Rhabdomyolysis Updates

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Introduction:

Characterized by destruction of skeletal muscle

Release of intracellular contents into the bloodstream

Leads to muscle necrosis

Clinical impact ranges from asymptomatic elevation of muscle enzymes to acute kidney injury and electrolyte abnormalities

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Introduction:

- Results in cell death and release of potentially toxic substances into the bloodstream
- Management often is directed in preventing the primary complication from rhabdomyolysis: Acute kidney injury

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Patient population that rhabdomyolysis occurs?

Traumatic causes are a common mechanism (20%)

- Multisystem trauma
- Crush injuries
- Compartment syndrome - leads to muscle ischemia
- Vascular injuries
- Falls with prolonged immobilization

Approximately 8.5% of critically injured patients in TICU

- 10% develop renal failure
- 5% require RRT

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Patient population that rhabdomyolysis occurs?

Metabolic & Medical causes are more common (80%)

- Suspect in patient with increased metabolic demands on myocytes in excess of available supply of ATP
- Prolonged exercise
- Status epilepticus
- Exogenous agents (Alcohol, drugs, or toxins)
- Lipid lowering agents (Statins)
- Genetic defects
- Myopathies
- Infection
- Malignant hyperthermia
- Neuroleptic malignant syndrome
- Heat stroke

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What clinical findings are expected with rhabdomyolysis?

- Asymptomatic to critically ill
- Clinical presentation can vary greatly

Resultant organ injury may include:

- Renal (AKI)
- Cardiac (Arrhythmia)
- Coagulopathy
- Dark tea colored urine is a common finding

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What laboratory findings aid in the diagnosis of rhabdomyolysis?

- Elevated serum CK concentration
- CK >5 times upper limit of normal or
- CK >1,000 IU/L

Elevated myoglobulin

Elevated LDH

Elevated potassium

Elevated Creatinine

Injury to skeletal muscle cellular membrane leads to influx of calcium

- Disruption of cellular homeostasis occurs
- Leads to cell death
- Resulting in accumulation of CK, myoglobulin, LDH, and potassium in the bloodstream

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Creatinine Kinase

- Usually elevated by 12 hours of injury
- Peak at 24 to 72 hours after injury
- Returns to normal in approximately 5 days

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What is the optimal crystalloid type, rate of administration, and urine output goals to prevent AKI in rhabdomyolysis?

Fluid of choice:

- No clear recommendation
- No randomized controlled trials
- Lactated ringers
- Saline (0.9% or 0.45%)
- Saline is promoted due to its lack of potassium
- Crush injuries = Hyperkalemia
- Recommendation is 200 mL/hour to 1,000 mL/hour
- 400 mL/hour can be initiated
- Goal directed therapy of urine output of 1 mL/kg/hour to 3 mL/kg/hour and up to 300 mL/kg/hour
- If the patient remains anuric, then RRT may be necessary

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Are diuretics and/or bicarbonate administration beneficial?

Exact mechanism of AKI is controversial

- Two factors in development of myoglobin induced renal toxicity are:
  - Hypovolemia
  - Acuduria

Ultimately, AKI results from:

- Vasoconstriction
- Oxidant injury (Ferrihemate - breakdown product of myoglobin, in the presence of low pH can generate free radicals, which lead to direct renal cell injury)
- Tubular obstruction (Pigmented casts - result of an interaction between Tamm-Horsfall protein and myoglobin)
- Decreased tubular filtration

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Can alkalization of urine may prevent AKI?

- Sodium bicarbonate
- Mannitol - an osmotic diuretic, may lead to renal vasodilation
- No strong clinical evidence to support on the use of either

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Are diuretics useful?

Loop diuretics: clinical evidence is sparse. Mostly only case reports. Loop diuretics:

- Have shown to reduce metabolic demand and oxygen consumption by proximal tubular cells
- But, also shown to worsen renal afferent arteriole vasoconstriction, acidify urine, and promote aggregation of Tamm-Horsfall protein within the tubular lumen

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What electrolyte abnormalities should be expected and what are the optimal methods for management?

Hyperkalemia:

- Often associated with high potassium levels
- Correlates with the volume of muscle breakdown
- When it occurs with rhabdomyolysis-induced AKI, it occurs early in the course of the disease
- Hypocalcemia aggravates electrical effects of hyperkalemia: Should be aggressively treated with calcium chloride or calcium gluconate
- Treat hyperkalemia with Insulin, glucose, B-2 agonist, potassium removal cations, and RRT as a last resort

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Hyperphosphatemia:

- Occurs as a result of phosphate release from damaged cells
- High phosphate levels are problematic: binds to calcium and these complexes deposit in soft tissues
- Treat with caution. Require a calcium chelator, which can increase precipitation of calcium phosphate in injured muscles
- Early hyperphosphatemia typically decreases as phosphate is excreted in urine

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Hypocalcemia:

- Occurs early in rhabdomyolysis due to calcium entry into damaged cells and calcium phosphate deposition in necrotic muscle
- Early treatment should be avoided unless patient is symptomatic or severe hyperkalemia is present
- Avoid correction with calcium chloride or calcium gluconate - calcium deposition can occur in injured muscle

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Hypermagnesemia:

- May occur, but id infrequent
- Typically occurs in association with AKI
- Should be treated with RRT

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What is the role of RRT in rhabdomyolysis:

- No role in dialysis or CRRT in preventing AKI
- Also, there is no significant evidence to determine that CRRT has any benefit over conventional RRT in preventing AKI in rhabdomyolysis
- In patients who either develop AKI, and need dialysis: Either CRRT or intermittent RRT can be considered
- AKI is associated with myoglobulinemia, thus extracorporeal removal is an effective strategy
- Plasmapheresis does NOT have an effect on myoglobin clearance
- CRRT and conventional RRT have been shown to be equally effective

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What is the role of RRT in Rhabdomyolysis?

- Since myoglobin has a molecular weight of 17 KDa, it is poorly cleared by diffusion (dialysis). Studies have been performed to evaluate benefits of:
  - Continued RRT
  - Intermittent RRT
  - Hemodiafiltration
  - Hemofiltration
  - Special high cut off membrane filters (Enhance clearance of large molecules)
    - Overall studies are small and lack sufficient evidence to make recommendations

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What complications should be suspected?

- Hyperkalemia: most significant electrolyte abnormality
- Hepatic dysfunction may occur in 25% of patients
- Dysrhythmia or cardia arrest: Most likely secondary to hyperkalemia
- Mortality in patients with CK >5,000 IU/L is approximately 14%
- AKI develops in approximately 15% of patients
- Among patients requiring RRT, mortality is as high as 59%
- DIC may occur, due to release of intracellular products that may activate the clotting cascade

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What complications should be suspected?

- Compartment syndrome: May be an early or late complication
  - Results from direct muscle injury
  - Vigorous muscle activity
  - Occurs primarily due to limited muscle expansion from enveloping tight fascia
  - Delay of more than 6 hours may lead to irreversible muscle damage or death

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