End-stage Renal Disease (ESRD) and Hemodialysis (HD) in CDU

Joseph J. Jean, MD
PGY-3

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General Overview

What is ESRD?

Irreversible loss of renal function that results in accumulation of >70 chemicals causing the clinical syndrome of uremia.

- Uremia is fatal without renal replacement therapy:
  - Renal transplant
  - Dialysis, either hemodialysis or peritoneal dialysis (PD)

What is hemodialysis?

- It is a substitution for the glomerulus of the kidney by using a filter to essentially replicate the function of the kidney
- Hemodialysis sessions are typically 3-4 hours long and require dedicated vascular access
- Blood is circulated through the dialysis machine where it flows through a filter with a dialysate flowing in the opposite direction

Brief pathophysiology of ESRD

Excretory Failure

- Uremic toxins include but not limited to: urea, cyanate, guanidine, polyamines, and ß2-microglobulin
- Uremia is more than just renal excretory failure leading to a toxidrome
  - Dialysis does not reverse all symptoms of uremia because many toxins are highly protein bound and thus non-dialyzable

Biosynthetic Failure

- Kidneys secrete erythropoietin and 1α-hydroxylase
  - 85% of erythropoietin produced by kidneys
  - 1α-hydroxylase catalyzes the conversion of calcifediol to calcitriol which is the active form of vitamin D
- Due to the erythropoietin and vitamin D deficiency, ESRD eventually leads to anemia and decreased GI Ca^{+} absorption, respectively

Regulatory Failure

- Due to regulatory failure in ESRD, an over-secretion of hormones disrupts the normal feedback mechanisms
- This results in excess free oxygen radicals which can react with carbohydrates, lipids, and amino acids to create advanced glycation end products
  - This process is linked to atherosclerosis and amyloidosis and may possibly explain the progressively worsening status of these conditions in ESRD

Overview of Clinical Complications Associated with ESRD and hemodialysis

Neurological Complications

- Peripheral neuropathy is a common complication of ESRD with greater lower extremity versus upper extremity involvement
  - Hemodialysis does not seem to improve autonomic dysfunction
  - Medical management is marginally effective
- Stroke occurs in 6% of hemodialysis patients
  - Approximately half are ischemic and the other half are hemorrhagic
- Subdural hematomas occur 10x more frequently in dialysis patients versus general population

Neurological Complications

- Uremic encephalopathy is a constellation of non-specific symptoms that may appear as a stroke mimic or a gradual decline in neurologic function over a few days
- Dialysis dementia presents with non-specific progressive neurological decline that is irreversible and often fatal
  - Usually takes at least 2 years since initiation of dialysis to become evident
  - 2-4 year survival is 24%
  - Not reversed nor progression halted by increased dialysis frequency or renal transplantation

Cardiovascular Complications

- Mortality from cardiovascular disease is 10-20x higher in dialysis patients versus general population
- Multifactorial etiology of cardiovascular disease that includes: pre-existing conditions, uremia, and dialysis related complications
- Elevated troponins in asymptomatic patients common and reflect left ventricular hypertrophy and microvascular disease

Cardiovascular Complications

- Hypertension in ESRD largely attributable to increased total peripheral resistance but other contributing factors include: increased blood volume, decreased vascular compliance, the vasopressor effects of native kidneys, the renin-angiotensin system, and the sympathetic nervous system
- Uremic cardiomyopathy is a diagnosis of exclusion and dialysis rarely improves left ventricular function

Cardiovascular Complications

- Uremic pericarditis will not have the typical EKG changes of acute pericarditis
  - Inflammatory cells do not penetrate into the myocardium, thus EKG changes are absent
  - Related to fluid overload, abnormal platelet function, and increased fibrinolysis and inflammation
- Dialysis-related pericarditis related to increased catabolism (such as trauma or sepsis), inadequate dialysis (such as missed sessions), or vascular access problems

Cardiovascular Complications

- In critically ill ESRD patients, cardiac tamponade can present without classic findings, instead presenting with altered mental status, hypotension, or shortness of breath
- Heart failure in ESRD commonly caused by (in descending order): hypertension, coronary artery disease, and valvular defects
  - Causes unique to ESRD include uremic cardiomyopathy, fluid overload, and AV fistula related high-output failure

Hematologic Complications

- Anemia not only due to decreased erythropoietin but also blood loss from dialysis, frequent phlebotomy, and decreased red blood cell survival times
- Bleeding diathesis caused by decreased platelet function, abnormal platelet-vessel wall interactions, altered von Willebrand factor, anemia, and abnormal production of nitric oxide
  - Increased risk of GI tract bleeding, subdural hematomas, subcapsular liver hematomas, and intraocular bleeding

Hematologic Complications

- Increased risk of infection due to depressed leukocyte chemotaxis and phagocytosis
  - Dialysis does not improve immune function and may exacerbate immunodeficient state by inappropriate complement activation after exposure to hemodialysis filter membranes
- Accumulation of phosphate leads to metastatic calcification and pseudogout

Hematologic Complications

- Dialysis-related amyloidosis (β2-macroglobulin) can occur in patients >50 years of age and on dialysis for >10 years
  - Amyloid can deposit in the GI tract, bones, and joints and consequently lead to GI perforation, bone cysts with pathologic fractures, and arthropathies
  - Patients with amyloidosis have higher mortality rates versus patients who do not

Emergent Hemodialysis in ESRD

Important history

- Cause of ESRD
- Dialysis schedule
- Any missed sessions?
- Currently making urine?
- Any recent complications of dialysis?
- Baseline dry weight, lab values, and vital signs
- Average weight gain between sessions
- Achieve dry weight by end of dialysis session?
- Hypotension during dialysis?
- Vascular access
- Symptoms of uremia
- Still have native kidneys?

Indications For Emergent Dialysis in ESRD

1. Fluid overload (51%)
2. Hyperkalemia (18%)
3. Severe acid-base disturbances

Fluid Overload

- Can cause pulmonary edema, though need to evaluate if acute myocardial ischemia is the potential cause
- Temporize with supplemental oxygen, BiPAP, nitrates, and ACEi
- Even in patients who make minimal urine, a loop diuretic may help due to their short-lived vasodilatory effect
- **Hemodialysis is the definitive treatment for fluid overload in ESRD**

Hyperkalemia

- Potassium is predominantly excreted by the kidneys (approximately 80-90%)
- Hyperkalemia defined as K^+ >5.5mEq/L
  - Normal range 3.5 to 5.5 mEq/L
- Cardiac dysrhythmias are the most serious sequelae
  - Other common symptoms are neuromuscular dysfunctional weakness, paresthesias, areflexia, ascending paralysis, and GI effects

Hyperkalemia

- Diagnosis is confirmed on a basic metabolic panel but can have high suspicion with EKG findings:
  - K^+ 6.5-7.5: prolonged PR interval, tall peaked T waves, short QT interval
  - K^+ 7.5-8.0: P wave flattening, QRS widening
  - K^+ 10-12: QRS complex degrades into a sinusoidal pattern
- In chronic or slowly developing hyperkalemia, the above noted EKG findings may not be seen until higher K^+ levels

Hyperkalemia

- If EKG changes are present while K^+ levels are unknown, initiate emergency treatment of hyperkalemia immediately
  - Place on continuous cardiac monitoring and establish IV access
- Emergency intervention can be split into 3 modalities based on mechanism of action:
  - **Cardiac membrane stabilization -- this must be prioritized and done immediately**
  - Intracellular shift of K^+
  - Increased removal/excretion of K^+

Hyperkalemia: Membrane Stabilization

- Give 10% calcium chloride or 10% calcium gluconate
- Calcium chloride versus calcium gluconate
  - Can give either but note that CaCl contains 3 times the elemental calcium compared to calcium gluconate
- Calcium has short duration and can give repeat doses up to 4 times per hour
- Avoid calcium if patient is on digitalis
  - But can consider giving with digibind in severe hyperkalemia with advanced intraventricular conduction impairment (EKG with wide, low-voltage QRS complexes)

Hyperkalemia: Intracellular Shift

- Start nebulized albuterol
  - Beta agonist upregulates cyclic AMP to shift K^+ into cells
- Give insulin 5 units IV (renal dosing due to ESRD) and glucose 25 grams
  - Perform frequent blood glucose monitoring for hypoglycemia
- Consider giving sodium bicarbonate 50-150mEq IV if patient is in metabolic acidosis

Hyperkalemia: Removal/Excretion

- Consider furosemide 40-80mg IV if patient still makes urine
- Consider sodium polystyrene sulfonate (Kayexalate) 25-50g PO or PR
  - Use caution due to association with intestinal necrosis
- **Hemodialysis is the definitive treatment for hyperkalemia in ESRD**

Complications of Vascular Access

Vascular Access For Hemodialysis

- Arteriovenous (AV) fistula is created from a native artery and vein and is the preferred choice of vascular access
- When a native artery or vein cannot be used to create an AV fistula, an interposing vascular graft is created from an autologous vein, polytetrafluoroethylene, or bovine carotid artery
  - Grafts have higher complication rates and shorter functional life expectancies than native AV fistulas
- Third form of vascular access is a tunneled-cuffed catheter
  - Most common site is right internal jugular (IJ) vein

Complications of Vascular Access

- Vascular access complications account for more inpatient hospital days than any other complication related to hemodialysis
- Most common complications related to vascular access are inadequate flow and infection
- Other complications include: bleeding, ulcerated hemodialysis fistula, aneurysms, pseudoaneurysms, vascular insufficiency, and high-output heart failure

Inadequate Flow

- Thrombosis and stenosis of the vascular access are the most common cause of inadequate flow
  - Grafts have higher rates of stenosis than fistulas
  - No audible bruit or palpable thrill on physical exam
- Diagnosis by ultrasound
- IR for clot removal if within 24 hours otherwise consult vascular surgery

Infection

- Infection rates in AV fistulas range from 2-5% and approximately 10% in AV grafts over their functional lifetimes
- Approximately 50% of patients develop bacteremia after 6 months after having a dialysis catheter placed with 5-10% developing a serious complication: septic arthritis, osteomyelitis, epidural abscess, endocarditis, and death
- Most common organism is *S. aureus* followed by gram negative bacteria

Infection

- Plan for admission and have high suspicion for sepsis
- Collect blood cultures from catheter and from separate peripheral site
- Start vancomycin IV and piperacillin/tazobactam IV for broad spectrum coverage
- Consider work up for endocarditis, epidural abscess, osteomyelitis, and/or septic arthritis depending on history and physical

Bleeding

- Life-threatening hemorrhage is a rare but serious complication of AV fistulas and grafts
  - Can result from aneurysms, anastomosis rupture, or supra-therapeutic anti-coagulation
- Significant bleeding will need admission and vascular surgery to provide definitive treatment

Bleeding

- Temporizing measures include:
  - Direct pressure at minimum 5-10 minutes
  - Hemostatic sponge such as Gelfoam or Surgicel
  - Protamine sulfate 10-20mg IV for heparin reversal
  - Tourniquet proximal and distal to vascular access site
    - This is very temporary, only to prepare to place sutures or await emergent vascular surgery consult
  - Apply figure-of-eight suture
  - Consider tranexamic acid 10mg/kg IV
  - Consider initiating massive transfusion protocol

Pseudoaneurysm Versus Aneurysm

- Aneurysms result from repeated punctures and true aneurysms are very rare but can be life threatening in the event of hemorrhage
- Pseudoaneurysms result from subcutaneous extravasation of blood from puncture sites
- Diagnosis by doppler US or angiography
- Consult vascular surgery if either present

Vascular Insufficiency

- Vascular insufficiency distal to the vascular access on an extremity occurs in approximately 1% of patients
- Caused by preferential shunting of arterial blood to the venous side of the access
  - Also known as “steal syndrome”
- Symptoms include exercise pain, non-healing ulcers, and cool, pulseless distal extremities
- Diagnosis by doppler US or angiography
- Consult vascular surgery if present

High-Output Heart Failure

- When >20% of cardiac output is diverted through the vascular access, high-output heart failure can develop
- Branham sign: a fall in heart rate when vascular access is temporarily occluded
- Diagnosis by doppler US
- Vascular surgery for definitive treatment
  - Requires surgical banding to decrease flow through the access

Complications During Hemodialysis

Hypotension

- Hypotension is the most common complication during hemodialysis, occurring in approximately 50% of treatments
- Though on average 1 to 3L of fluid is removed over a 4 hour session, sometimes up to 2L/hr is possible
- Excessive ultrafiltration due to underestimating a patient's dry weight is the most common cause of intradialytic hypotension
  - Optimum dry weight is clinically defined when hypotension prevents further fluid removal

Hypotension

- Timing of when hypotension occurs can help narrow the differential diagnosis
- Early hypotension is usually due to pre-existing hypovolemia prior to starting treatment
  - Suspect GI bleeding, sepsis, vomiting, diarrhea, or decreased intake of salt and/or fluids
- Hypotension near the end is usually the result of excessive ultrafiltration
- Pericardial or cardiac disease can cause hypotension any time during hemodialysis

Hypotension

- Symptoms associated with hypotension during hemodialysis include: nausea, vomiting, anxiety, orthostatic hypotension, tachycardia, dizziness, and syncope
- Initial treatment of intradialytic hypotension include stopping treatment and placing the patient in Trendelenburg position
- If hypotension still persists, can give salt containing fluid such as broth by mouth or normal saline 100 to 500mL IV and reassess

Dialysis Disequilibrium

- When large amounts of solutes are cleared during hemodialysis, an osmolar imbalance between the brain and blood form which favor water movement into the brain causing cerebral edema
- This causes a clinical syndrome called dialysis disequilibrium characterized by nausea, vomiting, and hypertension that can progress to seizure, coma, and death
- Can prevent by limiting solute clearance
- Treat by immediately stopping dialysis and giving 5mL hypertonic saline 10-23% IV or mannitol 0.25g/kg IV

Air Embolism

- Always risk of air embolism when blood is pumped extracorporeally
- Clinical presentation depends on patient position when air embolizes
  - If sitting up, air can pass retrograde through IJ vein into cerebral circulation
  - If recumbent, air can go into right ventricle and into the pulmonary circulation
  - If left-to-right shunt present, and arterial air embolism can lodge in the coronary or cerebral circulation causing an MI or CVA

Air Embolism

- Symptoms can be varied: acute shortness of breath, chest tightness or pain, syncope, and/or cardiac arrest
- If suspected:
  - **Immediately clamp venous blood line and place patient supine**
  - Place on 100% supplemental oxygen
  - Can consider IV steroids, heparinization, and hyperbaric oxygen treatment

Clinical Scenarios

Clinical Scenarios: Overview

- Will review possible scenarios in the CDU: hyperkalemia, intradialytic hypotension, and bleeding AV fistula
- **If at any point a patient becomes unstable, notify the attending on duty (if present) and call an RRT**

Hyperkalemia

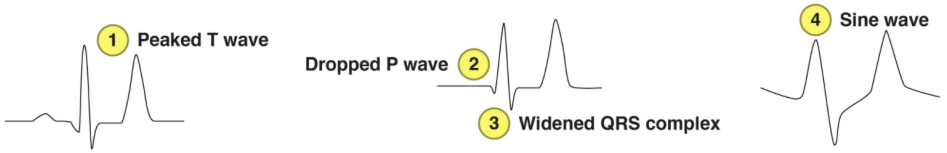
Patient admitted to CDU for scheduled HD with no complaints or symptoms. IV access obtained and blood work sent. EKG shows peaked T waves and K+ level is still pending.

Management: General Strategy

Definitive treatment is HD, so will goal is to provide temporizing measures until HD. This will largely be focused on cardiac membrane stabilization and intracellular shift of K+.

- Use the Hyperkalemia Order Set

ECG Changes Due to Hyperkalemia



Hyperkalemia Treatment			
Intervention	**Onset**	**Duration**	**Mechanism**
Membrane stabilization			
Calcium gluconate or chloride	Immediate	30–60 min	Membrane stabilization
Redistribution			
Insulin	20–30 min	4–6 hr	Shifts potassium into cell
Albuterol	15–30 min	2–4 hr	Upregulates cAMP & shifts potassium into cells
Sodium bicarbonate	5–10 min	1–2 hr	Shifts potassium into cell
Elimination			
Furosemide	15–30 min	2–3 hr	Increases renal potassium excretion
Sodium polystyrene *(no longer recommended)*	1–4 hr	4–6 hr	Increases GI potassium excretion
Hemodialysis	Immediate	2–6 hr	Removes potassium

Image from Rosh Review

Management

1. Assess patient and **start calcium gluconate**
   a. **Can repeat 4 times an hour as needed until HD**
2. Depending on clinical status consider nebulized albuterol and insulin/glucose
   a. Give 5 units insulin for renal dosing and monitor blood glucose
3. If concurrent metabolic acidosis present, consider giving sodium bicarbonate
4. Call nephrology to expedite HD

Hypotension

Patient admitted to CDU for scheduled HD with no complaints or symptoms. Approximately halfway into the dialysis session, patient complains of lightheadedness and is hypotensive when BP is taken.

Management: General Strategy

Hypotension is a common complication during HD. Initial evaluation will consist of trying to differentiate if the hypotension is related to overzealous fluid removal versus another process.

- **If patient does not improve with the measures on the following slide, call an RRT**

Management

1. Stop HD and place patient supine or in Trendelenberg
2. Assess patient for other symptoms/complaints
    a. May need further history to see if patient was already in a hypovolemic state prior to presenting for HD such as having vomiting, diarrhea, etc
    b. ACS work up when appropriate
    c. Septic work up when appropriate
3. Consider small IV fluid bolus
    a. Start at no more than 100mL at a time

Bleeding Fistula

Patient admitted to CDU for scheduled HD with no complaints or symptoms. After completing an entire dialysis session without any problem, AV fistula would not stop bleeding. You arrive to find excessive blood soaked gauze over the AV fistula. Patient is otherwise asymptomatic.

Management: General Strategy

A life-threatening bleed is uncommon but if present will require surgical intervention for definitive treatment. Initial evaluation will consist of determining extent of bleed and if bedside hemostasis can be achieved definitively. If bleeding cannot be controlled, then will need to temporize until vascular surgeon arrives.

- **If uncomfortable with bedside management, hold direct pressure and call an RRT**

Holding Direct Pressure

- Dr. Al Sacchetti's video shows a very good example of applying direct pressure to control hemorrhage:
  - https://www.youtube.com/watch?v=toFiGSfesZk
- This is an essential temporizing measure when attempting to assess bleeding or waiting for vascular surgery

Management

1. Get help and gather supplies
   a. Bring gelfoam/surgicel, suture kit and **non-cutting** sutures
   b. May need others to hold direct pressure
2. Assess AV fistula and visualize the extent of bleeding
3. Apply direct pressure and use hemostatic sponges
   a. **Hold direct pressure proximal and distal to the fistula**
4. Place figure-of-eight suture
   a. May need more than one suture

Bleeding Fistula

Patient admitted to CDU for scheduled HD with no complaints or symptoms. After completing an entire dialysis session without any problem, AV fistula would not stop bleeding. You arrive to find blood covering the floor with excessive amounts of blood soaked gauze held over the AV fistula by the nurse. The patient is lightheaded and hypotensive.

Management

1. Get help and gather supplies
    a. Bring gelfoam/surgicel, suture kit and **non-cutting** sutures
    b. May need others to hold direct pressure
2. Assess patient, AV fistula and visualize the extent of bleeding
    a. Consider activating massive transfusion protocol
    b. Consider protamine sulfate 10-20mg IV for heparin reversal
3. Apply direct pressure and use hemostatic sponges
    a. **Hold direct pressure proximal and distal to the fistula**
4. If still bleeding significantly, apply tourniquets for better visualization
5. Place figure-of-eight suture
    a. May need more than one suture
6. Emergent vascular surgery consult

References

Stapczynski, J. Stephan, et al. Tintinalli's Emergency Medicine: A Comprehensive Study Guide, 9th Edition. McGraw-Hill Education/Medical, 2019.

The End -- Thank You For Your Attention and Patience

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