

RENAL REPLACEMENT THERAPY IN ACUTE KIDNEY FAILURE - AN OVERVIEW

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Abstract

Renal failure is the loss of renal function, either acute or chronic, that results in azotemia and syndrome of uremia. Acute renal failure, is also known as acute kidney injury (AKI), is defined as an abrupt (within 48 hours) reduction in kidney function. The initial management of acute kidney failure involves treating the underlying cause, stopping nephrotoxic drugs and ensuring that the patient is euvolaemic with an adequate mean arterial blood pressure. However, no specific treatments have been shown to reverse the course AKF so Renal Replacement Therapy (RRT) is the cornerstone of further management. RRT therapy can be administered either intermittently or continuously. Multiple modalities of RRT are currently available. The purpose of this review is to familiarize different modalities of RRT for blood purification.

Keywords: acute kidney failure (AKF), renal replacement therapy (RRT), hemodialysis, peritoneal dialysis

INTRODUCTION

Main function of the kidney is to maintain the constancy of the 'interior environment' by eliminating waste products and by regulating the volume electrolyte content and p^H of the extracellular fluid¹. Renal failure is the inability of the kidney to excrete waste materials, concentrate urine and conserve electrolytes. It occurs suddenly (acute renal failure) in response to inadequate perfusion, kidney disease or urinary tract obstruction or it can develop slowly (chronic renal failure) as a result of kidney disease or anomaly. Acute renal failure refers to an abrupt, sudden deterioration in renal function resulting in retention of nitrogenous wastes and other biochemical derangement. Oliguria or anuria is the prominent feature, though rarely urine output may normal. The principal features of ARF are oliguria associated with azoemia, metabolic acidosis, and electrolyte disturbances². ARF associated with high mortality and morbidity (oliguric 50-80%) non oliguric (10-40%)³. Treatments of ARF include treatment of underlying cause, management of complications of renal failure and dialysis. RRT therapy indicated in patients with severe kidney injury. The initiation of RRT in patients with AKF prevents uremia and immediate death from adverse complications of renal failure⁴. The use of RRT becomes necessary when the kidney can no longer remove wastes, maintain electrolytes, and regulate fluid balance. This can occur rapidly or over a long period of time and need for replacement therapy can be acute (short term) or chronic (long term). The main RRT include various types of dialysis and kidney transplantation⁵.

RENAL REPLACEMENT THERAPY (RRT)

RRT is any treatment modality that seeks to replace the excretory function of the kidney. RRT always uses a semipermeable membrane to achieve blood purification. It can be intermittent or continuous⁶. Conventional indications for RRT in AKF include fluid volume excess, hyperkalemia, metabolic acidosis and uremia. This therapy can also be used for drug overdose⁷.

MECHANISM OF SOLUTE REMOVAL

Although the basic principles of these replacement therapies are similar, clearance rate, i.e. extent of solute removal varies. It involves mainly four mechanism, Diffusion, Convection, Adsorption and ultra filtration. In all types of RRT blood is presented to a dialysis solution across some form of semipermeable membrane that allows free movement of low molecular weight compounds⁸.

Semipermeable membrane is the basis of all blood purification therapy. They allow water and some solutes to pass through the membrane, while the cellular components and other solutes remains behind. The water and solutes that pass through the membrane are called ultra filtrate. Two types of membranes are used in RRT, cellulose and synthetic⁹.

1. Ultra filtration

Ultra filtration refers to the passage of water through a membrane under pressure gradient. Rate of ultra filtration will depend upon the pressure applied to the filter and on the rate at which the blood passes through the filter. Higher pressure increases the rate of ultra filtration.

2. Diffusion

Diffusion is the movement of solute across a membrane via a concentration gradient. When solute across a membrane they always shift from an area of higher concentration to an area of lower concentration until the solute concentration on both sides of the membrane are equal. Diffusion depends upon concentration differences between blood and dialysate and molecule size¹⁰.

3. Convection

It is the movement of solutes through a membrane by the force of water. Larger molecule cleared more effectively by convection¹¹.

4. Adsorption

Adsorption is the removal of solutes from the blood because they attach to the membrane. High level of adsorption can cause filters to clog and become ineffective¹².

TYPES OF RENAL REPLACEMENT THERAPY (RRT)

- Peritoneal dialysis
- Hemodialysis
- Hemofiltration
- Kidney transplantation

1. PERITONIAL DIALYSIS

Peritoneal dialysis is performed to remove toxic substance and metabolic wastes and reestablish normal fluid and electrolyte balance. It is a form of dialysis where special fluid is infused into the peritoneal cavity (a container in the stomach which is surrounded by arteries and veins through which blood flows). The excess waste from these blood vessels diffuses into the fluid through a semipermeable that encloses the peritoneal cavity. The peritoneal membrane used as semipermeable membrane across which excess waste and fluids move from blood in peritoneal vessels in a dialysate solution that has been instilled in to the peritoneal cavity. Peritoneal dialysis involve repeated cycles of instilling dialysate. Maximum exchange happening in first five min. Equilibrium happens between blood and dialysate with in 15-30 min.

PROCEDURE FOR PERITONIAL DIALYSIS

1. Preparation of the patient

Before catheter insertion, the client must be fully prepared for PD. The patients need to know exactly what will happen and what to do during the dialysis. Obtain informed consent from the patient. Monitor temp, BP, Pulse, respiration, body weight and serum electrolyte levels before dialysis. Encourage the patient to empty their bladder and bowel to decrease the risk of puncturing internal organs. Make tube air free and flush with dialysis solution. The dialysate is warmed to the body temperature to prevent the discomfort and abdominal pain and to dilate the vessels of the peritoneum to increase the urea clearance. Add heparin to prevent the blood clotting and result occlusion of the catheter. Administer the broad spectrum antibiotic to prevent infection.

2. Peritoneal dialysis access

A catheter or a flexible hollow tube is surgically placed in lower abdomen. The preferred insertion site 3-5cm below the umbilicus (an area that is relatively avascular). Before the procedure skin is prepared with a local antiseptic to decrease the skin bacteria and risk of contamination and infection. A peritoneal catheter is placed into the patient's peritoneal space between the two layers of the peritoneum below the waistline, which help to the exchange of draining dialysate from the abdomen and introduction of fresh dialysate in to the abdomen.

3. Peritoneal dialysis treatment

The entire exchange takes 1-4 hrs, depending on the prescribed dwell time (it is the length of time the dialysis solution stays in the peritoneal cavity during peritoneal dialysis). Exchange process has three steps a) filling or infusion b) dwell time c) draining

Filling step involves instilling a bag of sterile dialyzing solution into the patient's peritoneal cavity through catheter by gravity. The amount of solution 1500-2000ml which is infused with in 5-10 min. the solution is left to dwell in the abdomen for several hours, allowing time for the waste products from the blood to pass through the peritoneal membrane into the dialysate solution. At the end of dwell time the drainage occurs. The tube is unclamped and the solution drains from the peritoneal cavity by gravity. Drainage phase usually completed in 10- 30min. (figure: 1)

The drainage fluid is normally colorless or straw colored and should not be cloudy. Urea, creatinine, and metabolic end products are cleaned from the body by diffusion, osmosis across the peritoneal membrane. Urea is cleared at the rate of 15 -20 ml/min^{13,17}.

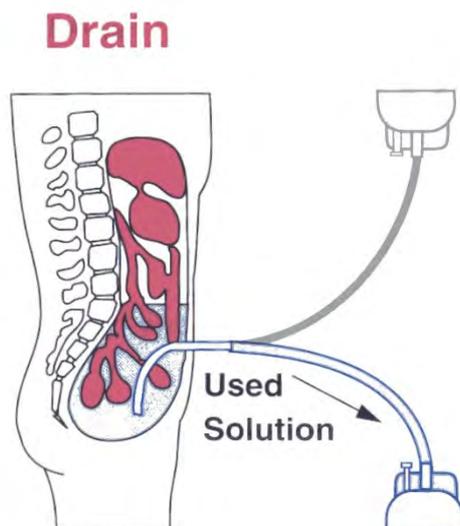


Figure 1:- peritoneal dialysis

COMPLICATIONS OF PERITONIAL DIALYSIS

Peritonitis is the most significant complication. It is frequently caused by *S. epidermidis* (30%) or *S. aureus* (10%), Catheter exit – site infection is most often caused by *S. aureus* and *pseudomonas* species. Weight gain - dextrose in dialysate solution serves as an osmotic agent for removal of fluid during each exchange and contributes about 500 – 1,000 calories absorbed from dextrose in peritoneal dialysis solutions Fluid leakage, back pain and abdominal hernias.^{14, 8}

2. HEMODIALYSIS

Hemodialysis is a therapy that filters waste, removes extra fluid and balances electrolytes. It is a form of dialysis where the blood in the body is continuously removed and passed through an artificial kidney which cleans it. Diffusion, osmosis, and ultra filtration are the principles on which hemodialysis is based. The dialysis machine pumps blood through the dialyzer. The newly cleaned blood flows out of the dialyzer and returned to blood stream. It removes extra fluid and wastes from body by constantly moving blood through the filter. The filter known as dialyser or artificial kidney is used with a dialysis machine. Hemodialysis usually lasts about 3-4 hours each week. This is the best therapy for sever hyperkalemia.¹⁵

1. DIALYZER

The blood is removed from the body and filtered through a manmade membrane called dialyzer, or artificial kidney, and the filtered blood is returned to the body .The dialyzer have semipermeable membrane composed of cellulose based or other synthetic material. These semipermeable membranes do not allow blood cells and protein to pass through because they are too big.

2. DIALYSATE

Also called dialysis fluid, it is a solution of pure water, electrolyte and salts such as bicarbonate and sodium. The purpose of dialysate is to pull toxins from the blood into dialysate. The way this works is through a process called diffusion. Due to difference in the concentration. The waste will move through the semipermeable membrane to create an equal amount on both sides. Electrolytes in the dialysis solution are used to balance electrolyte in the patient's blood¹⁶.

3. VASCULAR ACCESS

One important step before starting hemodialysis is preparing vascular access .An access create a way for blood to be removed from the blood , circulate through the dialysis machine and then return to the body at a rate that is higher than can be achieved through a normal vein. After the access is made and healed, two needles connected to the tubing are inserted into the access. One needle draws a small volume of blood out and pumps it through to the dialysis machine and filter. After the blood is filtered, it is return to the body through the other needle

Vascular access should be prepared weeks or months before the beginning of dialysis. In hemodialysis vascular access helps to the removal and replacement of blood with few complications.

In hemodialysis three methods to gain access to the blood.

1. Arteriovenous fistula
2. Arteriovenous graft
3. Central venous catheter

1. Arteriovenous fistula

This is more preferred type. It require a surgical procedure that create a direct connection between an artery and a vein either side of artery to side of vein or side of artery to end of vein or end of artery to side of vein .This can be done in the lower arm, can be done in upper arm well. The fistula takes 4-6 weeks to mature before it ready for use. This increase the amount of blood that flows through the vein and makes it bigger. This is the best access because fewer complications and long lasting.^{17, 25} figure: 2

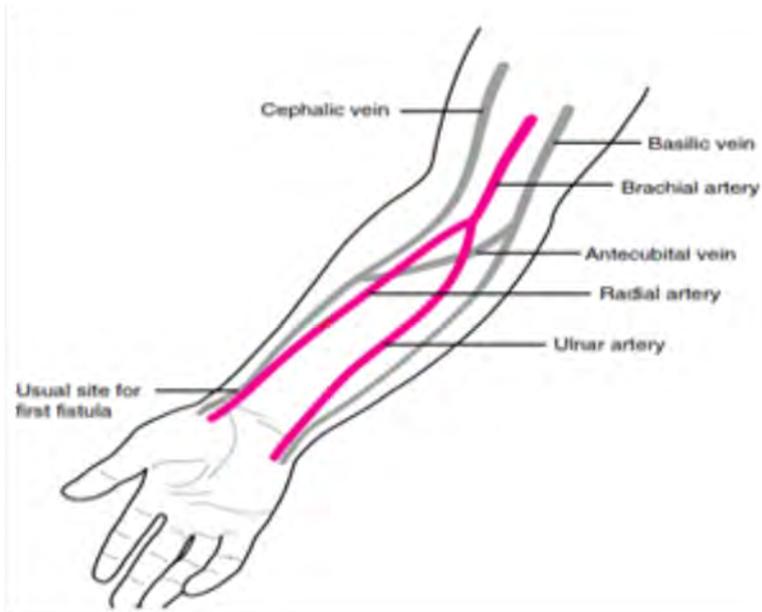


Figure 2:- Arteriovenous fistula

2. Arteriovenous graft

Sometime patient arm vein is not suitable for creating a fistula, in this case surgeon can use a flexible tube to create a path between artery and vein .this is called a synthetic bridge graft. Grafts are surgically placed between artery and vein. It can be placed in the upper arm forearm or upper thigh. Here artificial tubes are used to join between artery and vein. AV graft tend to mature fast and usable much faster than AV fistula, but they are artificial they tend to narrow and become infected more. Figure: 3

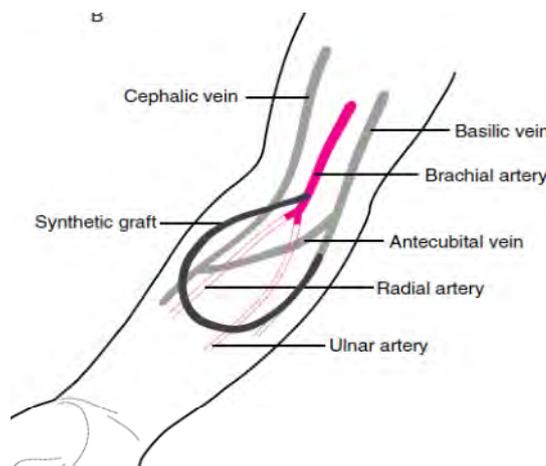


Figure 3:- Arteriovenous graft

3. Central venous catheter

Here a thin flexible tube that is placed in to a large vein. It may be recommended if dialysis must be started immediately and the patient does not have functioning AV fistula or graft. Central venous catheter will have two tubes from their access is connected to the blood tube that leads to the dialyzer and back to the body. Two types of catheter temporary and permanent. Temporary can use for one week. Permanent can be placed in the neck vein and tunneled under the skin. It is good for about one year. Catheter has a risk of infection and it is used only if a fistula or a graft can't be maintained^{17, 6 and 26}

PROCEDURE FOR HEMODIALYSIS

When a patient goes to hemodialysis a nurse or technician will check all vital signs. A small dose of anticoagulant may instill into the shunt in order to prevent the coagulation. Patient with vascular access (AV fistula or AV graft) have two needles one needle take blood out of the body, the other needles puts it back. There are two compartments within the dialyzer. Semipermeable membrane that will separate the two compartments. It will only allow the passage of certain sized molecule. As the blood pushed through the compartment in one direction at a flow rate of 200 – 500 ml/min. the suction or vacuum pressure pull the dialysate through the dialysate compartment in an opposite direction at a rate of 300 -900 ml/min. in this process the excess of fluid and water moves out of the blood stream . This process called ultrafiltration. second process is called diffusion, here the waste products in the blood moves through the membrane to the dialysate (mainly urea, creatinine and the nitrogen end product of protein metabolism). At the same time the electrolytes and other chemicals in the dialysate solution cross the membrane in to the blood compartment. Figure: 4

The purified, chemically balanced blood is then returned to the body through the second needle. Dialysis process lasts for 2 – 6 hrs. Most people undergo three dialysis sessions in each week. During dialysis patient receives medications to replace the hormones the kidney are unable to produce.^{18, 17, 13}

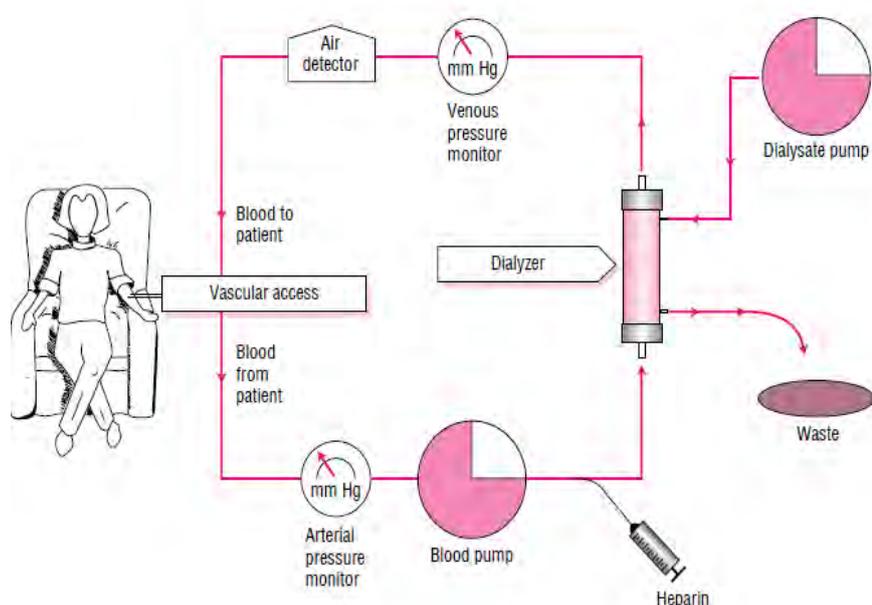


Figure: 4 hemodialysis

COMPLICATIONS OF HEMODIALYSIS

Hypotension is primarily caused by excessive fluid removal at a rate exceeding mobilization of fluid stores, or occasionally, by excessive heating of the dialysate and subsequent vasodilatations. Hypersensitivity - Anaphylaxis can develop secondary to dialyzer membrane or to ethylene oxide used to sterilize the dialyzer. Muscle cramps may be induced by excessive ultra filtration resulting in altered perfusion of the affected tissue. May be prevented with vitamin E 400 units nightly. Cerebral edema - rapid removal of urea lowers plasma osmolarity, shifts free water in to the brain, and induces cerebral edema. Thrombosis is the most common site cause for loss of vascular access site due to venous stenosis. Infection of the access site is usually caused by staphylococcus aureus or staphylococcus epidermidis^{19, 8}

3. HEMOFILTRATION

It is a type of renal replacement therapy similar to hemodialysis. It is the therapy in which the patient's blood passed through a machine which containing a semipermeable membrane where the waste products and water are removed. Replacement fluid is added and the blood is return to the patient body system. Various types of renal replacement therapy are available differentiated by whether arterial and or venous access is required²⁰.

Different types are available ie.

- Slow continuous ultra filtration(SCUF)
- Continuous venovenous hemofiltration(CVVH)
- Continuous venovenous hemodialysis(CVVHD)
- Continuous venovenous hemodiafiltration(CVVHDF)

Slow continuous ultrafiltration (SCUF)

It is used to removal of fluid by ultra filtration. This type is used when fluid removal is the prime therapeutic goal. While some urea is removed with plasma water, the rate of urea removal is slow. It is a slow process; it does not require a replacement fluid.^{21, 24} figure: 5

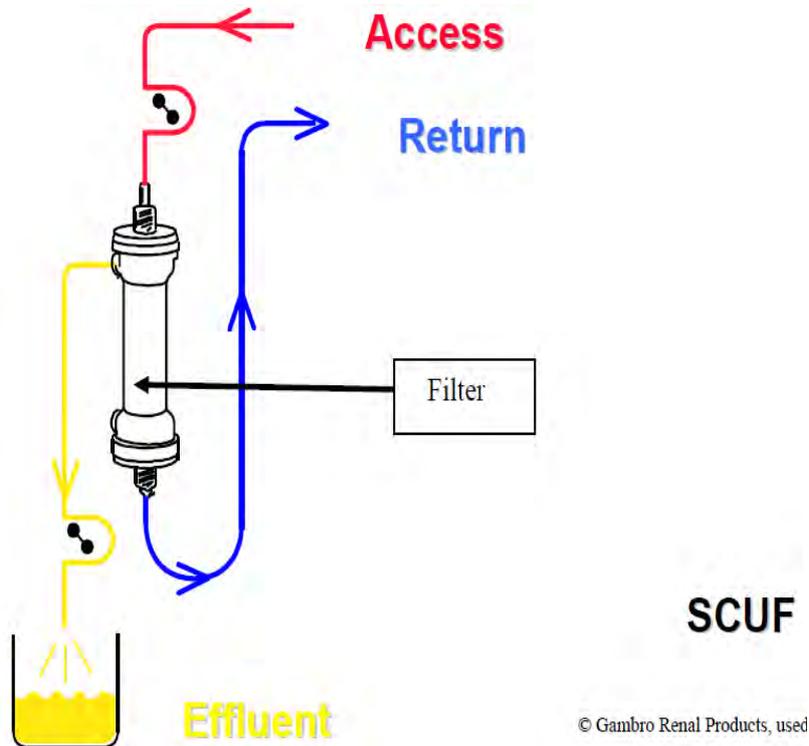


Figure 5:- slow continuous ultra filtration (SCUF)

Continuous venovenous hemofiltration (CVVH)

It works by convection. In CVVH the blood is removed and return through the venous access but in CAVH the blood is removed through the artery and return through the body by veins. Filtration rate is high, here replacement fluid is required. Figure: 6

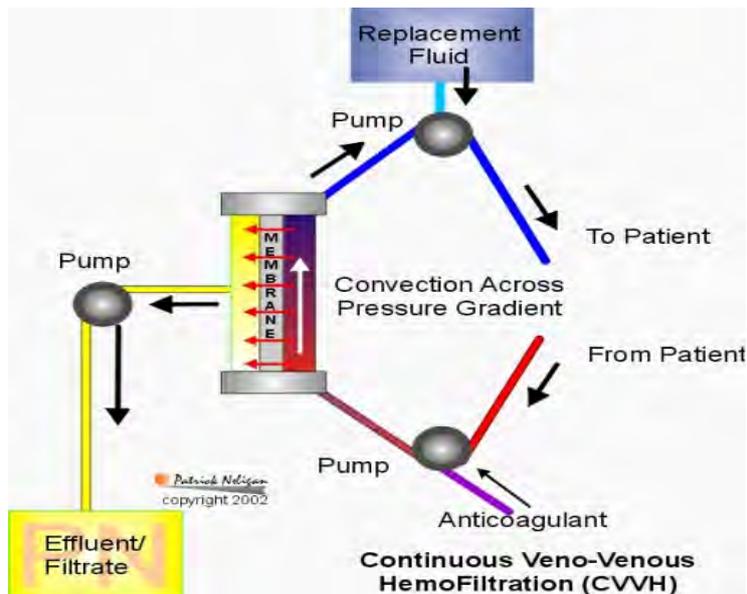


Figure 6: Continuous venovenous hemofiltration (CVVH)

Continuous venovenous hemodialysis (CVVHD)

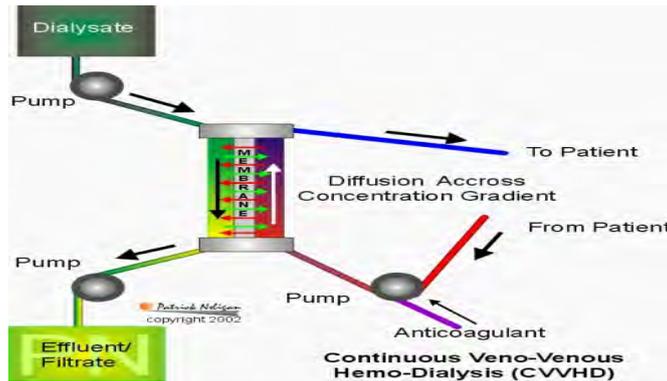


Figure 7:- Continuous venovenous hemodialysis (CVVHD)

It is a slow form of dialysis. Blood is removed and return through the venous access. Diffusion is the process used to remove waste and electrolytes. Mostly small molecules are removed .CVVH and CVVHD are most commonly used.²² figure: 7

Continuous venovenous hemodiafiltration (CVVHDF)

Here both convection and diffusion are the mechanisms remove fluids, waste particle and inflammatory mediators. Dialysis solution run in opposite to the blood flow and particle is removed by diffusion. In addition the replacement fluid is also added to promote convection. This method has best clearance but more expensive and technically challenging.^{23, 22} figure: 8

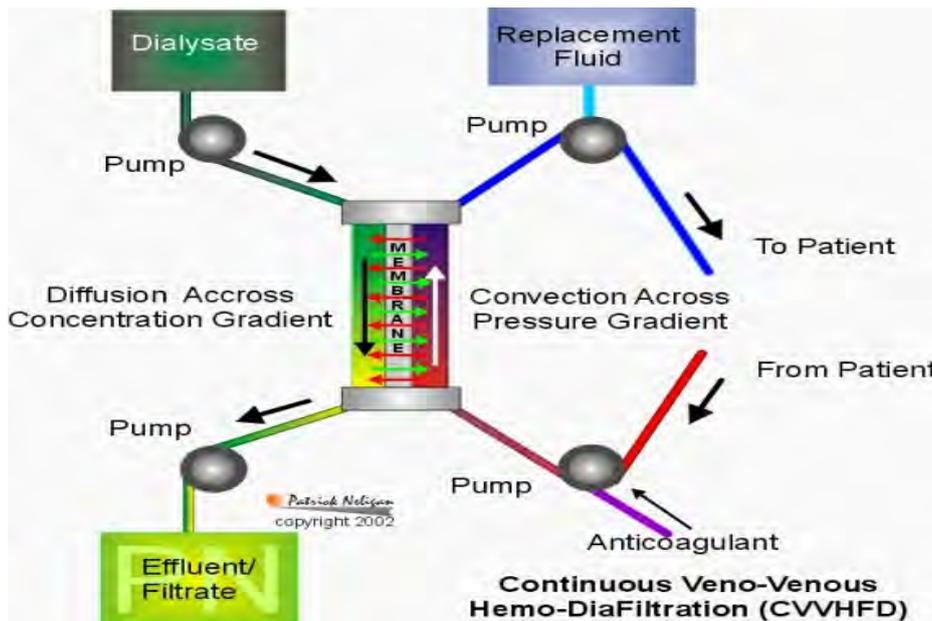


Figure 8: Continuous venovenous hemodiafiltration (CVVHDF)

4.KIDNEY TRANSPLANTATION

All patients with end stage renal disease are potential candidates for kidney transplantation unless contraindicated. Less than 50% of patients who undergo kidney transplant experience an acute allograft rejection episode and rates as low as 20% have been reported during the first year after transplantation. After kidney transplantation, the initial renal function can reflect excellent, moderate or delayed graft function (DGF). DGF reduces kidney graft survival and complicates a patients early management because of the need for dialysis, prolonged length of hospital stay, and increase cost of therapy. Rejection of transplanted kidney can be categorized as hyper acute (within minutes to hours); accelerated (within 2 – 6 days); acute (within 7 – 10 days); humoral (within 1 week to 3 months); or chronic (within 3 months – one year). High- dose corticosteroid therapy reverses the majority of acute rejection episodes and often is the first line therapy of acute kidney rejection.⁸

DONOR

Kidney transplantation means requirement of a failed kidney with a working kidney from other person called a donor. Donor should have compatible blood group. Age should be between 18 – 65 years. Should not have major disease.

DONOR AND RECIPIENT MATCHING

Can be divided into three distinct areas

- Blood group
- Tissue typing

WBC is a special marker called antigen on their surface. It is called human leukocyte antigen (HLA)

The HLA of donor and recipient should be match so the chance of success also increases.

- Cross match

Just prior to the transplant, blood is taken from donor and recipient and mixed to ensure no reaction i.e. Negative cross match.

THE TRANSPLANT OPERATION

The transplant operation takes around 3 -4 hrs. The transplant kidney is placed left or right side of the lower abdomen, below the navel. The new kidney's artery and vein are joined to an artery and vein in the pelvic area. The ureter from the kidney is attached to the bladder.^{13, 17}

CONCLUSION

RRT is indicated in a patient with ARF when kidney function is so poor that life is at risk. However, it is desirable to introduce RRT therapy early in ARF, as complications and mortality are reduced. Generally, the use of RRT becomes necessary when the kidney can no longer remove wastes, maintain electrolytes, and regulate fluid balance. There are various forms of RRT but they all are removing unwanted solutes using the process of diffusion (dialysis) and or convection (filtration). The main RRT include the various types of dialysis and kidney transplantation. Successful kidney transplantation eliminates the need for dialysis. Not only is the quality of life much improved in patients with ESRD who undergo transplantation, but physiologic function is improved as well.

REFERENCE

- [1] Rang and Dale's Pharmacology, sixth edition page no: 369
- [2] Essentials of pediatric nursing by Rimple Sharma page no: 470-475
- [3] 3. Purdava, ARF in Allman K. G and Wilson I.H, Oxford handbook of anesthesia, Oxford university press 2001; 116 -118.
- [4] <http://www.uptodate.com/contents/RRT>
- [5] Clinical pharmacy and therapeutics by Roger Walker, Cate Whittle Sea, Fourth edition, Page no: 250 – 260
- [6] Pharmacotherapy, A pathophysiological approach, By Joseph t. Dipiro, Robert L. Tolbert, Sixth edition Page no :761- 821.
- [7] Palevsky P, Indication and timing of RRT. Crit Care Med 2008;36, s224 – s228.
- [8] Handbook of applied therapeutics by Mary Anne Koda – Kimble, Lloyd yee young, Wayne a. Kradjan, eighth edition. Page no: 34.2, 32.1 – 32.3.
- [9] Konstantin P. Newer Membrane: Cuprophane Versus Polysulfone Versus Polyacrylonitrile In: Bosch Jp, Ed. Hemodialysis: High Efficiency Treatments. Contemporary Issues in Nephrology. New York, Churchill Livingstone 1993; 27:63 - 78
- [10] Cooper and Gunn's Tutorial Pharmacy Edited by S. J Carter, Page No: 55, 60,106.
- [11] Bentley's Text Book of Pharmaceutics, Eighth Edition Edited by E. A Rawlins Page No: 119.
- [12] Pharmaceutics the science of dosage forms edited by M. E Aulton, second edition, page no: 39,587
- [13] Brunner and Siddhartha's text book of medical and surgical nursing, twelfth edition, volume 2, page no: 1328- 1345.
- [14] Remington, The science and practice of pharmacy, vol II; page no: 1151-1152
- [15] Physical Pharmacy Fourth Edition Alfred Martin Page No: 324, 328,353.
- [16] A Text Book Of Hospital Pharmacy By Dr. R. K Goyal And R. K Parikh, B. S Shah, Page No: 106.
- [17] Assessment and management of Clinical Problem by Leiwis, Heitkemper Chintamani, Page no: 1222 – 1230.
- [18] Comprehensive Medical and Surgical Nursing, Part –A by Javed Ansari, Page no 700-720
- [19] Biopharmaceutics and clinical pharmacokinetics by Milo Gibaldi, page no: 275 - 277.
- [20] Applied biopharmaceutics and pharmacokinetics, 5th edition by Leon Shargel, Susanna Wu-pong, Andrew B.C Yu, page no: 675-692, 697-704.
- [21] O' Reilly P, Tolwani A, RRT III; IHD, CRRT, SLED. Crit care clin 2005; 21 (2); 367- 378
- [22] <http://www.baxter.com/healthcareprofessionals>
- [23] Metha RI, Mc Donald BR, Aquilar MM Ward DM; Regional citrate anticoagulation for continuous arteriovenous hemodialysis in critically ill patients kidney int 38 976-981.
- [24] Intensivecare.hsnet.gov.au
- [25] Ronco C, Bellomo R, continuous high flux dialysis an effect of renal replacement. In Vincent JL. Ed1996, 690-698
- [26] Lauer A, Saccaggin A, Ronco C, Belledone M, Glabmas, Bosch JP, continuous arteriovenous hemofiltration in critically ill patients Ann Intern Med 1983;- 99