III. Comparison of patients who started dialysis before and after 6 months of life at the age of 1 year. Data are presented as median value and 25-75% interquartile range

Time of PD initiation	< 6 months		≥ 6 months	
Number of patients	21		12	
	Start	**12 m**	**Start**	**12 m**
Serum creatinine [µmol/l]	292 (238-372)	323 (286-427)	336 (292-404)	345 (288-534)
Haemoglobin concentration [g/l]	107 (98-129)	114 (107-121)	93[1] (79-100)	100[1,2] (91-108)
Serum calcium [mmol/l]	2.3 (1.8-2.5)	2.4 (2.2-2.6)	2.2 (2.0-2.4)	2.3 (2.1-2.4)
Serum phosphate [mmol/l]	2.6 (1.5-4.5)	2.2 (1.5-2.9)	1.8[1] (1.7-2.6)	1.8[1] (1.7-1.8)
PTH [pg/ml]	200 (119-542)	429[2] (165-633)	850[1] (250-1324)	406[2] (190-525)
Body weight [kg]	3.3 (2.8-4.8)	7.3 (6.9-8.5)	8.5[1] (6.8-9.6)	8.0[1] (7.8-9.0)
SDS for body weight	–2.1 (–3.1 - –1.4)	–2.0 (–2.4 - –1.3)	–1.3[1] (–2.2 - –0)	–1.5[1] (–1.7 - –0.9)
ΔSDS for body weight	–	–0.4 (–1.1 - 0.5)	–	0[1] (–0.3 - 0.7)
Urine output [ml/kg]	41 (16-64)	58 (40-71)	58 (13-66)	58 (24-68)

ΔSDS = SDS at 12 m – SDS at the beginning of dialysis
[1]significantly different when compared to children who started PD before 6 m, $p < 0.05$, [2]significantly different when compared to beginning of PD, $p < 0.05$

done by the treating physician showed an adequate stage of development in 10 patients, while in 12 retardation was observed.

Based on the clinical criterion of < or > 6 months of age at the initiation of PD, the study group was divided into two subgroups (n = 21 and n = 12, respectively) (Table III). The analysis performed in this setting revealed that their initial renal function measured by serum creatinine did not differ significantly; however, children starting PD before 6 months of life had higher haemoglobin concentration both at the start and at the age of 12 months. The increase of haemoglobin during PD treatment was similar in both observed groups of infants, whereas serum calcium was at a comparable level. Patients starting PD earlier exhibited more severe hyperphosphataemia. Their PTH concentration at the beginning of dialysis was lower than in older infants, but we observed further increase, while in the latter group PTH concentration decreased during PD.

Infants from both subgroups were malnourished, but children commencing PD over 6 months of life had higher SDS for body weight (–1.3 vs. –2.1, p = 0.003). We observed no improvement in this parameter when compared to the age of 1 year, and the difference observed earlier persisted. The additional survey revealed that out of 10 participating centres only 2 (9 pts) applied gastroenteral feeding in the study period as a routine treatment for children undergoing peritoneal dialysis. Peritonitis occurred significantly more frequently in patients who commenced dialysis before 6 months (1.47 vs. 0.9 episodes/patient/year, 1/8 vs. 1/13 pm, p = 0.021).

Similarly, the frequency of Tenckhoff catheter reimplantation procedures was increased in these infants (0.56 vs. 0.31 episodes/patient/year, p = 0.041). There was no significant difference in ESI rate (0.56 vs. 0.29 episodes/patient/year, 1/21 vs. 1/13 pm).

When the transplanted children group (n = 12) was analysed in detail, we found that they had lower concentration of haemoglobin (105 vs. 118 g/l) and higher body weight (8.5 vs. 7.0 kg) at the 12th month of life. Seven of the transplanted children started dialysis after 6 months (58%) whereas 5 (42%) started earlier. There was a significant difference in the transplantation rate between those who started PD before and after 6 months of life (24% vs. 58%, p = 0.042).

Additional analysis revealed that the subjects who died during dialysis treatment (6 children) had significantly lower urine output when compared to those who survived.

Discussion

Although the results of peritoneal dialysis therapy in small children have been improving in recent years, chronic PD in infants still continues to present an extreme challenge for many clinicians [2, 5]. High mortality rate, frequent infections, technical problems, and poor growth are very common in this group of patients [1-3, 8, 9, 16]. The percentage of children who started PD under 2 years of age remains low (13.% in the 2001 NAPRTC report, 12.5% according to the Italian registry) [16-18]. In Finland there is a higher proportion of infants among all dialysed children (35%) than in other countries, mainly on account of the congenital nephrotic syndrome of the Finnish type [19]. In the Polish registry (2000-2004) children who started PD in infancy constituted below 10% of children requiring renal replacement therapy. In earlier studies, infants made up only about 1-2% of the paediatric ESRD population [9].

In our study, most children who started PD in infancy survived up to 12 m of life, but 3 children died during the study period. The mortality rate was 9%, which is comparable to the results reported by other authors [7, 9, 10], but lower than in the studies of Ellis *et al.* and Ledermann *et al.* [4, 20]. The mortality rate in infants starting dialysis is as many as 4 times higher than that of children beyond infancy [21]. Most deaths occur in the first year of life. A 1-year survival of 85% was found in this population by NAPRTC and in the UK, which is lower than the 95% reported in children starting dialysis after infancy [6, 18]. It should be noted that in the most difficult age group to treat with dialysis, i.e. those under 5 years, mortality has continued to fall in Europe. The 2-year survival in children on dialysis aged 0-4 years increased from 71.3% in 1980-1984 to 87% in 1995-2000 [22].

Complications related to the peritoneal catheter, such as peritonitis, exit site infection (ESI), tunnel infection, pericatheter leakage or mechanical dysfunction, are very common in infants undergoing PD [1, 8, 19, 23] and remain troublesome [1, 2]. In our study, 10 infants (30%) needed hernia repairs. Laakonnen *et al.* reported 23 infants on PD in Finland; among them 13 (56%) underwent operations due to inguinal or umbilical hernias or hydrocele [10]. Lederman *et al.* (12) documented hernias in 15 infants (75%) whereas Hölttä *et al.* (9) observed them in 92% of children under age 5 years [7, 24]. In our study, 7 patients (21%) needed catheter exchange, but the frequency of peritoneal catheter reimplantation was greater in infants who started PD under 6 months of age (revision ratio 0.56 vs. 0.31, $p < 0.05$). Laakonnen *et al.* described 10 patients (43%) who needed a catheter exchange at least once, with a revision ratio of 0.65 [10]. On the other hand, Lederman *et al.* reported 20 infants on PD, among whom in 10 (50%) the catheter was replaced once and in 2 (10%) twice [7]. Consequently, it seems that catheter-related technical problems remain very common in children who started PD under one year of age.

We observed a relatively high (1/8.8 ptm) peritonitis rate when compared to 1 : 22 ptm in all children undergoing PD in Poland [25]. This was confirmed by other authors in infants and small children – range 1/7.5 to 1/14.5 ptm [7, 10, 18]. The exit site infection rate (1/19 ptm) was also higher than in the general PD population in Poland (1/25-30 ptm). Kaluzynska and colleagues reported an ESI rate of 1/9.6 ptm in children under the age of 5 years when compared to older patients (1/26.5 pmt) [26]. The importance of ESI prevention is high because ESI can lead to tunnel infections and peritonitis [14]. Gram-positive bacteria were the most common cause of peritonitis in our patients (61%), similarly to other recent and earlier reports [7, 10, 13, 14, 25].

The concept that chronic renal failure occurring in the first 2 years of life may have a long-standing adverse effect on height prognosis is well known. Growth at this time is principally dependent on nutrition [8, 9, 20, 27].

The results of our analysis in terms of growth and nutrition are disappointing, and significantly worse than those reported by Ledermann *et al.* and Laakkonen *et al.* In our group, the mean SDS of body weight at the start was –2.0, at 1 year of age –1.7 [7, 10, 20]. Only 40% of infants analysed were adequately nourished at 1 year of age. Children commencing PD over 6 months of life had higher SDS for body weight (–1.3 vs. 2.1), and the observed differences persisted to the age of 1 year. Only two centres (of 10 participating) applied gastroenteral feeding as a routine treatment. Parents' disagreement, technical and economic problems or reluctance of the medical staff could be responsible for this situation. It should be strongly emphasised that the commencement of careful nutritional support early in the course of the dialysis treatment may not only improve growth but also limit mortality in children undergoing PD [27, 28].

There is a small number of reports which analyse long-term emotional and developmental outcome in children starting PD in infancy. Lederman *et al.* reported good results. Warady *et al.* found that of 28 survivors of 34 infants who began dialysis before 3 months of age, only 1 was significantly delayed [29, 30]. In our study, 55% of children were delayed. In the observed infants, developmental delay was attributed mainly to perinatal asphyxia or genetic disease.

To summarize, the results of our multicentre survey are comparable to data presented in other countries with regard to most of the analysed

parameters. However, there is a strong need to maintain adequate nutritional support to preserve normal growth and development in PD infants. The study revealed that the management of infants with ESRD remains a challenge for the medical team and families, but overall results are encouraging.

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