Acute renal failure in critically ill patients is common and can become very difficult to manage if the patient becomes oliguric. These proceedings will focus on acute renal failure, in particular its pathophysiology, typical causes, diagnostics, and specific treatments.

Pathophysiology

Acute renal failure (ARF) is due to an abrupt and sustained decrease in glomerular filtration rate (GFR). This leads to retention of nitrogenous wastes and toxins, as well as fluid, electrolyte, and acid-base imbalances. Both pre-renal and post-renal causes of azotemia need to be ruled out prior to a diagnosis of ARF. Most ARF is caused by ischemic events or exposure to nephrotoxins, leading to acute tubular necrosis. The kidneys receive 20% of the total cardiac output in the body, with the renal cortex receiving 90% of the renal blood flow and the medulla only receiving 10%. Total renal oxygen extraction from the body is about 10%, however the outer medullary oxygen extraction is about 80-90% of the total. The low pO2 and the high metabolic activity of the thick ascending loop of Henle and the pars recta of the proximal tubule make it at high risk for ischemia. Normally, the kidney is very good at maintaining intrarenal oxygen homeostasis by changes in arteriolar tone and blood flow regulation during normal blood pressure changes. The kidney also undergoes tubuloglomerular feedback (TGF), which induces preglomerular arterial constriction, reduces GFR, and ultimately reduces oxygen requirements when solute filtration is in excess of reabsorption capacity. TGF may be a protective mechanism in states of medullary ischemia and attempts to increase GFR may increase solute load to the kidney, therefore increasing medullary workload, and worsening ischemia. Whether it is cellular hypoxia from renal ischemia, or interference of normal cell function due to nephrotoxins, decreased GFR is common in both types of ARF. These insults lead to cell swelling, vascular congestion, vasomotor disturbance and ultimately leads to decreased glomerular permeability, afferent arteriolar vasoconstriction and efferent arteriolar vasodilation. Cell swelling also leads to direct tubular cell damage, causing tubular obstruction and tubular backleak.

Differentials

There are many differentials associated with ARF. These include, but are not limited to:

1. Ischemia: Hypovolemia, Shock, Addison’s disease, Decreased cardiac output, Cardiac disease, Thrombosis, DIC/Sepsis/SIRS, Anesthetic hypotension
2. Toxic/Drug: Ethylene glycol, Lilies (cats), Aminoglycosides, NSAIDS, Myoglobin/Hemoglobin, Radiocontrast agents, Snake/Bee venom, Amphotericin B, Chemotherapeutics, Raisins/Grapes
3. Infectious: Leptospirosis, Pyelonephritis
4. Acute on chronic
5. Secondary to dehydration or hypovolemia
6. Hypercalcemia
7. Obstructive: Ureteral obstruction, Chronic urethral obstruction, Hydronephrosis
8. Immune-mediated
9. Diabetes mellitus

Uremia

Uremia is when the body starts to have systemic side effects from decreased waste through the kidney of natural body toxins. It can lead to depressed leukocyte function and cellular immunity, decreased clearance of gastrin (which leads to stomach and oral ulcers), stimulation of chemoreceptor trigger zone (vomiting), pneumonitis, pericarditis, encephalitis, and altered platelet function and adhesion.

Detection of ARF

There are many aspects that go into diagnosing ARF. The history and physical examination can be very telling based upon hydration status, body weight, pulse quality/character, urine output, kidney pain or swelling, and blood pressure. Laboratory parameters will depend on PCV/TS, BUN/Creatinine, Urine specific gravity, urinalysis, acid/base status, electrolytes, quantitative enyzmuria (Gamma-glutamyl transpeptidase (GGT): brush border of proximal tubule and N-acetyl-beta-D-glucosaminidase (NAG): lysosomes of proximal tubule cells), and fractional excretion of electrolytes (with Increased Na/Cl excretion suggestive of renal damage). Normal urine output is 1-2 ml/kg/hr, with oliguria being defined as <0.5-1 ml/kg/hr and anuria being defined as no urine production at all.
Treatment

Treatment focuses on fluid therapy, treating the underlying cause, managing hyperkalemia and acid/base disturbances, and considering specific drug treatments. Drugs used to treat ARF may include furosemide, mannitol, dextrose, diltiazem, fenoldopam, anti-emetics, GI protectants, phosphate binders, and nutrition. Peritoneal or hemodialysis may need to be considered in some severe oliguric or anuric cases.

Fluid therapy is the first mainstay in treating ARF. The patient should be volume loaded in order to treat any underlying pre-renal disease. Until the patient is volume loaded, true oliguria cannot be determined because oliguria is the kidney’s natural response to hypovolemia and dehydration. The patient needs to be closely monitored for volume resuscitation and over-resuscitation needs to be avoided. Monitoring may include PCV/TS, Body weight monitoring, physical exam findings, central venous pressure monitoring, and urine output monitoring. Once volume resuscitation occurs, then fluid therapy should be altered to meet insensible losses and outs to avoid overhydration. Insensible losses are typically 20 ml/kg/day or 1/3 of maintenance needs. These insensible losses are then added to the patients sensible losses (measurable urine output) and that becomes the fluid rate. This is called “ins and outs” fluid therapy. If overhydration occurs and the patient is oliguric or anuric, dialysis may be the only way to treat the patient.

Potassium is excreted exclusively through the kidneys and hyperkalemia is very common in the oliguric ARF patient. ECG changes may occur in the hyperkalemic patient, however they do not occur consistently. ECG changes typically consist of shortening of the Q-T interval, spiked T-waves, widening of the QRS complex, prolonged P-R interval, bradycardia, loss of P-waves, sinoventricular rhythm, sine-wave rhythm, and ultimately ventricular fibrillation and asystole. Treatment of hyperkalemia is multifactorial and many of the treatments focus on protecting the heart or shifting potassium back into cells, as opposed to increasing potassium excretion. Fluid therapy should consist of potassium-free crystalloids, such as 0.9% NaCl. Calcium gluconate 10% at 0.5-1 ml/kg slowly IV over 10-20 minutes will help protect the heart against hyperkalemia induced arrhythmias. It will not lower the serum potassium level. ECG monitoring should be performed during calcium administration. Dextrose alone can be used to stimulate natural insulin release and drive potassium back into the cells. 0.5-1 g/kg IV Dextrose diluted is a typical dose. Regular insulin can also be given at 0.1-0.25 U/kg IV followed by 1-2 grams dextrose/unit insulin IV in fluids. Glucose needs to be closely monitored if insulin is given, as these animals typically aren’t diabetic and are prone to hypoglycemia. Sodium bicarbonate can be given if the patient is acidicotic, as fixing acidosis will drive potassium back into the cells. The calculation is 0.3 x base excess x kg = base deficit. Give 1/3 to ½ base deficit over 30 minutes. The rest of the deficit can be given over 4 hours in fluids. Loop diuretics, such as furosemide, have questionable efficacy for treatment of acute clinical hyperkalemia, as these need to reach the ascending loop of henle to work and many ARF patients have poor blood flow to the ascending loop of henle. Peritoneal or hemodialysis may be the only way to truly get rid of potassium in the oliguric or anuric patient.

Loop diuretics are frequently considered in oliguric or anuric patients. They should NOT be used if the pre-renal azotemia has not resolved. The purpose of using loop diuretics in these cases is that they may ease the management of oliguric patients by converting them to a non-oliguric state. However, there is no evidence that it decreases mortality or the need for dialysis in human studies. Loop diuretics decrease the metabolic demand on the renal tubular cell and greater urine flow may help prevent tubular obstruction. Animal studies indicate that loop diuretics may be useful within minutes to hours of renal insult. The cons of loop diuretics are that they may not be helpful once acute tubular necrosis is established because delivery of the drug is GFR dependent. Loop diuretics also may be harmful if a pre-renal state is still present. Continuous infusions of loop diuretics produced more net sodium excretion and less toxicity than bolus doses in some studies. Large bolus doses may cause transient renal vasoconstriction.

Mannitol administration has been advocated in cases of oliguria or anuria. Pros of mannitol use include that it is an intravascular volume expander, a free-radical scavenger, an osmotic diuretic, it decreases tubular swelling, increases tubular flow, helps prevent tubular obstruction, and has weak renal vasodilatory effects. Cons are that it reduces medullary pO2 and it may lead to volume overload if the kidneys do not respond to it.

High-dose glucose (10-20% solutions) have been suggested as an osmotic diuretic in oliguric patients. It has similar osmotic effects to mannitol, but mannitol may be slightly more effective because it is not metabolized or reabsorbed by the renal tubules. However, it is less likely to lead to volume overload compared to mannitol, if it happens to be ineffective.

Dopamine has remained very controversial regarding its use in ARF. The pros are that it may increase GFR. It causes direct vasodilation of the afferent and efferent arterioles via dopamine receptors, which tends to cause more of a rise in RBF than GFR. It may increase cardiac output via beta receptors, and can increase perfusion pressure via alpha receptors. It may cause natriuresis and diuresis via inhibitory effects of renal tubule Na/H antiporter and Na/K-ATPase pumps. Cons include the fact it increases outer medullary blood flow, but does not improve outer medullary oxygenation in rats. The increased solute delivery to the distal tubule may increase oxygen consumption. The dopamine effects can be unpredictable from animal to animal and of 30 human studies using low-dose dopamine, only 3 have had positive results. Regarding dopamine in cats, Flourney, et. al., in the Journal of Vet Pharmacology and Therapeutics, 2003 stated “There is a lower DA receptor density in feline renal cortices compared with other species suggesting that a higher dosage of DA may be required to effectively activate the lower population of DA receptors in cats vs. lower dosages used in rats, dogs and humans.” Fenoldopam may be a better choice in cats vs. dopamine. It is DA1 receptor specific
which causes renal vasodilation. There is higher activity in cats at D1 receptors with fenoldopam vs. dopamine. In one study, 0.5 mcg/kg/min x 2 hours lead to increased urine output and GFR 6 hours post administration. It also increases natriuresis.

Calcium antagonists may be useful in some cases of oliguria or anuria. They induce preglomerular arteriolar dilation, promote natriuresis, show a parallel rise in RBF and GFR, reduce intracellular calcium flux, block angiotensin induced cytokine formation, and have oxygen free-radical scavenging effects. All 3 classes of calcium antagonists act similarly on the renal vasculature, although some studies indicate that the negative inotrope effects of nonselective calcium channel blockers (i.e. Diltiazem) may be detrimental to renal blood flow due to decreased CO. One study indicated that diltiazem may be useful in dogs with leptospirosis ARF, although it may take up to 3 days to see therapeutic effects from it.

When medical management isn’t enough, dialysis (either hemodialysis or peritoneal dialysis) or continuous renal replacement therapy (CRRT) may need to be resorted to. Dialysis or CRRT is typically used for oliguric or anuric patients that need help with acid/base status, electrolyte issues, or are overhydrated. Early dialysis may help patients feel better and “recover” faster. The goal should not be focused on fixing the azotemia, but getting the patient back into a non-uremic state. Earlier dialysis may be considered in disease/conditions known to have a long course of recovery, such as lily toxicity or ethylene glycol toxicity.