

Rhabdomyolysis: Prolonged and high-intensity exercises, impact on renal function

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Abstract

Rhabdomyolysis is a syndrome caused by injury to skeletal muscle that usually leads to acute kidney injury (AKI) and has been linked to different conditions, including severe trauma and intense physical exercise. The Cases related to vigorous physical exercise are observed in individuals in whom the severity it is due the response to the prolonged and high-intensity exercises. Additionally, the excessive use of Nonsteroidal anti-inflammatory drugs (NSAIDs), commonly used by endurance competitors can cause renal insufficiency. This short communication presents general aspects about rhabdomyolysis, pathophysiological mechanism, clinical manifestation and treatment.

Introduction

Rhabdomyolysis is a syndrome caused by the destruction of musculoskeletal cells, which releases intracellular substances toxic to the circulation, including myoglobin, which are harmful to the body. Typically, rhabdomyolysis presents with myalgia, muscle weakness and dark urine. Clinical manifestations may range from an asymptomatic disease to a life-threatening condition with very high enzymes, acute kidney injury (AKI) and electrolyte disturbances.

The syndrome is reported in athletes having a higher prevalence in men. Can be induced by prolonged and high-intensity exercises [1] or by sudden and excessive contractions of the skeletal muscles, with typical appearance of prominent clinical manifestations between 24 and 48 hours after the activity. Being more often reported in certain running modalities than in cycling and triathlon. This case, rhabdomyolysis is related to excessive muscle activity, changes in body temperature, electrolyte, endocrine and circulatory changes.

Dehydration may be a key factor in triggering the syndrome, even in previously healthy and well-conditioned practitioners. Intake of isotonic fluids should be prioritized since hypotonic fluids can lead to varying degrees of hyponatremia. Reduced sodium rates, by mechanisms not yet well elucidated, are pre-disposed to rhabdomyolysis.

Clinical manifestations and treatment

The clinical presentation is extremely variable. In conscious patients, the main complaint may be of sensitivity, pain, stiffness and cramps accompanied by weakness and loss of function. However, myalgia may be absent or minimal initially. In comatose patients, the observation of stiffness in the extremities may suggest rhabdomyolysis. Skin changes due to ischemic tissue damage (discoloration, blistering) may be present in the affected area. Physical examination may reveal edema in muscles that may worsen after parenteral rehydration. Severe muscle edema may result in compartment syndrome, with no pulse.

Dark urine (reddish chestnut) is the classic manifestation of rhabdomyolysis. Signs of dehydration caused by the sequestering of

fluid by the affected muscles may be present along with oliguria. Signs related to the complications of rhabdomyolysis (hyperkalemia, acute renal failure, metabolic acidosis, disseminated intravascular coagulation and, rarely, respiratory failure) may also be present between clinical manifestations.

The treatment for rhabdomyolysis, if done immediately, usually does not cause sequelae and consists of the application of intravenous saline, absurd intake of fluids and administration of diuretics to dilute myoglobin in the blood and stimulate the kidneys with the production and release of urine. Depending on the patient's condition, more drastic procedures, such as hemodialysis or surgery to “unclog” may be applied [2].

Molecular mechanisms in rhabdomyolysis

The most accepted pathophysiological mechanism is that the deficit or even depletion of adenosine triphosphate due to strenuous exercise induces a dysfunction of Na-K-ATPase, impairing the redistribution of ionic balance that occurs physiologically during exercise. The increase in sodium concentration in myocytes causes the Na-Ca exchanger to work to reverse this state, in order to accumulate calcium in the high ion concentrations in muscle fibers are associated with cytotoxic events such as: activation of proteases and phospholipases, higher mitochondrial, sarcoplasmic calcium rates and stimulation of apoptosis signaling cellular [3].

Common final pathophysiological mechanisms among these causes of rhabdomyolysis include an uncontrolled rise in free intracellular calcium and activation of calcium-dependent proteases, which lead

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Key words: exercise, renal failure, nephrology

Received: November 24, 2018; **Accepted:** December 05, 2018; **Published:** December 10, 2018

to destruction of myofibrils and lysosomal digestion of muscle fiber contents [4]. Calcium is among the major ions involved in maintaining skeletal muscle homeostasis. On the other hand hyperkalemia may be important to the point of leading to cardiac arrhythmias, hyperphosphatemia, metabolic acidosis and oscillations in serum calcium, and depending on the magnitude of these complications, hemodialysis should be indicated.

Another fact, myoglobin is a low molecular weight protein that is freely filtered by the kidney, and when there is muscle damage its concentration in the bloodstream is high, when it is eliminated in high concentrations it gave a dark color to the urine. Normally, after the end of muscle injury myoglobin blood levels return to normal within a few hours due to hepatic metabolism and renal excretion. The problem is that myoglobin is toxic to the kidney, and although it does not cause kidney damage alone, together with decreased circulating blood volume and decreased kidney perfusion can lead to myoglobinuric AKI.

Finally, serum creatine kinase (CK) is the most reliable diagnostic marker of rhabdomyolysis. Studies confirm the elevation CK that occurs during strenuous exercise, healthy subjects who participated in long marches (50 and 80 km) with heavy load also showed a large increase of CK during each march, reaching levels 40 to 80 times higher than the typical value for healthy sedentary participants, reflecting continuous muscular damages [5].

Renal failure

Rhabdomyolysis produces multiple adverse effects on the kidney, such as vasoconstriction, oxidative stress, inflammation and apoptosis [6]. Renal vasoconstriction is caused by reduced renal blood flow due to excessive leakage of extracellular fluid into the damaged muscle cells and by secondary activation of the renin–angiotensin aldosterone system [7]. On the other hand, the key role of oxidative stress in acute kidney injury in rhabdomyolysis has also been demonstrated using antioxidants which effectively prevented oxidative renal damage and dysfunction [8].

The accumulation of myoglobin in the kidney is central in the mechanism that leads to kidney damage [9]. Myoglobin deposition associates with impairing the primary urine flow and reabsorption, apparently through induction of oxidative stress with subsequent nephron cell death [10]. Recent data show that myoglobin induces lipid peroxidation of cellular membranes ultimately producing malondialdehyde as well as isoprostanes [11].

In addition, it is agreed that renal failure is due to the combined effects of direct cytotoxicity due to the accumulation of renal tubular myoglobin, hypovolemia, and aciduria. Increased levels of uric acid may play an important role in the renal alterations induced by heat stress and continuous episodes of rhabdomyolysis. Therefore, treatments aimed to reduce hyperuricemia may help to decrease the renal burden in these conditions [12].

Nonsteroidal anti-inflammatory drugs and AKI

Nonsteroidal anti-inflammatory drugs (NSAIDs) permitted by the World Anti-Doping Agency, are commonly used by competitors including runners and ultra-marathon competitors to improve performance in endurance events performed over large distances. Recently a study [13] showed that high creatinine excretion correlated with NSAIDs (i.e. ibuprofen) intake indicating an increased risk of AKI in ultramarathoners. The excessive use of NSAIDs, can cause renal insufficiency, what will be aggravated during a test of long distance being able to increase the severity of the rhabdomyolysis.

The use of NSAIDs requires special attention because they inhibit the activity of satellite cells, potentially inhibiting muscle adaptation to exercise and cause renal hemodynamic changes including the stimulation of the renin-angiotensin aldosterone system, vasoconstriction, decreased renal blood flow, and water retention, which may lead to hyponatremia (i.e., low plasma sodium concentration) and increased stress on the kidneys during endurance competition [14].

Conclusion

This brief communication study illustrates the concern of exercise in prolonged and high intensity induction of AKI and rhabdomyolysis.

Ethics approval

Not applicable

Consent for publication

Not applicable

Availability of data and materials

Not applicable

Competing interests

The author declares that there are no competing interests

Funding

None

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