Renal Ischemia and Reperfusion

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Objectives

- Understand the importance of Acute Kidney Injury (AKI)
- Describe current theories to causes of AKI, focusing primarily on shock and reperfusion
- Describe methods to prevent AKI

Why do we care about AKI?

- Strong predictor of morbidity and mortality associated with sepsis
- Up to 10 fold increase in mortality in septic patients with AKI compared to septic patients without AKI
- Also increased length of stay and need for ventilator

Traditional Thought

- AKI is primarily related to renal hypoperfusion
- Inflammatory component, but not well understood
- If we increase renal blood flow (RBF), then we will decrease AKI
- Focus on maintaining perfusion and general hemodynamic parameters

Renal Blood Flow

- What actually happens in shock?
  - Decreased in approximately 2/3 of cases
  - Increased in 1/3
- Really depends on cardiac output (CO)
  - If CO is preserved or increased, then so is RBF (and vice versa)

Hyperdynamic Shock

- RBF increases in hyperdynamic shock
- RBF has greater correlation with cardiac output than with systemic blood pressure
- But does RBF actually matter?

Correlation? BP and AKI

- Incidence of AKI does not correlate well with systemic blood pressure
  - SBP, DBP, MAP
- Similarly limited correlation with hypotensive time or nature (continuous vs. episodic)
- Also limited correlation with RBF
- So what is it correlated with?

Inflammation

- AKI is correlated with degree of inflammation
  - Leukocyte activation
  - Various cytokines (IL-6, etc.)
  - Oxidative stress markers
  - Neutrophil gelatinase-associated lipocalin (NGAL)

Treatment

- If RBF is maintained in hyperdynamic shock, then do fluids make any difference?
  - Probably not
- What about diuretics?
  - Increase urine output
  - But worsens creatinine clearance

Treatment

- But more fluids certainly don't hurt, right?
  - Not exactly
  - Restrictive fluids may improve length of stay and days on ventilator
  - Increase inflammation in the lung
- But what about the kidney?

Treatment

- If inflammation is what leads to AKI, then should we focus on the lung or other organ systems?
- Maybe

Treatment

- Trend towards decreased need for renal replacement therapy in restrictive fluid group compared to aggressive hydration
- But no change in AKI with lung protective ventilator settings

So what causes AKI in sepsis?

- Since it's not a RBF issue, then:
  - Monitoring systemic blood pressure or RBF don't really help
  - Increasing RBF with IV fluids really doesn't help
- It's more complex, likely inflammatory
  - Success in many animal models with multiple agents that decrease oxidative stress
  - But so far little evidence of change in human trials or with ventilator changes

Recovery from shock

- Associated with decreased RBF
- AKI in septic shock isn't really a hypoperfusion problem
- So the recovery isn't really a "reperfusion" problem

Future Study

- Human studies are needed
- Multiple studies testing ways to decrease oxidative stress
  - Not quite ready for prime time

Conclusions

- Renal blood flow is often maintained or increased in septic shock
- AKI is not correlated with BP or RBF
- Optimize fluid replacement, but don't maximize it
- Minimize inflammation (from any source)
- Look for anti-inflammatory treatments in the future

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