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Rhabdomyolysis In Critically Ill Patients In ICU

an essay

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LIST OF ABBREVIATION

AKI : acute kidney injury

aPTT :activatedpartial thromboplastin time

ARF : acute renal failure

ATLS : Advanced Trauma Life Support

ATN : acute tubular necrosis

CHCT : Caffeine Halothane Contracture Test

CK : serum creatine kinase

CO : carbon monoxide

CPT I : carnitinepalmitoyltransferaseI

CPT II : Carnitine palmitoyltransferase

DIC : Disseminated intravascular coagulopathy

D5W :dextrose 5%

FA : fatty acid

½NS : half-normal saline

KIM-1 : kidney injury marker 1

MLCK : myosin light chain kinase

MRI : Magnetic resonance image

Na/K-ATPase : a sodium-potassium adenosine triphosphatase

NGAL : neutrophil gelatinase-associated lipocalin

NMS : neuroleptic malignant syndromes

OCTN2 :carnitine/organiccations transporter

PRIS :propofol-related infusion syndrome

PT :prothrombin time

PYR1 :the sarcoplasmic reticulum ryanodine receptor gene

SEARCH :the Study of the Effectiveness of Additional Reductions in Cholesterol and Homocysteine

TBSA : Total Body Surface Area

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INTRODUCTION

Rhabdomyolysis is the end result of any process that leads to the death of muscle tissue ***(Khan2009).***

Causes of rhabdomyolysis are divided into hereditary andacquired ones. The hereditary causes are mainly related to alack or insufficiency of enzymes that participate in the catabolism of different energy macromolecules.the acquired causes are classifiedas traumatic and non-traumatic: The traumatic ones, such as crush syndrome, accidents, natural disasters, or intense exercise, cause direct muscle injury and rupture of the sarcolemma. The non-traumatic causes are the most common ones during peacetime and include alcohol abuse, medicines e.g., statins***(Chatzizisis et al.,2008).***

Although the causes of rhabdomyolysis are so diverse the pathogenesis appears to follow a final common pathway, ultimately leading to myocyte destruction and release of muscle components into the circulation***(Khan, 2009).***

The classic triad of symptoms of rhabdomyolysis includesmuscle pain, weakness and dark urine***(Huerta-Alardín et al.,2005).***Diagnosis of rhabdomyolysis is based on elevated serum creatine kinase (CK) levels more than 1000 u/L **(*Luck and Verbin,* 2008).**

First line treatment for rhabdomyolysis is aggressive fluid repletion which reduces the accumulation of toxic intracellular content caused by rapid breakdown of muscle and subsequent renal damage, unfortunately few treatments are available for rhabdomyolysis beside those that address the underlying insult **(Cervellinet al., 2010).**

The complications of rhabdomyolysis include:hypovolemia,compartment syndrome, arrhythmia, disseminated intravascular coagulation, hepatic dysfunction and acute renal failure***(Khan, 2009).***

AIM OF THE WORK

Is to identify rhabdomyolysis both clinically and laboratory, discuss its causes and its complications in ICU, additional to that, highlighting main lines of therapy in rhabdomyolysis and its complications.

Chapter I

Epidemiology and Pathophysiology of Rhabdomyolysis

Epidemiology:

Luckily, rhabdomyolysis is a rare event of rapid destructionofskeletalmuscle cells***(Better and Abassi,2011).***

The historical background

Rhabdomyolysis has been described since biblical times.Its earliest reference was where migrating Jews ate quail while traveling in the desert. One of the more unusual elements in the bird's diet was hemlock; therefore, ingestion of vast quantities of quail(and thus hemlock) may have led to rhabdomyolysis. Diets rich in quail have also been reported in the contemporary literature as being an inciting etiology of rhabdomyolysis ***(Schepet al.,2009).***

Widespread casualties from other world events have also brought rhabdomyolysis to the forefront, including crush injuries sustained during **:** 1908 Messina earthquake in southern Italy;1941 Blitz bombing of London, England; collapse of the US embassy in Beirut, Lebanon, in 1982; 1989 LomaPreita earthquake that triggered the collapse of the San Francisco–Oakland Bay Bridge; Hanshin-Awaji

earthquake of 1995; and 1999 earthquake in Izmir, Turkey ***(Gunalet al.2004)*.**

Rhabdomyolysis has been recognized for thousands of years as a cause ofmyoglobinuric renal failure, but a report byBywaters was among the first to document the major clinical sequels***(Bywaterset al.,, 1941).*** Rowlandand Penn described a series of patients with rhabdomyolysis secondary to a variety of enzymatic disorders ***(Rowland and Penn,1972).***

Prevalence and frequency

In the ICU setting, the most common causes of rhabdomyolysis are muscular trauma and vascular obstruction***(De Meijer et al.,2003).***Rhabdomyolysis occurs in up to 85% of patients with traumatic injuries. Alcohol has been implicated in the development of rhabdomyolysis in up to 20% of cases***(Brown et al.,2004).***About a third of all patients with rhabdomyolysis will develop AKI and it is suggested that5-25% of all acute kidney injury (AKI) results from rhabdomyolysis***(Khan, 2009).***Patients with severe injuries that develop rhabdomyolysis-induced renalfailure, have a mortality of approximately 20% but is higher if multiple organ dysfunction is present**(Huerta-Alardín et al, .2005).**

Pathophysiology:

Although the causes of rhabdomyolysis are so diverse, the pathogenesis appears to follow a final common pathway, ultimately leading to myocyte destruction and release of muscle components into the circulation ***(Khan,2009).***

In the normal myocyte, the sarcolemma, a thin membrane that encloses striated muscle fibers, contains numerous pumps that regulate cellular electrochemical gradients. The intercellular sodium concentration is normallymaintained by a sodium-potassium adenosine triphosphatase (Na/K-ATPase) pump located in the sarcolemma***(Luck andVerbin,2008).***

The Na/K-ATPase pumpactively transportssodium from the interior of the cell to the exterior. As a result, the interior of the cell is more negatively charged than the exterior because positive charges are transported across the membrane. The gradient pulls sodium to the interior of the cell in exchange for calcium by a separate ion exchange channel. Moreover, low intracellular calcium levels are also maintained by an active calcium exchanger (Ca2+ ATPase pump) that promotes calcium entry into the sarcoplasmic reticulum and mitochondria (**figure1.1**).The aboveprocesses depend on ATP as a source of energy***(Khan,2009).***

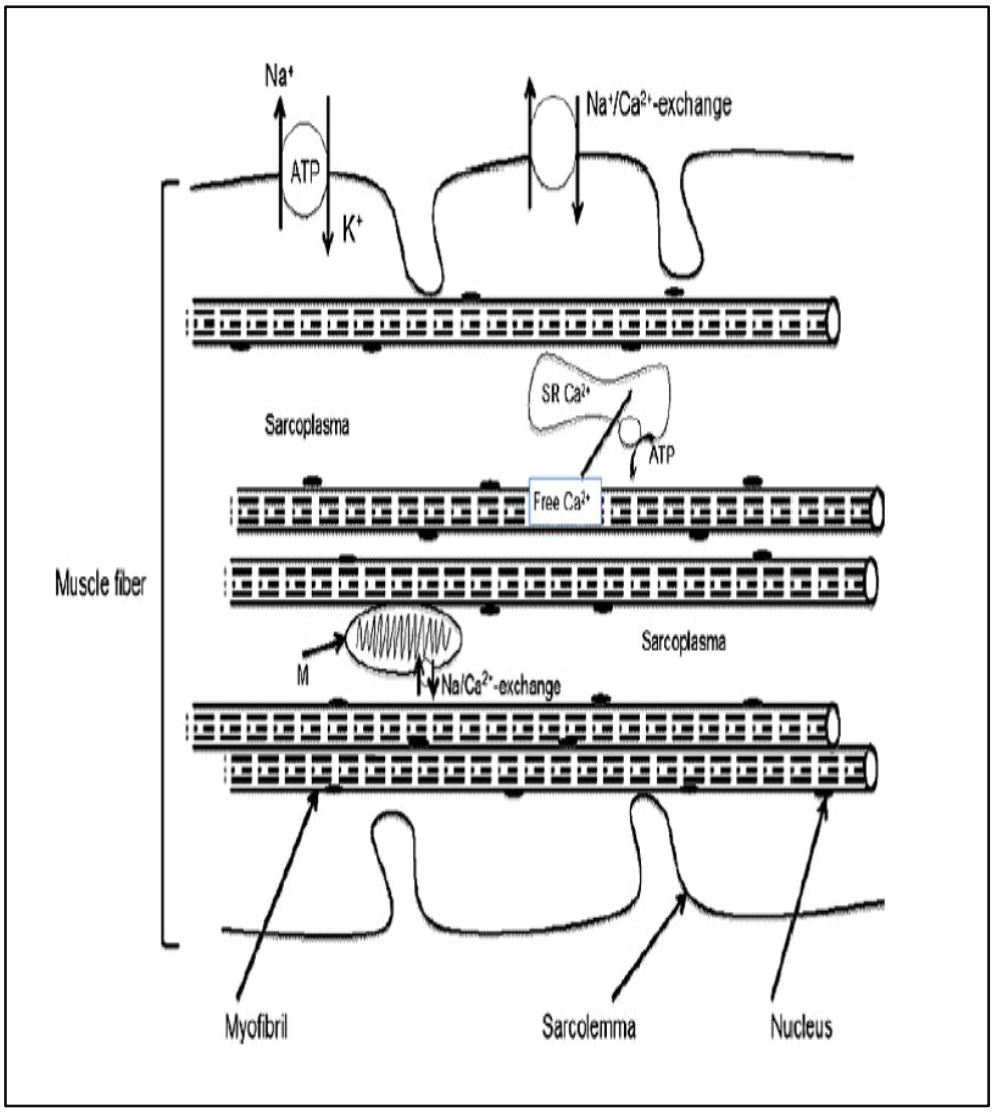

Figure 1.1 Mechanism of muscle contraction***(Al-Ismailiaet al., 2011).***

Mechanisms of rhabdomyolysis

ATP depletion, which appears to be the end result of mostcauses of rhabdomyolysis, results in Na/K-ATPase andCa2+ ATPase pump dysfunction ***(Figure 1.2)***, the end result of whichis an increased cellular *permeability* to sodium ions dueto either plasma membrane disruption or reduced cellularenergy (ATP) production.Accumulation ofsodium in thecytoplasm leads to an increase in intracellular calciumconcentration (which is normally very low relative tothe extracellular concentration). This excess calciumthen increases the activity of intracellular proteolytic enzymes that degrade the muscle cell. As the myocytedegenerates, large quantities of potassium, aldolase, phosphate, myoglobin, CK, lactate dehydrogenase, aspartatetransaminase and urate leak into the circulation ***(Huerta-Alardínetal., 2005).***

Underphysiological conditions, the plasma concentration of myoglobin is very low (0 to 0.003 mg per dl). If more than 100 g of skeletal muscle is damaged, the circulating myoglobin levels exceed the protein-binding capacity of the plasma and can precipitate in the glomerular filtrate. Excess myoglobin may thus cause renal tubular obstruction, direct nephrotoxicityand acute renal failure***(Mannix et al, 2006).***