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ACUTE RENAL FAILURE: STRATEGIES FOR THE MANAGEMENT AND TREATMENTS

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ABSTRACT

Acute renal failure (ARF) recently known as Acute Kidney Injury(AKI), characterized by sudden loss of ability of the kidney to excrete waste, concentrate urine, conserve electrolyte, and maintain fluid balance is a common condition. There is a rapid decline in glomerular filtration rate (GFR) and is usually marked by rapid rise in serum creatinine level. In sudden acute renal failure no biochemical changes occur and the only sign of ARF is low urine output. Azotemia is also a characteristic feature of ARF. Management includes correction of fluid and electrolyte levels; avoidance of nephrotoxin and kidney replacement therapy, when appropriate. The purpose of this review is to discuss the differential and possible treatments of acute renal failure. It also includes the discussion about possible etiologies, biochemical changes and recovery pattern of the patients.

KEYWORDS: Electrolytes, GFR, Nephrotoxin, Creatinine, Azotemia, Electrolytes.

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INTRODUCTION

Acute renal failure is defined as sudden and reversible decline in kidney functions, to excrete nitrogenous waste and maintain fluid and electrolyte homeostasis. ARF occurs rapidly (over hours to weeks).[1] It is a reversible condition if proper treatments are given but can progress to chronic stage and later end stage renal failure (ESRF) if not treated. ARF is common, complicating 5% of all medical and surgical admissions in a large American study.[2] ARF, the traditionally used name was replaced recently by Acute Kidney Injury (AKI). Normally the kidneys filter the blood and remove waste and excess salt and water. A moderate increase in creatinine and reduction in glomerular filtration rate (GFR) increases the risk of mortality. As ARF is often preventable, identification and administration of medications are crucial.[3]Acute renal failure has various etiologies including pre-renal, renal, post-renal or diabetic nephropathy and so on. Co-existence of any of these causes in same patient reveals that even mild and reversible ARF can be fatal and should be given great care. [4, 5] Biochemical changes include rise in serum creatinine level, blood urea nitrogen level, potassium level, and urine osmolarity.[6] The etiological factors responsible for acute renal failure, its biochemical changes, and management and treatment possibilities are discussed below.

ETIOLOGICAL FACTORS OF ACUTE RENAL FAILURE

PRE RENAL FACTORS

These factors causes following changes:

- Hypovolaemia: Due to excessive loss of water from body in dehydration condition, the concentration of extracellular fluid and plasma volume get disturbed that leads to less flow of blood, hence there will be Hypovolaemia.
- Oedematous changes: these changes leads to low blood flow such as cardiac failure or other heart conditions, liver failure or cirrhosis causing changes in hormones that affect blood flow and pressure of kidneys .[7,8]
- Vascular embolism: blockage or narrowing of renal artery due to mild clot formation.
- Hypotension: due to cardiac shock and sepsis.
- Less renal perfusion: due to drugs action such as NSAID's, ACE inhibitors or receptor antagonists.[9]

RENAL FACTORS

These factors are also known as intrinsic factors that affect the internal parts of kidney or majorly give direct impact on kidney .[10] These factors cause ATN (acute tubular necrosis) means damage to the cellular organization of renal tubules. These factors are as follows:

- Inflammatory events: inflammation in kidney tubules may occur in case of glomerulonephritis, interstitial nephritis. This inflammation occurs due to certain nephrotoxin such as excessive use of drugs like aminoglycosides, abnormal protein accumulation, heavy metals deposition, bacterial infections such as post Streptococcal infection .[11]
- Vascular diseases such as microangiopathies, embolism, cholesterol, renal vein blockage, hypertension etc.

POST RENAL FACTORS

These factors are responsible for causing problems that affecting the movement of urine out of the kidneys .[12,13] These factors could be:

- Cancer of UT (urinary tract) organs.
- Calculi formation in ureter, urethra.
- Benign prostate hyperplasia.
- Hypertrophy.
- Urethra stricture.
- Bladder tumor.
- Pelvic malignancy.
- Septic shock and excessive use of antibiotics and pain killers.

RISK FACTORS OF ARF [14,15]

The following patients could be more prone for ARF due to some pre complications inside their body those are considered as risk factors. These are as following:

- Advanced age ≥ 65 years.
- Diabetes.
- High blood pressure.
- Heart failure.
- Liver disease such as cirrhosis.
- Emergency surgery.
- Nephrotoxin medications.[16]
- Neurological impairment or disability.

BIOCHEMICAL CHANGES IN ARF

1. ELECTROLYTES IMBALANCE

- Hyperkalemia: Due to excessive loss of sodium ions from body, potassium ions get accumulated in blood and leads to hyperkalemia condition.
- Hyperphosphatemia: Due to excessive loss of calcium ions from body in case of acute renal failure, potassium ions will be accumulates in body. As these both ions are antagonist to each other.
- Hyponatremia: in case of dehydration and heavy loss of sodium ions from body leads to Hyponatremia condition.
- Hypocalcaemia: in acute kidney failure, DCT (distilled convoluted tubule) will lose its property to reabsorb calcium, hence hypocalcaemia.[18]

2. UREA AND CREATININE LEVEL RAISED IN BLOOD

In case of acute renal injury, kidney will unable to excrete nitrogenous waste, so nitrogenous compounds such as urea and creatinine will get accumulated in blood. This leads to increased level.

3. METABOLIC ACIDOSIS

due to failure, kidney will not be able to excrete extra hydrogen ions from body and there will be imbalance between HCO_3^- (hydronium ions) and H^+ hydrogen ions and this will be leads to retention of hydrogen ions inside body and causes metabolic acidosis. [12, 19]

4. DECREASE IN GLOMERULAR FILTRATION RATE

In acute renal failure the condition of oliguria or anuria occurs that is due to less glomerular filtration rate. Means glomerular apparatus of nephron will not be able to filter the blood plasma due to any etiological factor.

5. PULMONARY EDEMA

This occurs due to volume overload or fluid deposition in intracellular tissue space. That leads to swelling in legs, feet or another part of body . [15]

MANAGEMENT OF ARF

- Restriction of nephrotoxic drugs by Rhabdomyolysis. [17](forced alkaline diuresis)
- Volume overload in body should be managed by restriction of salt and water, by diuresis.
- Hyponatremia could be managed by restriction of enteral free water intake, minimization of hypotonic IV solutions.
- Hyperkalemia could be managed by restricting dietary potassium intake, loop diuretics to promote urinary potassium loss etc.
- Metabolic acidosis could be managed by sodium bicarbonate, administration of bases such as THAM (Tris hydro methyl amino methane). [18]
- Hyperphosphatemia could be managed by restricting phosphate dietary intake, by taking phosphate binding agents such as Calcium acetate, aluminum hydroxide in meals.
- Hypocalcaemia if symptomatic could be managed by administration of calcium carbonate or calcium gluconate.
- Sufficient proteins and calories should be taken in nutrients to avoid negative nitrogen balance.
- Patient should consult with urologist if appropriate such as in obstruction cases . [19, 20] Drug medications should be administered with doctor's prescription and guidelines.

TREATMENTS

The treatments for acute renal failure should begin at the earliest indication of renal dysfunction. Maintenance of volume homeostasis and correction of biochemical abnormalities remain the primary goals of treatment.

CORRECTION OF HYPERKALEMIA

Hyperkalemia (serum potassium level more than 6 millimol/l) in patients of ARF is life threatening because of cardiac arrhythmias. Rise in potassium level leads to changes in ECG pattern. Patient should be given urgent treatment for hyperkalemia if potassium level rises above 6 millimol /L . [21]

CALCIUM RESONIUM AND RESONIUM A MECHANISM

Potassium binding resins bind to the gut lumen, in exchange for calcium or sodium and result in increased potassium excretion in stool. These are the most commonly used drug for the treatment of hyperkalemia associated with anuria or severe oliguria. Calcium Resonium is for oral or rectal administration only. Together with this drug lactulose, an osmotic laxative is given to prevent constipation. Side effects include hypercalcaemia, salt or water overload, and hypomagnesaemia.

Table 1
Summary of treatment strategies in hyperkalemia

Treatment	Action immediacy	Reduction in $[K^+]$	Duration of action
Insulin	15-30 min.	0.65-1.0 mmol/L	4-6 hrs.
Salbutamol	30 min.	0.6-1.0 mmol/L	2-4 hrs.
Ion exchange resins	2-3 hrs.	0.5-1.0 mmol/L	4-5 hrs.

INSULIN WITH GLUCOSE AND SALBUTAMOL MECHANISM

Insulin therapy along with glucose and salbutamol promotes the intracellular shift in potassium by indirectly activating the cell membrane Na+/K+ ATPase. Insulin with glucose is given so as to prevent hypoglycemia. After the infusion of this solution reduction in potassium is seen within 20-30 minutes. [22, 23] Salbutamol is beta 2 adrenergic agonists that binds to b2 receptors and through cytosolic second messengers activates the Na+/K+2ATPase, thus Promoting cellular potassium uptake. Nebulized or intravenous administration is preferred for Salbutamol]. [24] Prevention of further potassium accumulation can be achieved by low potassium diet.

CORRECTION OF FLUID OVERLOAD

Fluid overload could be minimized by using diuretic drugs for more excretion of urine from body.

LOOP DIURETICS

Furosemide is a potent loop diuretic frequently used in different stages of acute renal failure. Urine concentration of Furosemide determines its diuretic effect. The response of kidney to Furosemide depends on the severity of acute renal failure . [25] Mechanism: Furosemide is a weak organic acid. It is highly protein bound and about 85% is cleared by Kidneys. Half of it is metabolized and half is secreted in unchanged form. Furosemide acts in the thick ascending limb of loop of Henle. Furosemide acts on the sodium-chloride-

potassium [Na-K-Cl2] co-transporters at the intra-luminal side of the ascending limb of the loop of Henle. Furosemide act by diminishing these ions, thereby increased urinary loses of these ions].[26] Other loop diuretic drugs are Ethacrynic acid and Bumetamide.

THIAZIDE DRUGS

Mechanism: They reduce fluid accumulation in the body by reducing the ability of the Kidneys to reabsorb salt and water from the urine and into the body thereby increasing the product and output of urine. Thiazide drugs act in the proximal convoluted tubule of nephron.

CORRECTION OF METABOLIC ACIDOSIS

Metabolic acidosis often accompanies acute renal failure. Metabolic acidosis a condition that, occurs when the body produces excessive quantities of acid or when the kidneys are not able to excrete enough acid (blood pH more than 7.2).

SODIUM BICARBONATE THERAPY

Mechanism: To reverse metabolic acidosis sodium bicarbonate therapy is preferred. Sodium bicarbonate is an alkaline solution. If bicarbonate is given then it should be monitored

DIALYSIS AND RELATED THERAPIES

Acute kidney injury is associated with morbidity and mortality rates of more than 50% in critically ill patients despite the potential for recovery of renal function and many advances in medical management.[27] For managing the care of patients with acute kidney injury we must optimize their hemodynamic and volume status, correct metabolic abnormalities check for adequate nutrition and minimize progression of injury .Dialysis is often required and critical factors to consider when designing a dialysis strategy for patients with acute kidney injury for determining the extent of dialysis and fluid removal determining when to start and selecting the most appropriate method and dialysis membrane.[28]

INDICATIONS

The indications for dialysis treatment in acute kidney injury is not specific and must be individualized by nephrological consultation. [29]The standard indications for dialysis are symptoms and signs of uremia, volume overloaded ,hyperkalemia and metabolic acidosis that is refractory to medical management . Initially, levels of blood urea nitrogen and serum creatinine were not considered to be primary indicators for dialysis unless they could be related to mental status changes. One of the more challenging issues in the management of acute kidney injury is determining the modality of renal replacement therapy].[30]

DIALYSIS DOSE AND SELECTION OF DIALYSIS MEMBRANE

The optimal dose of dialysis in patients with acute kidney injury is not known. Higher than usual doses have been proposed as beneficial , whether therapy is intermittent ,for 3-4 hours a day or continuous .[31,32,33] A link between the hemodialysis dose and outcome has been previously established in chronic hemodialysis patients. Recent studies have also suggested similar correlation in acute renal failure.[34] In the critically ill patient adequate RRT is probably one of the several factors affecting morbidity and mortality of acute renal failure. In general, a reasonable goal is to maintain adult predialysis blood urea nitrogen less than 80mg/dl. The effect of the type of dialysis membrane on morbidity and mortality in acute renal failure is continuously debated among nephrologists. Recent studies have suggested that biocompatible membranes, when used in patients with ARF are associated with better outcomes including a lower incidence of sepsis when compared with typical cellulosic membranes. These studies suggest that in patient with ARF who require dialysis, biocompatible membranes should be used.[29,35,36]

CONVENTIONAL HEMODIALYSIS

This is the definitive means by which potassium can be removed from the body, and is indicated in refractory severe hyperkalemia .It is more effective than peritoneal dialysis at potassium removal and has an immediate effect once started. In the first hour of dialysis maximum removal occurs. The higher concentrations may be used for the patients who are at the risk of arrhythmias and lower concentration where there is continuous increase in potassium such as rhabdomyolysis, tumor lysis and hemolysis .[37]

PERITONEAL DIALYSIS (PD)

It is effective in the treatment of ARF, but there has been a decline in the use of peritoneal dialysis during the last stage. It is still used in regions where access to acute hemodialysis is not readily available. Peritoneal dialysis has been shown to be effective in hyper catabolic patients [38,39,40,41] and in correction of acidosis .[42]

INTERMITTENT HEMODIALYSIS (IHD)

It has been the standard form of dialysis used to treat ARF but some have suggested this form of renal replacement therapy may actually prolong the course of ARF. Intermittent therapy is typically applied daily or on alternate days depending on the catabolic state usually for 3-4h. ISD is preferable in patients with hemorrhagic diathesis because it can be easily performed without anti coagulation. It is associated with wide swings in bodyweight, blood pressure and solute concentration .[34] The efficiency of dialysis impaired by hypotension which further decreases renal perfusion and exacerbates tabular necrosis. The new modes of dialysis therapy have been developed that minimize hypotension.[34]

CONTINUOUS RENAL REPLACEMENT THERAPY (CRRT)

It is regarded as one of the most important advanced treatment of ARF. CRRT offers the advantage to minimize hypotension in the perpetuation of renal

injury.[36] CRRT can potentially correct some of the problems associated with IHD. This modality has several theoretical advantages over intermittent hemodialysis. [43]CRRT avoids fluctuation in level of metabolites and allows for elimination of septic mediators. CRRT's have been shown to remove proinflammatory mediators such as thromboxane B_2. TNF-α, interleukin-1β and platelet activating factor Removal of these factors may play a role in treating various cause of ARF

DOPAMINE

Dopamine is commonly prescribed in the early phase of acute renal failure to enhance renal blood flow and induce diuresis. Dopamine is endogenous catecholamine, and it acts as a non-specific agonist. Dopamine stimulates both dopaminergic and adrenergic receptors in dose dependent manner. Lower doses (0.5-3.0mcg/kg/min) predominantly stimulate dopaminergic receptors which in turn produce renal and mesenteric vasodilation. Higher doses produce cardiac stimulation and renal vasodilation. Potential complications of dopamine use include cardiac arrhythmias, myocardial ischemia, and intestinal ischemia. Despite the lack of evidence supporting the use of dopamine interest remains in dopamine agonists for the treatment of ARF. Fenoldopam is a selective dopamine receptor agonist that is currently approve for the treatment of hypertensive emergencies. It increases renal perfusion at doses that do not lower systemic blood pressure in normal volunteers. [44] Fenoldopam maintains renal perfusion and GFR in the presence of hypovolemia. The finding suggests that a selective dopamine agonist may confer renal protection during renal ischemia .[45]

CONCLUSION

Acute renal failure is one of the dangerous conditions that should be minimized before occurrence of End stage renal disease. Advancement in medical sciences is still dealing with inventions of new techniques and treatments that would be beneficial to minimize the mortality rate and increase health improvement of patient. But prevention is always better than cure, so this could be prevented at an earlier stage with proper management of biochemical defect that occurs due Acute Renal Failure, So that the severity of Acute Kidney Injury condition could be minimized. This could be prevented at earlier stage by keeping a biochemical check at an initial stage and changes in sign and symptoms. This alertness can lead to detection of actual defect and treatment could be given for better treatment and minimization of the acute renal failure.

CONFLICT OF INTEREST

Conflict of interest declared none.

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