Dialyzing challenging patients: 
Patients with hepato-renal conditions

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Acute kidney injury in Acute liver failure (ALF)

• Patients with ALF have a 50% risk of developing AKI

• Acetaminophen-induced liver injury and liver failure from ischemic shock are most likely to develop AKI

• Other causes include
  – Infections that cause combined liver and kidney failure (such as leptospirosis)
  – Hepatorenal syndrome after Fulminant liver failure
Acute kidney injury in Chronic Liver Disease

- Pre-renal state
- Acute tubular injury
- Toxins (e.g. Contrast agents, NSAIDS, Antibiotics)
- Infection
- Hepatorenal syndrome
  - Type 1
  - Type II
Pre renal state

- Hypoalbuminemia
- Diuretic therapy
- High volume paracentesis
- GI bleed
- Sepsis
- Reduced renal perfusion
Hepatorenal Syndrome

Affected patients usually have portal hypertension due to

- Cirrhosis
- Severe alcoholic hepatitis
- Fulminant hepatic failure from any cause
Hepatorenal Syndrome

- It represents the end-stage of a sequence of reductions in renal perfusion induced by increasingly severe hepatic injury
  - Splanchnic vasodilatation
  - Hypovolemia
  - Renal vasoconstriction and decrease in GFR from activation of potent hormonal systems

- It is a diagnosis of exclusion and is associated with a poor prognosis.
Hepatorenal syndrome

Characterized by the following features in a patient with acute or chronic liver disease

- A progressive rise in serum creatinine
- An often normal urine sediment
- No or minimal proteinuria (less than 500 mg/day)
- A very low rate of sodium excretion (ie, urine sodium concentration less than 10 meq/L)
- Oliguria
Hepatorenal syndrome

Type I
• More serious type
• At least two fold increase in serum creatinine to a level >2.5mg/dl within <2 weeks
• Some pts will have urine output <500 ml/day

Type II
• Less severe
• Usually manifests as ascites that is resistant to diuretics
CKD in Chronic Liver disease

• Glomerulonephritis in Hep B, C infections

• IgA nephropathy in alcoholic liver disease

• Interstitial nephritis in Primary biliary cirrhosis or Wilson’s disease

• Rarely Polycystic liver and kidney disease
AKI after Orthotopic liver transplant

- Ischemic injury (Intra or post op bleeding or hypotension)
- Toxic (e.g., drugs or radiological dyes)
- Hepatorenal syndrome if there is primary allograft failure
- Sepsis or septic shock
- Immunosuppressant toxicity

Often, renal failure persists in the peri and postop period, requiring a continuation of RRT
Prognosis of AKI in liver failure

• Mortality reaches 60-70% in pts with AKI requiring RRT before OLT

• Occurrence of AKI after OLT is also an important risk factor for death

• Yearly survival of pts undergoing dialysis for AKI after OLT was 45% vs 96% in pts without AKI.

Areas that need dialysis provider attention

• Severe hemodynamic instability
• Increased intracranial pressure (ICP)
• Electrolyte abnormalities
• Acid/base disturbances
• Medication dosing
Hemodynamic instability

– Hypovolemia from hypoalbuminemia and splanchnic vasodilation resulting in pooling of all fluids to the peritoneal cavity

– Liver failure, SIRS and hypotension induced damage to heart, brain and adrenal glands

– High Nitric Oxide concentrations makes them prone for post dialytic hypotension

Brain edema

• Rapidly progressing liver failure pts with AKI are at high risk of developing brain edema

• OLT itself may cause elevation of intracranial pressure and result in death during or immediately after OLT

• Brain edema leads to Intracranial hypertension, reduction in cerebral perfusion and in some cases, brain herniation
Hyponatremia

- Can be severe (<120mmol/l or less) in some cases

- Brain loses osmotically active molecules in chronic hyponatremia

- If sodium level is suddenly corrected, then sudden hypertonicity of extra cellular fluid may lead to rapid dehydration of cells, risking myelinolysis.
Key Factors Relevant to RRT in ALF

• ALF pts may require RRT to closely control volume status, in addition to conventional indications, due to concern for intracranial hypertension (ICH)

• Line placement - Pts often have significant coagulopathy, but the risks and benefits of blood product transfusion must be weighed closely since volume overload may exacerbate ICH

• Consider femoral line placement (at least temporarily) to avoid Trendelenburg position if there is concern for ICH
RRT Modality

• Options include
  – Intermittent hemodialysis (lasting 3-4 hours/day)
  – Continuous methods (lasting 24 hours/day e.g., CVVHF, CVVHD or CVVHDF)
  – Sustained low efficiency dialysis (SLED – lasting 8-12 hours/day)

• In general, continuous modalities of therapy are preferred for tight control of volume status and lower risk of neurologic complications
Continuous blood volume measurement during IHD

Davenport A. Kidney international; Vol 56, S62-S66 (Nov 1999)
Patient with AKI and ICH treated by Automated PD

Davenport A. Kidney international; Vol 56, S62-S66 (Nov 1999)
Risk of IHD

- Rapid reduction in serum osmolality, may cause relative hyperosmolarity of intracellular compartment and water influx to brain cells resulting in edema

- Hypovolemia resulting from hypotonia (removal of NO) may lead to cerebral hypoperfusion

- Rapid correction of hyponatremia may result in myelinolysis

- Rapid correction of acidosis may result in transient intracellular acidosis
Benefits of CRRT

• Stable hemodynamic parameters and intracranial pressure

• Gradual correction of hyponatremia and acidosis

• Improves UF tolerance

• Allows use of large volume of fluids (e.g., use of blood products for correction of coagulopathy, TPN or oral nutrition etc)
Limitations

- Studies comparing various RRT in pts with AKI undergoing OLT are scarce
- They are mainly observational or retrospective
- Results are often contradictory
- No data on optimal time for initiation of RRT
  (Matuskiewicz-Rowniska et al; Ann Transplant, 2013: 18: 248-255)

American association for the study of liver disease (AASLD) recommends continuous RRT modalities in their position paper
Anticoagulation for RRT

• Pts are at greater risk of bleeding due to low platelets, impaired hepatic synthesis of clotting factors, portal HT and varices.
• On the other hand, risk of filter clotting is considerable due to inflammation and increase in tissue factor release from endotoxemia
• Avoidance of heparin is preferred
• Saline flushes (250mls) every 30 minutes into the circuit generally works
• Pre-dilution technique during CRRT may help, but reduces clearance.
Regional citrate anticoagulation

- Citrate works by chelation of ionized calcium

- Risk of citrate accumulation and toxicity

- Evidenced by systemic hypercalcemia, ionized hypocalcemia and high anion gap metabolic acidosis

- Avoid in pts with severe liver dysfunction, hypoxemia, serum lactate $\geq 3.4$ mmol/l, PT $\leq 26\%$ and in pts receiving multiple citrate containing blood products
Electrolyte disorders

• With significant transfusion requirements, patients are at increased risk of hypocalcemia, which can exacerbate hypotension.

• As hepatocytes start to regenerate, these patients are at increased risk of severe hypophosphatemia.
Medication dosing

• Adjust the antibiotic dosing and other medications while patients are on RRT

• NAC (given in Tylenol poisoning) is dialyzable and the optimal dose of NAC for patients on RRT is not well defined.

• Consider empirically increasing the dose of NAC while patients are on RRT
Indications for Intraoperative RRT

• Continuation of preoperative therapy

• Extra-renal indications
  – Hypervolemia or to enable large volume of blood products
  – High risk of brain or pulmonary edema
  – Severe lactic acidosis or prediction of aggravation
  – Threat of hyperkalemia
  – Very high portal venous pressures
  – Minimize the risk of rapid correction of hyponatremia
• Townsend et al reported use of intra operative CVVHDF in 6.4% of OLT recipients
  Townsend et al. Liver transplant, 2009; 15:73-78

• Recruitment for a large, multicenter, randomized trial to compare intraoperative CRRT with standard supportive therapy in pts underlying OLT with multi organ damage and GFR <60mls/mt is currently underway.
Summary

• Liver failure pts have very high risk of developing AKI

• Mortality reaches 60-70% in pts with AKI requiring RRT before OLT

• Occurrence of AKI after OLT is also an important risk factor for death

• In general, continuous modalities of RRT are preferred over IHD.
Thank you