

Dialysis in the Acute Setting

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October 8, 2015

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Citation: Malhotra K, Dialysis in Acute Setting. Journal of Academic Hospital Medicine 2015, Volume 7, Issue 4.

Acute kidney injury (AKI) is frequently encountered in the hospital setting. It may be present on admission or may develop during the hospital stay. Early and consistent recognition of AKI has been a challenge. This has led to the development of RIFLE and AKIN criteria for the definition of AKI. Acute Kidney Injury Network (AKIN) defines AKI as an abrupt (within 48 hours), absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dL from baseline; a percentage increase in the serum creatinine concentration of ≥ 50 percent; or oliguria of < 0.5 mL/kg per hour for more than six hours. Additionally, the definition should be applied after volume resuscitation and exclusion of urinary tract obstruction if oliguria was used as the sole criterion[1].

Acute tubular necrosis (ATN), sepsis and pre-renal causes account for majority of the cases of AKI [2, 3] in hospitalized patients. The recovery can be rapid or delayed depending on the severity of initial insult, its duration, hemodynamic status, comorbid conditions including pre-existing chronic kidney disease, nephrotoxic agents and urinary output. The management of AKI is usually supportive and includes volume optimization, management of potassium, calcium, acidosis and signs of uremia. Renal replacement therapy (RRT) or dialysis is indicated in severe disease.

Indications for Dialysis

1. Refractory fluid overload
2. Hyperkalemia- refractory to medical management, life threatening or rapidly rising
3. Metabolic acidosis
4. Dialyzable drug (medication, recreational or illicit)
5. Signs of uremia

The timing for initiation of dialysis is a controversial topic. While it is recommended that early initiation of RRT has better outcomes, most studies have limitations like lack of randomization, low power, selection bias, non-standardization of definitions of AKI, modality of RRT and indication for dialysis. This has led to variation in clinical practice and lack of consensus. Clinical practice guidelines for AKI[4] recommend

1. Initiating RRT emergently when life-threatening changes in fluid, electrolyte, and acid-base balance exist.
2. Considering the broader clinical context, the presence of conditions that can be modified with RRT, and trends of laboratory tests rather than single BUN and creatinine thresholds alone when making the decision to start RRT.
3. Discontinuing RRT when it is no longer required.

Acute hemodialysis prescription

This involves decision on the modality of dialysis, the choice of hemodialysis membrane, the choice of dialysate, blood flow rate, ultrafiltration amount and rate, choice of anticoagulation, dialysis dose, and the length of dialysis.

Dialysis access

Arteriovenous (AV) – In patients with pre-existing AV fistula or graft. Here the systemic blood pressure drives the blood into the extracorporeal circuit via an arterial needle, which after dialysis is then returned via a venous needle.

Venovenous (VV) – Requires one double lumen catheter (occasionally two catheters are used) to be placed in a vein. It requires an extracorporeal blood pump to circulate blood through the dialysis machine.

Dialysis Modality

There are many dialysis modalities available including peritoneal dialysis (if already being used as an outpatient), intermittent hemodialysis (IHD), sustained low efficiency hemodialysis (SLED) and continuous renal replacement therapy (CRRT). CRRT includes continuous hemofiltration, hemodialysis or a combination of the two i.e. hemodiafiltration.

Hemofiltration is a convective therapy in which hydrostatic transmembrane pressure (TMP) gradient forces plasma water across the membrane. Small and middle molecular weight solutes move in the same direction across the membrane due to solvent drag, resulting in their removal. A replacement or substitution fluid is required to prevent excessive fluid removal and optimization of electrolytes.

Hemodialysis involves diffusion of solutes from high concentration compartment to low concentration compartment across the dialysis membrane. The blood and the dialysate move in opposite direction across the membrane to maximize the concentration gradient. Toxins, urea, creatinine, potassium and phosphorus usually move from blood to dialysate and bicarbonate moves from dialysate into blood.

General principles of diffusion that apply are

1. Solutes diffuse across the dialysis membrane down the concentration gradient.
2. Net diffusion stops when concentration is equal on both sides
3. Greater the concentration gradient, greater is the rate of diffusion. As a result, as the

concentration gradient decreases over time, rate of diffusion decreases as well.

Diffusion flux (J_x) is also influenced by –

1. Surface area of membrane (A)
2. Thickness of membrane (dx)
3. Temperature of dialysate (T)
4. Concentration gradient across membrane (dc)
5. Diffusion coefficient of the solute (D)

$$J_x = D \cdot T \cdot A \cdot (dc/dx) [5]$$

Hemodiafiltration is a combination of both convection and diffusion.

Continuous replacement therapies

1. Continuous arteriovenous hemofiltration (CAVH)
2. Continuous venovenous hemofiltration (CVVH)
3. Slow continuous ultrafiltration (SCUF)
4. Continuous arteriovenous hemodialysis (CAVHD or CAVD)
5. Continuous venovenous hemodialysis (CVVHD or CVVD)
6. Continuous arteriovenous hemodiafiltration (CAVHDF)
7. Continuous venovenous hemodiafiltration (CVVHDF)
8. Continuous equilibrium peritoneal dialysis (CEPD)
9. Continuous-flow peritoneal dialysis
10. Sustained low efficiency (SLED) or extended daily dialysis (EDD)

Dialysis membranes

The membrane can be low flux or high flux membranes. High flux membranes contain larger sized pores that allow diffusion of large molecules. Low flux hemodialysis is defined as ultrafiltration coefficient of dialyzer less than 20 mL/h/mmHg whereas high flux hemodialysis is more than that. Studies have demonstrated no statistical significant difference in all-cause mortality between high flux versus low flux groups and in fact have shown a lower relative risk for mortality for patient undergoing dialysis with high flux membranes [6-8]. A Cochrane database systemic review concluded that high flux hemodialysis may reduce cardiovascular mortality by about 15% [9]. This has been generally attributed to enhanced middle molecular clearance by the high flux membranes. The downside to high flux membranes is that they can also allow waterborne pathogens and endotoxins to come into blood, therefore it should be used with only ultrapure water [6]. When a patient with chronic kidney disease is initiated on dialysis for the first time, a rapid reduction in blood urea nitrogen (BUN) levels can cause dialysis disequilibrium syndrome. To prevent this the first few sessions admit to be deliberately less efficient for a gradual decline in BUN levels. This is achieved by utilizing a low flux membrane, although surface area membrane, lower blood flows and shorter duration.

Dialysate composition [5, 10, 11]

The dialysate is made up of sodium, potassium, bicarbonate buffer, calcium, magnesium, chloride and glucose. For the purpose of acute hemodialysis, dialysate composition can be customized to meet the needs of a particular patient. Trace elements, including water-soluble metals, micronutrients, minor acids and folate are lost during dialysis since they are absent in the dialysate.

Bicarbonate – The amount of bicarbonate added to dialysis depends on patient's acid base status. If the predialysis plasma bicarbonate level is 28 mmol/L or higher, or if the patient has respiratory alkalosis then the dialysis solution should contain an appropriately lower bicarbonate level, for example 25-28 mmol/L, depending on the degree of alkalosis [10]. This is important since even mild metabolic alkalosis can cause the blood pH to rise to a high level. In patients with severe metabolic acidosis and plasma bicarbonate level less than 10 mmol per liter the goal of treatment should be to reach plasma bicarbonate level of 15-20 mmol per liter post dialysis. Excessive correction of severe metabolic acidosis can cause lowering of the ionized calcium level, paradoxical acidification of cerebrospinal fluid and increased tissue production of lactic acid.

Sodium- Sodium is generally kept at physiological concentration except when patient has hypo-or hypernatremia. If the patient has chronic hyponatremia then sodium shouldn't be corrected rapidly to prevent osmotic demyelination syndrome. The maximum safe rate of correction of serum sodium is recommended to be in the range of 6-8 mmol per liter in 24 hours. This can be achieved by using the lowest possible dialysate sodium with or without other hypotonic solutions like 5% dextrose. Similarly in hypernatremic patients dialysate sodium should be set closer to plasma sodium with gradual administration of hyponatric fluids and then gradually decreasing dialysate sodium to normal plasma level. In such cases the serum sodium should be monitored on an hourly basis. Since CRRT is a slower treatment, it is safer than intermittent hemodialysis for such patients.

Potassium- In patients with hyperkalemia and a potassium level of more than 5.5 mmol per liter, dialysis solution potassium level of 2.0 is appropriate in stable patients who are undergoing intermittent hemodialysis. In extended therapies, care should be taken to avoid life-threatening hypokalemia, especially in patients prone to arrhythmias. Dialysate solution potassium of 4 mmol per liter is appropriate for extended therapies. If the potassium level is more than 7.0 mmol per liter then it may be appropriate to use a lower potassium bath that can be raised later when the serum potassium level is in safe range. The dialysate potassium of zero is extremely dangerous and should not be prescribed.

Calcium- The dialysate calcium concentration is usually 2.0-3.0 mEq per liter. Dialysis can be used to lower the calcium level in acute hypercalcemia, with a 2.0-2.5 mEq per liter dialysate calcium level to avoid rapid decrease in serum calcium level that can cause tetany or seizures. Serum ionized calcium concentration should be measured frequently, along with frequent clinical examination. Patients who undergo extended dialysis treatments with citrate anticoagulation need a calcium chloride drip that needs to be titrated to achieve desired normal serum calcium level. Citrate is infused in the extracorporeal circuit and it chelates calcium thus anticoagulating the circuit.

Phosphate- Patients who are on intermittent hemodialysis usually have high phosphate levels however hypophosphatemia can occur in extended dialysis treatments and is usually avoided by giving phosphate as a supplement in the CRRT fluids or as a separate supplement by enteral or parenteral route.

Magnesium- The usual dialysate magnesium concentration is 0.5-1.0 mEq per liter.

Ultrafiltration [4, 10, 12, 13]

In a critically ill patient with acute kidney injury, the estimation of volume status is challenging. It is determined by physical examination, laboratory values, vital signs and other hemodynamic indices like CVP.

In ESRD patients undergoing chronic maintenance hemodialysis the determination of the 'target weight' aka 'dry weight' is done empirically as the weight at which clinical sign of extracellular fluid expansion (hypertension, edema and shortness of breath) are absent and when they develops signs of volume depletion (hypotension, tachycardia, symptoms of orthostatic hypotension and cramping). These variables can change based on clinical acute events in the hospital. For example, if the patient undergoes limb amputation, the dry weight would have to be reestablished, or if the patient is admitted for acute coronary syndrome then rapid removal of fluid may lead to worsening ischemia.

In patients who are critically ill and have acute renal failure, fluid removal goals have to be taken in a broader clinical picture that includes hemodynamic status that is necessary to maintain optimal circulatory and oxygenation needs.

Fluid overload is being increasingly recognized as an important factor associated with adverse outcomes.

Anticoagulation[5]

Anticoagulation is needed to prevent blood from clotting after contact with the plastic and artificial surfaces in the extracorporeal dialysis circuit.

Reasons for clot in the circuit

1. Suboptimal or inadequate anticoagulation
2. Poor quality vascular access
3. Poor attention to optimal machine operation
4. Sudden changes and patient positioning that can alter catheter function
5. Decreased blood flow
6. Induced clotting due to stasis

Increasing the dose of anticoagulation for all the causes other than the first one can be dangerous. Therefore every clotting episode should be analyzed and troubleshooted accordingly.

Different options for anticoagulation are

1. Heparin anticoagulation-
2. Most commonly used
3. May cause heparin induced thrombocytopenia
4. Patient's clotting time is less frequently monitored for the purpose of circuit anticoagulation. APTT is monitored to ensure adequate therapeutic anticoagulation.
5. Regional Citrate anticoagulation-
6. This involves infusion of citrate into the blood circuit which combines with ionized calcium to form citrate calcium complexes. This decreases the ionized calcium in the circuit and prevents coagulation of the blood. Calcium is then infused separately into patient in the form of calcium chloride.
7. Some citrate leaks into the patient's blood and is metabolized by the liver. Therefore, patients with liver failure can develop citrate toxicity.
8. Argatroban- this can be used in patients with heparin-induced thrombocytopenia
9. Bivalirudin- this is an alternative to Argatroban in patients with both kidney and liver failure. It has a short half-life, reversible thrombin binding and extrarenal and extrahepatic clearance mechanism.
10. No anticoagulation

Peritoneal dialysis[10, 14]

ESRD patient already on PD can continue on their home prescription while they are admitted to the hospital. Although underutilized, PD is also a viable option for acute renal failure in patients who have hemodynamic instability, coagulation issues or when other modalities are not readily available. PD requires a catheter the tip of which rests in peritoneal cavity in the pelvic region. The dialysate fluid is then delivered by the catheter into the peritoneal cavity and allowed to sit there for 1-4 hours depending on clinical need and then drained subsequently. This is called an exchange and PD prescription may require multiple exchanges to achieve the goals. Its salient features are as follows-

1. Acute PD requires long sessions since it's a slower treatment. An average session may last for 48-72 hours with multiple 1-2 hour exchanges.
2. PD dialysate comes in standard solutions of 1.5, 2.5, 4.25% dextrose. 4.25% dextrose achieves maximum ultrafiltration because of higher dextrose gradient and is the fluid of choice for rapid fluid removal.
3. PD solution should be warmed to body temperature to avoid discomfort and vasoconstriction.
4. The usual volume or exchange is around 2 L in a 60 to 80 kg adult. It may be more in the patient who is bigger in size or in a patient who is not achieving effective clearance. It may be less in a patient who is small in size or in patients with respiratory insufficiency, hernias or leakage.
5. Heparin may be added to the dialysate to prevent fibrin clot formation that can obstruct the peritoneal catheter. It should be noted that heparin is not absorbed through peritoneal cavity so it does not cause systemic anticoagulation.

6. Insulin can be administered intraperitoneally in diabetic patients on PD.
7. Standard PD solutions do not contain potassium but it can be added to the PD solution to prevent hypokalemia and to maintain normal serum potassium level.
8. In ESRD patient who are undergoing regular PD and are using icodextrin solution, regular glucometer should not be used and serum glucose testing should be done in the lab or by special glucometers that are more specific for glucose. Absorbed icodextrin is metabolized to maltose that reacts with GDH-PQQ test strips in point-of-care glucose meters [15]

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