Original Article

The Outcome of Iranian Children on Continuous Ambulatory Peritoneal Dialysis: The First Report of Iranian National Registry

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Background: **Continuous ambulatory peritoneal dialysis is not a very common modality to treat Iranian children with end-stage renal disease; however, there is sometimes no choice but to offer this therapy to salvage the patient. Obviously, promotion in each program needs re-evaluation to find the pitfalls. Therefore, a nation-wide survey on pediatric continuous ambulatory peritoneal dialysis was conducted to find the cause of death or termination of dialysis.**

Methods: **All children, younger than 14 years old, treated by continuous ambulatory peritoneal dialysis in nine main pediatric nephrology wards in Iran between 1993 and 2006 were included in this historical cohort study. Patient and technique survival rates were determined. Kaplan-Mayer and Cox-regression analysis were used to compare the survival. 2×2 table was used to calculate the risk ratio. A *P*<0.05 was considered significant.**

Results: **One hundred twenty children with a mean age of 47.6 months were on continuous ambulatory peritoneal dialysis. The most frequent cause of renal failure was hereditary-metabolic-cystic disease. One hundred eighty-two peritoneal dialysis catheters were inserted surgically. The median first catheter exchange was 0.74 year (95%CI: 0.5 – 0.98). The most frequent cause of catheter replacement was catheter outflow failure due to displacement, adhesion, and infection (persistent peritonitis or tunnel infection). The mean patient survival was 1.22 years (95%CI: 0.91 – 1.53). The mortality rate was 55% before 1997, and 60% between 1998 and 2001, which declined to 23% after 2002 (*P*<0.05). Young age (<24 months) was the only independent factor that predicted mortality (*P*<0.05). The outcome of children was as follows: recovery of renal function (6.7%), renal transplantation (8.3%), switch to hemodialysis (16.7%), still on continuous ambulatory peritoneal dialysis (23.3%), death (43.3%), and lost to follow-up (1.7%).**

Conclusion: **The mortality is still high among Iranian children on peritoneal dialysis. Young age is the most important factor influencing on survival and mortality.**

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Keywords: Continuous ambulatory peritoneal dialysis • mortality • pediatric • survival

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Introduction

Chronic peritoneal dialysis is the most frequently prescribed dialysis modality for children all over the world. Since continuous ambulatory peritoneal dialysis (CAPD) was introduced in Iran in 1993, it has remained as the only applicable modality for neonates, infants, and young children. Whereas, older children with end-stage renal disease (ESRD) are usually treated by hemodialysis (HD) until a matched donor is

found or transplanted preemptively. Compared with other countries, the reported rate of peritonitis and mortality is high among Iranian children on CAPD.[1,2] We studied the cause of death or termination of CAPD in Iranian children to improve patient survival and reduce the complications.

Patients and Methods

All children, younger than 14 years old, treated by CAPD in nine main pediatric nephrology wards in Iran between 1993 and 2006 were included in this historical cohort study. The records were reviewed to collect the clinical data, the complications of CAPD, and the outcome.

The indication of starting CAPD was elective (glomerular filtration<10 mL/min/1.73 m^2), emergent (uremic symptoms, fluid overload, or incorrectable fluid imbalance), or selective (all patients <10 kg, aged <24 months with ESRD).

Two-cuffed straight Tenckhoff or coiled swan neck peritoneal dialysis catheters were placed surgically under general anesthesia. CAPD commenced in two weeks postoperatively in elective situations. In the case of an emergency, dialysis was started by 5 mL/kg and gradually increased to 20 mL/kg in following days. Conventional dialysate containing 1.5 – 4.35% glucose was used. Using Gomez criterion, a weight <60% of the median weight for chronological age was defined as "failure to thrive." Surgical complications were recorded. Patient and technique survival rates were calculated. Student's *t*-test, χ^2, Kaplan-Mayer survival analysis, and Cox-regression analysis were used to compare means, frequency, survival, and the risk factors. Data censored at the following events: switch to HD, transplantation, death, lost to follow-up, and recovery of native kidney function, with the exception of death for patient survival calculation, and the exception of switch to HD for technique survival calculation. A *P* value <0.05 was considered statistically significant.

Results

Between 1993 and 2006, 120 children (58 girls, 62 boys) were on CAPD. The mean age at the beginning of dialysis was 3.96 years (range: two days – 16 years). Sixty-six (56%) patients were younger than 24 months, whereas 16 (13.6%) children were older than 10 years. Of the studied patients, 29.2% lived in rural areas and only 18.3% were educated.

The most common etiology of ESRD was hereditary-metabolic-cystic disease (47.5%), and the urologic problems (Table 1).

There was a slow increase in the number of patients who underwent peritoneal dialysis each year in comparison to the low number of children who remained on CAPD (Figure 1).

One-hundred and two peritoneal dialysis catheters were inserted surgically. The most frequent surgical complications were hernia (inguinal in 15, umbilical in eight, and incisional in two), and leakage in 18 patients. Fourteen patients had bleeding after surgery; hydrocele appeared in five.

The mean patient survival was 1.22 (95% CI: 0.91 – 1.53) years. Using Cox-regression analysis, age <24 months (Figure 2) was a risk factor predicting the mortality (Table 2) (risk ratio: 3.25, 95%CI: 1.82 – 5.79). However, though not statistically significant, patients on CAPD with failure to thrive had lower survival time. The reasons for termination of CAPD included persistent peritonitis (19.6%), catheter outflow failure (8.7%), generalized edema or cardiomegaly (4.3%), bowel obstruction (1.1%), transplantation or recovery of native renal function (18.5%), and death (47.8%). The causes of death were infection (40%), pulmonary edema/ineffective dialysis (29.1%), bowel perforation (5.4%), and undetermined (25.5%). The mean survival time in these patients was two (95%CI: 1.45 – 2.56) years. The mortality rate was 55% from 1993 through 1997, and 60% between 1998 and 2001, which declined to 23% from 2002 through 2006. Thus, the mortality was significantly (*P*=0.0001) higher in children who were treated before 2001 as compared with the time-being (risk ratio: 2.78, 95%CI: 1.64 – 4.72).

The mean survival of the first implanted catheter was 8.16 (95%CI: 6.43 – 9.90) months. The reasons for the first catheter exchange were persistent peritonitis (37.5%), outflow failure (35.4%), catheter displacement (12.5%), and others (14.6%) including tunnel infection, cuff extrusion, bleeding, dehiscence, and catheter break.

The outcome was: recovery of renal function (6.7%), renal transplantation (8.3%), switch to HD (16.7%), still on CAPD (23.3%), death (43.3%), and lost to follow-up (1.7%). Between 2001 and 2006, more children remained on CAPD and the number of death decreased significantly (*P*<0.0001) (Figure 3).

Table 1. Etiology of end-stage renal disease in patients on CAPD.

Condition	N	%
Urologic problems/tubulointerstitial disease	**21**	**17.5**
Posterior urethral valve/neurogenic bladder	8	
Vesicoureteral reflux	7	
Tubulointerstitial nephritis/uric acid nephropathy	2	
Chronic pyelonephritis	3	
UPJO	1	
Primary glomerulopathy	**10**	**8.3**
Focal segmental glomerulosclerosis	6	
Crescentic glomerulonephritis/diffuse mesangial proliferative	4	
Cystic renal disease	**20**	**16.7**
Polycystic kidney disease	10	
Juvenile nephronophthisis	10	
Hereditary/metabolic	**37**	**30.8**
Atypical hemolytic-uremic syndrome	13	
Cystinosis	5	
Primary hyperoxaluria/renal stone	10	
Congenital nephrotic syndrome/diffuse mesangial sclerosis/Denys Drash Syndrome	9	
Renal hypoplasia/dysplasia	**11**	**9.2**
Unknown	**14**	**11.7**
Miscellaneous	**7**	**5.8**
Acute tubular necrosis	1	
Hepatorenal syndrome	1	
Asphyxiated thoracic syndrome	1	
Renal coloboma syndrome	1	
Down syndrome	2	
Postchemotherapy	1	
Total	**120**	**100**

Discussion

Demographic data reveal that in our country, there is an inclination to start CAPD in very young age. As though, 71% of the patients had been younger than 60 months. Short course of HD and preemptive renal transplantation are the preferred modalities for older children (weight more than 15 kg and age more than five years). Otukesh et al.[3] reported that 97 out of 278 children with ESRD were preemptively transplanted, and 159 of them had been hemodialyzed for 8.2 months before finding a matched donor. In our series, only 8.3% of the patients who had been for a mean of 10.68 months on peritoneal dialysis, received renal transplantation. This ratio is much lower than those reported in the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS),[4] Japanese series,[5] TUPED Registry,[6] Korea,[7] and India[8] with ratios of 68%, 29.5%, 15.4%, 38.5%, and 23.3%, respectively. This means that we should keep more attention on ideal management of CAPD to achieve the criteria of transplantation.

According to the previous reports from Iran, hereditary-cystic disease and urologic disorders were the two most common etiologies of ESRD. [3,9]

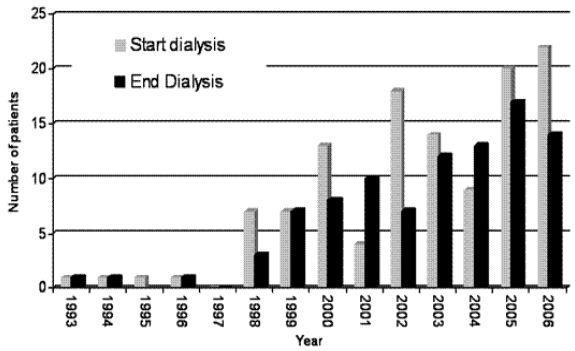

Figure 1. Number of patients who started and terminated CAPD per year.

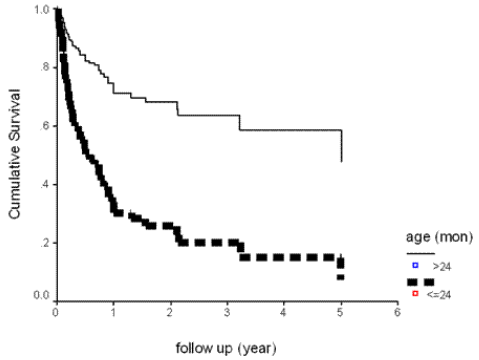

Figure 2. The effect of age on survival of patients on CAPD.

Table 2. Variables predicting mortality in children on CAPD (Cox-regression analysis).

Variables	Univariate				Multivariate			
	P value	Exp (B)	95% CI for Exp (B)		*P* value	Exp(B)	95% CI for Exp(B)	
			Lower	Upper			Lower	Upper
Illiteracy	0.89	0.95	0.46	1.95	.50	1.33	0.57	3.08
Age <24 months	0.001	0.29	0.14	0.59	.008	3.39	1.38	8.35
Gomez <60%	0.44	1.29	0.66	2.55	.60	.74	0.23	2.30
Fungal peritonitis	0.7	0.83	0.33	2.1	.61	1.40	0.37	5.30
Persistent peritonitis	0.26	0.59	0.24	1.47	.09	2.46	0.85	7.09
Rural inhabitant	0.55	1.19	0.66	2.15	.91	1.04	0.42	2.59
Sex	0.08	1.64	0.94	2.86	.07	2.02	0.93	4.38
Year of initiating CAPD<2003	0.018	0.45	0.23	0.87	0.69	0.83	0.32	2.1

Because of selecting younger population for CAPD, the hereditary disease was the most common cause of ESRD in comparison to those who were transplanted.[3] The high rate of consan guinity might be the reason for this higher proportion of hereditary-congenital nephropathies among Iranian children. Some studies reported urologic problems including vesicoureteral reflux and primary glomerulonephritis as the most common etiology of ESRD in children on CAPD.[6–8,10] Hypoplasia/dysplasia was the most frequent cause of CAPD in Japan.[5,11]

This study showed that in spite of increasing number of patients on CAPD, the survival rate has not improved proportionately. Approximately, half of the patients died and 38.5% of this death occurred during the first three months of being on CAPD. Young age and those with severe malnutrition had poor outcome. Comparing the three periods of introducing CAPD (1993 – 1997), launching (1998 – 2001), and expanding program (2002 – 2006), the survival of patients on CAPD has been improved in the last period.

Although the standard survival of patients on peritoneal dialysis has been improved to 90% at first year and 70 – 90% at five years,[4–6,12–14] the survival of children who initiated dialysis at a younger age has remained a problem. Japanese Registry reported first- and five-year survival of 94% and 76% in children, younger than six years old.[5] Reviewing the reports of CAPD from developing and eastern countries, Indians had a mean cumulative survival of 45 months with 26.6% death.[8] Another study from Saudi Arabia reported 33% death with a mean treatment of nine months.[15] Elhassan el al.[16] did a retrospective study on all Sudanese on CAPD and were included two pediatric centers. They showed a higher peritonitis rate in pediatric units with 27 patients but the exact survival rates of children were not clear. We observed that our patients had a significantly lower survival rate than those reported in NARTCPS, European, Japanese, and TUPED studies. In addition, we observed that illiteracy and residing in rural areas had no significant effect on patient and catheter survival. Gruenberg et al. evaluated the effect of socioeconomic status and the distance from dialysis center on the outcome in Uruguay. They found that 86% of the patients survived after five years of follow-up, and that neither socioeconomic status nor the distance from dialysis center had significant influence on the outcome.[17]

Twenty-five percent death was the dramatic observation of our study; it predominantly happened from 1993 through 2001. It occurred suddenly at home despite regular visits by local physicians. None of them was autopsied. We suggest that hypertensive crisis and overload might be the reasons of these unexpected events. Therefore, the care givers of these children need more education and better supervision. Less than half of the patients died of infection (systemic or peritonitis); two-third of such deaths occurred before 2002. Using Y system of disconnection,

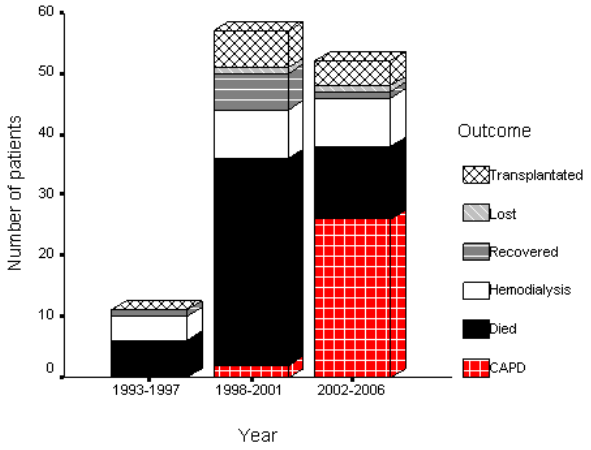

Figure 3. Outcome of patients on CAPD in three periods.

changing the policy of care, and closer follow-up might be the reasons for the observed improvement.

Catheter outcome was even more disappointing. On the average one point five catheters were used for each case. Moreover, the first catheters had only a mean survival of eight months. The reported catheter survival on different registries are above 90% after the first year and about 70 – 80% after five years.[4–6,8,11–14,17–19] Our survey revealed that neither carrier state, omentectomy, exit site, straight vs. coiled catheter, nor peritonitis had significant predictors of catheter survival. However, the place where the center of catheter implanted, obviously affects the catheter function. It displays the importance of expert hands on successful catheter implantation and its function.

The limitation of this study was using retrospective data filled by various medical staff; therefore, by providing a national registry we are going to conduct a prospective cohort study.

In conclusion, the mortality is still high in Iranian children on peritoneal dialysis. Young age is the most influential factor for survival and mortality. Sudden death at home is an alarm to establish on education programs for parents, nurses, and medical staff. Close observation of young children for adequacy of dialysis, fluid overload, and blood pressure control in early months of starting dialysis is more emphasized.

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