Pharma Health SciencesS

International Journal of Pharma Research and Health Sciences

Available online at www.pharmahealthsciences.net


**Review Article**

# Management of Acute Renal Failure

S Navaneetha Krishnan *, G shaji, S Salma, Y Pallavi

Department of Pharmacy Practice, Browns College of Pharmacy, Khammam, AndraPradesh, India.

ARTICLE INFO

Received: 14 Feb 2014

Accepted: 26 Feb 2014

Key words:

Acute renal failure, etiology, complication, management, prognosis.

ABSTRACT

Acute renal failure is the generic term for an abrupt and sustained decrease in renal function resulting in retention of nitrogenous (urea and creatinine) and non-nitrogenous waste products. Depending on the severity and duration of renal the renal dysfunction, this accumulation is accompanied by metabolic disturbance, such as metabolic acidosis and Hyperkalemia, change in fluid balance and effect on many other organ systems. Acute renal failure (ARF) is the major causes of mortality and morbidity in world wide. Death rate for ARF with superimposed with Coronary artery disease, cerebral ischemia and hypertension etc. The present work summarise etiology, complication issues, management and prognosis of acute renal failuredrug release.

## 1. INTRODUCTION

Acute renal failure (ARF) is a common complication of critical illness, which is associated with high mortality and has a separate independent effect on the risk of death[1, 2]. Acute renal failure is now being more often referred to as acute kindney injury (AKI). Which defined as an abrupt or rapid decline in glomerular filtration rate (GFR) usually accompanied by a rise in serum creatinine and blood urea nitrogen (Azotaemia) .it is important to note that a rise in creatinine and urea may not present after the kidney injury and that the

Corresponding author *

E-mailaddress:nasveen@gmail.com(S.Navaneetha Krishnan)

only sign of acute kidney injury may be decreased urine production.[3]

### *1.1 Etiology*

The causes of ARF traditionally have been divided into three major categories based on pathophysiology: pre-renal, intrinsic renal, and postrenal (Table-1). Prerenal etiologies are the most common, accounting for 30% to 60% of all cases of ARF [4]. Prerenal azotemia results from either an absolute or relative decrease in blood volume or altered intrarenal hemodynamic, decreasing renal perfusion without cellular injury. It is rapidly reversible if the hemodynamic insult is corrected. If the insult is sustained, then overt cellular injury results (i.e., acute tubular necrosis [ATN] with transition from prerenal to intrinsic ARF. Postrenal ARF is less common in the hospital setting, accounting for between 1% and 10% of cases of hospital-acquired ARF, and is characterized by structural and functional obstruction of the urinary tract.

**Table 1: Common causes of hospital Acquired Acute Renal Failure**

| |
|---|
| **Prerenal** |
| True volume depletion nausea/vomiting, hemorrhage, burns, diarrhea/ostomy output, diuretics. |
| Effective volume depletion: congestive heart failure, hepatorenal syndrome, sepsis/third spacing of fluids, pancreatitis. |
| **Intrinsic** |
| Ischemic acute tubular necrosis: shock from any cause,vasopressors |
| Nephrotoxic acute tubular necrosis Medications aminoglycosides, amphotericin B, radiocontrast agents, osmotic agents, crystal forming agents acyclic nucleotide phosphonates, zoledronate/pamidronate, oral sodium phosphate solution. |
| Endogenous toxins: light chains, hemo pigments, uric acid |
| Vascular injury: renal cholesterol emboli (atheroemboli) |
| **Postrenal** |
| Retroperitoneal obstruction: hematoma, cancer |
| Bladder outlet obstruction: structural, functional |

Obstruction occurs at any level from renal pelvis to the urethra; either complete or partial obstruction can cause ARF. Postrenal cause should be quickly recognized and treated because recovery of renal function is inversely related to the duration of obstruction[5].

Intrinsic renal failure is considered after prerenal and Postrenal causes have been excluded and clinical data point to a structural problem within the kidneys. Intrinsic renal diseases are characterized according to the primary site of injury, including the vasculature, glomerulus, tubules, and interstitium. The most common form of hospital-acquired intrinsic renal failure is ATN. This term is misleading because there is a spectrum of tubular necrosis. The most common causes of ATN are ischemia, exogenous toxins (drugs and radio contrast agents), endogenous toxins (heme pigments and toxic light chains), and natural or drug-induced urinary crystals [6].

### *1.2 Complications*

Complications of kidney failure can affect multiple systems of the body. When the kidneys are effected, less urine output occurs which will lead to fluid retention. Fluid retention causes the swelling of hands, feet and legs. As fluid backs up, it can affect the cardiovascular system, causing the patient to have high blood pressure and possibly heart failure because the heart cannot pump the additional fluid. As fluid overload continues, the respiratory system is affected, and the patient will develop shortness of breath. Waste products will build up in the blood and can affect the patient's mental status. Confusion, decreasing level of alertness and seizures are complications associated with the build-up of toxins in the blood stream. Acute kidney failure will impact red blood cell production, which means there is a decreased in the amount of red blood cells that carry oxygen to the tissues. Kidney failure causes nausea, vomiting and anorexia. When a patient is not getting the necessary nutrition, she will lose body mass and muscle [7].

ARF impairs renal excretion of sodium, potassium, and water perturbs dilavent cation homeostasis and urinary acidification mechanisms. As a result, ARF is frequently complicated by intravascular volume

overload,hyponatremia,hyperkalemia,hyperphosphotamia, hypocalcemia, hypermagnesemia, and metabolic acidosis. In addition, patients are unable to excrete nitrogenous waste products and are more prone to develop the uremic syndrome. The speed of the development and the severity of these complications reflect the degree of renal impairment and catabolic state of the patient.

Expansion of the extracellular fluid volume is an inevitable consequence of diminished salt and water excretion in oliguric or anuric individuals. Whereas milder forms are characterized by weight gain, bibasilar lung rales, raised jugular venous pressure, and dependent edema, continued volume expansion may precipitate life-threatening pulmonary edema. Excessive administration of free, either through ingestion or nasogastric administration or as hypoosmolality and hyponatremia, if severe leads to neurologic abnormalities, including seizures [8].

## 2. MANAGEMENT

The initial care of patients with ARF should focus on reversing the underlying cause (prerenal and postrenal) and correcting fluid, electrolyte, and acid-base imbalances (Table 2). Every effort should be made to prevent further kidney injury and to provide supportive care (including dialysis), until recovery occurs.

### *2.1 Fluids*

An important goal of patient management is maintaining euvolemia. Careful physical examination and, when appropriate, invasive monitoring is vital to this process. Achieving appropriate fluid balance involves two conflicting goals: providing sufficient volume to ensure adequate renal perfusion and avoiding volume overload with resulting pulmonary congestion. Attention to all sources of fluid intake and output, including surgical drains, nasogastric suction, diarrhea, and insensible losses is required. There is no substitute for daily weights. Rapid restoration of intravascular volume may reverse prerenal azotemia and prevent ischemic damage. Crystalloid solutions are often the best fluid choice. In situations of increased vascular permeability, colloid solutions may provide enhanced restoration of intravascular volume. Albumin therapy should be restricted to situations where synthetic colloids cannot be used,[9] the synthetic colloids, hydroxyethyl starch (HES) solutions with low in vivo molecular weight (HES, 200/0.5) demonstrate the best risk/benefit ratio,[10] but these should be avoided in patients with underlying kidney disease due to enhanced risk of ARF.

**Table 2: Strategies for Management of Acute Renal Failure**

| |
|---|
| Exclude urinary tract obstruction by utilizing clinical suspicion, assessment of postvoid urine residual, and renal ultrasonography |
| Evaluate for the presence of a prerenal state |
| If evidence of intravascular depletion is present, restore intravascular volume |
| Always consider the possibility of intrarenal causes that require early diagnosis |
| Discontinue all potential nephrotoxins or drugs associated with acute interstitial nephritis |
| Search for and treat acute uremic complications such as hyperka-lemia, hyponatremia, acidosis, and volume overload Optimize nutritional status and avoid foods high in potassium and phosphorus |
| Dose drugs appropriately according to estimated renal clearance using glomerular filtration rate estimation formulas, recognizing their limitations in the setting of acute renal failure |
| Initiate renal replacement therapy before uremic, metabolic, or volume-related complications develop |

### *2.2 Vasoactive Agents*

If hypotension persists despite adequate fluid replacement, vasopressors are indicated. However, intrarenal vasoconstriction develops with these drugs and may negate the hemodynamic benefit of increased blood pressure. Norepinephrine reduces renal blood flow in normal humans but improves renal blood flow

and augments urine output and GFR in patients with septic shock.[11] Vasopressin also increases urine output and GFR in patients with septic shock,[12] Inotropic agents such as dobutamine increase cardiac output and augment renal blood flow in patients with systolic dysfunction and ARF. Low-dose dopamine (0.5–0.2 µg/kg body weight) is commonly used to increase urine output in oliguric patients. Several studies have demonstrated that dopamine does not promote renal recovery or reduce mortality,[13–15] and is associated with tachyarrhythmias, pulmonary shunting, and gut or digital necrosis.[16] Dopamine should not be employed in the treatment of ARF.

***2.3 Diuretics***

Diuretics are often required to treat ARF when volume overload develops. Loop diuretics (furosemide, ethacrynicacid, torsemide) diminish active transport and energy requirements in the thick ascending limb. Although a favorable diuretic response occurs with these drugs when administered within the first 24 hours of onset of oliguria, this effect does not translate into enhanced renal recovery or a mortality benefit. In a prospective study of loop diuretics in ARF, no significant difference in renal recovery, requirement for dialysis, or death was observed, [17] In another study, diuretics were associated with non-recovery of renal function and increased risk of death in critically-ill patients,.[18] Other diuretics such as mannitol are used in limited clinical situations such as rhabdomyolysis with myoglobinuric ARF. Thiazide diuretics may increase urine output when combined with loop diuretics. Thus, diuretics should be used only in ARF for management of volume with no expectation that these agents improve outcomes.

***2.4 Metabolic Management***

Acidosis: Metabolic acidosis in ARF can be explained largely by (1) reduced renal excretion of acid and several organic and inorganic anions and (2) excessive acid production via catabolism. Correction of metabolic acidosis enhances response to vasopressors, improves cardiac contractility, ameliorates bone injury due to acid buffering, and reduces catabolism. Bicarbonate containing intravenous fluids correct acidosis, but proper use is required to limit excess volume repletion and minimize symptoms of hypocalcemia. Depending on the serum sodium concentration, sodium bicarbonate (50–150 mEq) can be added to a liter of either 5% dextrose in water or 0.45% normal saline to make an isotonic solution. Oral bicarbonate or bicarbonate precursors (citrate) are preferable in patients able to take pills or a liquid preparation. The goal is to correct the serum bicarbonate to approximately 22 mEq/L, depending on respiratory status and arterial pH.

Hypernatremia: Hypernatremia is the most common electrolyte abnormality in oliguric renal failure and usually is the result of excess water in the setting of reduced renal free water clearance. Sources of free water in hospitalized patients are hypotonic solutions (5% dextrose, 0.45% normal saline), parenteral medications administered in 5% dextrose, or excessive amounts of hypotonic fluid with enteral or parenteral feeds. Restriction of these types of fluid often minimizes worsening of hypernatremia and allows slow correction.

Hyperkalemia: Hyperkalemia is the most serious electrolyte abnormality associated with ARF. Cardiac toxicity as manifested by several forms of arrhythmia is a life-threatening complication. Serum potassium concentrations greater than 6.0 to 6.5 mEq/L require rapid therapy. The electromechanical effects of hyperkalemia are potentiated by hypocalcemia, acidosis, and certain medications. The ECG, which measures the summation of these effects, should be examined in concert with serum potassium concentration. The earliest change is peaked T waves,

followed by shortening of the QT interval and flattening of P waves, which eventually disappear. Later, QRS complex widening, prolongation of the QT interval, and ultimately a sine wave pattern develop.

Therapy is based on stabilization of excitable membranes, rapid reduction in serum potassium concentration utilizing cellular shift, and removal of potassium from the body (Table 3). Along with these interventions, limited potassium intake is an obvious therapy. Hyperphosphatemia and hypocalcemia. Impaired renal function limits phosphate excretion and promotes hyperphosphatemia. Cell release of phosphate in certain settings (rhabdomyolysis, tumor lysis syndrome, and hemolysis) exacerbates hyperphosphatemia. Severe hyperphosphatemia can cause hypocalcemia and soft tissue calcium and phosphate deposition as well as impair renal function. Hypocalcemia is often asymptomatic, although tetany can develop with overly aggressive correction of acidosis.

**Table 3: Treatment of Hyperkalemia**

| |
|---|
| **Stabilize excitable tissues (cardiac and neuromuscular):** Calcium gluconate (10% solution), 10 to 20 mL given as an intravenous bolus Calcium chloride (10% solution), 5 mL given as an intravenous bolus Each may be repeated every 5 min if the electrocardiogram appearance does not improve. Calcium gluconate should be mixed in 100 mL of 5% dextrose and infused over 10 to 20 min if the patient has been treated with digoxin. |
| **Shift potassium into cells:** Regular insulin, 10 U plus 50 mL of 50% dextrose given as an intravenous bolus, followed by 10% dextrose at 50 mL/min until definitive therapy is instituted. Check glucose levels at 1 to 2 h intervals. Albuterol (5 mg/mL concentration), 10 to 20 mg nebulized over approximately 10 min Terbutaline, 7 µg/kg administered via subcutaneous injection Combination therapy of insulin/dextrose and nebulized albuterol |
| **Remove potassium from the body:** Acute hemodialysis (low potassium dialysate) to remove potassium in patients with severe renal insufficiency Sodium polystyrene sulfonate, 15 to 30 g plus 15 to 30 mL of sorbitol administered orally or rectally (without sorbitol) |

Treatment of hyperphosphatemia is based on reducing gastrointestinal absorption. Reduced dietary phosphate (including parenteral nutrition) and oral phosphate binders with meals are the mainstay of treatment. Phosphate-containing bowel-cleansing regimens should be avoided. Hypocalcemia rarely requires therapy in the absence of symptoms of tetany. If symptoms develop, intravenous calcium gluconate should be administered to acutely improve symptoms, followed by oral calcium carbonate to correct the calcium to the lower limit of normal.

### *2.5 Renal Replacement Therapy*

Multiple modalities of renal replacement therapy (RRT) are available to manage ARF, including intermittent hemodialysis (IHD), peritoneal dialysis (PD), continuous renal replacement therapy (CRRT), and new "hybrid" therapies such as sustained low efficiency dialysis. Despite 4 decades of experience with RRT in ARF, there are no strict guidelines on the appropriate indications for initiation of therapy, the most appropriate modality, and the optimal dose of dialysis. Despite the absence of solid evidence, there is general consensus regarding some of these issues. Treatment should be initiated before uremic, metabolic, and volume-related complications occur.[19] Commencement of RRT is appropriate for volume overload that is unresponsive to diuretics, hyperkalemia and metabolic acidosis, refractory to conservative measures, and pericarditis or encephalopathy due to uremia. Strict laboratory values per se are not an indication for initiation of RRT, although a low threshold develops when the BUN level exceeds 100 mg/dL.

Until CRRT emerged as a form of therapy, IHD, and less commonly, acute PD was utilized for severe ARF. The advantages of CRRT over IHD include more precise fluid, electrolyte, and metabolic control; increased hemodynamic stability; and the ability to

administer unlimited nutritional support. The disadvantages of CRRT include requirements for prolonged anticoagulation, patient immobilization, and sophisticated nursing surveillance. PD is utilized in hypotensive patients where CRRT is unavailable. Although CRRT is often considered to be superior to IHD, studies have not demonstrated a significant difference in patient outcomes.[20] However, CRRT is preferable in patients with cerebral edema, liver failure, severe lactic acidosis, and profound hypotension. Sustained low efficiency dialysis has promise as a hybrid therapy that combines the advantages of both continuous and intermittent therapies.

***2.6 Prognosis***

When acute renal failure is severe enough to necessitate renal replacement therapy, in-hospital mortality is high, exceeding 50%. [21-23]. The long-term effects of acute renal failure are unclear and controversial because of the diverse (and in many cases multiple) causes of the disorder and the paucity of long-term follow-up studies. Nevertheless, the view that recovery is complete is simplistic, and progressive renal dysfunction after severe acute renal failure is commonly observed [24-27]. ARF is irreversible in 5% of patients, but in elderly people this proportion is as high as 16%[28]. Recent reports on children suggest that residual damage after acute renal failure by adolescence or early adulthood.[28]

## 3. CONCLUSION

Hospitalized patients may develop ARF from various etiologies, although ATN is the most common cause. Rapid diagnosis utilizing history, chart review, physical examination, and laboratory data enhances the chances for renal recovery. Appropriate management of ARF and its complications is required to improve patient outcome. ARF that requires RRT is associated with increased mortality.

## 4. REFERENCES


1. Chertow GM, Levy EM, Hammermeister KE, Grover F, Daley J. Independent association between acute renal failure and mortality followingcardiac surgery. J American Med Asso 1998; 104:343-348.
2. De Mendonca A, Vincent JL, Suter PM, Moreno R, Dearden NM, Antonelli M, Takala J, Sprung C, Cantraine F. Acute renal failure in the ICU: risk factors and outcome evaluation by SOFA score. Int care Med 2000; 26:915-921.
3. http://www.pediatriconcall.com/fordoctor/diseases andcondition/pediatric_nephrology/acute_renal_failure.asp (accessed on 20 June 2012)
4. Shapiro SR, Bennett AH. Recovery of renal function after prolonged unilateral urethral obstruction. J Urol 1976; 115:136-40.
5. Kaufman J, Dhakal M, Patel B, Hambuger R Community acquired acute renal failure. Am J Kidney Dis 1991; 17:191-8.
6. Richards NT, Darby S, Howie AJ, etal. Knowledge of renal histology alters patient management in over 40% of cases. Nephrol dial Transplant 1994; 9; 1255-1259.
7. http://www.livestrong.com/article/250938-acute-renal-failure complication/#ixzz24vSrWrg6 (accessed on 21 June 2012)
8. http://www.mhprofessional.com/downloads/products/0071663398/jameson_nephrology_ch10_p097-112.pdf(accessed on 22 June 2012)
9. Cochrane IGAR. Human albumin administration in critically ill patients; systematic review of randomized controlled trials. Cochrane injuries

groupa albumin reviewers. British Med J 1998; 317; 235-240.

10. Rageller MJ, Theilen H, Koch T. volume replacement in critically ill patients with acute renal failure. J Am Soc Nephrol 2001; 12: Suppl 17 S33-39.
11. Schetz M. Vasopressors and the kidney. Blood Purif 2002; 20:243–51.
12. Patel BM, Chittock DR, Russel JA, Walley KR. Beneficial effects of short term vasopressin infusion during severe septic shock. Anathesiology 2002; 96; 576-82.
13. Bellomo R, Chapman M, Finfer S. Low-dose dopamine in patients with early renal dysfunction: a placebo controlled randomised trial. Australian and New Zealand Intensive Care Society (ANZICS) Clinical Trials Group. Lancet 2000; 356: 2139–43.
14. Denton MD, Chertow GM, Brady HR. Renal-dose dopamine for the treatment of acute renal failure: scientific rationale, experimental studies and clinical trials. Kidney Int 1996; 50: 4–14.
15. Kellum JA, Decker J. Use of dopamine in acute renal failure: a meta-analysis. Crit Care Med 2001; 29: 1526–31.
16. Thompson BT, Cockrill BA. Renal-dose dopamine: a siren song? Lancet 1994; 344:7–8.
17. Shilliday IR, Quinn KJ, Allison ME. Loop diuretics in the management of acute renal failure: a prospective, double- blind, placebo-controlled, randomized study. Nephrol Dial Transplant, 1997; 12:2592–6.
18. Mehta RL, Pascual MT, Soroko S, et al. Diuretics, mortality, and nonrecovery of renal function in acute renal failure. PICARD Study Group. J American Med Asso 2002; 288:2547–53.
19. D'Intini V, Ronco C, Bonello M, Bellomo R. Renal replacement therapy in acute renal failure. Best Pract Res Clin Anaesthesiol 2004; 18:145–57.
20. Tonelli M, Manns B, Feller-Kopman D. Acute renal failure in the intensive care unit: a systematic review of the impact of dialytic modality on mortality and renal recovery. Am J Kidney Dis. 2002; 40:875–85.
21. Metcalfe W, Simpson M, Khan IH, et al. Acute renal failure requiring renal replacement therapy: incidence and outcome. Quaterly J Med 2002; 95: 579–83.
22. Liano F, Junco E, Pascual J, Madero R, Verde E. The spectrum of acute renal failure in the intensive care unit compared with that seen in other settings. Kidney Int Suppl 1998; 66: S16–24.
23. Karsou SA, Jaber BL, Pereira BJ. Impact of intermittent hemodialysis variables on clinical outcomes in acute renal failure. Am J Kidney Dis 2000; 35: 980–91.
24. Finn WF. Recovery from acute renal failure. In: Molitoris BA, Finn WF, eds. Acute renal failure: a companion to Brenner and Rector's the kidney, 1st edn. Philadelphia: WB Saunders, 2001: 425–50.
25. Alon US. Neonatal acute renal failure: the need for long-term follow-up. Clin Pediatr (Phila) 1998; 37: 387–89.
26. Polito C, Papale MR, La Manna A. Long-term prognosis of acute renal failure in the full-term neonate. Clin Pediatr (Phila) 1998; 37: 381–85.
27. Shaw NJ, Brocklebank JT, Dickinson DF, Wilson N, Walker DR. Long-term outcome for children with acute renal failure following cardiac surgery. Int J Cardiol 1991; 31: 161–65.
28. Bhandari S, Turney JH. Survivors of acute renal failure who do not recover renal function. Quaterly J Med 1996; 489: 415–21.