Treatment of Acute Renal Failure

General Therapy for Acute Renal Failure

Treatment of acute renal failure usually should be conservative and largely supportive. It requires careful and precise management. All patients will require close monitoring, many of them within intensive care settings.

Supportive care includes stabilizing the patient, monitoring input and output strictly, weighing daily, determining electrolyte values frequently, preventing sepsis via reducing the number of intravenous lines and removing an indwelling urinary catheter, culturing periodically, and using antibiotics when indicated clinically. It is important to adjust medication dosage according to renal function and to avoid nephrotoxins whenever possible. Because serum creatinine values increase daily, it is best to calculate drug doses based on GFR <10 mL/min per 1.73 m², rather than on the serum creatinine level.

Conservative therapy may be symptomatic or specific. Symptomatic therapy consists of treating the underlying prerenal conditions that led to renal failure; maintaining the fluid and electrolyte balance; initiating therapy for complications such as hyperkalemia, hypertension, acidosis, and infection; and instituting appropriate nutrition. Specific therapy consists of using medications for specific underlying causes and may include steroids (conventional or high-dose pulse steroid therapy) and other immunosuppressive agents, anticoagulation agents, plasmapheresis, or intravenous immunoglobulin.

THERAPY FOR PRERENAL FAILURE

Rapid volume replacement and treatment of the underlying condition that resulted in prerenal failure are the cornerstones of therapy. Initial fluid administration of isotonic saline (0.9%) or 5% albumin (10 to 20 mL/kg per dose) should be used to restore intravascular volume. This can be both a diagnostic and a therapeutic trial. Fluid administration also can convert oliguric to nonoliguric renal failure in its early stage.

Unless a patient is suffering congestive heart failure (CHF), fluid administration should be repeated, followed by the use of loop diuretics, including furosemide (2 to 5 mg/kg per dose) or bumetanide (0.25 to 0.5 mg/dose IV). After each bolus, the patient’s volume needs to be reevaluated. Response to the therapy will be indicated by a urine output of greater than 1 to 3
mL/kg per hour.

Patients who have CHF will need inotropic support, such as dopamine (5 µg/kg per minute IV), dobutamine (5 to 20 µg/kg per minute), or digoxin. Therapeutic digitalis values should be achieved slowly and the maintenance dose reduced as dictated by renal function (Table 6).

THERAPY FOR POSTRENAL FAILURE

Therapy for postrenal failure includes removal of obstruction by decompression or diversion of the urinary tract, stabilization of electrolyte abnormalities, management of postobstructive diuresis, and therapy for voiding dysfunction and for urinary tract infection. Surgical intervention will require urologic consultation. The site of the obstruction will determine the approach: placement of a Foley catheter, vesicostomy, ureteral catheters (stents), or nephrostomy tubes. Prompt relief of a partial obstruction is indicated in cases of severe pain, where the possibilities for severe renal damage predominate, and whenever there is a history of frequent urinary tract infections.

Postobstructive diuresis is characterized by marked polyuria. The excessive excretions of salt and water may result in hypokalemia, hyponatremia, and hypotension and lead to collapse. Fluid replacement should be guided by what is excreted and based on frequent measurements of urine volume, urinary electrolytes, and serum electrolytes, including calcium and phosphorus.

THERAPY FOR ESTABLISHED RENAL FAILURE

Maintaining Balance of Fluid and Electrolytes

In a euvolemic state, fluid intake, including water generated from endogenous metabolism (insensible fluid gain), is balanced by fluid output. Most of the fluid output involves sensible fluid losses by urine, stool, and sweat and insensible losses by water evaporation from the skin and respiratory tract. Only small amounts of water normally are lost in the stool (100 to 150 mL/d), and fluid loss by sweat is minimal. Therefore, patients who are in ARF should have fluid restricted to net insensible water loss (insensible losses minus endogenous water production, which is 400 mL/m² per day or 25% to 30% of caloric expenditure) plus all measured fluid losses (urine output, gastrointestinal losses, chest tube drainage). Net insensible loss should be restored with 5% to 10% dextrose in water (D5%W - D10%W). Urine output should be replaced with fluid that has the composition and quantity of these losses. Usually, normal saline (0.45% NS) mL for mL of losses every 4 to 6 hours is appropriate. If this therapy is sufficient, the patient will lose
0.5% to 1% of body weight per day over the initial few days. The patient should be weighed at least once daily, and input and output should be monitored strictly, with clinical status assessed constantly. Once urine output begins to rise, fluid intake should be increased. Fluid balance is easier to manage in children who have nonoliguric renal failure. Dialysis is indicated in the case of a severe fluid overload (Table 6).

Metabolic acidosis will change the activity of cellular enzymes and depress cardiac function. A serum bicarbonate (HCO₃) of less than 12 mEq/L may require correction. The goal is to keep the serum pH greater than 7.2 or serum bicarbonate level above 16 mEq/L. The amount of NaHCO₃ needed to correct metabolic acidosis can be estimated by using this formula:

Base deficit (BD) = 0.6×BW (kg) × (desired - observed serum HCO₃)

The base deficit can be added to the urine output or maintenance fluid. Half of the replacement can be given within the first 2 to 3 hours and the rest evenly over 24 hours. Caution must be taken to avoid salt and fluid overload. In the patient who has hypocalcemia, sodium bicarbonate must be administered cautiously because it may lead to tetany.

Patients who have CHF will not tolerate a large sodium load, and the use of intravenous tromethamine (THAM) can be considered; it is available as a 0.3 M solution. The dose of THAM in mL can be calculated as:

mL of 0.3 M THAM = BW (kg) × base deficit (mEq/L)

THAM can be given only in intensive care settings. If the patient has respiratory acidosis (increased pCO₂), administration of base will not be effective and it is not indicated.

Hyponatremia can lead to cerebral overhydration and neurologic symptoms. It is necessary to keep the serum sodium in the range of 130 to 135 mEq/L, restricting excessive free water.

Hyperkalemia is the most life-threatening condition in ARF, resulting in muscular weakness and abnormal cardiac conduction, which can lead to fatal arrhythmias. Potassium must be monitored by serial determination and electrocardiogram. A peaked T wave, prolongation of the PR interval, widening of the QRS, disappearance of the P wave, and ventricular fibrillation are electrocardiographic (EKG) changes associated with an elevated serum potassium level.

The effects of hyperkalemia can be reversed by direct antagonism of its membrane actions and by lowering of the serum K⁺ concentration either by promoting K⁺ uptake into the cells or by removing K⁺ from the body. Severe symptoms usually do not occur until the serum
level is above 7.5 mEq/L, but acid-base disbalance and a low serum Ca^++ level can modify the toxicity of hyperkalemia. In the absence of obvious artifactual changes (extravascular hemolysis, thrombocytosis, leukocytosis), an asymptomatic elevation of the serum K^+ to >5.8 mEq/L should be treated via a cation exchange resin (sodium polystyrene sulfonate). All sources of potassium should be eliminated in ARF. Usually ignored sources of K^+ are blood transfusions and drugs (penicillin).

If serum K+ is greater than 6.5 mEq/L and is accompanied by EKG changes, emergency steps must be instituted to lower the potassium level (Table 6).

1. Calcium gluconate--10% solution (0.5 to 1.0 mL/kg per dose) will oppose the effect of hyperkalemia on the heart and stabilize myocardial membranes. It should first be given intravenously (IV) slowly over 10 to 15 minutes under careful EKG monitoring. The protective effect of Ca++ is relatively short and can be repeated within 5 minutes if indicated by EKG.

2. Glucose and insulin will promote the cellular uptake of potassium by increasing the Na+-glucose cotransport and Na+-K+ ATP-ase. Regular insulin in a dose of 0.1 to 0.2 U/kg and dextrose 0.5 to 1.0 g/kg are given after calcium gluconate. One can mix 100 mL D25%W with 6 U of regular insulin and administer slowly (1 to 2 mL/kg per dose IV).

3. Sodium bicarbonate (NaHCO3 7.5% 1 to 2 mEq/kg per dose IV slow push or fast drip) will raise the blood pH and shift potassium into cells. An increase of serum pH by 0.1 will lower serum K+ by 0.6 to 1 mEq/L, but this effect in ARF is transient; there is only a moderate, unpredictable response on the serum potassium concentration, which often is accompanied by significant volume expansion.

4. Albuterol aerosol and other beta2-adrenergic agonists can be given in an emergency. Like insulin, the beta2-adrenergic agents will cause a shift of potassium from the extracellular space into the cells. In some patients, albuterol aerosol can lower the serum K+ level by 1.0 to 1.5 mEq/L within 30 minutes. This measure is safer than giving sodium bicarbonate. All of these steps are only temporizing measures and must be accompanied by removal of potassium from the body.

5. Sodium polystyrene sulfonate, an ion exchange resin, will bind potassium in the gut in exchange for sodium (1 mEq K+ for 1 mEq Na+) and remove excess potassium from the body. The usual dose is 1 g/kg orally or by nasogastric (NG) tube given with 70% sorbitol or rectally (1 g in 2 to 4 mL of 25% to 30% sorbitol or 10% dextrose in water) as a retention enema placed through a Foley catheter for 30 to 60 minutes. Doses can be repeated every 2 to 4 hours.

When all of the aforementioned therapies fail to control plasma K^+ excess adequately, dialysis, usually in the form of hemodialysis, should be initiated.

Mild hyperphosphatemia does not require therapy. Higher levels of phosphate in serum...
can be controlled with calcium carbonate as a phosphate binding agent (300 to 400 mg/kg per day orally). The dose should be adjusted to maintain the serum phosphorus level in the 5- to 6-mg/dL range. In general, magnesium or aluminum phosphate binders should be avoided in ARF.

Hypocalcemia does not require therapy unless tetany is present. If the child has tetany, 10% Ca gluconate (0.5 to 1.0 mL/kg per dose IV) should be administered.

Treating Hypertension

ARF in any form can present as hypertension and hypertensive encephalopathy. It is essential to lower the blood pressure quickly and safely. The blood pressure should be reduced by at least 25% within 1 hour with an antihypertensive medicine whose onset of action is rapid. It is advisable to start with one antihypertensive medicine and increase the dose to its maximum recommended level. Therapy is individualized and needs titration (Table 6). In most cases, hypertension is the result of sodium and fluid retention, but other factors, such as activation of the renin-aldosterone-angiotensin II and/or the alpha-adrenergic system, may have roles as well.

For immediate control of blood pressure, orally administered medication is less feasible in severely sick patients. Rather, a dose of the following should be considered:

1. Nifedipine, a calcium channel blocker (0.25 to 1.0 mg/kg per dose sublingually intrabuccally) usually is very effective. The dose can be repeated within 30 minutes and then every 3 or 4 hours as needed. Maximum is 30 mg/dose or 180 mg/24 hours.

2. Diazoxide, a vasodilator, given as a rapid IV infusion (3 to 5 mg/kg per dose) will lower blood pressure effectively within a few minutes. Its effect lasts several hours. Slow infusion should be avoided because it allows diazoxide to bind to plasma proteins and lose its efficacy. If the first dose is ineffective, another higher dose (maximum 10 mg/kg per dose) can be given. Doses can be repeated every 30 minutes. The maximum dose is 150 mg.

3. Hydralazine is a peripheral vasodilator that acts within 5 to 20 minutes when administered as 0.1 to 0.5 mg/kg per dose IV bolus or IM. Doses can be given every 4 to 6 hours as needed, but subsequent doses usually will result in undesirable side effects, such as headache, flushing, and tachycardia. The maximum to be given is 3.5 mg/kg per 24 hours.

4. Labetalol, with its alpha1- and nonselective beta-adrenergic blocking characteristics, can be used in a single dose. The starting dose is 0.25 mg/kg IV. It should be increased by 0.5 mg/kg per dose after 10 minutes, if needed, to 1.0 mg/kg IV, or it should be given as a continuous infusion (1 to 5 mg/kg per hour). The maximal dose is 300 mg/day.

5. Sodium nitroprusside continuous IV infusion (0.5 to 10 µg/kg per minute) will correct the
blood pressure rapidly, but close monitoring of vital signs, lactic acid, and the thiocyanate level are needed. This agent probably should be used only in an intensive care setting. The maximum dose to be used is 800 µg/min.

Treating Anemia

There is no need for transfusion unless the patient is symptomatic and the hematocrit falls below 25%.

Nutrition

The provision of adequate and appropriate nutrition is a fundamental part of the nondialytic therapy of ARF, regardless of the etiology. Generally, enteral nutrition is preferred, either by oral intake or gastric tube. In many cases, the oliguric phase of ARF is short and self-limited, and special nutritional support is not needed. Some experimental studies suggest that infusion of nutrients (amino acids) in the early phase of ARF may increase oxygen requirements and aggravate tissue injury. The goal is to provide sufficient nutrients and adequate caloric intake to restrain the catabolic response and to hasten renal recovery. About 400 kcal/m² per day (45 to 50 kcal/kg per day) are required mainly as simple carbohydrates (>70%) and fats (<20%) orally and/or glucose solution (10%) parenterally. A patient whose nutritional status is normal and in whom ARF is uncomplicated may resume a normal diet within 5 to 7 days. If renal function is below 30% of normal (GFR <50 mL/min per 1.73 m²), the nutritional requirement should be adapted to renal failure. There are special formulas designed for enteral feedings in patients who are in renal failure.

Hyperalimentation should be considered early in the hypercatabolic patient. With dialysis, daily protein and caloric intake can be more generous (0.5 to 1 g/kg per day high biologic value protein), but more frequent dialysis may be necessary to control azotemia. If the BUN is greater than 50 mg/dL, a patient can benefit from special "nephro" solutions (essential amino acids and various nonessential amino acids). Depending on serum electrolyte concentrations, solutions should contain minimal amounts of sodium and no potassium or phosphorus.

Nutritional therapy requires monitoring for potential metabolic complications, such as fluid and electrolyte derangements, excessive BUN accumulation, hyperglycemia, and hypertriglyceridemia.

Renal replacement therapy (dialysis) usually is needed in about 20% of patients. The use
of dialysis always should be individualized, but in general, the indications include severe fluid overload resulting in severe hypertension, CHF, pulmonary edema, and/or metabolic derangements refractory to therapy, such as severe acidosis, severe hyperkalemia, hyponatremia, hypernatremia, hyperuricemia, or hyperphosphatemia. Dialysis is indicated when the BUN is greater than 100 mg/dL and there are symptoms of uremia, usually manifested in children as central nervous system depression. Preemptive dialysis can be used to prevent rather than treat uremic symptoms, as in the case of rapidly decompensating hemolytic-uremic syndrome and acute uric acid nephropathy or for removal of toxins as in oxalate overload. Early dialysis can simplify management and help in the administration of a specific therapy (chemotherapy) or diet (hypercatabolic cases).

The choice between hemodialysis, continuous arteriovenous hemofiltration, continuous venovenous hemofiltration, continuous arteriovenous hemodialysis, and peritoneal dialysis will depend on the availability of the technique, the etiology of the renal failure, and specific indications and relative contraindications. In patients whose major problem is excess extracellular volume (eg, in patients who have cardiac problems), hemofiltration offers some distinct advantages because this technique removes excess fluid quickly.

Prevention

Prevention of ARF, obviously, is the best form of therapy. Certain clinical situations may predispose to the development of ARF and should be recognized. Some preventive measures include:

1. Monitor the patient at risk.
2. Provide adequate hydration and maintenance of extracellular fluid volume (ECV) prior to the administration of radiocontrast material, amphotericin B, or aminoglycosides.
3. Administer nephrotoxic drugs in appropriate doses and monitor drug levels carefully. If possible, use alternative medication and limit the length of patient exposure.
4. Alkalize urine (pH >6.5) and adequately hydrate patients who have hyperuricemia or pigmenturia.
5. Use xanthine oxidase inhibitors to prevent hyperuricemia, such as in tumor lysis syndrome.
6. Treat prerenal conditions promptly via intravenous fluid to expand ECV and via osmotic and loop diuretics to increase blood flow and decrease cast formation if cardiovascular status allows.
7. Administer low-dose dopamine infusion (3 to 5 µg/kg per minute) to patients who are in
cardiac failure and have other conditions that compromise renal perfusion.

8. Ameliorate ARF with nutrients and hormones; vasodilators and cytoprotective agents can help. Experimental studies have indicated a role for the following agents in animal studies and limited clinical trials. However, the beneficial effects of thyroxine, atrial natriuretic factor, insulin growth factor, prostaglandin analogs, adenosine triphosphate-magnesium chloride, calcium channel blockers, and dopamine need to be established more firmly.