Initiation of Maintenance Renal Replacement Therapy in Infants

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Keywords
Renal replacement • Infants • Hemodialysis • Peritoneal dialysis • Dialysis initiation

Introduction

Decisions concerning the initiation of dialysis during infancy are complex and serve as a prime example of why a pediatric dialysis healthcare team must be comprised of a multidisciplinary group of experts. Team members should include a social worker, nutritionist/dietician, nurses with experience in management of end-stage renal disease (ESRD) in infants, as well as the medical staff. In addition, the views of the parents must be seriously considered in the decision process. The complexity of the medical and psychosocial issues mitigates against care being provided by a single individual, if results are to be optimized. Additional input may be required from the dialysis technologist or from home or community providers. Finally, although dialysis in infants often poses significant clinical and technical challenges, it is frequently psychosocial and economic issues that dominate the patient management decisions.

The use of maintenance hemodialysis (HD) for children was first described by Fine and colleagues in 1968 [1] and was limited to a small group of adolescents. More than a decade later, the use of continuous ambulatory peritoneal dialysis (CAPD) was reported [2], and seemed to provide an opportunity to extend dialysis to younger children. Subsequent reports confirmed that long-term peritoneal dialysis (PD) was possible for infants [3, 4], although concerns about growth and development in this age group were emphasized. Whereas improvements in technology have permitted the successful use of HD for infants with acute renal failure [5], the use of this renal replacement modality for long-term care of this population may be problematic. Nonetheless, maintenance treatment of infants with both peritoneal and hemodialysis is possible, although before starting, parents should be cautioned about the demands of therapy, that desired outcomes may not be achieved, and that the emotional cost of treatment is considerable.

The ensuing discussion will review the options that exist with respect to the provision of

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B.A. Warady et al. (eds.), *Pediatric Dialysis*, DOI 10.1007/978-1-4614-0721-8_7,

maintenance renal replacement therapy (RRT) for infants, focusing on those factors unique to this population. This chapter addresses issues related to the initiation of dialysis, potential complications, and ethical considerations with this population. Lastly, the outcomes of infant dialysis, as reported in the literature, will be summarized.

Dialysis Options

Hemodialysis

HD is rarely the modality of choice for the initiation of maintenance dialysis in infants [6]. Estimates of its use in infants have ranged from 3% to 14% [7–9]; however, in most observational studies, HD was utilized only after PD failed [10, 11]. Mortality rates notwithstanding, the drawbacks of infant HD include its special equipment needs and the labor intensity. For successful HD, each component of the equipment (machine, filters, bloodlines, and vascular access) must be specifically adapted for infants. More frequent dialysis (> thrice weekly) is also often required in younger patients because of the difficulty that can occur achieving consistent blood flow rates with this equipment [12]. In addition, because the infant diet is predominantly liquid-based, more frequent treatments are often required to achieve appropriate ultrafiltration and to allow for optimal nutrition, especially in the oliguric infant. This increase in dialysis frequency places great demands both on the family and the dialysis staff.

Another potential drawback to infant HD has been the need for blood priming for treatments and the associated risk for increased antigen exposure, all of which can have a negative impact on subsequent transplant availability. However, larger infants (>5 kg) have been treated chronically using albumin or saline priming with success [11], potentially diminishing this drawback. On a positive note, published experience does provide evidence that it is possible to maintain infants on chronic HD and achieve adequate growth and development [10, 11].

Peritoneal Dialysis

PD has long been the dialysis modality of choice for infants, since the introduction of CAPD in the late 1970s, in large part due to the lack of need for vascular access and the excellent patient tolerance of the procedure. Its technical requirements include a flexible catheter small enough for insertion into an infant and a supply of dialysate in small bags to allow for the infusion of appropriately smaller volumes, compared to older children and adults. The introduction of cycling machines allowed for frequent, small volume exchanges and overnight dialysis with less caregiver burnout. Salusky et al. reported their successful clinical experience with cycling PD in eight infants (aged 2.5–8.5 months) in the mid-1980s [13]. However, these initial cycling machines had excessive dead space in the tubing, such that the recirculated volume of dialysate in infants could be nearly 40% of the exchange volume. The development of machines with smaller tubing dead space and less dialysate recirculation has further facilitated and improved this dialysis modality in infants.

PD is, however, fairly rigorous for parents, as it is most often performed nightly in infants. Some have speculated that on occasion, the sudden death that may occur in an infant on PD may actually be secondary to hyperkalemia from dialysis not being performed in the prescribed manner. However, the rigors on the family may be less overall than with HD, which often requires a constant parental presence during treatments, in addition to regular travel to and from the dialysis center, allowing less time to be spent at home. For those situations in which care provision or home scenarios are not acceptable for home dialysis, PD may be provided in the hospital setting.

Timing of Dialysis Initiation

There are no scientific data stating exactly when dialysis should be initiated during infancy, especially if all infants with impaired kidney function are considered. For those who are oligo-anuric or with life-threatening metabolic disturbances, the

decision is straightforward as death will occur, often within a few days, if dialysis is withheld. However, for infants who are capable of maintaining neutral fluid and metabolic balance, the optimal time to start dialysis is much less clear. There is frequent reticence on the part of parents and staff to institute therapy, even in the absence of potential ethical dilemmas, which may lead to delays in dialysis initiation.

Renal Function Considerations

The guidelines presented by both the Kidney Disease Outcomes Quality Initiative (KDOQI) [14] and the European ad hoc committee for elective PD in pediatric patients [15], which recommend the level of renal dysfunction at which dialysis should be initiated, have no proven validity in infants in whom the glomerular filtration rate (GFR) in the normal state is quite low. An analysis of data from the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) derived from 300 infants who initiated dialysis revealed that those less than 12 months of age at dialysis initiation had a median GFR of 6 mL/min/1.73 m^2, compared to 8–11 mL/min/1.73 m^2 for those 12–24 months old [12]. These data, in turn, show that the estimated GFR is not used as an absolute threshold for dialysis initiation in this population.

Delays in the initiation of dialysis may be warranted by the need for urologic surgical procedures, for long-term preparation of the genitourinary system and reduction of infection risk, and possibly by preservation of renal function following surgical correction of severe, persistent upper tract obstruction with severe hydronephrosis [16, 17]. Criteria for surgical intervention in pediatric patients with upper tract obstruction have been published and include renal failure and worsening hydronephrosis; however, these indications are also not absolute and will vary by surgeon [18].

Some reticence about early dialysis initiation during infancy may also be secondary to the hopes, of both staff and parents, that renal function will improve as a result of postnatal maturation. Whereas the GFR of a normal term newborn is less than 10% of that in adults, it increases rapidly, doubling within the first 2 weeks of life and continuing to increase up to 2 years of age [19]. This rise in total GFR is secondary to increases in single nephron GFR, paralleled by an increase in renal plasma flow and individual glomerular hypertrophy (increases in size, surface area, and capillary permeability). Similarly, these changes may also occur, although less pronounced, in infants with renal dysplasia or acquired postnatal hypoxic insults to the kidney. Studies looking at the progression of renal dysplasia in children not requiring RRT have shown that GFR may improve in this population at an early age, but significant improvement is less likely in those with a lower initial GFR [20, 21]. Nevertheless, single-center reports of infant dialysis populations have cited their reason for terminating dialysis as recovery of renal function in 10–15% of their subjects [10, 22] and a NAPRTCS review by Carey et al. reported that up to one-eighth of all neonates on dialysis were able to discontinue dialysis because of recovered renal function [23]. In contrast, Coulthard et al. reported a much lower percentage (4.6%) of patients experiencing recovery of function when all infants with ESRD, including those not treated, were considered [24]. Therefore, the prospect of dialysis being only a temporary measure in infants with severely impaired kidney function is not great and likely should not be overemphasized in discussions with most families about the prospect of initiating long-term RRT.

Nutritional Considerations

Nutrition is a primary concern in all children with chronic kidney disease (CKD), but its importance is greatest during infancy. At this stage, statural growth and increase in brain growth and head circumference is primarily driven by nutrition and early deficits may be difficult to overcome later. The recently published KDOQI guidelines for nutrition in children with CKD recommend evaluation of nutritional parameters in infants, as frequently as every 2 weeks [25], as shown in Table 7.1 [25]. Additionally, most of the primary indications for dialysis initiation, as cited by the KDOQI guidelines, are conditions (acidosis, hyperkalemia, hyperphosphatemia, growth failure, fluid overload, and neurologic sequelae of uremia) which may be amenable to intense dietary

Table 7.1 Recommended parameters and frequency of nutritional assessment for children with CKD Stages 2 to 5 and 5D

	Minimum interval (mo)									
	Age 0 to <1 year			Age 1–3 years			Age >3 years			
Measure	CKD 2–3	CKD 4–5	CKD 5D	CKD 2–3	CKD 4–5	CKD 5D	CKD 2	CKD 3	CKD 4–5	CKD 5D
Dietary intake	0.5–3	0.5–3	0.5–2	1–3	1–3	1–3	6–12	6	3–4	3–4
Height or length-for-age percentile or SDS	0.5–1.5	0.5–1.5	0.5–1	1–3	1–2	1	3–6	3–6	1–3	1–3
Height or length velocity-for-age percentile or SDS	0.5–2	0.5–2	0.5–1	1–6	1–3	1–2	6	6	6	6
Estimated dry weight and weight-for-age percentile or SDS	0.5–1.5	0.5–1.5	0.25–1	1–3	1–2	0.5–1	3–6	3–6	1–3	1–3
BMI-for-height-age percentile or SDS	0.5–1.5	0.5–1.5	0.5–1	1–3	1–2	1	3–6	3–6	1–3	1–3
Head circumference-for-age percentile or SDS	0.5–1.5	0.5–1.5	0.5–1	1–3	1–2	1–2	N/A	N/A	N/A	N/A
nPCR	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1[a]

Abbreviation: N/A, not applicable

[a]Only applies to adolescents receiving HD

and medication management [14]. Therefore, early and frequent evaluation of both biochemical and growth parameters are necessary to minimize sequelae of malnutrition, but also to anticipate potential nutritional needs once starting dialysis.

Precise documentation of dietary intake in infants should be recorded, although this is somewhat more complex in breastfed infants. It is mandatory to document intake accurately in uremic infants so that any reduction below recommended calorie and protein intakes for age can be identified and corrected quickly. Similarly, meticulous care is also required to ensure that calcium and age specific phosphate values are maintained in the normal range, the latter goal often requiring the initiation of dialysis. Lastly, though difficult to confirm, renal salt wasting may occur in infants and a therapeutic trial of sodium chloride supplementation in the infant with advanced CKD may be advised to determine any possible contribution to growth, especially given that additional sodium loss will typically occur with the initiation of PD [25].

Whereas the amelioration of uremia by dialysis may improve appetite and reduce vomiting, this does not frequently occur. In fact, the installation of large dialysate volumes into the peritoneal cavity may aggravate these symptoms. Therefore, the introduction of enteral tube feeding, if possible, prior to the initiation of dialysis is recommended [26] and decisions to start dialysis should include discussions about a long-term tube feeding strategy. Adequate nutritional outcomes may be achieved by either a nasogastric or gastrostomy tube; however, the timing of their introduction is often closely tied to the plan for dialysis initiation. PD catheters and gastrostomy tubes may be inserted as part of the same surgical procedure [15]. When performed in this manner, dialysis should be withheld for the first 48 h to ensure there is no leakage from the gastrostomy tube site. A gastrostomy tube may be added after PD catheter insertion, but with increased risk of infection, particularly if inserted percutaneously [27]. Prophylactic antibiotics and antifungals have been shown to reduce this risk [28]. Some would also suggest the initial use of a nasogastric tube when the patient is significantly malnourished to enhance nutrition prior to surgery for gastrostomy placement as a means of decreasing the risk for postoperative complications (e.g., infection, poor wound healing).

Growth and Development Considerations

Although the precise cause of developmental and growth delay in uremic infants has not been clarified, one must consider the uremic milieu as potentially harmful and as an important clinical indicator for dialysis initiation. Improved developmental outcomes in uremic infants have been noted over the past few decades, coinciding with the elimination of aluminum containing phosphate binders, optimization of nutrition, use of erythropoiesis-stimulating agents, and increasing awareness of the potential benefits of earlier and "adequate" dialysis. However, it is impossible to separate the individual contributions of each of these factors on the observed improvement in development; therefore, each (including earlier dialysis) should be factored into the decision to initiate dialysis.

The most objective measure of the need to start dialysis in infants may be growth impairment. Growth delay, like developmental delay, is most often multi-factorial and may require a period of months rather than weeks to manifest and, therefore, should not be the sole criterion upon which the decision to initiate dialysis is based. However, an inability to correct several of the factors that contribute to growth delay (inadequate nutrition, persistent acidosis, and renal osteodystrophy) through dietary and pharmacologic measures alone should have a strong influence on the decision to initiate dialysis.

Ethical Considerations

The ethical and legal issues that need to be considered when deciding whether or not to proceed with dialysis during infancy, have been debated for many years. In 1987, Cohen reviewed these issues and suggested that dialysis for infants could be considered more of an experimental or innovative intervention than an accepted therapy. She concluded that "when parents elect conservative treatment for their very young infants who are born with End-Stage Renal disease (ESRD), rather than dialysis or transplantation, this is a choice that is medically, ethically, and legally

Table 7.2 Ethical decisions: Guidelines for practice

1.	Always act in the child's best interests
2.	Never rush the decision; continue treatment until it can be properly made
3.	Assemble all the available evidence
4.	Respect the opinions of everyone in the team
5.	Discuss the issues with the whole family
6.	Attempt a consensus whenever possible
7.	Make sure everyone appreciates the burden of care
8.	Try to avoid adding to the guilt of anyone involved
9.	Consider the child's palliative and terminal care
10.	Offer support for all those affected, parents and staff alike
11.	Remember, we can only do the best we can and sometimes there is no ideal solution

acceptable [29]." Nine years later, when considering the same issue, despite substantial improvements in technology that had been achieved in the interim, Bunchman concluded that "the decision by the family or the medical team not to institute dialytic therapy must be honored and offered as a reasonable option [30]." Bunchman added that "early intervention with aggressive management of infants would be optimal, with the understanding that discontinuation or withdrawal of care in the future is an option." He also drew attention to the need for the healthcare team to objectively outline the long-term care burden and outcomes associated with dialysis to the patients' families and emphasized the difficulty of truly obtaining "informed consent" at such a stressful time. These issues were again discussed in 2000 by Shooter and Watson [31] who stated that decision-making for pediatric patients should be in the hands of the patient, the hospital team, and the parents; since infants cannot speak for themselves, decisions must be made by proxy. They pointed out that when there is disagreement between family members about the course of action to take, as well as potential conflicts between hospital staff members, these very difficult decisions become even more complex. They provided some guidelines, as outlined in Table 7.2 [31], on actions to consider when confronted with such complex patient issues.

In an attempt to clarify the ethical dilemmas that doctors face when deciding whether or not to treat patients with ESRD, the Spanish Pediatric Nephrology Association also produced guidelines on this issue [32]. These authors also mentioned how difficult, but important it is to try to obtain informed consent for procedures in young children. They stated that information should be provided to families that includes a discussion of quality of life as a major consideration. Parents should be counseled, advised, and supported before, during, and after decision-making. Withholding or withdrawing dialysis was considered a reasonable option in these guidelines if the net benefit to the child would not justify the risks and burdens of the treatment. These guidelines are outlined in Table 7.3 [32].

It is of interest that the first guideline listed in Table 7.3 states that "a patient must have real possibilities for kidney transplantation." Whereas this has also historically been a consideration for patients starting dialysis at The Hospital for Sick Children in Toronto, it is no longer so. Provided the expected quality of life for the child is considered satisfactory and members of the healthcare team in conjunction with the family elect dialysis, then it is considered reasonable to initiate this treatment even for those in whom the likelihood of transplantation is considered small.

The second guideline in this table suggests that "patients with irreversible disease that makes survival extremely unlikely will not be considered as candidates for dialysis." Whereas we are in general agreement with this philosophy for children, dialysis may be offered to some children with a terminal illness if the child's quality of life is satisfactory and the patient or the family do not want to terminate life early because of a complication resulting from non-treatment of renal failure. However, given the intensity of care necessary and the frequent medical interventions required of infants on dialysis, it is difficult to envisage a situation in which an infant should be dialyzed when the likelihood of survival is extremely poor.

The ethical and legal issues outlined above are extremely useful to help guide decision-making about initiating or withholding dialysis treatment for infants with ESRD. However, it is also of great value to understand what the attitudes are of medical professionals with respect to this decision-making process. In a survey published in 1998, 93% of an international group of pediatric

Table 7.3 Guidelines for treatment of ESRD in children

1.	All pediatric patients receiving dialysis must meet the following criteria
	(a) The patient must be diagnosed with ESRD
	(b) Signed informed consent must be given by the parents/legal guardian
	(c) The patient must have real possibilities for kidney transplantation
	(d) There must be reasonable expectation that the patient will have an acceptable quality of life during dialysis therapy and after kidney transplantation
	(e) The patient and parent/guardian must demonstrate a willingness to participate in and cooperate with the dialysis procedures and medical advice
2.	Patients with irreversible diseases that make survival extremely unlikely will not be considered as candidates for dialysis
3.	Those patients meeting the criteria stated in guideline 1 will not be refused treatment for economic, social, or psychological factors, nor in relation to age, sex, race, or a physical handicap
4.	Dialysis treatment will not be withdrawn against the wishes of the patient and parents/guardian
5.	The cessation of dialysis will be considered if therapeutic results are not satisfactory or will not be reasonably achieved. A decision to stop treatment must always be made with the agreement of the responsible physician, the patient, and the parents/guardian

nephrologists responded that they offered dialysis treatment for ESRD to *some* infants aged <1 month and 41% reported that they offered RRT to *all* infants in this age group; 53% offered RRT to *all* such infants aged 1–12 months [33]. The presence of coexisting serious medical abnormalities or anticipated morbidity for the child ranked as the most important factors influencing their decision to withhold such treatment. The least influential factor concerning the decision to initiate or withhold such treatment was consideration of hospital or governmental budgetary issues. Most importantly, more than 80% of pediatric nephrologists believed that it was sometimes ethically acceptable for parents to refuse RRT for their children <1 month of age, and 61% held this belief concerning older (1–12 months) children.

Additional information about how nephrologists make decisions about life sustaining treatment in children was obtained from interviews with 46 French speaking pediatric nephrologists [34]. This study was not restricted to infants in early life, but nonetheless 97.8% answered that in their opinion it is sometimes necessary to withdraw or to withhold life sustaining treatment in children and the quoted reasons for this were "to avoid poor quality of life or to avoid artificial prolongation of life by medical means and to limit suffering for children when there's no hope for improvement." Interestingly, when asked if there was a difference between withdrawal of treatment or withholding of the same treatment, it was felt by the great majority that withdrawal of life-sustaining treatment is more difficult because this act may provoke or accelerate death. It was also interesting that in contrast to the survey by Geary, most doctors in this French survey (85%) did not wish to involve parents in the decision-making process.

Coulthard and Crosier reviewed the treatment of infants aged less than 2 years with ESRD in the UK and Ireland [24]. Of 192 such children, 177 (92%) were treated with dialysis or transplantation. Decisions not to treat were typically made by mutual agreement between clinicians and families. Although a relatively large number of children aged <1 month (n = 31) were treated, 45% of these patients died. In addition to physician advice, other influences on parental decision-making may include religious authorities [11], depending on the importance families place in their faith.

To determine if attitudes toward withholding care from infants with ESRD had changed over a 10 year period, the survey published by Geary in 1998 was repeated in 2008. In recognition of the fact that many of these decisions now often involve interdisciplinary members of the pediatric nephrology team, nurses and social workers were also surveyed. Ninety-eight percent (98%) of respondents stated that they offer RRT to some infants less than 1 month of age, compared with only 93% in 1998 ($p < 0.05$). In contrast, only 30% of nephrologists surveyed in 2008 offered RRT to all children <1 month of age compared to the figure of 41% in the earlier study. This

suggests that technology and patient outcomes have not advanced sufficiently to make the provision of RRT mandatory or the expectation for all young infants. As in 1998, 50% of nephrologists recommended treatment for all children aged 1–12 months. It is noteworthy that nurses rated the presence of oligo-anuria as an important factor influencing the decision to withhold RRT more so than nephrologists. Also, nurses rated the families' right to decide about the initiation of life sustaining therapy more highly than did respondent nephrologists. These disagreements of opinion between different members of the health care team emphasize the need for open discussion among team members when confronted with an infant with ESRD to aim for a consistent approach to treatment prior to speaking to the family so that the parents are not further confused during this stressful period of time.

Economic Considerations

The survey of Spanish pediatric nephrologists suggested that the economic cost of dialysis is the least important criterion in a long list of potential factors determining the advisability of starting dialysis in infants [35]. Similarly, in the previously mentioned international survey of pediatric nephrologists, hospital and governmental budget constraints ranked very low as considerations whether or not to initiate RRT for ESRD in infants [33]. Nonetheless, it is appropriate to consider the costs to the healthcare system of dialysis in infants.

In 1982, Baum at al. estimated the overall annual costs of dialysis as US $19,600 and $54,300 for pediatric CAPD and HD, respectively [36]. This study was based on a review of Medicare costs throughout the United States, provided no information about laboratory or medication costs, and was restricted to children between the ages of 3 and 20 years. A more detailed study by Coyte et al. found that the cost of pediatric CAPD was US $36,000, continuous cycling PD $37,000, and HD $57,000 annually [37]. This study was based on the detailed analysis of only a small number of patients older than age 2 and greater than 20 kg of body weight. Neither study addressed the added costs that characteristically occur in infants due to the greater number of average hospital days per annum [38] and the common need for more frequent dialysis sessions per week when compared to older children [12]. The common need for supplemental enteral feeding inherently increases direct costs in this population as well.

Both studies reflected only a healthcare system perspective rather than a total societal perspective of costs. It is likely that the cost of dialysis for infants, from both a societal and family perspective, is much greater than the sample values outlined above. The rigorous nature of dialysis in infants may preclude a family member from working full-time, unless other care arrangements can be made. The family's socioeconomic status, although not ranked as a highly influential factor by healthcare providers, must be considered. This is not to suggest that economically disadvantaged people should have less opportunities for dialysis than others, but rather that the financial burden to be carried by the families should be detailed in advance and discussed because of the influence it may have on this decision. The importance of the contribution from the social service team members on this issue cannot be overemphasized.

Unique Features of Infant Dialysis

As the infant with ESRD prepares to initiate dialysis, a number of issues should be considered to enhance the efficacy of the procedure and minimize treatment related complications.

Infant Hemodialysis

More infant-specific HD equipment has become available over the past two decades which has facilitated the use of this modality. Smaller dialysis circuits and tubing are available which may avoid the need for blood priming of lines and which requires less than 10% of the infant's intravascular blood volume to be in an extracorporeal location. If blood priming is needed, diluting the blood to a hematocrit of 30–40% may decrease

its viscosity and the associated increased resistance, while the use of leukopore blood may decrease the white blood cell load and potential antigen exposure. The infant's vascular access should also be characterized by low resistance to help avoid thrombosis. Therefore, the access should have a wide diameter and the shortest length possible, while still permitting appropriate surgical placement of the access tip in the atrial-vena caval junction. The standard blood flow rate for an infant's HD treatments is [39]:

$$(\text{body weight}\,[\text{kg}]+10)\times 2.5 = \text{blood flow rate}\,(\text{mL/min})$$

which translates to a rate of ≤50 mL/min in infants under 10 kg. Adequate anticoagulation is especially important in the setting of these low blood flow rates to decrease the risk of thrombosis. Heparinization is best accomplished with a heparin load of 10–20 units/kg and a maintenance rate of 10–20 units/kg/h to achieve standard activated clotting times of 150–200 s [40].

The infant HD treatment requires great circumspection by the dialysis staff, as the infant is at risk for complications throughout the session. In the hypervolemic infant, there may be an increased susceptibility to pulmonary edema and the need for supplemental oxygen. At the same time, ultrafiltration rates may be limited to 0.2 mL/kg/min as higher rates may cause hemodynamic instability. Additionally, the ultrafiltration monitors on HD machines have an error rate of ±50 mL/h, so infants could theoretically have an inadvertent excessive or reduced ultrafiltrate of as much as 150–200 mL during a 3–4 h treatment. This error rate may be minimized for a particular dialysis machine, once the variation rate is known and its range can be tightened by the biomedical support team [40]. Strict attention to maintaining accurate infant scales are also needed to minimize the risk for volume related complications. Maintenance of the infant's body temperature may be challenging with such large blood volumes in an extracorporeal location. As such, increased dialysate temperatures may be needed to maintain normothermia. Lastly, the return of blood to the infant must be performed slowly if it represents more than 10% of the patient's blood volume, as it may in essence represent a transfusion to the patient with a risk of hemodynamic compromise if performed rapidly.

Infant Peritoneal Dialysis

Specific technical details about performing PD in infants are covered elsewhere in this book. However, there are several issues which should be considered at therapy initiation.

The frequency of peritonitis is higher in infants under 1 year of age (once every 14.2 months) than in all children (once every 18 months) [7] and is a major cause of patient morbidity. One related issue that is especially pertinent to the infant initiating dialysis, but about which there is conflicting evidence, is the impact of a gastrostomy tube/button on the peritonitis rate. Ledermann et al. reported that the incidence of peritonitis in their gastrostomy fed infants was comparable to that reported for all children on PD by the NAPRTCS registry [27]. However, the peritonitis incidence in this study was twice as great when gastrostomy tube insertion was conducted after, compared to prior to dialysis initiation. Ramage et al. similarly noted a markedly increased incidence of peritonitis in children with gastrostomy tubes, and that the organisms causing peritonitis were similar to those infecting gastrostomy tube exit-sites [26]. Therefore, the PD catheter exit site should, if possible, be placed contralateral to the stomach and any current/potential gastrostomy site, as well as away from any other ostomy openings, as shown in Fig. 7.1. Additional recommendations regarding the gastrostomy placement strategy as it relates to peritonitis risk, with particular reference to the timing of placement, are noted above refer to the Nutrition chapter. Downward pointing dialysis catheter exit-sites have been associated with lower peritonitis rates in older children, but this has not been confirmed in infants. Concerns also exist that a downward pointing site may be a risk factor for infection in children with frequently soiled diapers; therefore, the location of the exit-site should be outside of the diaper region, and occasionally on the chest wall.

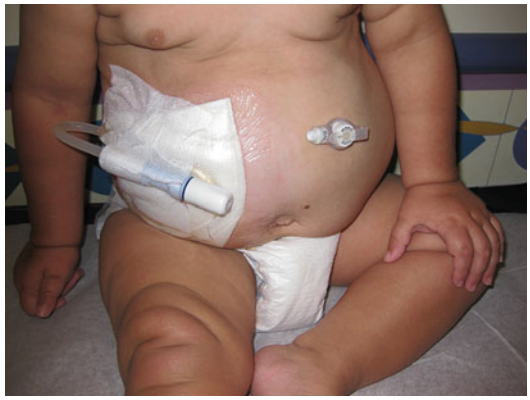

Fig. 7.1 Infant with PD catheter

Another potential factor that may contribute to an increased frequency of peritonitis during infancy may be a selective IgG deficiency associated with this therapy [41, 42]. While regular infusions of intravenous immunoglobulin have not yet been shown to decrease the risk of peritonitis in children, the subject has not been well studied [43]. Relative immaturity of other parts of the infant's immune system may also contribute to this risk [44]. Since membrane failure is associated with the number and severity of peritonitis episodes in children, all possible steps to minimize infections and, hence, preserve the peritoneum should be undertaken [45].

Whereas the use of double-cuffed catheters is recommended for pediatric PD [15], the possibility of erosion of the proximal cuff through the skin is probably greater in infants than in older children, particularly if the infant is malnourished. No specific recommendation is therefore possible regarding the number of cuffs that an infant PD catheter should have. Although the institution of dialysis in older children is often delayed for several weeks to allow healing of the exit-site, this may lead to more catheter occlusion in infants and may not be desired or even possible, based on the urgency of the clinical situation. If dialysis is started soon after catheter placement, the frequency of dialysate leakage may be increased, especially in the youngest infants [8], which may require a reduction in fill volumes, use of fibrin glue [46], or even temporary conversion to HD to allow for healing. Occlusion of the catheter by omentum may occur more frequently in infants as well and partial omentectomy should be considered at the time of catheter placement. Lastly, the development of hernias in young infants on PD is much more common than in older children [8, 13]. Prophylactic surgery to prevent hernia development is not mandated, but identification and correction of hernias at the time of catheter placement is recommended [38].

When PD is prescribed for infants, the exchange volume should be scaled to body surface area (BSA) and not weight, as a result of the age independent relationship between peritoneal surface area and BSA. In addition, the exchange volume at dialysis initiation should be only 600–800 mL/m^2 to optimize patient tolerance and minimize intraperitoneal pressure (IPP). It has been suggested that PD may also be particularly suitable for infants because of the potentially better preservation of residual renal function, or at least urine volumes [47]. Whereas, this has been documented in children on PD, in contrast to those on HD [48, 49], it has not been documented specifically in infants. Noteworthy is the fact that the presence of preserved renal function has been associated with improved growth in children on PD [50].

Outcomes of Infant Dialysis

The pediatric nephrology team should be well versed on the outcome of infants receiving dialysis so that they can provide this important data to families who are being asked to help make decisions regarding the long-term care of their infant with ESRD.

Growth and Development

Historically, growth and development have been significantly impaired in most infants requiring dialysis, but advances in treating the sequelae of ESRD have permitted normal or near normal development and reasonable growth. Nearly a decade ago, Warady et al. showed improved developmental outcomes in patients who initiated dialysis during infancy (<3 months old) with the

avoidance of aluminum binders and the regular use of supplemental feedings [51]. Of 28 surviving infants followed long-term, nearly 80% had normal developmental scores and only 4% had significant developmental delay. Coulthard et al. reported that 87% of their cohort was able to attend school and be placed in regular classrooms [24] while Shroff et al. reported that none of her 68 subjects without significant comorbidities were found to have learning difficulties [9]. Growth tends to be most severely impaired with an earlier age of ESRD onset and with the coexistence of comorbid conditions [52]. However, catch-up growth may occur in patients once on dialysis, especially in the case of infants [9]. As an example, Laakkonen et al. reported catch-up growth in 64% of their infants on PD with early dialysis initiation and aggressive nasogastric tube feeding [38]. Much the same has been demonstrated by the NAPRTCS. Most of the studies that have addressed growth were conducted without the use of recombinant growth hormone, which has now been shown to produce catch-up growth in treated infants (<1 year old) with CKD [53], increasing the likelihood of achieving near normal growth on dialysis.

Mortality

There is limited data available reporting long-term (>5 years) outcomes of patients who initiated maintenance RRT during infancy. However, there is a growing body of evidence from single-center observational experience and registry data that does provide short-term outcomes and may prove helpful when advising families. Early reports on young children receiving dialysis gave mortality rates of nearly 16% per year [40] and infant PD mortality rates >40% [54]. However, national registry data give a much less bleak picture. Children less than 1 year of age when initiating dialysis have had 5-year survival rates reported as high as 73% in Australia and New Zealand [55] and 66% in the United Kingdom [56]. Laakkonen et al. reported a mortality rate of only 9% in children <2 years old at the time of PD initiation [38]; however, these subjects were followed only during their time on dialysis (14 months), limiting the availability of outcome data. Similarly, the NAPRTCS found the 1-year survival of infants <2 years of age at dialysis initiation in 2001–2006 to be 86.1%. A more recent retrospective study by Wedekin et al. reported a 5-year survival of 82% for infants who received PD [57]. Mortality rates of patients receiving HD have seemingly been higher, with retrospective single-center studies giving overall rates of 30–40% [10, 11] but data has been limited to a very small numbers of patients.

Many feel that these studies and registry data underestimate the improvement in the survival rates of most infants who receive dialysis, as younger infants and those with substantial comorbidities are currently being treated [45]. While likely true, it should also be recognized that nearly all of these studies and registries analyze a selected population, those infants already deemed worthy candidates for dialysis, and do not include those to whom dialysis was not offered.

There are several risk factors associated with mortality in infants on dialysis that must be considered as part of the decision process regarding dialysis initiation. Oligo-anuria has been associated with the worst outcomes [10, 54] in several case series. Recently, Hijazi et al. found oligo-anuria to be the greatest risk factor for mortality in their analysis of 52 infants, with an odds ratio of 41 [8]. Interestingly, the international survey of pediatric nephrologists noted that the presence of oligo-anuria was only a minor influence on their decision-making regarding offering infant dialysis [33], highlighting a potentially concerning discrepancy between the clinical data that exists and practice recommendations.

Additional risk factors for infant mortality consist of a number of comorbidities, [54] namely, neurodevelopmental delay, congenital heart disease, malignancy, heritable metabolic disorders, and syndromes with multisystem involvement. Shroff et al. found the presence of other comorbidities to be associated with a relative mortality risk of 7.5 [9] while Hijazi et al. calculated an associated odds ratio of nearly 4.5 [8]. Unfortunately, the presence of other comorbidities is not always known at the time decisions are

being made about dialysis initiation and their presence has been cited as the leading reason for treatment withdrawal in infants [24].

Finally, younger age at the time of dialysis initiation has been associated with higher mortality, with neonates noted to have poor outcomes associated with the provision of both HD and PD [11, 24]. Rheault et al. specifically analyzed this population and noted a 3-year survival rate of only 48% [22]. However, mortality was highest during the initial hospitalization as 70% of those surviving to discharge went on to renal transplant. A specific analysis of NAPRTCS data on neonatal dialysis revealed an overall mortality of 24%, comparable to that of young infants [23]. In this analysis, however, a significantly better outcome was found in the neonatal cohort dialyzing since 1999 when compared to those who received dialysis prior to that time, suggesting that overall outcomes in neonates seem to be improving with advances in knowledge and technology.

Summary

The increasing number of reports of successful dialysis during infancy have been encouraging, such that no longer can RRT in infants be considered experimental [58]. However, this therapy remains demanding for the healthcare team and most importantly, for the family. Therefore, decision-making regarding the initiation of therapy in infants can by complex and should involve the multi-disciplinary team to address anticipated problems with care and to give realistic expectations of outcome. Lastly, the socioeconomic and ethical issues surrounding each individual case, which have also evolved with advances in technology and will likely continue to do so, should always be considered.

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