Management Critically Ill Patients with AKI

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- ***Definition and importance***

Definition and importance

- Acute kidney injury (AKI) is defined by a decline in kidney function or reduction in urine output occurring over hours to days.

- AKI is associated with prolonged hospitalization, substantial resource utilization, high mortality, and progressive chronic kidney disease (CKD) and end-stage renal disease (ESRD) in survivors.

Definition and importance

- The principles of management of AKI include timely recognition of the problem, identification and correction of the underlying cause, and steps to avoid further kidney injury.

- After AKI is established, current therapeutic options are limited, and mortality remains high despite recent technologic advancements.

- Management including supportive care, management of complications, and use of renal replacement therapy (RRT).

Definition and importance

- AKI is usually identified based on an increase in SCr; however, SCr is an insensitive early marker of changes in kidney function, and AKI may develop before such changes become apparent.

- Oliguria or anuria is an important sign that can identify AKI before changes in SCr become apparent.

- Several novel biomarkers for AKI have been identified in recent years, including KIM-١, NGAL, IL-١٨ and cystatin C, which may identify a decline in GFR or kidney damage earlier, and be more sensitive than changes in serum creatinine or urine output.

- *Definition and importance*
- **Conservative management**

Conservative management

١. Identifying the etiology of AKI

- Initial management includes careful assessment of the etiology of kidney dysfunction and patient volume status.
- History and examination are required to identify potential causes of AKI.
- Ischemia, sepsis, and exposure to nephrotoxic agents are the most common causes of AKI in hospitalized patients.

Conservative management

٢.Treating reversible causes

- A search for pre renal and post renal causes should be performed because their correction can lead to rapid recovery of kidney function.

- AKI due to hypovolemia may be rapidly reversed by the administration of intravenous fluids. Volume status should be frequently reassessed to determine the response to intravenous fluids and to avoid volume overload.

- Selected use of kidney ultrasound is useful for identifying hydroureter and/or hydronephrosis, indicative of a postrenal cause.

Conservative management

٣.Removing any active insults to minimize injury

- Stopping medications that impair glomerular filtration, including NSAIDs, diuretics (when there is volume depletion), and drugs that cause direct nephrotoxicity, such as aminoglycosides and intravenous radiocontrast.

- Doses of medications cleared by the kidney should be adjusted for the level of kidney function.

- This can be particularly important for antimicrobial agents so as to maintain appropriate therapeutic levels in patients with sepsis, while avoiding drug toxicity.

- *Definition and importance*
- Conservative management
- Intravenous fluid and hemodynamic support

Intravenous fluid and hemodynamic support

- Volume status should be assessed in all patients with AKI by physical exam.
- Correction of Volume depletion or Volume overload should be a primary aim of therapy.
- Early correction of hypovolemia and hypotension not only reverses most pre renal causes of AKI but also likely prevents extension and allows recovery from ATN.
- Vasopressors such as norepinephrine, dopamine, or vasopressin may be required when hypotension persists despite intravascular fluid resuscitation.

Intravenous fluid and hemodynamic support

- Small degrees of fluid overload are associated with a higher risk of mortality and other poor outcomes, and therefore, fluid therapy should be used with careful attention to net fluid balance and avoiding overload.

- A restrictive fluid strategy may be more appropriate in some patients, particularly those with concomitant lung injury.

- IV fluid therapy should be administrated to patients with a clinical history consistent fluid loss (such as vomiting and diarrhea),a physical exam consistent with hypovolemia (such as hypotension and tachycardia),or oliguria.

Intravenous fluid and hemodynamic support

- The overall goal of fluid therapy is to increase cardiac output and improve tissue oxygenation in patients who are preload dependent or volume responsive.
- Prompt reversal of volume depletion in patients with a prerenal state may improve renal perfusion and prevent progression to ATN.
- With certain causes of AKI, maintenance of tubular flow rate and urine output may increase excretion of nephrotoxins and protect against tubular injury. This is especially true for certain etiologies such as rhabdomyolysis.

Intravenous fluid and hemodynamic support

- In certain patients, such as those with cirrhosis or the nephrotic syndrome, patients may appear to be volume overloaded but have low effective circulating volume and may respond with increased urine output, improved GFR, and improved hemodynamics after fluid therapy.

Intravenous fluid and hemodynamic support

- Isotonic crystalloids are the principal intravenous fluid for intravascular volume expansion of AKI patients.
- Normal (٠,٩%) saline is considered the standard crystalloid for most patients.
- Colloid solutions such as albumin and starches are theoretically attractive alternatives for intravenous volume expansion, given their oncotic properties, but their appropriate use remains controversial and be appropriate for some patients, including those with ascites, spontaneous bacterial peritonitis, or burns, or following surgery.

Intravenous fluid and hemodynamic support

- Choice and quantity of fluid depends upon the presence of other underlying conditions, the clinical assessment, and the patient's response to initial fluid that is confirmed by clinical assessment, we administer ١ to ٣ liters of crystalloid with assessment of clinical response.

- For volume responsive patients with a robust response in urine output and improvement in GFR, and with persistent evidence of hypovolemia or inability to maintain fluid balance, we continue maintenance isotonic fluids at ٧٥ mL/hour or greater depending upon the ongoing losses.

Intravenous fluid and hemodynamic support

- Among patients with AKI who have a volume status that is difficult to interpret, we administer a smaller volume trial (up to ١ liter) of an isotonic fluid. Based upon the response, a decision regarding continuation of fluid therapy may be made.

- *Definition and importance*
- Conservative management
- Intravenous fluid and hemodynamic support
- DIURETICS

DIURETICS

- Oliguria has long been recognized as an important prognostic sign in AKI.
- In many studies, oliguric AKI has been associated with worse outcomes than non oliguric AKI.
- Conversion oliguric to non oliguric AKI makes fluid and electrolyte management easier but might perpetuate renal insult if given after the onset of ATN.
- The loop diuretics are clearly the most effective diuretics in the acute care setting.

DIURETICS

- The most common loop diuretics used clinically are furosemide, bumetanide and torsemide.
- The loop diuretics may be more effective and less toxic when given as a continuous infusion rather than as a bolus .
- Large boluses of loop diuretics may cause transient renal vasoconstriction, adversely affecting renal medullary oxygenation.

DIURETICS

- Diuretics can induce hypovolemia, leading to prerenal AKI, and their use has been associated with increased mortality and delays in kidney recovery in observational studies.
- However, when volume overload is present, diuretics are often prescribed to control fluid balance.
- Diuretics can be used effectively to achieve fluid balance and may facilitate mechanical ventilation and improved outcomes in patients with lung injury.

DIURETICS

- As a part of the strategy to avoid fluid retention in patients with co-existing acute lung injury reduce the risk of AKI, duration of mechanical ventilation, and length of ICU stay Using urinary response to furosemide (١ to ١,٥ mg/kg) as a prognostic test to predict the risk of requiring RRT.

- we start with ٨٠ mg of IV furosemide and assess for response. Patients who were on diuretics prior to the onset of AKI should receive a dose that is at least double their prior (home) dose.

- If there is no definite augmentation in the urine output within two hours of an IV diuretic dose, then we administer double the initial dose (maximum of ٢٠٠ mg in a single dose of IV).

DIURETICS

- Lack of response to a ٢٠٠ mg dose of IV furosemide, may suggest the need for extracorporeal removal of excess volume

- Among patients who respond to diuretics, we continue to give repeated doses to avoid hypervolemia if kidney function is improving or improvement is thought to be imminent.

DIURETICS

- Although loop diuretics are often prescribed in established AKI , recent meta-analysis have shown that loop diuretics do not affect mortality, need for dialysis, or number of dialysis sessions required. In regard to morbidity, diuretics are associated with an increased risk of ototoxicity.

- Among hospitalized patients, diuretics are generally given intravenously rather than orally since the absorption of oral agents is variable in patients with decreased intestinal perfusion and motility and in those with mucosal edema.

DIURETICS

- BENEFITS Furosemide:

١. Decrease O٢ Demand

٢. improve urine flow by flushing out debris and denuded epithelium, thus avoiding intratubular obstruction.

٣. reduce the back leak of glomerular filtrate into the renal interstitium which tends to worsen acute kidney injury.

٤. decrease renal vascular resistance and therefore increase renal blood flow.(PGE٢)

DIURETICS

Potential pitfalls of using furosemide :

١. Induces hypovolaemia, hypokalaemia, hypophosphataemia, hypomagnesaemia, and metabolic alkalosis

٢. Induces ototoxicity

٣. High doses can induce systemic vasoconstriction.

٤. Reduces mucociliary transport and sputum clearance by inhibiting Na-K-Cl٢ co-transporters of the respiratory tract

٥. Acidifies urine and reduces solubility of myoglobin and haemoglobin in patients with rhabdomyolysis and intravascular haemolysis (including cardiopulmonary bypass).

٦. Aciduria may also promote free radical formation in the urine by radiocontrast agents .

DIURETICS

KDIGO guideline :

- We recommend not using diuretics to prevent AKI.
- We suggest not using diuretics to treat AKI, except in the management of volume overload.
- There is no evidence that the use of diuretics reduces the incidence or severity of AKI.

- *Definition and importance*
- Conservative management
- Intravenous fluid and hemodynamic support
- Diuretics
- Vasodilators agents

VASODILATORS AGENTS

- Several pharmacologic agents with renal vasodilatory properties have been studied, with the aim of increasing renal blood flow and ameliorating ischemic damage in AKI. However, none of these agents are proven to improve the clinical outcomes of AKI.

- Dopamine was once commonly used for renal protection in the critically ill.

- Low-dose dopamine administration(۱-۳mg/kg/min) to healthy individuals causes renal vasodilation, natriuresis, increase urine out put and increased GFR but does not affect on survival, need for dialysis, or adverse clinical events and AKI outcome.

VASODILATORS AGENTS

- Dopamine is associated with tachyarrhythmias and myocardial ischemia, decrease intestinal blood flow, cause hypopituitarism, and suppress T-cell function.

- No RCTs have assessed the effect of norepinephrine on prevention of AKI.

- Fenoldopam mesylate is a pure dopamine type-١ receptor agonist that has similar hemodynamic renal effects as low-dose dopamine, without systemic a-orb-adrenergic stimulation.

VASODILATORS AGENTS

KDIGO guideline

- We recommend not using low-dose dopamine to prevent or treat AKI.
- We suggest not using fenoldopam to prevent or treat AKI.
- We suggest not using atrial natriuretic peptide (ANP) to prevent or treat AKI
- We recommend not using recombinant human (rh)IGF-١ to prevent or treat AKI.

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- Renal Replacement Therapy

Renal Replacement Therapy:

Best modality :

- Several modalities of RRT may be used in AKI, including peritoneal dialysis, continuous renal replacement therapy (CRRT) , conventional intermittent hemodialysis (IHD), and prolonged IHD .

- Peritoneal dialysis is used for AKI in some pediatric settings and in adults in developing countries where infrastructure for hemodialysis is not available.

- In industrialized countries, IHD and CRRT are the mainstays of RRT for AKI.

Renal Replacement Therapy:

- Available resources, expertise, hemodynamic stability, and patient comorbidities usually influence the decision of renal replacement modality.

- When both therapies are available, the indication of CRRT or IHD is based on the patient's neurologic, hemodynamic, and catabolic status.

Renal Replacement Therapy:

Best time :

- Initiating RRT is influenced by several factors, including assessments of fluid, electrolyte, and metabolic status.
- Thresholds for starting RRT appear to be lower when AKI is accompanied by multiple organ failure.
- earlier initiation may avoid adverse AKI consequences, including metabolic abnormalities and fluid overload, and could improve outcomes.

Renal Replacement Therapy:

- However, earlier initiation RRT expose some patients to the risk associated with vascular access (infection, thrombosis), anticoagulation (hemorrhage), and RRT itself (hypotension, dialyzer reactions) , and leukocyte activation from contact with dialysis membranes.

- early RRT in CIP" is associated with:

a- improved survival

b- improved renal recovery

c- shorter duration of RRT support

d- reduced ICU-LOS

Renal Replacement Therapy:

- Urgent indication for renal replacement therapy in patients with AKI:

- ✓ Refractory fluid overload
- ✓ Severe hyperkalemia (k>٦,٥ or rapidly rising k level)
- ✓ Sign of uremia such as pericarditis , encephalopathy, or an otherwise unexplained decline in mental stats .
- ✓ Sever metabolic acidosis (PH<٧,١)
- ✓ Certain alcohol and drug intoxication

Renal Replacement Therapy:

- Even if one of the urgent indications is not satisfied, we electively initiate RRT in patients with AKI that is unlikely to resolve quickly and who , in addition have one or more of the following :

- ✓ Serum potassium >٦ or > ٥,٥ mEq/l
- ✓ PH<٧,٢
- ✓ Hypervolemic patients

- Neither creatinine nor BUN should be used to absolutely determine when to initiate dialysis.

- We typically initiate RRT for volume overload in patients who have anuria for more than ٢٤ hours, who fail to respond to diuretics, or whose response to diuretics is insufficient .

Renal Replacement Therapy:

DOSE OF RENAL REPLACEMENT THERAPY

- One small trial that evaluated the effect of daily versus alternate-day IHD in AKI reported lower mortality and shorter duration of dialysis in the daily IHD group.

- Patients dialyzed for control of both azotemia and volume overload experienced the worst outcome than those patients dialyzed predominantly for control of both azotemia and solute control .

- If the patient is hemodynamically unstable during this period, it may be difficult to remove any fluid.

Renal Replacement Therapy:

VASCULAR ACCESS :

- Venous access is a necessity for CRRT and IHD, and access dysfunction can limit blood flow and the delivery of dialysis.

- Nontunneled catheters are the initial choice for most patients starting RRT.

- Cuffed, subcutaneous tunneled catheters are more complex to insert; however, they may be less prone to dysfunction, infection, or thrombosis and thus appropriate if longer (greater than ٣-week) durations of RRT are anticipated.

Renal Replacement Therapy

ANTICOAGULATION FOR RENAL REPLACEMENT THERAPY:

- Clotting of the dialysis filter can lead to extracorporeal blood loss, a reduction in dialysis efficiency, and procedural interruptions.

- Use of anticoagulation for CRRT and IHD may reduce these problems; however, the benefits of anticoagulation must be balanced against the risk of bleeding complications in acutely ill AKI patients with significant comorbidities.

Renal Replacement Therapy

- Patients with coagulopathy and thrombocytopenia may not benefit from additional anticoagulation, and CRRT and IHD can often be provided without anticoagulation.
- Unfractionated heparin is the most widely used anticoagulant for dialysis.
- Low-molecular-weight heparin may also be used, although it has unpredictable clearance in patients with kidney failure.
- Citrate anticoagulation has become more common in recent years, especially for anticoagulation on CRRT.

Renal Replacement Therapy:

DISCONTINUING RENAL REPLACEMENT THERAPY

- Many patients with AKI will experience partial or complete recovery of kidney function, although recovery is less likely in those with severe injury or preexisting CKD.

- Little is known about the optimal time to stop RRT; however, increasing urine output often identifies patients recovering kidney function. Changes in interdialytic measurements of serum creatinine, urea, and urinary creatinine clearance can be used to assess kidney function in patients receiving IHD.

- *Definition and importance*
- Conservative management
- Intravenous fluid and hemodynamic support
- Diuretics
- Vasodilators agents
- Renal Replacement Therapy
- Supportive care and management of complications of AKI

Supportive care and management of complications of AKI :

- Supportive care in patients with AKI requires maintenance of fluid, electrolyte, and acid-base balance.

- Disorders of sodium and water handling, metabolic acidosis, and hyperkalemia are common complications of AKI.

Supportive care and complications management of AKI

Potassium:

- A rise in plasma potassium concentrations to ٥,٥ mEq per L is a frequent complication seen in ٥٠% of patients with AKI.
- in conditions such as tumor lysis syndrome and rhabdomyolysis, dangerous levels of hyperkalemia can occur quickly.
- AKI induced by NSAIDs can also be associated with marked hyperkalemia.

Supportive care and complications management of AKI

- Management of hyperkalemia depends on its severity, etiology of the AKI (readily reversible or likely to be prolonged), clinical manifestations (cardiac conduction abnormalities), and effect of medical management.

- All patients with hyperkalemia should be on a potassium-restricted diet (less than ٢ g per day).

- Discontinuing exogenous sources (oral or IV)of potassium and drugs with effect on potassium handling such as potassium-sparing diuretics, ACE inhibitors, ARBs, and other drugs that inhibit renal potassium excretion.

Supportive care and complications management of AKI

- Specific treatment of hyperkalemia is directed at antagonizing the membrane effects of potassium, driving extracellular potassium into the cells, or removing excess potassium from the body.

- If echocardiogram (ECG) changes are present, the administration of intravenous calcium is urgent.

- Beta-agonists, insulin, and sodium bicarbonate can shift potassium out of the plasma and into cells. For example The onset of action parenteral glucose and insulin infusions is within ٢٠ to ٣٠ minutes, and the effect lasts for ٢ to ٦ hours.

Supportive care and complications management of AKI

- Potassium excretion should be increased by the administration of loop diuretics and cation exchange resins, such as Kayexalate .

- Attempts to eliminate potassium through the GI tract with ion exchange resins may be used; however, these agents are slow to take effect, have limited efficacy, have been associated with bowel necrosis or perforation, and are unlikely to be adequate in patients with severe hyperkalemia.

Supportive care and complications management of AKI

- When medical management of these abnormalities is unsuccessful, or medical interventions cannot be tolerated by the patient, or occurs in patients with ESRD, RRT is usually necessary unless recovery of kidney function is imminent.

- As it may take some time to initiate RRT, medical management should always be used while waiting for dialysis to be started.

Supportive care and complications management of AKI

- Sodium bicarbonate also promotes shift of K into the intracellular space, the effect occurs in less than ١٥ minutes, and has ١ to ٢ hours' duration.
- This therapy can be started if there is no concern of fluid overload ; however, the potassium-lowering effect of sodium bicarbonate is most prominent in patients with metabolic acidosis.
- Beta adrenergic agonists given as aerosols are also effective but more likely to produce side effects and so are not often prescribed to treat hyperkalemia.
- Monitoring for K should continue following conservative or dialytic management to prevent and treat rebound hyperkalemia from the underlying process.

Supportive care and complications management of AKI

Acid- Base Disorders :

- In AKI, metabolic acidosis is the most common acid-base abnormality.
- The approach to acid-base disturbances in AKI needs to be adjusted to the underlying causes.
- Bicarbonate administration in lactic acidosis due to an underlying shock is controversial given the possibility of an increase in CO_2 generation, worsening of the intracellular acidosis, and volume overload.

Supportive care and complications management of AKI

- Rapid improvement in the metabolic status may also enhance hypocalcemia.

- most physicians would restrict the administration of sodium bicarbonate to patients with severe metabolic acidosis (arterial pH below ٧,١٠ to ٧,١٥) to maintain the pH above ٧,١٥ to ٧,٢٠ until the primary process can be reversed.

Supportive care and complications management of AKI

- RRT is preferred to the administration of bicarbonate among hypervolemic patients with reduced urine output because bicarbonate administration results in a large sodium load that may worsen volume overload.

- Among patients who are not hypervolemic but who have oliguria or anuria, bicarbonate therapy may produce volume overload and should therefore be used cautiously.

- Among patients with AKI, bicarbonate administration may be associated with serious side effects due to hypocalcemia and hypokalemia.

Supportive care and complications management of AKI

- As in patients without AKI, bicarbonate administration could cause hypernatremia, an increase in the partial pressure of carbon dioxide (pCO_2), and increased intracranial pressure in patients with diabetic ketoacidosis.

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- Avoidance of hyperglycemia

Avoidance of hyperglycemia

- The kidney also metabolizes insulin and reduced renal function prolongs the half-life of insulin and can contribute to hypoglycemic events.

- In a large observational study, patients who did and did not have diabetes and required glycemic control had more infections, anemia, and AKI (١١% and ٧% versus ٤%; P ٠,٠٠١) compared with control subjects.

Avoidance of hyperglycemia

- On the basis of these conclusions hyperglycemia should be considered a major risk factor for AKI in the ICU and should prompt specific measures.

- Severe hypoglycemia was significantly more common with intensive glucose control.

Avoidance of hyperglycemia

KDIGO guideline

- In critically ill patients, we suggest insulin therapy targeting plasma glucose ۱۱۰-۱۴۹ mg/dl (۶,۱-۸,۳ mmol/l).

- Tight glycemic control can reduce the incidence and severity of AKI.

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- Nutritional Support

NUTRITIONAL SUPPORT

- AKI patients present an increased risk of protein–energy malnutrition due to poor nutrient intakes and high catabolic rates and has been consistently associated with mortality.

- Severe malnutrition occurs in up to ۴۲% of patients with AKI.

NUTRITIONAL SUPPORT

- The enteral route should be the first choice for nutritional support if the GI tract is functioning, whereas parenteral nutrition should be reserved when the GI tract cannot be used, or when the enteral route appears inadequate to reach nutrient intake goals.

- AKI itself and other factors commonly present in critically ill patients, such as medications, hyperglycemia, and electrolyte disorders, can impair gastrointestinal motility.

NUTRITIONAL SUPPORT

- Consultation with a registered dietitian is valuable to estimate the appropriate energy and protein requirements for an individual patient.
- Electrolytes (potassium, phosphate) should be monitored following initiation of enteral feeding.
- A total energy intake of ٢٠ to ٣٠ kcal/kg per day is recommended to maintain nitrogen balance in patients with AKI.

NUTRITIONAL SUPPORT

KDIGO guideline :

- We suggest to avoid restriction of protein intake with the aim of preventing or delaying initiation of RRT.

- We suggest administering ٠,٨-١,٠ g/kg/d of protein in noncatabolic AKI patients without need for dialysis , ١,٠-١,٥ g/kg/d in patients with AKI on RRT , and up to a maximum of ١,٧ g/kg/d in patients on continuous renal replacement therapy (CRRT) and in hypercatabolic patients.

Thanks for your attention