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The Use of Acute Peritoneal Dialysis in Critically Ill Newborns

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Background: To evaluate the efficacy, complications, and mortality rate of acute peritoneal dialysis (APD) in critically ill newborns.

Material/Methods: The study included 31 newborns treated in our center between May 2012 and December 2014.

Results: The mean birth weight, duration of peritoneal dialysis, and gestational age of the patients were determined as 2155.2±032.2 g (580–3900 g), 4 days (1–20 days), and 34 weeks (24–40 weeks), respectively. The main reasons for APD were sepsis (35.5%), postoperative cardiac surgery (16%), hypoxic ischemic encephalopathy (13%), salting of the newborn (9.7%), congenital metabolic disorders (6.1%), congenital renal diseases (6.5%), nonimmune hydrops fetalis (6.5%), and acute kidney injury (AKI) due to severe dehydration (3.2%). APD-related complications were observed in 48.4% of the patients. The complications encountered were catheter leakages in nine patients, catheter obstruction in three patients, peritonitis in two patients, and intestinal perforation in one patient. The general mortality rate was 54.8%, however, the mortality rate in premature newborns was 81.3%.

Conclusions: APD can be an effective, simple, safe, and important therapy for renal replacement in many neonatal diseases and it can be an appropriate treatment, where necessary, for newborns. Although it may cause some complications, they are not common. However, it should be used carefully, especially in premature newborns who are vulnerable and have a high mortality risk. The recommendation of APD therapy in such cases needs to be verified by further studies in larger patient populations.

MeSH Keywords: Emergency Treatment • Infant, Newborn • Peritoneal Dialysis • Sepsis

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Background

Despite other advances in neonatal intensive care units (NICUs), acute peritoneal dialysis (APD) – the nonvascular treatment method for acute kidney injury (AKI) and critical metabolic disorders – has been increasingly used of late [1–3]. The use of other forms of renal replacement therapy, such as hemodialysis (HD) and hemofiltration, which are technically more difficult in newborns, have recently been replaced by APD, as wide extracorporeal circuit volumes, anticoagulation, and weak arterial access are limiting factors for other therapies, particularly in newborns [4,5]. In contrast to HD, APD does not require any expertise for its application, is readily performed, and is effective in treating many neonatal disorders [4,6]. In recent years APD, which is better tolerated than HD, has been increasingly used as an alternative to HD in renal replacement therapy of critically ill newborns [3,7,8]. The use of APD had previously been limited due its high rate of complications, primarily having to do with infections, until the introduction of techniques developed by Popovich and Tenckhoff [6–8]. There have been scant new studies on many aspects of APD treatment in both term and preterm neonates.

The purpose of this study was to evaluate the efficacy, complications, and mortality rate of APD treatment in critically ill newborns.

Material and Methods

This retrospective study included newborns undergoing APD in the NICU at Yuzuncu Yil University (which serves as a medical reference center for eastern and southeastern Turkey), between May 2012 and December 2014. Approval from the local ethical board and consent from the babies' parents were obtained for the study. The patients' demographic characteristics, and laboratory and clinical data were obtained from the patients' medical files. The decision for APD treatment was made by the attending pediatric nephrologist and neonatologist. The indications, results, and complications of APD were recorded.

APD indications were as follows [1,3]: 1) impairment of kidney function (urine output of <0.5 mL/kg/hour within 24–48 hours) in spite of therapy with fluids, diuretics, and inotropic agents; 2) serious edema despite medical treatment; 3) findings of uremia (impairment of cardiac function or convulsions); hyperkalemia, hyperammonemia (blood ammonia level >200 mg/dL), and metabolic acidosis irresponsive to bicarbonate therapy; and 4) excess fluid loading causing impairment of respiratory functions.

PD catheters were inserted percutaneously under sterile conditions with local anesthesia by pediatric surgeons or neonatologists. The catheters used were either Tenckhoff or one-cuffed newborn catheters (Quintin® Convidien, Mansfield, USA). After placing the newborn in a supine position, the catheter insertion site was cleaned. After making a 0.5 cm-horizontal incision 0.5–1 cm below the umbilicus, cutaneous and subcutaneous tissues were dissected down to the sheath of the rectus abdominal muscle. The guided PD catheter was inserted through the rectus abdominal muscle and advanced along the peritoneum, and placed in the left lower quadrant of the abdomen at a 45° angle. After removing the catheter guide, the inside of the catheter was washed with 25–30 mL of heparinized fluid to check that it was functioning properly. In order to avoid leakage, the PD catheter was circularly sutured for fixation to the skin.

For APD, standard dialysis fluid containing 1.36% or 2.27% glucose (Baxter Healthcare, Deerfield, USA) was used. The dialysis fluid was given by starting with a dose of 10–20 mL/kg and gradually increasing up to 30–40 mL/kg, based on the tolerance of the patient on the first day. The one hour-PD cycle comprised three stages: 10 minutes for filling, 30 minutes for dwelling, and 20 minutes for draining of the fluid. Before use, first heparin (500 IU/L) and an antibiotic (cefazolin 500 mg/L) were added to the dialysis fluid, followed by potassium chloride, based on the patient's blood potassium level. The efficacy of APD was evaluated based on the resolution of the underlying disorders, such as hyperkalemia or hyperammonemia.

Catheter obstruction was defined as slow drainage of the dialysis fluid, the need to irrigate, or dysfunction of the catheter. In the case of obstruction, a new catheter was inserted. Peritonitis was suspected in instances of cloudy dialysis fluid or fever. Peritonitis was defined as the presence of ≥100/mm^3 leucocytes (neutrophils more than 50%), the presence of microorganisms in a Gram stain, or culture-positive peritoneal fluid [9]. Visible fluid leakage or wetness around the PD catheter site was interpreted as catheter leakage.

For the statistical analyses, SPSS version 15 software program (SPSS Inc., Chicago, Illinois, USA) was used. The descriptive analyses were expressed as mean ± standard deviation (SD) for variables with normal distribution and as median for variables with non-normal distribution. The Fisher exact test was used to analyze the relationships between the survival rate, clinical findings and complications. A *p*-value of less than 0.05 was considered statistically significant.

Results

The mean birth weight and gestational weeks of the 31 newborns, 16 of whom were preterm, were 2155.2±1032.2 g (580–3900 g) and 34 weeks (24–40 weeks), respectively. The average

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duration of PD was four days (1–20 days), and the average age of the dialyzed patients was eight days (2–28 days).

The urea, creatinine, sodium, and potassium values of the patients before and after PD are shown in Table 1.

The main reasons for the use of APD were sepsis (35.5%), postoperative cardiac surgery (16%), hypoxic ischemic encephalopathy (13%), salting of the newborn (9.7%), congenital metabolic disorders (6.1%), congenital renal diseases (6.5%), nonimmune hydrops fetalis (6.5%), and acute kidney injury (AKI) due to extreme fluid loss or insufficient fluid intake (dehydration) (3.2%). There were no patients with AKI due to nephrotoxic drug exposure in our study (Table 1).

APD-related complications were observed in 48.4% of the patients. The complications encountered were catheter leakages in nine patients, catheter obstruction in three patients, peritonitis in two patients, and intestinal perforation in one patient (Table 1). Of the two patients with peritonitis, isolated micro-organisms included one case of *Acinetobacter baumannii* and one culture-negative case. Systemic and intraperitoneal antibiotic therapy was started in patients with peritonitis based on culture results.

Of the 31 patients, 17 (54.8%) died, and 14 (45.2%) were discharged to be followed by the Pediatric Nephrology Outpatient Clinic. Of the 17 infants who died, nine had sepsis and 13 (76.5%) were premature newborns. Out of the 16 premature newborns, 13 (81.3%) died. When the surviving infants were compared with those who died, no statistically significant difference was found between pre-therapy levels of creatinine, sodium, and potassium and the rate of dialysis-related complications, duration of dialysis, and time spent undergoing dialysis. On the other hand, there was a significant difference in gestational age, birth weight, and preterm and term status between infants who survived and those who died (p=0.003 and p=0.039, respectively) (Table 2). The average pre-dialysis creatinine values of the surviving infants were found to be significantly higher than those of the infants who died. These factors may affect patient survival rates (p=0.025) (Table 2).

Discussion

AKI, which is prevalent in newborns, can be caused by many factors. The most frequent causes of AKI are dehydration secondary to insufficient nutrition with mother's milk, congenital heart diseases, sepsis, hypoxia, congenital metabolic disorders, and congenital kidney anomalies [4,5,10–12]. In NICUs, the rate of AKI in critically ill newborns is estimated to be between 8% and 24%, but the mortality rate can be as high as 61% [11,13,14]. Our study showed that APD is a practical and safe method that can be used in both critically ill term and preterm newborns. Our study differs from other studies because our study included a considerable number of critically ill premature infants.

The most frequent reason for the use of APD in our study was sepsis. The other common conditions requiring APD were postoperative cardiac surgery, hypoxic ischemic encephalopathy, salting of the newborn, congenital metabolic disorders, congenital kidney diseases, nonimmune hydrops fetalis, and AKI due to severe dehydration. Hakan et al. [3], Yıldız et al. [4], and Matthews et al. [16] previously reported that the most frequent reason for performing APD is oliguric AKI, followed by metabolic disorders. Alparslan et al. [1] reported that APD was most frequently indicated by metabolic disorders, asphyxia, and sepsis. In the present study, in contrast to the literature, we determined that neonatal sepsis was the most frequent cause of renal impairment and thus the most frequent reason for use of APD. This may be explained by the fact that our study population included a large number of critically ill premature newborns and very low-birth-weight neonates who were susceptible to sepsis and the severity of underlying diseases.

In one of our previous studies carried out in the same region, we reported salting of newborns as one of the rare causes of serious hypernatremia [17]. Salting is a practice performed by grandparents in order to increase the likelihood that the baby will be healthy. The practice covers the process of scrubbing the whole body of the baby with table salt for an hour in a manner that facilitates thorough contact of salt with the skin. This custom is not unique to Turkey. In the present study, we observed serious hypernatremia-dehydration and AKI due to salting of the newborns in three cases.

APD is an invasive procedure that can cause some complications [16]. The most common complications of this procedure are leakage around the catheter, catheter obstruction, peritonitis, and perforation [1,4,11,18]. With the introduction of Tenckhoff catheters, there has been a significant decrease in the complication-related death rate [19]. In the present study, the Tenckhoff catheter was used in all of our patients, and our complication rates were consistent with those in the literature. Hakan et al. [3] reported hyperglycemia as metabolic complication, but in our patients no such complication was encountered. In the present study, APD-related complications were observed in 46.7% of the patients, but the complications were managed and no complication-related deaths occurred.

Mortality in patients undergoing APD is more closely related to the underlying disorder than to complications [17,21]. Matthews et al. [16] reported a mortality rate of 61.3% in cases undergoing PD. Hakan et al. [3] and Alparslan et al. [1] in their studies carried out in different medical units in Turkey,

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Table 1. Clinical and Laboratory features of the study group.

Patient no.	Sex	Gestatinal age (weeks)	Age (days)	Weight (g)	Underlying cause	PD duration (days)	Compli-cations	Cr pre/post PD (mg/dL)	Urea pre/ post PD (mg/dL)	Na^+ pre/ post PD (mg/dL)	K^+ pre/ post PD (mg/dL)	Outcome
1	M	34	15	2500	NIH+DS	2	Peritonit	1.35/1.25	132/118	148/142	4.2/5.3	Died
2	M	31	10	1200	CB	4	Leakage	2.7/1	208.4/66.5	174/140	9/3.4	Survived
3	M	39	16	3900	PPHN+VGAE	8	Leakage	2.3/2.15	112/103	132/136	3/3.13	Died
4	M	34	6	2900	PKD	20	CO	5.6/2.77	116/57	122/127	7/5.6	Died
5	M	39	7	2750	HIE	3	Leakage	5.5/1.1	231/49	130/127	5.7/3.3	Survived
6	M	30	28	3000	Galactosemia	10	Leakage	0.2/0.3	68/28	135/140	5.4/2.8	Died
7	FM	38	2	2160	HIE	3	ND	1.3/2.35	32/44	139/158	7/4.2	Died
8	M	26	14	600	Sepsis	3	ND	4.1/3.1	301/318	188/169	8.1/4.6	Died
9	M	25	11	750	Sepsis	1	ND	3.3/3.6	355/415	148/146	8.1/8.2	Died
10	M	39	5	3000	PBS	14	Leakage	2.69/1.7	72/26	141/131	4/3.1	Died
11	FM	32	25	2300	NIH	2	ND	2.72/2.56	282/248	120/128	10/6.2	Died
12	M	24	7	580	Sepsis	3	ND	1.2/1.8	181/182	157/146	8/4.5	Died
13	FM	39	28	3400	d-TGA+PPHN	8	Leakage	3.6/0.9	142/71	135/131	3.3/3.6	Survived
14	FM	32	5	1900	UCD	5	Leakage	1.5/1.2	76/50	124/133	9.9/4.8	Died
15	FM	30	12	780	Sepsis	4	Peritonit	3.8/1.4	302/196	138/134	6.6/3.2	Died
16	FM	39	7	3000	HIE	11	ND	4.2/1.5	91/35	131/142	2.8/4.1	Survived
17	FM	32	28	1300	Sepsis	10	Leakage	4.2/4.24	217/236	133/140	6.5/5.8	Died
18	M	24	8	700	Sepsis	1	ND	3.4/2.84	300/369	165/159	8.5/6.8	Died
19	M	39	18	3050	Salting*	3	ND	5.7/1	455/78	171/143	5.6/2.8	Survived
20	M	39	7	1950	Salting*	5	CO	7.4/0.6	379/39	184/140	6.5/2.8	Survived
21	FM	39	5	3450	HIE	5	ND	4/0.8	285/135	143/144	4/3.5	Survived
22	FM	28	2	1250	Sepsis	2	ND	1.52/1.6	81/88	138/140	8.1/6.9	Died
23	FM	27	5	1040	Sepsis	2	Perforation	3.1/1.3	218/113	159/143	7.6/5	Survived
24	M	39	4	3800	HLHS	3	ND	2.5/1	89/30	148/130	6.6/3.2	Survived
25	M	40	8	3100	APW+ CoA	3	CO	2.2/1.1	156/61	149/129	5.4/3.8	Survived
26	FM	38	3	2100	Sepsis	6	ND	3.4/0.8	200/23	138/142	7/3.1	Died
27	FM	38	7	2000	Salting*	4	ND	6.7/0.8	449/39	195/149	7.4/2.7	Survived
28	FM	39	6	2300	inability to feed	5	ND	9.6/0.6	157/39	155/142	4.4/3.3	Survived
29	FM	28	19	1300	Sepsis	4	ND	3.3/1.4	70/19	130/142	4.6/3.5	Survived
30	FM	30	11	1250	Sepsis	6	Leakage	4.2/1.74	320/88	143/142	5.3/4.8	Died
31	FM	39	25	3500	d-TGA	6	ND	3.75/1.29	139/71	129/128	2.9/3.1	Survived

NIH – non immun hidrops; DS – Down syndrome; CB – collodion baby; VGAE – vein of Galen aneurysmal malformations; PKD – polycystic kidney disease; HIE – hypoxic ischemic encephalopathy; PBS – Prune Belly syndrome; UCD – urea cycle defects; d-TGA – transposition of the great arteries; PPHN – persistent pulmonary hypertension; HLHS – hypoplastic left heart syndrome; APW – aortopulmonary window; CoA – coarctation of the aorta; CO – catheter obstruction; ND – not defined; M – male; FM – female; PD – peritoneal dialysis; * Hypernatremia.

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Table 2. Comparison of characteristics between survived and died.

	Survived (n=14)	Died (n=17)	p
Sex, female, n (%)	8 (57)	8 (47)	0.582
Birth weight (g)	2560±927.4	1821.8±1018.5	0.039*
Gestatinal age (weeks)	36.8±4.49	31.5±5.1	0.003*
Age (days)	11.1±7.9	11.7±8.5	0.921
PD duration (days)	4.7±2.37	5.9±5.16	0.904
Complication, n (%)	7 (50)	8 (47)	0.629
Predialysis Cr (mg/dL) Mean ±SD	4.6±2.1	2.8±1.4	0.025*
Predialysis Urea (mg/dL) Mean ±SD	219.2±128.4	185.1±107.1	0.427
Predialysis Na+ (mg/dL) Mean ±SD	152.4±21.7	142.1±16.5	0.233
Predialysis K+ (mg/dL) Mean ±SD	5.4±1.9	6.9±2	0.051
Preterm, n	3	13	0.002*
Term, n	11	4	0.003*

have reported mortality rates of 74% and 59.3%, respectively. Other studies have reported mortality rate of 69% to 80% in preterm newborns with AKI [21,22]. Tetta et al. [23] reported that the rate of mortality can climb to 95% in cases of AKI with multi-organ failure. Many clinicians think that mortality in premature infants with AKI is generally caused by multi-organ failure and thus initially avoid the use of APD. However, Mathur et al. [24] have shown that the presence of AKI even in term newborns with sepsis increases the mortality rate almost three-fold (25% versus 70%). Alparslan et al. [1] have claimed that APD can yield good results in premature newborns with AKI, observing that five preterm newborns out of 13 survived with APD. When compared with the results in the literature, our overall mortality rate of 54.8% initially seems to be a good result, but, unfortunately, the death rate in our premature infants was 81.3%.

The limitation of this retrospective study was sample size; a larger sample size might well have yielded different results.

Conclusions

APD can be an effective, simple, safe, and important therapy for renal replacement in many neonatal diseases and it can be an appropriate treatment, where necessary, for newborns. Although it may cause some complications, they are not common. However, it should be used carefully, especially in premature newborns who are vulnerable and have a high mortality risk. The recommendation of APD therapy in such cases needs to be verified by further studies in larger patient populations.

Statement

No conflicts of interest and no financial support were declared in relation to this article.

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