Acute tubular necrosis(ATN)

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TUMS

DEFINITION of AKI

- A rise in serum creatinine of at least 0.3 mg/dL (26.5 micromol/L) over a 48-hour period

and/or

- ≥1.5 times the baseline value within the seven previous days
- Urine volume ≤0.5 mL/kg per hour for six hours

ETIOLOGY

- Causes of prerenal disease:

1. True volume depletion
2. Hypotension
3. Edematous states
4. Selective kidney ischemia
5. Drugs affecting glomerular hemodynamics

ETIOLOGY

- Causes of acute tubular necrosis :

1. Kidney ischemia
2. Sepsis
3. Nephrotoxins (Tenofovir, Vancomycin, mTOR inhibitors, Aminoglycosides, Radiocontrast media, Intravenous immunoglobulin)

Frequency

Approximately 65 to 75 percent of cases of AKI in the hospital are due to either prerenal disease or ATN

- ● ATN – 45 percent
- ● Prerenal disease – 21 percent
- ● Acute on chronic kidney failure – 13 percent (mostly due to ATN or prerenal disease)
- ● Urinary tract obstruction – 10 percent
- ● Glomerulonephritis or vasculitis – 4 percent
- ● Acute interstitial nephritis – 2 percent
- ● Atheroemboli – 1 percent

EVALUATION

- Vomiting, diarrhea, bleeding, or sepsis
- Hypotension, intraoperative events, aminoglycoside therapy, or the administration of radiocontrast media
- Careful perusal of the patient's chart
- Unexplained tachycardia, dry mucous membranes, decreased skin turgor, cool extremities, supine and/or orthostatic hypotension

EVALUATION

- Heart failure and cirrhosis can result in edema, ascites, and other signs of specific organ dysfunction
- Abdominal distension leading to intra-abdominal hypertension and abdominal compartment syndrome

Distinction of prerenal disease from ATN

1. Urinalysis and urine microscopy.
2. Fractional excretion of sodium (FENa) and, to a lesser degree, the urine sodium concentration.
3. Response to fluid repletion in patients who have evidence of volume depletion, which is the gold standard for the diagnosis of prerenal disease.

Other parameters:

- Blood urea nitrogen (BUN)/serum creatinine ratio.
- Rate of rise of serum creatinine concentration.
- Urine osmolality.
- Urine volume.
- Bedside ultrasound measurements of the inferior vena cava

Urinalysis

- Normal
- Cell sloughing and cast formation are less prominent in patients with less severe disease and nonoliguric ATN
- muddy brown granular, epithelial cell casts, and free renal tubular epithelial cells

FENa

- $$\text{FENa(percent)} = \frac{\text{UNa x SCr}}{\text{SNa x UCr}} \times 100$$

FENa

- Preferred test
- A patient with prerenal disease who is highly water avid due to increased secretion of antidiuretic hormone may have a higher than expected urine sodium concentration, despite a low rate of sodium excretion.
- Conversely, decreased water reabsorption in ATN due to impaired concentrating ability can lower the urine sodium concentration by dilution.

Response to fluid repletion

- Gold standard for the distinction between prerenal disease secondary to volume depletion and postischemic or nephrotoxic ATN is the response to fluid repletion
- If sufficient fluid is given to reverse any signs of volume depletion (eg, hypotension, cool extremities, low FENa and urine-sodium concentration), return of the serum creatinine to the previous baseline within 24 to 72 hours

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- Although prerenal disease and postischemic ATN are usually discrete entities, some patients have an intermediate presentation, with overlap between features of both prerenal disease (eg, low FENa) and ATN, such as coarse granular casts and/or renal tubular epithelial cells on urine microscopy and urinary biomarkers of renal tubular injury.

Fluid selection

- Fluid repletion is typically initiated with intravenous isotonic saline.
  - severe hypovolemia or hypovolemic shock : one to two liters of isotonic fluid (ie, isotonic saline or a balanced crystalloid solution)
  - The rate of further fluid repletion : the blood pressure response and other clinical signs such as peripheral perfusion, mental status, and urine output.

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- Patients with mild-to-moderate hypovolemia : isotonic fluid at a slower rate.
- The goal of therapy: volume repletion, requires that the rate of fluid administration be greater than the rate of ongoing fluid losses.
- Rate that is 50 to 100 mL/hour above ongoing fluid losses. These include insensible losses (usually 30 to 50 mL/hour) plus any other fluid losses

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- Concurrent abnormalities in serum sodium or potassium
- The presence of metabolic acidosis
- Patients who are hypernatremic may be treated with one-half isotonic saline
- The choice of initial replacement fluid in hypernatremic patients is dependent upon the degree of hypernatremia.
- The type of replacement fluid may influence outcomes and lower the risk of AKI. Balanced crystalloid solutions (eg, lactated Ringer's lactate, Plasma Lyte, Hartman solution) are associated with reduced risk compared with normal saline.

Blood urea nitrogen/serum creatinine ratio

- The BUN/serum creatinine ratio is normal at 10 to 15:1 in ATN
- A high ratio suggests prerenal disease
- Other causes: gastrointestinal bleeding, which disproportionately increases the BUN, or loss of muscle mass in a chronically ill individual, which lowers creatinine

Rate of rise of serum creatinine concentration

- The serum creatinine concentration tends to rise progressively and usually at a daily rate greater than 0.3 to 0.5 mg/dL (26 to 44 micromol/L) per day in patients with ATN.
- A slower rate of rise with periodic downward fluctuations (due to variations in kidney perfusion) is suggestive of prerenal disease.

Urine osmolality

- Loss of concentrating ability is an early and almost universal finding in ATN, with the urine osmolality being below 450 mosmol/kg in almost all cases and usually below 350 mosmol/kg
- A urine osmolality above 500 mosmol/kg is highly suggestive of prerenal disease.
- lower values similar to those in ATN may be seen in prerenal disease and are therefore of little diagnostic help.

Urine volume

- The urine volume is typically, but not always, low (oliguria) in prerenal disease due to appropriate increases in both sodium and water reabsorption, which limits further fluid loss.
- One exception is effective diuretic therapy, which will acutely raise the urine volume while the diuretic is acting.
- In comparison, patients with ATN may be either oliguric or nonoliguric.

Limitations with underlying kidney disease

- None of the above criteria for the diagnosis of prerenal disease may be present in a patient with underlying kidney disease.
- The ability to conserve sodium and the ability to concentrate the urine are often impaired.
- As a result, a cautious trial of fluids may be given (independent of the urinary findings) if it is suspected from the history and physical examination that an acute rise in the serum creatinine concentration may be due to volume depletion.

PREVENTION

- Identify the patient at increased risk
- We optimize volume status with intravenous (IV) fluids (if necessary), with the goal of optimizing cardiac preload, cardiac output, and ultimately renal blood flow.
- Avoiding nephrotoxins
- Medications

high-risk patients

- Chronic kidney disease (CKD; either reduced estimated glomerular filtration rate [eGFR] or proteinuria with normal eGFR)
- Severe atherosclerosis
- Diabetes mellitus, even in the absence of microalbuminuria or reduced eGFR
- Advanced malignancy, obesity, and/or poor nutrition
- Heart failure

Interventions to decrease risk

- Change modifiable risk factors:
- Optimizing volume status, avoiding or stopping nephrotoxins, if possible, and dose adjustment for drugs excreted by the kidney
- Do not administer any pharmacologic agent (such as diuretics or dopamine/fenoldopam) for the prevention of ischemic ATN.
- Their efficiency is yet to be confirmed

We do not give…

- We do not give sodium bicarbonate to prevent ischemic ATN.
- We do not give statins to prevent ischemic ATN.
- We do not use corticosteroids to prevent ischemic ATN.
- We do not use erythropoietin to prevent ATN.

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“No role for diuretics”

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THANK YOU