Acute Kidney Injury (AKI)

Acute renal failure (ARF) is an abrupt reduction (usually within a 48-h period) in kidney function (glomerular filtration rate (GFR) or creatinine clearance (CrCl)). This results in an accumulation of nitrogenous waste products and other toxins. Many patients become oliguric (low urine output) with subsequent salt and water retention.

The clinical course of AKI: AKI has three distinct phases

• Oliguric Phase: a progressive decrease in urine production after kidney injury

• Diuretic Phase: initial repair of the kidney insult with resultant diuresis of accumulated toxins, waste products, and fluid

• Recovery Phase: return of kidney function depending on the severity of injury

Classification and causes:

AKI can be categorized as

1-Pre-renal: resulting from decreased renal perfusion in the setting of undamaged parenchymal tissue. It is usually a consequence of Decreased intravascular volumes (hypovolemia) Examples of this include diarrhea and vomiting, burns and excessive use of diuretics. and/or decreased intravascular pressures (hypotension).

2- Intrinsic: resulting from structural damage to the kidney tubule from an ischemic or toxic insult.

3- Post-renal: resulting from obstruction of urine flow downstream from the kidney) these can be divided into causes within the ureters (e.g., calculi or clots), a problem within the wall of ureter (malignancies, benign strictures) and external compression (e.g., retroperitoneal tumors).

Clinical manifestations

The signs and symptoms of AKI are often non-specific. The patient may exhibit signs and symptoms of volume depletion or overload, depending upon the precipitating conditions, course of the disease and prior treatment. In those patients with volume depletion, a classic pathophysiological picture is likely to be present with tachycardia, postural hypotension, and reduced skin turgor and cold extremities. The most common sign in AKI is oliguria, where urine production falls to less than 0.5 mL/kg/h for several hours. In those patients with volume overload, a classic pathophysiological picture is likely to be present with ankle swelling, oedema, Jugular venous distension and effusion.

Diagnosis

In hospitalized patients, ARF is usually diagnosed incidentally by the detection of increasing serum creatinine and/or a reduction in urine output. **Common Diagnostic Procedures:**

Urinary catheterization (insertion of a catheter into a patient's bladder; an increase in urine output may occur with post renal obstruction)**.** Renal ultrasound (uses sound waves to assess size, position, and abnormalities of the kidney; dilatation of the urinary tract can be seen with post renal ARF). Renal angiography (administration of intravenous contrast dye to assess the vasculature of the kidney).

Laboratory Tests

- Hyperkalemia
- Metabolic acidosis
- Elevated serum creatinine concentration (normal range approximately 0.6 to 1.2 mg/dL [53 to 106 µmol/L].
- Elevated BUN concentration (normal range approximately 8to 25 mg/dL [2.9 to 8.9 mmol/L].
- Decreased creatinine clearance (normal 90 to 120mL/minute.
- BUN: creatinine ratio (elevated in prerenal ARF) Greater than 20:1 (prerenal ARF) and Less than 20:1 (intrinsic or post renal ARF)

General approach to treatment

- A primary goal of therapy is ameliorating any identifiable underlying causes of ARF such as hypovolemia, nephrotoxic drug administration, or ureter obstruction.
- Currently, there is no definitive therapy for AKI. Supportive care is the mainstay of AKI management regardless of etiology.
- There is no evidence that drug therapy hastens patient recovery in ARF, decreases length of hospitalization, or improves survival. Therefore, options are limited to supportive therapy, such as fluid, electrolyte, and nutritional support, renal replacement therapy (RRT).

Restoration of renal perfusion

Restoration of renal perfusion would improve renal blood flow, reducing renal vasoconstriction and flushing nephrotoxins from the kidney. The use of **crystalloids** in the form of **0.9% sodium chloride** is an appropriate choice of intravenous fluid since it replaces both water and sodium ions in a concentration approximately equal to serum.

The effect of fluid replacement on urine flow and intravascular pressures should be **carefully monitored**. **fluid loading with 1–1.5 L saline at <0.5 L/h is** unlikely to cause harm.

Establishing and maintaining an adequate diuresis

Diuretics

Loop diuretics have not been shown to accelerate AKI recovery or improve patient outcome; however, diuretics can facilitate management of fluid overload. Doses of up to **100 mg/h of furosemide** can be given by **continuous intravenous** infusion. to produce a more effective dieresis with a lower incidence of side effects than seen with bolus administration. Higher infusion rates may cause transient deafness. The addition of **small oral doses of metolazone** may also be considered which is a weak thiazide diuretic alone but produces a synergistic action with loop diuretics. Metolazone is commonly used because, unlike other thiazides, it produces effective diuresis at GFR < 20 ml/min.

Patients with renal insufficiency often encounter a decreased response to loop diuretics often referred to as "diuretic resistance." Some common causes of diuretic resistance in ARF are excessive sodium intake, inadequate diuretic dose or inappropriate regimen, reduced bioavailability (from gastrointestinal edema), reduced renal blood flow (drugs, intravascular depletion) and nephrotic syndrome (in nephrotic syndrome, diuretics bind to proteins in the renal tubule, reducing diuretic effects). Strategies to overcome diuretic resistance may include increasing the dose or the dosing frequency; continuous intravenous infusion of the diuretic; and concomitant administration of loop diuretics with diuretics that act at the distal convoluted tubule (thiazides) or the collecting duct (amiloride, triamterene, and spironolactone).

Mannitol

The rationale for using mannitol in ARF arises from the concept that tubular debris may contribute to oliguria. Mannitol 20% is typically started at a dose of 12.5 to 25 g IV over 3 to 5 minutes. **Mannitol can cause volume overload**. Consequently, mannitol is now not recommended for patients with ARF.

Fenoldopam

Fenoldopam is a selective dopamine-1 receptor agonist that is approved for short term management of severe hypertension. Because it does not stimulate dopamine-2, α-adrenergic, and β-adrenergic receptors, fenoldopam causes vasodilation in the renal vasculature with potentially fewer non-renal effects than dopamine.

Treatment of hyperkalemia

This is a particular problem in AKI because urinary excretion is reduced and intracellular potassium may be released. Rapid rises in extracellular potassium are to be expected when there is tissue damage as in burns, crush injuries and sepsis. Acidosis also aggravates hyperkalemia by provoking potassium leakage from healthy cells. The condition may be life-threatening causing cardiac arrhythmias and, if untreated, can result in asystolic cardiac arrest.

Dietary potassium should be restricted to less than 40 mmol/day and potassium supplements and potassium-sparing diuretics removed from the treatment schedule. Emergency treatment is necessary if the serum potassium level reaches 7mmol/L (normal range 3.5–5.5 mmol/L) or if there are the progressive changes in the electrocardiogram (ECG) associated with hyperkalemia. **Emergency treatment of hyperkalemia** consists of the following:

- 10–30 mL (2.25–6.75 mmol) of calcium gluconate 10% intravenously over 5–10 min; this improves myocardial stability but has no effect on the serum potassium levels.
- 50 mL of 50% glucose together with 8–12 units of soluble insulin over 10 min. to stimulates intracellular potassium uptake, thus removing it from the serum.
- Nebulized salbutamol has also been used to lower potassium; however, this is not effective for all patients and does not permanently lower potassium.

Treatment of acidosis

The inability of the kidney to excrete hydrogen ions may result in a metabolic acidosis. This may contribute to hyperkalemia. It may be treated orally with sodium bicarbonate 1-6g/day in divided doses or 50–100 mmol of bicarbonate ions (preferably as isotonic sodium bicarbonate 1.4 % or 1.26 %, 250–500 mL over 15–60 min) intravenously may be used. The administration of bicarbonate in patients with metabolic acidosis will also tend to reduce serum potassium concentrations.

Treatment of hypocalcaemia

Calcium malabsorption, probably secondary to disordered vitamin D metabolism, can occur in AKI. Hypocalcaemia usually remains asymptomatic, as tetany of skeletal muscles or convulsions does not normally occur until serum concentrations are as low as 1.6–1.7 mmol/L (normal 2.20–2.55 mmol/L). Oral

calcium supplementation with calcium carbonate is usually adequate, and although vitamin D may be used to treat the hypocalcaemia of AKI, it rarely has to be added. Effervescent calcium tablets should be avoided as they contain a high sodium or potassium load.

Treatment of hyperphosphataemia

Hyperphosphataemia can occur in ARF but rarely requires treatment. phosphate-binding agents may be used to retain phosphate ions in the gut. The most commonly used agents are calcium containing such as calcium carbonate or calcium acetate and are given with food.

Treatment of hyponatremia

Moderate or asymptomatic hyponatremia may require only **fluid restriction**. **Sodium chloride** may be given for severe symptomatic hyponatremia (i.e., a serum sodium level below 120 mEq/L). Sodium chloride replaces and maintains sodium and chloride concentration, thereby increasing extracellular tonicity. A 3% or 5% sodium chloride solution may be administered by slow IV infusion. Typically, 400 mL or less is administered.

Treatment of infection

Bladder catheters, central catheters and even peripheral intravenous lines should be used with care to reduce the chance of bacterial invasion. Antibiotic therapy should be broad spectrum until a causative organism is identified.

Uraemia and intravascular volume overload

The symptoms of uraemia include **nausea, vomiting and anorexia**, and result principally from accumulation of toxic products of protein metabolism including urea. Unfortunately, severely ill patients are unable to tolerate any kind of diet. **The use of enteral or parenteral nutrition** should be considered at an early stage. **Restricting NaCl intake to about 1–2 g/day** if the patient is not hyponatraemic **and total fluid intake to less than 1 L/day**. Care should be taken with the so-called '**low salt**' **products**, as these usually **contain KCl,** which will exacerbate hyperkalaemia.

Renal replacement therapy

Renal replacement therapy is indicated in a patient with ARF **when life is at risk**. Generally, replacement therapy is urgently indicated in ARF to:

1. **remove toxins** when severe symptoms are apparent, for example, impaired consciousness, seizures, pericarditis, rapidly developing peripheral neuropathy

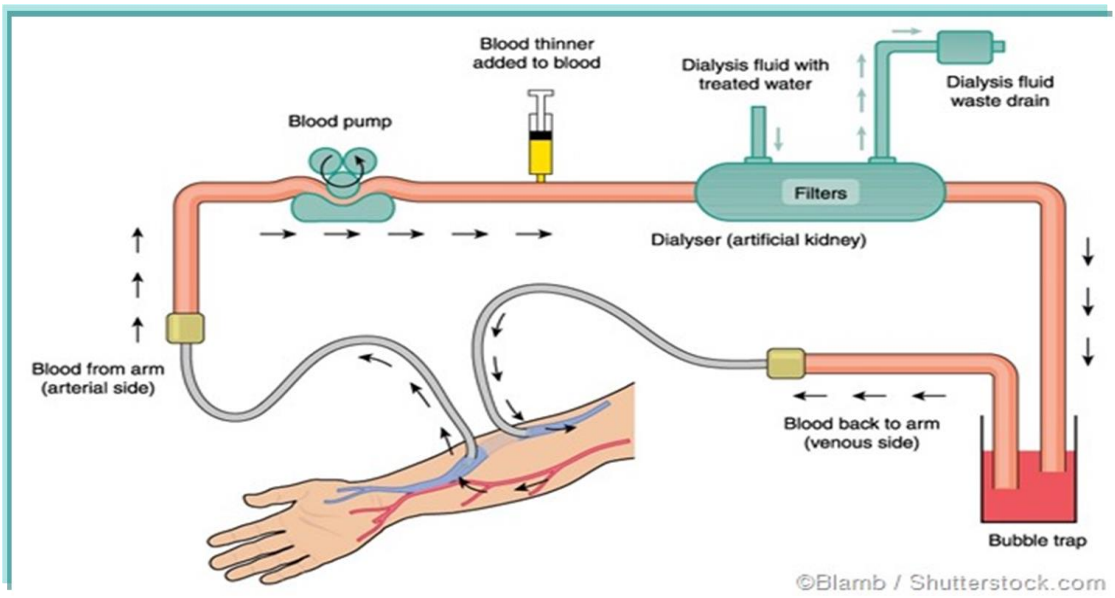
2. **remove fluid resistant to diuretics**

3. **correct electrolyte and acid–base imbalances**, for example, hyperkalaemia >6.5 mmol/L or 5.5–6.5 where there are ECG changes, increasing acidosis (pH < 7.1 or serum bicarbonate <10 mmol/L) despite bicarbonate therapy, or where bicarbonate is not tolerated because of fluid overload. The common types of renal replacement therapy used in clinical practice are: haemodialysis and peritoneal dialysis. In all types of renal replacement therapy, **blood is presented to a dialysis solution** across some form of **semi-permeable membrane** that allows free movement of **low molecular weight compounds**.

Haemodialysis

A dialysis catheter is a catheter used for exchanging blood to and from a hemodialysis machine and a patient. The dialysis catheter contains two lumens: venous and arterial. Although both lumens are in the vein, the "arterial" lumen, like natural arteries, carries blood away from the heart, while the "venous" lumen returns blood towards the heart. The arterial lumen (typically red) withdraws blood from the patient and carries it to the dialysis machine, while the venous lumen (typically blue) returns blood to the patient (from the dialysis machine). The catheter is placed in a vein (the jugular, femoral or sub- clavian).

Heparin is added to the blood as it leaves the body to prevent the dialyzer clotting. In those patients at high risk of haemorrhage, the amount of heparin used can be reduced or even avoided. Haemodialysis can be performed in either intermittent or continuous schedules. The latter regimen is preferable in the critical care situation, providing 24-h control, and minimizing swings in blood volume and electrolyte composition that are found using intermittent regimens.



peritoneal dialysis

Peritoneal dialysis is rarely used now for ARF except in circumstances where haemodialysis is unavailable. A semi-rigid catheter is inserted into the abdominal cavity. A warmed sterile dialyzing solution (up to 2 L for adults and 1 L for children) is introduced in to the peritoneal cavity over a period of 15 to 20 min. The fluid is left in place for 45 to 60 min for equilibration to occur and then removed. A fresh solution is reintroduced & the process repeated. Up to 30L or more of dialysis fluid may be used. Peritoneal dialysis is relatively cheap and simple, does not require specially trained staff. It is associated with a high incidence of peritonitis and permits protein loss, as albumin crosses the peritoneal membrane.