ORIGINAL ARTICLE

Renal Replacement Therapies in Kidney Disease

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ABSTRACT
Renal replacement therapy (RRT) artificially replaces function of the kidney when it is damaged. Plethora of modalities has developed, each having its unique indication and advantages. The first step in choosing RRT is to establish whether damage is acute or chronic. There are specific indications in starting RRT in each. Hemodialysis and hemofiltration utilizes external "filters" while in peritoneal dialysis, peritoneal membrane of the patient is used for the purpose. Slow continuous therapies such as 'sustained low-efficiency dialysis' and 'continuous renal replacement therapy' have developed as variant of hemodialysis and hemofiltration making it possible to dialyze hemodynamically unstable patients. Except the transport characteristics of the peritoneum all other variables in RRT can be adjusted to achieve the desired response. Understanding of the underlying principles of each modality helps in choosing a right RRT for the patient. Various types of dialysis have been discussed in detail in the article.

Key words: renal replacement therapy, hemodialysis, hemofiltration, peritoneal dialysis, sustained low-efficiency dialysis, continuous renal replacement therapy.

INTRODUCTION

Kidney is the only organ in the body whose function can be artificially replaced. If damage occurs to kidneys, the kidneys may become inefficient or may stop functioning altogether. Hemodialysis is the traditional method for replacing renal function. Over the last three decades, there has been rapid evolution of various modalities designated as renal replacement therapies (RRTs). RRTs, their indications, advantages and advances are reviewed in this article to help physicians chose a specific therapy as per patient's needs.

DISCUSSION

The first step in the administration of a specific RRT is to esablish whether the damage to kidney is acute or chronic.

Acute Kidney Injury (AKI): An acute injury to kidneys can occur due to various causes such as toxins, drugs, infection or immune response.[1] The subsequent damage is largely reversible if the underlying cause is removed. However, the process may take days to weeks. Hence in the intermittent period RRT may be required for patient's survival in certain conditions.

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Table1: Indications for RRT in the patient with acute kidney injury

1.	Uremic complications, such as pericarditis, encephalopathy, or gastrointestinal bleeding.
2.	Volume overload not treatable with diuretics.
3.	Severe hyperkalemia.
4.	Resistant acidosis
5.	Acute poisoning with a dialyzable substance

Chronic Kidney Disease (CKD): If an acute kidney injury does not reverse, it may progress to chronic stage. Chronic damage to kidneys also occur due to continuous insult from systemic diseases such as Diabetes & Hypertension. In such cases, the kidney function decreases progressively. Finally, a stage is reached when survival is compromised and RRT is mandated.

Table-2: Indications for RRT in the patient with chronic kidney disease

1.	GFR below 10mL/min
2.	Fluid overload refractory to diuretics
3.	Hypertension poorly responsive to antihypertensive medications
4.	Refractory metabolic disturbances such as hyperkalemia, metabolic acidosis, hypercalcemia, hypocalcemia, and hyperphosphatemia
5.	Persistent nausea and vomiting
6.	Evidence of malnutrition
7.	Pericarditis or pleuritis
8.	Uremic encephalopathy or neuropathy
9.	Bleeding diathesis

RRT can be done by Dialysis or Hemofiltration which have further evolved into various specific categories. Renal transplantation can also be said to be a type of RRT. Dialysis is divided into two broad categories: Hemodialysis & Peritoneal dialysis.

Hemodialysis: In Hemodialysis, waste products & excess water are removed extra corporeally using a dialyser. A vascular access, dialyser, dialysate and a hemodialysis machine are the basic requirements.

1. Vascular access: It is the site on the body where blood is removed and returned during dialysis. The vascular access should allow continuous high volumes of blood flow. A vascular access may be temporary or permanent.

a. Temporary vascular access:

i. Venous catheter: A venous catheter is placed in jugular vein or femoral vein. In acute & emergency conditions and in non ambulatory patients, femoral vein may be used. Otherwise, jugular vein is used which is safer & lasts longer. Catheter in subclavian vein is now largely abandoned due to high incidence of stenosis.[2]

ii. Arterio-venous graft: An arteriovenous graft is a synthetic tube made of Polytetrafluoroethylene (PTFE) that is grafted between an artery and vein. The graft becomes an artificial vein that can be used repeatedly for needle placement and blood access during hemodialysis. A graft can be used within 2 or 3 weeks after placement and can last several years.

b. Permanent vascular access:

Arterio-venous fistula (A-V fistula): It is made by joining an artery and a vein. Fistulas are usually made in the nondominant arm. They are generally created on the following sites:

On the dorsum of the hand below the thumb: the 'snuffbox' fistula - the dorsal branch of the radial artery is anastomosed to the cephalic vein.

The forearm: Brescia-Cimino fistula - the radial artery is anastomosed to the cephalic vein.

The elbow: Brachiocephalic fistula - the brachial artery is anastomosed to the cephalic vein.

A fistula takes on an average 4–6 weeks to mature.

2. Dialyser: A dialyser is different from a typical filter as the blood is not filtered out. Rather the undesirable elements in the blood and excess of water are absorbed. The main element in a dialyser is a semipermeable membrane through which small molecules can pass by diffusion. It consists of a cylindrical bundle of hollow fibers, whose walls are composed of semi-permeable membrane. It is then assembled into a clear plastic cylindrical shell with four openings. One opening or blood port at each end of the cylinder communicates with each end of the bundle of hollow fibers. This forms the "blood compartment" of the dialyzer. Two other ports are cut into the side of the cylinder. These communicate with the space around the hollow fibers and forms the "dialysate compartment." Blood is pumped via the blood ports through this bundle of very thin capillary-like tubes and the dialysate is pumped through the space surrounding the fibers. Initial membranes were made of cellulose. Cellulose acetate and modified cellulose dialysers are still used. But most membranes are now made from synthetic materials, using polymers such as polyarylethersulfone, polyamide, polyvinylpyrrolidone, polycarbonate, and polyacrylonitrile.[3] The main advantage of synthetic membranes is that they activate complement to a lesser extent than cellulose membranes.[4]

3. Dialysate: It is the fluid consisting of solutes that flow through the dialyser (Table-3). It helps in filtering out of the toxins from the blood. The composition can be varied depending upon the biochemical profile of the patient.

4. Hemodialysis Machine: It supplies the blood and the dialysate to the dialyser. The blood pump takes the blood from the patient via the vascular access and supplies it to the dialyser. The blood is confined to the disposable plastic tubing and does not come in contact with any part of the machine. The dialysate pump mixes the concentrate with water and moves the dialysate through the dialyser. The blood pump in the hemodialysis machine can control the rate of blood flow. It is generally kept in the range of 300-450 mL/min. To prevent clotting, it is periodically mixed with heparin. Simultaneously, the dialysate pump mixes the concentrate with water thus making the dialysate of desired concentration. The dialysate is also pumped to the dialyser but from opposite end. In the dialyser, blood and dialysate flow in opposite direction (counter current). This counter current mechanism helps to maintain the concentration gradient along the whole length of the dialyser The dialysate pump also has adjustable flow rate and it is typically kept in the range of 500-800 mL/min. In the dialyser, blood is pumped through the bundle of very thin capillary like tubes and the dialysate is pumped through the space surrounding the fibers. The impurities in the blood like urea diffuses to the dialysate. Pressure gradients are applied to move fluid from the blood to the dialysate compartment (ultrafiltration). During ultrafiltration, the solutes in the blood also move out by convection. The purified blood is then returned to the body. A typical hemodialysis session lasts 4 hours and needs to be repeated every 48-72 hours.

Table-3: Composition of a typical dialysate

Glucose	200mg/dL
Sodium (Na)	140 mEq/L
Potassium (K)	1-3 mEq/L
Bicarbonate	30-35 mEq/L
Calcium (Ca)	2.5 mEq/L
Magnesium (Mg)	1mEq/L

Hemofiltration: The procedure of hemofiltration is somewhat similar to hemodialysis but the principle involved is different. In hemofiltration, dialysate is not used. Solute movement with hemofiltration occurs by convection[5]. When the blood flows through the dialyser, a positive hydrostatic pressure drives water and solutes across the filter membrane. This filtrate is drained. The excess fluid that is drained (after considering for required ultrafiltration) is replaced by an isotonic replacement fluid. The advantage of hemofiltration is that convection overcomes the reduced removal rate of larger solutes (due to their slow speed of diffusion) seen in hemodialysis. Thus clearance of phosphate, many uremic toxins such as complement factor D, leptin, erythropoiesis inhibitors is increased.[6] When hemofiltration is combined with hemodialysis, the process is known as hemodiafiltration.

Slow Continuous Therapies: Slow Continuous Therapies are used for hemodynamically unstable, fluid overloaded, catabolic septic patients.[7] These patients are generally having AKI or multi organ failure. The following types of slow continuous therapies have developed.

Sustained Low-efficiency Dialysis (SLED): In SLED, standard HD equipment is used with reduced dialysate and blood flow rates. The blood flow rate is kept at 100-200 mL/min while dialysate flow rate is kept at 100 ml/min. The session is continued for 6-10 hours.

Continuous Renal Replacement Therapy (CRRT): There are many variations of CRRT. They are categorized according to the access characteristics and also according to the modality chosen. In Arteriovenous (AV) an arterial catheter allows blood to flow into the extracorporeal circuit by the driving force of the systemic blood pressure. The blood is returned by the venous catheter. It does not require an extracorporeal blood pump. But there is risk of arterial embolization and blood flow may be unreliable in hypotensive patients. In Venovenous (VV) both catheters are placed in veins. An extracorporeal blood pump is required to circulate blood through the extracorporeal circuit. Irrespective of the access, any of the three modalities viz hemodialysis (HD), hemofiltration (H) or hemodiafiltration (HDF) can be used. Thus the possible variations are CAVHD, CAVH, CAVHDF, CVVHD, CVVH & CVVHDF.

Peritoneal Dialysis: The Peritoneal dialysis utilizes the peritoneum as the dialyser. Peritoneal dialysis may be done acutely or chronically with different types of catheter and machines but the underlying basic principle is the same. To understand Peritoneal dialysis it is necessary to have a knowledge of structure of peritoneum.

Structure of the Peritoneum: Peritoneum is a serous membrane of the abdominal cavity. It consists of two parts: Visceral, which forms 80% & covers the gut and other viscera. It also forms the omentum and the mesentry. Parietal forms 20% & lines the inner surface of the abdominal wall. Peritoneum consists of mesothelial cells resting on the basement membrane. Its Interstitium contains the peritoneal capillaries & lymphatics.

Principle: All types of peritoneal dialysis are performed by introducing peritoneal dialysate in the peritoneal cavity. This is achieved by inserting peritoneal dialysis catheter which permits bi-directional flow of dialysate.[8] The passage of fluid or solutes from the blood vessels in the peritoneum to the dialysate in the peritoneal cavity or vice versa is met with six resistance sites viz fluid film, endothelial layer, capillary basement membrane, interstitium, mesothelium & fluid film of peritoneal cavity. The most important principle for solute removal in PD is diffusion, for which the driving force is the concentration gradient between the blood and the dialysis fluid. Small solutes move quickly through the membrane creating equilibrium during the dwell period. Larger solutes move slowly across the peritoneum, reaching equilibrium point takes a long time. Fluid removal in PD is by osmosis. Both solute and fluid removal in PD is controlled by various factors listed in.

Table-4: Factors controlling solute and fluid removal in PD

1.	Glucose concentration of the dialysate
2.	Dwell time of the dialysate
3.	Volume of the dialysate
4.	Peritoneal membrane characteristics

Types of Peritoneal Dialysis

Acute Peritoneal Dialysis: It is done for acute kidney injury. For acute peritoneal dialysis, a short term, hard PVC catheter is used. Before insertion, patient's bladder is emptied to prevent accidental puncture. The catheter is inserted by puncturing the abdominal wall about 2.5 cm below the umbilicus in the midline. Through the catheter, the dialysate of 1-2 L is introduced over a 10 minute period (inflow time). The dialysate remains in the cavity for around 30 minutes (dwell time) after which it is allowed to drain over a 20 minute period (outflow time). The cycles are then repeated. During acute PD, it is essential to monitor electrolytes particularly Na & K. Potassium is generally required to be supplemented after 4-8 cycles. The cycles can be continued for 48-72 hrs after which risk of peritonitis increases considerably.

Long-term Peritoneal Dialysis: It is prescribed to CKD patients. It is of two main types: Continuous Ambulatory Peritoneal Dialysis (CAPD) and Continuous Cycling Peritoneal Dialysis (CCPD). The catheters inserted in both remain for many years and are softer and flexible. The double cuff straight Tenckhoff catheter, a silicone catheter, is the most commonly used catheter. The distal (intraabdominal) segment of the catheter is positioned freely in the intraabdominal pelvic area. The catheter's midportion is implanted within the wall of the abdomen via one to two Dacron velour cuffs. The deep cuff is embedded in the abdominal rectus muscle. The superficial cuff in both double cuff and single cuff catheters is placed subcutaneously approximately 2 cm from the catheter exit site on the abdominal wall.

Continuous Ambulatory Peritoneal Dialysis (CAPD): CAPD involves manual exchange of dialysate and does not require any machine. The patient may remain ambulatory while the dialysate remains in the peritoneal cavity. The fluid is allowed to stay in the abdomen for several hours allowing excess fluid and toxins to move from the blood to the dialysate. At the end of the dwell, the fluid is drained by gravity into a collecting bag and the same process is repeated. Draining dialysate and replacing it with fresh solution takes about 30 minutes and is repeated three to five times every day. The last exchange of the day may be done before going to sleep, and the dialysate is left in overnight.

Continuous Cycling Peritoneal Dialysis (CCPD) / Automated Peritoneal Dialysis (APD): It uses a machine called a cycler. A cycler circulates dialysate solution in and out of the peritoneal cavity at evenly spaced intervals during the night for eight to 10 hours. In the morning, dialysate flows into the abdomen and the dialysate is carried in the peritoneal cavity during the day. During that time, patients do their daily activities. Before the patient goes to sleep, the catheter is reattached to the cycler, the fluid is drained out and the night exchanges are started. This cycle is repeated daily.

CONCLUSION: RRT has evolved into a unique modality that provides both short and long term support for patient's survival in the absence of renal function. Except the transport characteristics of the peritoneum, all other variables in RRT can be adjusted to achieve the desired response. Specific type of RRT for a particular patient should be carefully chosen considering various factors such as residual renal function, co-morbidities, hemodynamic stability, access to hospital services, work profile of the patient, physical environment and patient's desire.

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