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Mini-Review Article

Rhabdomyolysis in Severe Covid19: A Mini Review Study

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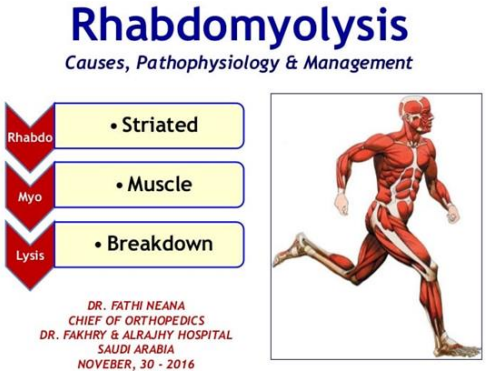
ABSTRACT

Introduction: Rhabdomyolysis can be a symptom of COVID-19, with very few cases described so far. AKI and renal failure following rhabdomyolysis are a potentially dangerous complication. Diagnosis of rhabdomyolysis in COVID-19 is difficult due to overlap.
Materials and Method: The present study was a PICO review that examined rhabdomyolysis in COVID-19. The documents browsed by Google Scholar, Sid and Mag Iran databases were analyzed using the keywords rhabdomyolysis, creatine kinase, COVID-19, acute renal failure.
Results: Rhabdomyolysis following COVID-19 and SARS-CoV-2 reports of viral contamination of striated muscle may result in muscle destruction. Rhabdomyolysis in COVID-19 is a late complication. Evaluation of CK and myoglobin levels is important for the diagnosis of rhabdomyolysis in COVID19 patients. The mechanism of rhabdomyolysis in COVID-19 is unknown and various mechanisms are used.
Conclusion: Rhabdomyolysis may cause acute kidney damage (AKI). Prompt diagnosis is a prerequisite for successful treatment and prevention of complications.

GRAPHICAL ABSTRACT



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Introduction

When it comes to fitness, sometimes it can be exaggerated. Rhabdomyolysis is a complication that may be caused by excessive exercise [1-3]. Motivated people are encouraged by trainers and tutors to go beyond the limits of the body. Whether in the gym, sports complex or in front of the TV practicing with the film, there are potential dangers in lifting, crushing and stretching for a long time (Figure 1). Many lessons can be learned from top athletes who have not followed the proper limits. These people may be called 13 badmen [4]. At the end of an intense workout, thirteen Iowa University football players were taken to hospital for rhabdomyolysis (rhabdo = skeleton + meow = muscle + slip = analysis), a condition in which muscles rapidly degenerate and turn their contents into the flow into the bloodstream. Myoglobin is a protein found in muscle cells that, if taken in sufficient amounts into the bloodstream, can block the kidney filtration system, leading to kidney failure and many other serious medical consequences [5]. Although muscles naturally become sore after physical activity, rhabdomyolysis takes this muscle injury to the next level [6-8].

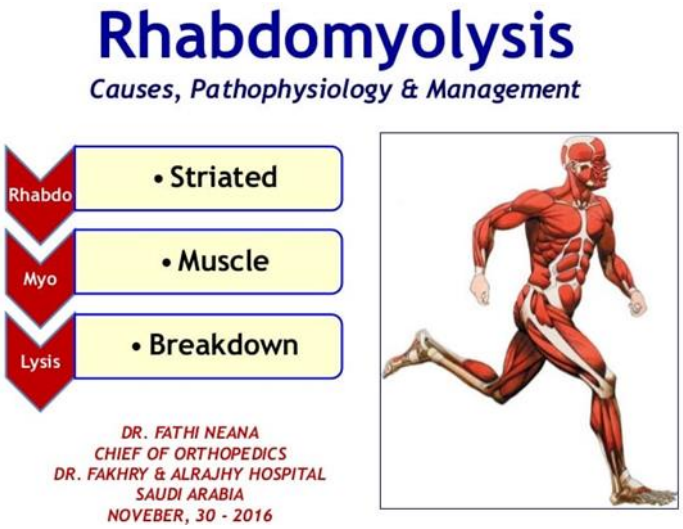

Figure 1: Rhabdomyolysis [2]

Ardehali (2005) wrote that rhabdomyolysis is basically a clinical syndrome that occurs following injury to the striated muscles and the release of intracellular elements into the bloodstream. Historically, accidents caused by accidents and muscle bruises and crush injuries have been the main causes of rhabdomyosis, which increases the incidence of acute renal failure during natural disasters such as earthquakes and man-made events such as war. [9-11]. The most common symptoms of this syndrome are pain and muscle weakness. The two symptoms (triad) of muscle weakness are muscle pain and dark urine (hallmark) of the syndrome. The severity of the disease is in a range where in one hand there is an asymptomatic increase in muscle enzymes in the serum and on the other hand there is acute renal failure and electrolyte disorders [12].

Mousavi *et al*. (2009) reported that most common causes of acute poisoning were rhabdomyolysis (opium use (28%), tricyclic antidepressants (14%) and benzodiazepines (14%). Types of severe acute poisoning related to rhabdomyolysis are presented [13]. The ratio of men to women was higher in all causes leading to severe poisoning. Acute renal failure was detected in 23 patients (13.94%), of which 1 was female and 22 were male (Figure 2); opium and alcohol were the most common causes of poisoning [14]. Of these, only 9 patients (all males) underwent hemodialysis. Finally, 7 patients (4.2%) died. The only cases leading to death in the study population were the same 7 ones. Out of 2 other patients, 1 had chronic renal failure and the other recovered. There was a significant positive linear relationship between CK level and serum creatinine in patients with renal failure due to the disease [15].

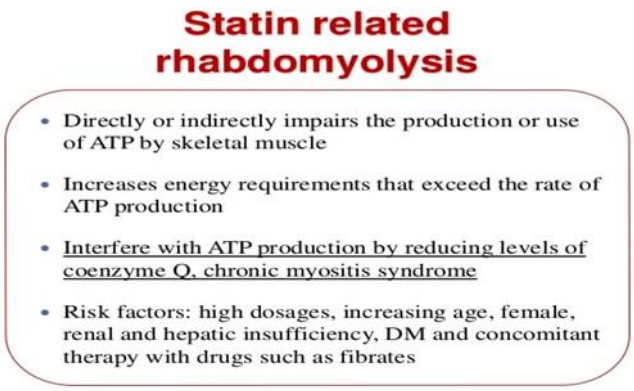

Figure 2: Statin related Rhabdomyolysis [5]

Causes of rhabdomyolysis

Rhabdomyolysis is the result of massive muscle injury and there are many reasons, including: Very aggressive exercises such as lifting weights, intense exercises with film or doing various exercises. This is especially true when a person moves from a small activity to an exercise for an hour or more [16]. Muscle cell injury leading to kidney failure can happen to anyone who over-exercises, and rhabdomyolysis should not be considered a sign of pride; also, a wise decision to stop exercising at the right time should not be considered a failure. Injury to victims of traumatic injuries can happen in earthquakes, bombings or lightning strikes if a person falls and lies motionless for several hours (for example, due to a stroke, drunkenness, or drug overdose), the weight of the body then crushes their muscles and rhabdomyolysis occurs (Figure 3). Harmless causes include side effects of certain medications, such as statins used to treat high cholesterol, and some psychiatric medications [17].

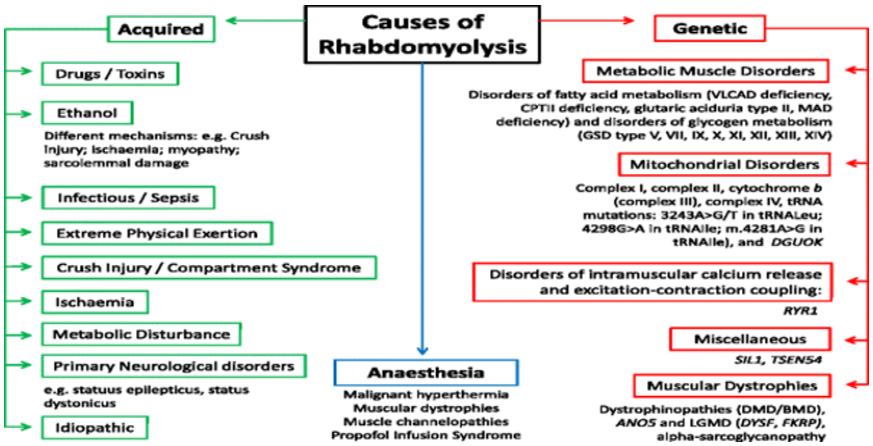

Figure 3: Rhabdomyolysis: a genetic perspective

How is rhabdomyolysis diagnosed?

The specialist doctor will diagnose the disease by examining the skeletal muscles of the person's body and touching the areas that are associated with pain, as well as by performing urine and blood tests. Tests performed to determine the health of muscles and kidneys are performed by examining the following values: Creatine kinase, an enzyme found in skeletal muscle, brain and heart [17]. Myoglobin is a protein that is found in the blood and urine as a result of muscle breakdown. Potassium is a mineral in the body that may leak from damaged bones or muscles. Creatinine in the blood and urine is a product of the breakdown of skeletal muscle that is normally excreted by the kidneys. The presence of high levels of these substances in the blood and urine is a sign of muscle injury [18].

In late December 2019, a case of unidentified pneumonia was reported in Wuhan City, Hubei Province, China, whose clinical features were very similar to those of viral pneumonia. The

World Health Organization (WHO) named the virus COVID-19 and the International Committee on Taxonomy of Viruses (ICTV) SARS-CoV-2. Corona virus 2019 (COVID-19) is caused by severe acute respiratory syndrome. For about three months, it spread throughout the world and was declared epidemic [19].

Material and methods

This article was based on a review study and was relied on observation and documentation. The first part was based on library studies and Internet searches on Web of Science, PubMed Scopus, Google Scholar, Direct Science, and Advanced Google. Articles on WHO and the US CDC were also reviewed.

Treatment of Rhabdomyolysis

Fluid intake

If you are lucky enough and only need home remedies to treat your illness, the best way to manage the condition is to use fluids. At the hospital you can use venous fluids to flush toxins out of the bloodstream, but you can do the same at home. Drinking water and other fluids can help with bowel movements and proper kidney function. This will eliminate toxins from the body [20].

Stop exercising

If your illness is due to strenuous physical activity, it is best to stop doing so. If you do not reduce the volume and pressure of your workouts, you will do more injury to your muscles. In this case, it is better to consult a doctor [21].

Discontinuation of drugs

Drug use can cause or worsen the symptoms of the disease. Try to stop taking these substances quickly, especially cocaine. These substances can hurt the kidneys and make the disease worse.

Increased blood circulation

Since most of the complications of this disease are related to muscles and tissues and its release into the bloodstream, it will be essential to have a complete blood circulation and sufficient and fresh oxygen. Some healthy foods to increase blood circulation include oranges, peppers, garlic, ginger, dark chocolate, watermelon and goji berries. As for improving kidney function, it is clear that if you find a way to improve the efficiency and function of the kidneys to remove toxins from the body, you will be able to improve the disease. Some foods and herbs that help with kidney health and improve kidney function include red pepper, cabbage, garlic, apples, egg whites and olive oil [22].

Stop taking unnecessary drugs

Taking certain medications or a combination of powerful medications can lead to this disease. If you have experienced symptoms of this disease, it is better to discontinue some medications or use alternative medications after consulting your doctor [23].

Warning

Although home remedies are helpful in preventing or reducing the symptoms of rhabdomyolysis, you should keep in mind that the condition can be very serious and life-threatening, so referring to a specialist doctor can be very helpful. If your illness is not very acute and serious, you can also use home remedies in consultation with your doctor.

Result and Discussion

A 38-year-old man with type 2 diabetes, gout and mild obesity with a 1-week history of fever, myalgia, nausea, vomiting, dry cough, shortness of breath and abdominal pain was brought by ambulance but was conscious at the time of admission. 91% oxygen saturation and other vital signs were normal and suspected SARS-CoV-2 infection at the time of admission due to the presence of classic combination symptoms. CT showed large double-sided glass chests. On the fourth day, the urine was stained, myoglobin levels gradually increased (from normal at baseline to> 21000 µg / L) and renal function was deteriorated (lowest relative glomerular filtration rate 18 ml. per minute / 1.73 square meters). Rhabdomyolysis was very high. And intermittent hemodialysis was required for the patient [24-26]. Early reports from China showed that 25% of patients with COVID-19 in intensive care had AKI [27-29].

Myoglobinuria is pathognomonic of rhabdomyolysis, and evidence suggests that myoglobin disrupts glomerular filtration through several mechanisms, including intrarenal vasoconstriction, ischemic tube injury, and tubular obstruction [30-32]. Jin and Tang reported a 60-year-old man with COVID-19, who developed lower extremity pain and weakness and rhabdomyolysis on the ninth day of hospitalization [32]. Rhabdomyolysis is the breakdown of skeletal muscle myocytes and the release of intracellular contents. For this reason, rhabdomyolysis is characterized by elevated levels of CK, myoglobin, potassium, aldolase, lactate dehydrogenase, urate, and ALT. Rhabdomyolysis can be a potentially life-threatening condition due to the side effects of releasing excessive amounts of this intracellular content. Rhabdomyolysis can cause harm to kidney. Myoglobin secretion exceeds the protein binding capacity and excess pigment is deposited in the glomerulus. Hyperkalemia, acute renal failure, metabolic acidosis, diffuse intravascular coagulation, ventricular syndrome, arrhythmias, and cardiac arrest are potential complications of rhabdomyolysis [33-36].

Hydroxychloroquine and oseltamivir were used in the early cases of COVID-19, having been reported to be associated with rhabdomyolysis [37-39]. According to Fadila *et al*., about one-third of reports of rhabdomyolysis are due to the influenza. Recently, there have been several reports of rhabdomyolysis following COVID-19 and SARS-CoV-2, possibly causing viral infection of the striated muscle and causing muscle destruction [4]. Jin and Tang reported the first case of rhabdomyolysis in COVID-19 as a late complication [35].

Dissection and Conclusion

From the first description of the causal relationship between rhabdomyolysis and AKI in people who suffered crush injuries during World War II, the range of causes of rhabdomyolysis, myoglobinuria, and renal failure has expanded. Rhabdomyolysis is most commonly caused by trauma or other types of injury that can lead to muscle compression, ischemia, increased muscle activity with exercise or seizures, metabolic disorders (hypokalemia and hypophosphatemia), medications and infections, cocaine use, and Noravalp syndrome. Malignancies and the use of hydroxymethylglutaryl coenzyme A reductase inhibitors (statin drugs) used to treat hypercholesterolemia have also been implicated in the development of rhabdomyolysis. Muscle pain and dark brown urine that is orthotoloidin positive and lacks RBCs are important diagnostic clues, but must be accompanied by elevated creatine phosphokinase and myoglobin to confirm the diagnosis. About one-third of patients with rhabdomyolysis develop ARF, which is usually associated with hyperkalemia, hyperuricemia, hyperphosphatemia, premature hypocalcemia, and decreased BUN to creatinine ratio due to excessive release of creatinine from muscle. Late hypercalcemia is also a prominent feature of this disease. The most important aspect of treatment is rapid fluid replacement. Intravenous fluids should be started with a normal saline solution at a rate of 200 to 300 ml per hour. If urinary output increases within 4-6 hours, fluids should be continued in proportion to the urinary tract to eliminate rhabdomyolysis. But if the patient is still oliguric (urinary retention less than 400 mL per day), venous fluid should be stopped and conservative AKI treatment should be started. Experiences from the catastrophes of recent years have shown that aggressive and immediate injections of fluids and alkalisation (3 ampoules of sodium bicarbonate in one liter of 5% glucose serum at a rate of 250 mL per hour) can protect the kidneys against the toxicity of myoglobin and urate, which prevent acute harm to kidney caused by myoglobin.

In sum, this study reports the following findings:

1. The patients complained of worsening muscle pain and weakness with the findings of simultaneous imaging of symmetrical bilateral calcification of the shoulder and chest muscle in the posterior, which progressed in attenuation and its extent in serial CT scan. General muscle pain and fatigue are common symptoms of COVID-19, but physicians should consider diagnosing rhabdomyolysis in patients with focal muscle pain and fatigue.

2. Gradual increase in creatinine kinase (33,000 µg / L), developing hypocalcemia, and refractory hyperkalemia (proportional to renal function) were all in favor of rhabdomyolysis.
3. The levels of aspartate aminotransferase (AST) and alanine aminotransferase (ALT) were significantly increased [30].

Case reports of SARS-CoV-2 causing rhabdomyolysis were reported. Rhabdomyolysis has been described as both a presentation feature and a late complication of COVID-19. The mechanism of rhabdomyolysis in COVID-19 is unknown and various mechanisms are used. Rhabdomyolysis is characterized by muscle necrosis and the release of intracellular muscle components into the systemic circulation. Prompt diagnosis is a prerequisite for successful treatment and prevention of complications. Rhabdomyolysis may cause acute kidney damage (AKI). Hence, timely detection is the key to preventing AKI.

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Authors' contributions
All authors contributed toward data analysis, drafting and revising the paper and agreed to be responsible for all the aspects of this work.

Conflict of Interest
The authors declare that they have no competing interests.

Ethical considerations
The ethical issues (including plagiarism, data fabrication, double publications) were fully noted by the authors.

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