MEDICAL UNIVERSITY - PLEVEN
FACULTY OF MEDICINE

DISTANCE LEARNING CENTRE

DEPARTMENT OF „NEPHROLOGY, HEMATOLOGY AND GASTROENTEROLOGY“

LECTURE № 6

FOR E-LEARNING IN „NEPHROLOGY“

FOR MEDICAL STUDENTS

TITLE: **ACUTE RENAL FAILURE**

PREPARED BY:

PROF. DR. VASIL TODOROV DSC

PLEVEN, 2020

ACUTE RENAL FAILURE

Definition

Acute renal failure (ARF) is a severe clinical-laboratory syndro-me as a result of sudden fast reduction of intact renal function.

Epidemiology

ARF is commonly encountered in the contemporary practice of medicine. For example 4,9% of the admitted to a general medical-surgical hospital develop an abrupt rise of serum creatinine. In patients undergoing nonemergent surgery, 25% develop either a mild rise of serum creatinine or a fall of creatinine clearance in the early postoperative period. In intensive care units (ICU) 5-15% of patients develop a significant abrupt rise of serum creatinine.

Etiology

It may complicate a wide range of diseases, which for purposes of diagnosis and management are conveniently divided into two categories: (1) diseases that cause renal hypoperfusion without compromising the integrity of renal parenchyma (prerenal ARF) ; (2) diseases that directly involve renal parenchyma (intrinsic renal ARF) .

The *prerenal or extrarenal* etiologic factors include **shock** as a main and often cause. As a result renal blood flow decreases markedly. Common clinical situation in which this is the major or only mechanism of ARF include hypotension from any cause, severe extracellular volume depletion, hemorrhage, gastrointestinal loses, and third-space loses from burns, peritonitis, pancreatitis, as well as renal salt loses, severe congestive heart failure, hepatorenal syndrome.

The most common causes of *intrinsic renal failure* are the antimicrobial agents, such as acyclovir, aminoglycosides, amphotericin B, and pentamidine, and chemotherapeutic agents, such as cisplatin. ARF complicates 10 to 30% of courses of *aminoglycoside antibiotics*, even in the presence of therapeutic levels.

The most common *endogenous nephrotoxins* are myoglobin, hemoglobin, urate, oxalate, and myeloma light chains.

Common causes of the latter include traumatic crush injury, muscle ischemia, seizures, excessive exercise, heat stroke or malignant hyperthermia, alcoholism, and infectious or metabolic disorders. ARF due to hemolysis is relatively rare and is observed following massive blood transfusion reactions.

The severe forms of acute glomerulonephritis and acute interstitial nephritis lead to ARF.

Pathogenesis

Hypovolemia leads to a fall in mean systemic arterial pressure, which is detected as reduced stretch by arterial and cardiac baroreceptors. As a result – glomerular hypoperfusion anr reduction/decrise of GF.

Intrinsic renal azotemia can complicate many diverse diseases of the renal parenchyma. From a clinicopathologic viewpoint, it is useful to divide the causes of acute intrinsic renal azotemia into (1) diseases of large renal vessels, (2) diseases of the renal microcirculation and glomeruli, (3) ischemic and nephrotoxic ARF, and (4) tubulointerstitial diseases. Most intrinsic renal azotemia is triggered by ischemia (ischemic ARF) or nephrotoxins (nephrotoxic Prerenal azotemia and ischemic ARF are part of a spectrum of manifestations of renal hypoperfusion. Ischemic ARF differs from prerenal azotemia in that the hypoperfusion induces ischemic injury to renal cells, particularly tubular epithelium, and recovery typically takes 1 to 2 weeks after normalization of renal perfusion as it requires regeneration of tubular cells.

The most common cause of intrinsic renal failure is acute tubular necrosis. Tubular necrosis leads to sloughing of tubular cells into tubular lumen, with partial or total obstruction of nephrons flow. Damaged tubules do not transport solutes normally, leading to elaboration of dilute urine with high sodium concentration. The severe forms of acute glomerulonephritis and acute interstitial nephritis lead to ARF, due to injury of GF and injury of tubules respectively.

Direct toxicity to tubule epithelial cells and/or intratubular obstruction is major pathophysiologic event in ARF induced by many antibiotics and anticancer drugs.

Pathology of ARF

The classic pathologic features of ischemic ARF are patchy and focal necrosis of tubule epithelium with detachment from its basement membrane and occlusion of tubule lumens with casts composed of intact or degenerating epithelial cells, cellular debris, Tamm-Horsfall mucoprotein, and pigments.

Clinical assessment

ARF impairs renal excretion of sodium, potassium, and water and perturbs divalent cation homeostasis and urinary acidification mechanisms. As a result, ARF is frequently complicated by intravascular volume overload, hyponatremia, hyperkalemia, hyperphosphatemia, hypocalcemia, hypermagnesemia, and metabolic acidosis. In addition, patients are unable to excrete nitrogenous waste products and are prone to develop the uremic syndrome. The speed of development and severity of these complications reflects the degree of renal impairment and catabolic state of the patient.

Hyperkalemia is a frequent complication of ARF. Mild hyperkalemia (more than 6.0 mmol/L) is usually asymptomatic. Higher levels are typically associated with electrocardiographic abnormalities. Potentially fatal hyperkalemia rarely occurs unless the

plasma K^+ concentration exceeds 7.5 mmol/L and is usually associated with profound weakness and absent P waves, QRS widening, or ventricular arrhythmias on the electrocardiogram.

ARF is typically complicated by *metabolic acidosis*, often with an increased serum anion gap. Acidosis can be particularly severe when endogenous production of hydrogen ions is increased by other mechanisms.

Anemia develops rapidly in ARF and is usually mild and multifactorial in origin. Contributing factors include impaired erythropoiesis, hemolysis, bleeding, hemodilution, and reduced red cell survival time. Prolongation of the *bleeding time* and *leukocytosis* are also common. Common contributors to the bleeding diathesis include mild thrombocytopenia, platelet dysfunction, and/or clotting factor abnormalities.

Infection is a common and serious complication of ARF, occurring in 50 to 90% of cases and accounting for up to 75% of deaths. It is unclear whether patients with ARF have a clinically significant defect in host immune responses or whether the high incidence of infection reflects repeated breaches of mucocutaneous barriers (e.g., intravenous cannulae, mechanical ventilation, bladder catheterization).

Cardiac complications of ARF include arrhythmias, myocardial infarction, and pulmonary embolism. Mild *gastrointestinal bleeding* is common (10 to 30%) and is usually due to stress ulceration of gastric or small intestinal mucosa.

Urinalysis

Anuria suggests complete urinary tract obstruction but may be the MAIN symptom of prerenal or intrinsic renal ARF.

Diagnosis

Diagnosis of *ARF* requires careful review of the clinical data and pharmacy, nursing, and radiology records for evidence of recent exposure to nephrotoxic medications or radiocontrast agents or to endogenous toxins (e.g., myoglobin, hemoglobin, uric acid, myeloma protein, or elevated levels of serum calcium).

ARF due to ischemia is likely following prolonged or severe renal hypoperfusion complicating hypovolemic or septic shock or following major surgery. The likelihood of ischemic ARF is increased further if ARF persists despite normalization of systemic hemodynamics.

Treatment

Prevention. Because there are no specific therapies for treatment of ischemic or nephrotoxic ARF, prevention is of paramount importance. Many cases of ischemic ARF can be avoided by close attention to cardiovascular function and intravascular volume in high-risk patients.

Specific Therapies. By definition, *prerenal azotemia* is rapidly reversible upon correction of the primary hemodynamic abnormality. **To date, there are no specific therapies for**

established intrinsic renal ARF due to ischemia or nephrotoxicity. Management of these disorders should focus on elimination of the causative hemodynamic abnormality or toxin, avoidance of additional insults, and prevention and treatment of complications. Specific treatment of other causes of intrinsic renal azotemia depends on the underlying pathology.

SUPPORTIVE MEASURES. Following correction of hypovelemia, salt and water intake are tailored to match losses. *Hypervolemia* can usually be managed by restriction of salt and water intake and diuretics. Indeed, there is, as yet, no proven rationale for administration of diuretics in ARF except to treat this complication.

Severe hyperkalemia requires emergent treatment directed at minimizing membrane depolarization, shifting K^+ into cells, and promoting K^+ loss. In addition, exogenous K^+ intake should be discontinued. Administration of calcium gluconate decreases membrane excitability. The usual dose is 10 ml of a 10% solution infused over 2 to 3 min. The effect begins within minutes but is short-lived (30 to 60 min), and the dose can be repeated if no change in the electrocardiogram is seen after 5 to 10 min. Insulin causes K^+ to shift into cells. Although glucose alone will stimulate insulin release from normal pancreatic □ cells, a more rapid response generally occurs when exogenous insulin is administered (with glucose to prevent hypoglycemia). A commonly recommended combination is 10 units of regular insulin and 50 g of glucose. Obviously, hyperglycemic patients should not be given glucose. If effective, the plasma K^+ concentration will fall by 0.5 to 1.5 mmol/L in 15 to 30 min and the effect will last for several hours. Alkali therapy with intravenous $NaHCO_3$ can also shift K^+ into cells.

Removal of K^+ can be achieved using cation-exchange resin, or dialysis. Sodium polystyrene sulfonate is a cation-exchange resin that promotes the exchange of Na^+ for K^+ in the gastrointestinal tract. Each gram binds 1 mmol of K^+ and releases 2 to 3 mmol of Na^+. When given by mouth, the usual dose is 25 to 50 g mixed with 100 ml of 20% sorbitol to prevent constipation. This will generally lower the plasma K^+ concentration by 0.5 to 1.0 mmol/L within 1 to 2 h and last for 4 to 6 h. The most rapid and effective way of lowering the plasma K^+ concentration is hemodialysis.

Metabolic acidosis is not treated unless serum bicarbonate concentration falls below 15 mmol/L or arterial pH falls below 7.2. More severe acidosis is corrected by oral or intravenous sodium bicarbonate.

INDICATIONS AND MODALITIES OF DIALYSIS. Dialysis replaces renal function until regeneration and repair restore renal function. Hemodialysis and peritoneal dialysis appear equally effective for management of ARF. Thus, the dialysis modality is chosen according to the needs of individual patients (e.g., peritoneal dialysis may be preferable if the patient is

hemodynamically unstable, and hemodialysis after abdominal surgery involving the peritoneum), the expertise of the nephrologist, and the facilities of the institution.

Outcome and long-term prognosis

The mortality rate among patients with ARF approximates 50% and has changed little over the past 30 years. Twenty-one day mortality is higher (30%) in patients with acute tubular necrosis of ischemic, compared to nephrotoxic (10%), etiology.

It should be stressed, however, that patients usually die from sequelae of the primary illness that induced ARF and not from ARF itself. Indeed, **the kidney is one of the few organs whose function can be replaced artificially (i.e., by dialysis) for protracted periods of time**. In agreement with this interpretation, mortality rates vary greatly depending on the cause of ARF: ~15% in obstetric patients, ~30% in toxin-related ARF, and ~60% following trauma or major surgery. Mortality rates are higher in older debilitated patients and in those with multiple organ failure. Most patients who survive an episode of ARF recover sufficient renal function to live normal lives. However, 50% have subclinical impairment of renal function or residual scarring on renal biopsy. Approximately 5% of patients never recover function and require long-term renal replacement with dialysis or transplantation. An additional 5% suffer progressive decline in GFR, following an initial recovery phase, probably due to hemodynamic stress and sclerosis of remnant glomeruli.