RENAL REPLACEMENT THERAPY IN CHILDREN

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Abstract : *Chronic kidney disease (CKD) is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Once the estimated GFR declines to less than 30 mL/min per 1.73 m2 and the child is in Stage 4 CKD, it is time to start preparing the child and the family for renal replacement therapy. Some form of renal replacement therapy will be needed when the weekly renal Kt/Vurea falls below 2.0, which approximates a creatinine clearance between 9 to 14 mL/min per 1.73 m^2. Children usually have a range of treatment options for kidney failure. The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. The best rehabilitation of uremic children can be achieved by renal transplantation. This is the only modality that facilitates growth and development in children. In an ideal scenario, pre-emptive kidney transplantation is the gold standard as it gives superior patient and graft survival with minimal side-effects. The other advantages are economic because of the cost savings in terms of dialysis expenses. The aim of dialysis is to bridge the period of terminal renal insufficiency until transplantation becomes possible. Many children begin with dialysis to stay healthy until a suitable kidney becomes available. Sometimes, a transplant itself may stop working, and the child may need to return to dialysis. Peritoneal dialysis is much more common in infants and younger children, in large part due to vascular access issues, and hemodialysis becomes more common in older adolescents. Although transplantation is the treatment of choice for children with ESRD, maintenance dialysis can provide satisfactory life expectancy for patients with no possibility of transplantation or highly sensitized patients. Peritoneal dialysis can be performed by parents at home, overnight with a cycling machine. Hemodialysis usually takes place three times a week, but it may be required more often in smaller children. Each treatment lasts from 3 to 4 hours. An early diagnosis of CKD and prompt referral to an appropriate centre would help in increasing the rates of pre-emptive renal transplantation in children in our country. For those in whom transplant is not an immediate option dialysis offers a bridge till this therapy becomes an option.*

INTRODUCTION

Chronic kidney disease (CKD) is characterized by an irreversible deterioration of renal function that gradually progresses to end-stage renal disease (ESRD). Children develop end-stage renal disease (ESRD) at an annual rate of 0.5 to 5.5 per million population. CKD has emerged as a serious public health problem. In the past decade, the incidence of the CKD in children has steadily increased, with poor and ethnic minority children disproportionately affected[1].

The definition and classification of chronic renal disease may help identify affected individuals, possibly resulting in the early institution of effective therapy. To achieve this goal, the Kidney Disease Outcomes Quality Initiative (K/DOQI) working group of the National Kidney Foundation of the United States defined CKD as "evidence of structural or functional kidney abnormalities (abnormal urinalysis, imaging studies, or histology) that persist for at least 3 months, with or without a decreased glomerular filtration rate (GFR), as defined by a GFR of less than 60 mL/min per 1.73 m^2" [2].

ESTIMATION OF GFR

The GFR is equal to the sum of the filtration rates in all of the functioning nephrons; thus, estimation of the GFR gives a rough measure of the number of functioning nephrons. A reduction in GFR implies either progression of the underlying disease or the development of a superimposed and often reversible problem, such as decreased renal perfusion due to volume depletion. The normal GFR varies with age, gender, and body size. Children achieve adult values for mean GFR at approximately two years of age The estimation of the GFR by the creatinine clearance in a 24-hour urine collection is easy to perform, but has limitations including frequent incomplete collections, especially in infants and young children who are not toilet-trained.

The work group on chronic kidney disease (CKD) for the Kidney Disease Outcome Quality Initiative (K/DOQI) recommends that in children, the level of GFR should be estimated from the Schwartz. In the Schwartz equation, GFR is calculated by the following:

GFR = k X Height (cm) / Pcreat

Height represents the body height measured in centimeters, and Pcreat is the plasma creatinine. The constant k is directly proportional to the muscle component of body, and varies with age. The value for k is 0.33 in premature infants through the first year of life, 0.45 for term infants through the first year of life, 0.55 in children and adolescent girls, and 0.7 in adolescent boys.

CLASSIFICATION

The observation that many of the complications of CKD can be prevented or delayed through early detection and treatment prompted the K/DOQI workgroup to develop a formal staging system for stratification of CKD based on the level of kidney function, independent of the primary renal diagnosis:

- **Stage 1** disease is defined by a normal GFR (≥ 90 mL/min per 1.73 m^2)
- **Stage 2** disease is a GFR between 60 to 89 mL/min per 1.73 m^2
- **Stage 3** disease is a GFR between 30 and 59 mL/min per 1.73 m^2
- **Stage 4** disease is a GFR between 15 and 29 mL/min per 1.73 m^2
- **Stage 5** disease is a GFR of less than 15 mL/min per 1.73 m^2 or ESRD.

TREATMENT CHOICES FOR KIDNEY FAILURE IN CHILDREN

Once the estimated GFR declines to less than 30 mL/min per 1.73 m2 and the child is in Stage 4 CKD, it is time to start preparing the child and the family for renal replacement therapy. Some form of renal replacement therapy will be needed when the weekly renal Kt/Vurea falls below 2.0, which approximates a creatinine clearance between 9 to 14 mL/min per 1.73 m2. However, renal replacement therapy is often initiated before children reach these levels for the following reasons:

- Limitations of total calorie intake resulting in failure to thrive
- Clinical symptoms attributable to uremia
- Delay in psychomotor development and/or educational issues from progressive CKD

Children usually have a range of treatment options for kidney failure.The family should be provided with information related to preemptive kidney transplantation, peritoneal dialysis, and hemodialysis. In most cases, the goal is to have a successful transplant that allows the child to lead the most normal life possible. The best rehabilitation of uremic children can be achieved by renal transplantation[3]. This is the only modality that facilitates growth and development in children[4]. The aim of dialysis is to bridge the period of terminal renal insufficiency until transplantation becomes possible[5].

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In an ideal scenario, pre-emptive kidney transplantation is the gold standard as it gives superior patient and graft survival with minimal side-effects. The other advantages are economic because of the cost savings in terms of dialysis expenses[6]. There is a greater potential for preemptive renal transplantation in children due to having parents who are a half haplotype match, are relatively young and healthy, and are willing to donate a kidney. But viable kidneys are not always readily available, and not all children can have a transplant. Many children begin with dialysis to stay healthy until a suitable kidney becomes available. Sometimes, a transplant itself may stop working, and the child may need to return to dialysis. The registry of the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS) reports that of patients initiating renal replacement therapy in pediatric centers:

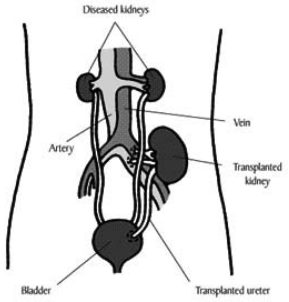
- One quarter of children underwent preemptive renal transplantation
- One half were started on peritoneal dialysis
- One quarter were started on hemodialysis

TRANSPLANTATION

Transplantation means that a healthy kidney from a donor is placed inside a child's body to take over the job of filtering wastes and extra fluid from the blood. The donor may be a stranger who has just died or a living family member or friend. Once kidneys fail because of chronic kidney disease, function cannot be restored, so transplantation is the closest thing to a cure we have. A child with a transplant will still need to take medicines every day, follow a restricted diet, and get regular checkups to make sure the new kidney is accepted and functioning in the body. Over the last decade there has been a progressive improvement in result sof kidney transplantation in children. A retrospective analysis was done of 39 pediatric transplants (age at transplant <18 yrs) done at our centre over the last 10 years. The 1-year patient and graft survival was 89%. Three year patient and graft survival was 70%. Kaplan Meier revealed actuarial graft survival at 5 years of 50%. The major cause of graft loss was noncompliance with immunosuppressive agents[7]. An analysis of the next 61 transplants however revealed a distinct improvement when due attention was paid to compliance. In a long-term Swedish study of children who received cyclosporine, prednisolone, and azathioprine, 5- and 10-year allograft survival rates were 77 and 66 percent, respectively. Patient survival is better in pediatric renal transplant recipients than adults[8,9].

Preemptive Transplantation

Preemptive transplantation means that the child receives a donated kidney before dialysis is needed. Some studies indicate that preemptive transplantation reduces the chances of rejecting the new kidney and improves the chances that it will function for a long time. Another advantage especially in a country like ours is the cost saving because of avoidance of dialysis[6].



Kidney transplantation

Living Donor Kidneys

About half of the kidneys transplanted into children are donated by family members—usually a parent—or a family friend. Potential donors need to be tested for matching factors and to make sure that donating a kidney will not endanger their health. Most people can donate a kidney with little risk.

A kidney from a living donor often has advantages over a kidney from a person who has just died.

- A kidney from a parent is guaranteed to match on at least three of six proteins; mismatched proteins may cause rejection.
- Living donation allows for greater preparation and for the operation to be scheduled.
- A kidney from a living donor may be in better condition because it does not have to be transported from one site to another.

Deceased Donor Kidneys

The cadaveric transplant programme in India is in infancy. In US every person who needs an organ from a deceased donor is registered with ta central network which maintains a centralized computer network linking all regional organ gathering organizations and transplant centers. How long the child will have to wait for a transplant depends on many things but is determined primarily by how good the match is between the child and the cadaveric donor. When a kidney becomes available, the hospital that has obtained the kidney reports to the network registry, where the central computer generates a list of compatible recipients. In our country the cadaveric donor programme is yet to take off and living donor transplantation remains the predominant choice.

DIALYSIS

There are 2 types of dialysis : hemodialysis and peritoneal dialysis. When preemptive transplantation is not an option, the choice between the two forms of dialysis is generally dictated by technical, social, and compliance issues, as well as family preference. Peritoneal dialysis is much more common in infants and younger children, in large part due to vascular access issues, and hemodialysis becomes more common in older adolescents. However, hemodialysis can be performed successfully in infants and very young children.

(a) Hemodialysis

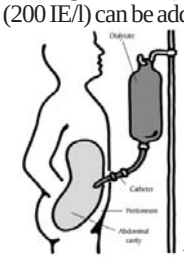
Although transplantation is the treatment of choice for children with ESRD, maintenance HD can provide satisfactory life expectancy for patients with no possibility of transplantation or highly sensitized patients. In hemodialysis, the child's blood is sent through a filter to remove harmful wastes, extra salt, and extra water. Hemodialysis helps control blood pressure and keep the proper balance of potassium, sodium, calcium, and bicarbonate. Hemodialysis uses a special filter called a dialyzer. During treatment, blood travels from the child's body through tubes into the dialyzer, which filters out wastes and extra water. Then the cleaned blood flows through another set of tubes back into the child's body. The dialyzer is connected to a machine that monitors blood flow and disposes of the wastes. Regarding *dialysis technique* , the extracorporeal circuit ('tubing') must be adapted to the size of the patient. The entire circuit volume should not exceed 10–15 per cent of the total blood volume of the child. In small children and infants, dialyser and tubing should be 'primed' with blood to prevent circulatory collapse. Heparin is used to prevent clotting in the extracorporeal circuit. The usual loading dose at initiation of HD is 2000 U/m^2, the maintenance dose 400 U/m^2/h; monitoring is usually performed by measuring activated clotting times (ACT). In patients with high risk of bleeding or heparin-induced thrombopenia, regional citrate anticoagulation should be used.

Hemodialysis usually takes place in a centre three times a week, but it may be required more often in smaller children. Each treatment lasts from 3 to 4 hours. A recent advancement is home hemodialysis, which allows more flexibility in scheduling but requires the caregiver to take weeks of training. During treatment, the child can do homework, read, write, sleep, talk, or watch TV10. Children who are to receive

hemodialysis will need evaluation of their vasculature for placement of an arterio-venous (AV) fistula several months before the first treatment. Alternatively a cuffed double lumen catheter can be placed. The use of AV fistula, the recommended type of vascular access in adults, is limited in children due to the size of their vessels. The NAPRTCS database reports that 78.6 percent of children receiving hemodialysis use an external percutaneous catheter for vascular access, 11.8 percent have an AV fistula, and 9.2 percent have an arterio-venous graf[11]t. The 5 year patient survival rate for children receiving chronic HD was 95 per cent, being comparable with the results of living-related donor transplantation (92 per cent). Long-term results of chronic HD in infants are worse; in one single-centre report (including 20 infants with 11 receiving transplants) the overall 14 year survival was 60 per cent and significantly better in children weighing greater than 5 kg (73 per cent) than those weighing less (20 per cent) at initiation of HD[12].

(b) Peritoneal Dialysis

Peritoneal dialysis can be performed by parents at home, overnight with a cycling machine. This potentially allows the least disruption of home life, school, and work attendance, when compared to ambulatory peritoneal dialysis, which often requires a dialysis exchange procedure to be conducted during school hours and hemodialysis which requires three weekly treatments of at least 3 to 4 hours (not counting travel time). In developing countries like India, pediatric hemodialysis facilities are scarce and there is no maintenance hemodialysis program in most of the nephrology centers. Thus CPD remains the only available option as a bridge between ESRD and transplant in remaote areas[13]. In addition, access to a nearby hemodialysis center may not be readily available to patients and their families or the personnel may not be trained to care for children, especially pre-pubertal children and infants. Peritoneal dialysis uses the lining of the child's abdomen, called the peritoneal membrane, to filter blood. CPD is most often based on patient and family preference, center philosophy and availability of desired expertise. Children who are to initiate peritoneal dialysis undergo abdominal surgery for placement of a peritoneal dialysis catheter. Ideally, there should be a period of 10 days to 3 weeks to provide for healing of the abdominal wound to occur prior to the initiation of dialysis [14]. Peritoneal dialysis is more common in infants and young children than hemodialysis due to the above mentioned vascular access problem. The peritoneal dialysis solution contains a mixture of minerals and dextrose dissolved in water and is inserted into the abdomen through a soft tube. The dextrose, draws nitrogenous wastes, electrolytes and extra water from the tiny blood vessels in the peritoneal membrane into the dialysis solution. After some time, the used solution—now loaded with the wastes and extra fluid that the kidneys would have filtered out—is drained from your child's abdomen through the tube. The period that dialysis solution is in the abdomen is called the dwell time. The abdomen is filled again with fresh dialysis solution, and the cycle repeats. The process of emptying and refilling the abdomen is called an exchange and takes about 30 to 40 minutes. Following catheter placement, PD is started with a low exchange volume (300 ml/m ^{2} or 10 ml/kg). Small amounts of heparin (200 IE/l) can be added to prevent catheter obstruction by fibrin clots.



Peritoneal dialysis

The exchange volume is slowly increased over several days and the exit site is repeatedly checked for leakage of dialysis fluid. The exchange volumes are increased to 1000–1500 ml/m ^{2}, the final volume, during the second week. Some centres have gained experience with intra-abdominal pressure measurements, which may be helpful in adjusting the dialysis dose to the individual need of the patient[15]. Peritoneal dialysis can be done with or without a cycling machine.

- **Continuous ambulatory peritoneal dialysis (CAPD).** CAPD requires no machine and can be done in any clean, well-lit place. The dialysis solution passes from a plastic bag through the catheter and into the abdomen, where it stays for several hours with the catheter sealed. After the dwell time, the child drains the dialysis solution into a drain bag for disposal. Then the same catheter is used to refill the abdomen with fresh solution so the cleaning process can begin again. With CAPD, the dialysis solution stays in the abdomen for 4 to 6 hours or more. Most people change the dialysis solution at least four times a day and sleep with solution in their abdomen at night. With CAPD, it is not necessary to perform an exchange during the night.
- **Continuous cycling peritoneal dialysis (CCPD).** CCPD uses a machine called a cycler to fill and empty the child's abdomen many times at night during sleep. In the morning, the child begins one exchange with a dwell time that lasts the entire day. An additional exchange without the cycler may be added in the middle of the afternoon to increase the amount of waste removed and to reduce the amount of fluid left behind.

Both types of peritoneal dialysis can be performed in the home without help from a nurse or doctor[15]. If your child is very young, you will need to help with the exchanges or set up the cycler. Older children can do it themselves. The child and the family needs detailed instructions and extensive training so that they feel confident when performing these exchanges.

The most common problem with peritoneal dialysis is peritonitis, a serious abdominal infection that can occur if the opening where the catheter enters the body becomes infected or if contamination occurs as the catheter is connected or disconnected from the bags. Peritonitis requires antibiotic treatment.

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