Introduction

Acute kidney injury is characterized by a sudden decrease in kidney function over a period of hours to days, resulting in accumulation of creatinine, urea, and other waste products. It may be associated with retention of sodium and water and the development of metabolic disturbances such as metabolic acidosis and hyperkalemia ***(Bedford et al., 2014).***

Acute kidney injury has been estimated to account for 1% of hospital admissions and to develop in 5 to 7% of hospitalized patients. In the intensive care unit (ICU), acute kidney injury develops in 5 to 25% of patients. Acute tubular necrosis is the most common cause of hospital-acquired acute kidney injury and usually results from ischemic or nephrotoxic injury to the tubules. In the ICU, acute tubular necrosis is usually multifactorial and may develop from a combination of sepsis, impaired renal perfusion, and nephrotoxic medications ***(Tolwani, 2012).***

Renal Replacement Therapy (RRT) is one of the most common clinical procedures in the intensive care unit (ICU). Approximately 4-5% of critically ill patients require RRT during the ICU stay. RRT has long been used as supportive treatment of Acute Kidney Injury (AKI), and has

traditionally focused on averting the life threatening derangements associated with kidney failure (i.e. metabolic acidosis, hyperkalemia, uremia, and/or fluid overload), while allowing time for organ recovery. In patients with AKI, RRT is regarded as a type of organ support aimed at achieving metabolic homeostasis and preventing fluid overload and new organ failure. The benefits of RRT must be balanced by potential harm, including risks related to vascular access, infections and anticoagulation ***(Gupta, 2013).***

A number of strategies for RRT may be used. RRT can be applied intermittently (IRRT), e.g. intermittent haemodialysis (IHD) or continuously (CRRT), as in continuous venovenous haemofiltration (CVVHF). IRRT was defined as any form of RRT [haemodialysis (HD), haemofiltration (HF), haemodiafiltration (HDF), isolated ultrafiltration (UF)] prescribed for a period of < 24 hours. CRRT was defined as any form of RRT (HD, HF, HDF, UF) intended to run on a continuous basis until recovery of renal function ***(Lins et al., 2009).***

There is evidence for both IRRT and CRRT, that increasing the delivered dialysis dose improves outcome. What is less clear is which, if any, approach is preferable.

Individual studies comparing the therapies have suggested that CRRT offers superior biochemical control and improved patient outcomes. However, a number of authoritative reviews, that have addressed the pros and cons of IHD versus CRRT for patients with AKI, have been unable to provide objective evidence of the superiority of one approach over the other ***(Rabindranath et al., 2008).***

Aim of the Work

The aim of work is to identify the role of renal replacement therapy technique in management of patients with acute kidney injury, different modalities of therapy and respective patient outcomes.

Chapter (1)
Acute Kidney Injury

Pathogenesis:

Acute kidney injury is defined as any of the following: increase in Serum Creatinine (SCr) by ≥0.3 mg/dl (≥ 26.5 μmol/l) within 48 hours; OR increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within prior 7 days; OR Urine volume <0.5 ml/kg/h for 6 hour ***(Kidney Disease Improving Global Outcomes, 2012)***.

Epidemiology

Acute kidney injury is common among hospitalized patients. It affects 3-7% of patients admitted to the hospital and approximately 25-30% of patients in the intensive care unit ***(Renal Medicine, 2013)***.

Staging of AKI

Rifle Criteria

The RIFLE criteria consists of three graded levels of injury (Risk, Injury, and Failure) based upon either the magnitude of elevation in serum creatinine or urine output, and two outcome measures (Loss and End-stage renal

disease). The RIFLE strata are as follows ***(Bellomo et al., 2004).***

- Risk - 1.5 fold increase in the serum creatinine or Glomerular Filtration Rate (GFR) decrease by 25 percent or urine output <0.5 mL/kg per hour for six hours.
- Injury - Two fold increase in the serum creatinine or GFR decrease by 50 percent or urine output <0.5 mL/kg per hour for 12 hours.
- Failure - Three fold increase in the serum creatinine or GFR decrease by 75 percent or urine output of <0.5 mL/kg per hour for 24 hours, or anuria for 12 hours.
- Loss - Complete loss of kidney function (eg, need for renal replacement therapy) for more than four weeks.
- End-Stage Renal Disease (ESRD) — Complete loss of kidney function (eg, need for renal replacement therapy) for more than three months.

The RIFLE criteria correlated with prognosis in a number of studies. As an example, a systematic review of 13 studies demonstrated a stepwise increase in the relative risk of death in patients who met the RIFLE criteria for various stages of AKI ***(Ricci et al., 2008).***

Causes of acute renal failure:

1- Prerenal causes:

Decreased effective extracellular volume:

Renal losses: hemorrhage, vomiting, diarrhea, burns and diuretics

Redistribution: hepatopathy, nephrotic syndrome, intestinal obstruction, pancreatitis, peritonitis and malnutrition.

Decreased cardiac output:

Cardiogenic shock, valvulopathy, myocarditis, myocardial infarction, arrhythmia, congestive heart failure, pulmonary emboli and cardiac tamponade

Peripheral vasodilation:

Hypotension, sepsis, hypoxemia, anaphylactic shock, treatment with interleukin L2 or interferons

Renal vasoconstriction:

Prostaglandin synthesis inhibition, adrenergics, sepsis, hepatorenal syndrome and hypercalcemia.

Efferent arteriole vasodilation:

Converting-enzyme inhibitors.

(Pascual and Liaño, 1998)

2- Intrarenal causes:

Acute tubular necrosis

Hemodynamic: cardiovascular surgery, sepsis and prerenal causes.

Toxic: antimicrobials, iodide contrast agents, anesthesics, immunosuppressive or antineoplastic agents, Chinese herbs, mercurials, organic solvents, venoms, heavy metals, mannitol and radiation.

Intratubular deposits: acute uric acid nephropathy, myeloma, severe hypercalcemia, primary oxalosis, sulfadiazine, fluoride and anesthesics.

Organic pigments (endogenous nephrotoxins):

Myoglobin (rhabdomyolisis): Muscle trauma, infections and dermatopolymyositis.

Metabolic alterations: hyperosmolar coma, diabetic ketoacidosis, severe hypokalemia, hyper or hyponatremia, hypophosphatemia or severe hypothyroidism, toxins such as ethylene glycol, carbon monoxide and mercurial chloride drugs such as fibrates, statins, opioids and amphetamines, hereditary

diseases such as musculardystrophy, metabolopathies, McArdle disease and carnitine deficit.

Hemoglobinuria:

Malaria mechanical destruction of erythrocytes with extracorporealcirculation or metallic prosthesis transfusion reactions, or other hemolysis heat stroke burns chemicals such as aniline, quinine, glycerol, benzene, phenol, hydralazine and insect venoms.

Acute tubulointerstitial nephritis

Antimicrobials: penicillin, ampicillin, rifampicin and sulfonamides.

Analgesics, anti-inflammatories: Fenoprofen, ibuprofen and naproxen.

Immunological: Systemic lupus erythematosus and rejection.

Neoplasia: Myeloma, lymphoma and acute leukemia.

Principal vessels: bilateral (unilateral in solitary functioning kidney) renal artery thrombosis or embolism or bilateral renal vein thrombosis.

Small vessels: atheroembolic disease, thrombotic microangiopathy, hemolytic-uremic syndrome or thrombotic thrombocytopenic purpura, postpartum acute renal failure, antiphospholipid syndrome, disseminated intravascular coagulation,scleroderma, malignant arterial hypertension, radiation nephritis and vasculitis.

Acute glomerulonephritis

Postinfectious: streptococcal or other pathogen associated with visceral abscess, endocarditis, or shunt Henoch-Schonlein purpura Essential mixed cryoglobulinemia Systemic lupus erythematosus ImmunoglobulinA nephropathy Mesangiocapillary With antiglomerular basement membrane antibodies with lung disease (Goodpasture is syndrome) or without it Idiopathic, rapidly progressive, without immune deposits Cortical necrosis, abruptio placentae, septic abortion and disseminated intravascular coagulation**.**

Postrenal causes:

Congenital anomalies: Ureterocele, bladder diverticula, posterior urethral valves and neurogenic bladder.

Acquired uropathies: Benign prostatic hypertrophy, urolithiasis, papillary necrosis and iatrogenic ureteral ligation.

Malignant diseases: Prostate, bladder, uurethra, cervix, colon and breast metastasis.

Gynecologic non-neoplastic: Pregnancy-related, uterine prolapse and endometriosis.

Drugs: Aminocaproic acid and sulfonamides.

Infections: Schistosomiasis, tuberculosis, candidiasis, aspergillosis and acitnomycosis,

(Pascual and Liaño, 1998)

Pathophysiology

The mechanisms involved in the etiology of AKI are as follows:

- endothelial injury from vascular perturbations

- direct effect of nephrotoxins

- abolishment of renal autoregulation

- formation of inflammatory mediators

Necrosis and apoptosis of tubular cells lead to tubular obstruction, which contributes to the reduction of GFR. In

addition, elevated intracellular calcium levels from tubular damage cause a series of cellular-level alterations that culminate in increased tubuloglomerular feedback, and thus, diminished GFR.

Vascular compromise causes increased cytosolic calcium, elevated endothelial injury markers, and production of inflammatory mediators (eg, tumor necrosis factor α, interleukin 18, intercellular adhesion molecule 1), which result in reduced GFR ***(Schrier et al., 2004).***

These pathophysiologic mechanisms are perpetuated by a persistent imbalance between the mediators of vasoconstriction and dilatation that result in intrarenal vasoconstriction and, eventually, ischemia. The vasoconstrictors include angiotensin II, endothelin, thromboxane, and adenosine. The vasodilators include prostaglandin I2 and endothelial-derived nitric oxide. High levels of vasoconstrictors and low levels of vasodilators cause continued hypoxia and cell damage or cell death ***(Marin and Sessa, 2007).***

Diagnosis

The presentation will depend on the underlying cause and severity of AKI. There may be no symptoms or signs, but oliguria (urine volume less than 0.5 ml/kg/hour) is common. There is an accumulation of fluid and nitrogenous waste products demonstrated by a rise in blood urea and creatinine.

Symptoms

- Urine output:
  - AKI is usually accompanied by oliguria or anuria. However polyuria may occur due to either reduced fluid reabsorption by damaged renal tubules, or the osmotic effect of accumulated metabolites.
  - Abrupt anuria suggests an acute obstruction, acute and severe glomerulonephritis, or acute renal artery occlusion.
  - Gradual diminution of urine output may indicate a urethral stricture or bladder outlet obstruction - eg, benign prostatic hyperplasia.
- Nausea, vomiting.
- Dehydration.
- Confusion.

Signs

- Hypertension.
- Abdomen: may reveal a large, painless bladder typical of chronic urinary retention.
- Dehydration with postural hypotension and no edema.
- Fluid overload with raised jugular venous pressure (JVP), pulmonary edema and peripheral edema.
- Pallor, rash, bruising: petechiae, purpura, and nosebleeds may suggest inflammatory or vascular disease, emboli or disseminated intravascular coagulation.
- Pericardial rub.

(UK National Institute for Health and care Excellence Guidelines,2013)

Investigations:

Kidney function tests:

Although increased levels of blood urea nitrogen (BUN) and creatinine are the hallmarks of renal failure, the rate of rise depends on the degree of renal insult and, with respect to BUN, on protein intake. BUN may be elevated in patients with gastrointestinal (GI) or mucosal bleeding, steroid treatment, or protein loading.

The ratio of BUN to creatinine is an important finding. The ratio can exceed 20:1 in conditions in which enhanced reabsorption of urea is favored (eg, in volume contraction); this suggests prerenal AKI ***(Lowes, 2014)***.

Assuming that the patient has no renal function, the rise in BUN over 24 hours can be roughly predicted using the following formula: 24-hour protein intake in milligrams ´ 0.16 divided by total body water in mg/dL added to the BUN value.

Assuming no renal function, the rise in creatinine can be predicted using the following formulas: For males: Weight in kilograms ´ [28 - 0.2(age)] divided by total body water in mg/dL added to the creatinine value For females: Weight in kilograms ´ [23.8 - 0.17(age)] divided by total body water added to the creatinine value. As a general rule, if serum creatinine increases to more than 1.5 mg/dL/day, rhabdomyolysis must be ruled out ***(Lowes, 2014)***.

CBC, peripheral smear, and serology:

The peripheral smear may show schistocytes in conditions such as hemolytic uremic syndrome (HUS) or thrombotic thrombocytopenic purpura (TTP). A finding of increased rouleaux formation suggests multiple myeloma, and the