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Rhabdomyolysis in Critically Ill Surgical Patients

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ABSTRACT

Introduction: Rhabdomyolysis is a syndrome of injury of skeletal muscles associated with myoglobinuria, muscle weakness, electrolyte imbalance and often, acute kidney injury as severe complication. **The aim** of this study is to detect the incidence of rhabdomyolysis in critically ill patients in the surgical intensive care unit (ICU), and to raise awareness of this medical condition and its treatment among the clinicians. **Material and methods:** A retrospective review of all surgical and trauma patients admitted to surgical ICU of the University Surgical Clinic "Mother Teresa" in Skopje, Macedonia, from January 1st till December 31st 2015 was performed. Patients medical records were screened for available serum creatine kinase (CK) with levels > 200 U/l, presence of myoglobin in the serum in levels > 80 ng/ml , or if they had a clinical diagnosis of rhabdomyolysis by an attending doctor. Descriptive statistical methods were used to analyze the collected data. **Results:** Out of totally 1084 patients hospitalized in the ICU, 93 were diagnosed with rhabdomyolysis during the course of one year. 82(88%) patients were trauma patients, while 11(12%) were surgical non trauma patients. 7(7.5%) patients diagnosed with rhabdomyolysis developed acute kidney injury (AKI) that required dialysis. Average values of serum myoglobin levels were 230 ng/ml,with highest values of > 5000 ng/ml. Patients who developed AKI had serum myoglobin levels above 2000 ng/ml. Average values of serum CK levels were 400 U/l, with highest value of 21600 U/l. Patients who developed AKI had serum CK levels above 3000 U/l. **Conclusion:** Regular monitoring and early detection of elevated serum CK and myoglobin levels in critically ill surgical and trauma patients is recommended in order to recognize and treat rhabdomyolysis in timely manner and thus prevent development of AKI.

Key words: rhabdomyolysis, critical illness.

1. INTRODUCTION

Rhabdomyolysis is a syndrome of injury of skeletal muscles first described in 1941 by Beall, in a victim of the London bombing (1). The injury of a skeletal muscles fibers is followed by release of myoglobin, creatine phosphokinase (CK) and lactate dehydrogenase, which are most important biochemical markers that indicate rhabdomyolysis.

The etiology of rhabdomyolysis includes hereditary and acquired causes. Hereditary causes of rhabdomyolysis are metabolic myopathies (2). Acquired causes of rhabdomyolysis are: trauma and crush syndrome, surgery, extreme physical activity, influence of extreme temperatures, metabolic disorders of water and salts, vascular ischaemia, surgery, various drugs (statins, corticosteroids, antidepressants, neuroleptics, barbiturates, benzodiazepines, salicylates, theophylline, aminocapronic acid) and anesthetics, alcohol abuse, cocaine abuse, neuroleptic malignant syndrome, seizures, toxins, infections or sepsis, prolonged immobilization,carbon monoxide (CO), endocrine disorders, malignant hyprtermia, electrical current and

connective tissue disorders (2-6). Despite the vast variety of causes of rhabdomyolysis, the pathogenesis follows common pathway that ultimately leads to destruction of myocytes and release of its components into circulation (2, 3, 7-10). Clinical manifestations of rhabdomyolysis are myoglobinuria, myalgia, muscle weakness, swelling, electrolyte imbalance and often, acute kidney injury as severe complication. Nonspecific symptoms such as fever, nausea and vomiting might also be present. Tea colored urine is a classical manifestation of rhabdomyolysis. The severity of clinical manifestations of rhabdomyolysis can vary from mild and subclinical cases, to severe cases with acute kidney injury and other complications that include disseminated intravascular coagulopathy, changes in micro and macrocirculation, hyperkaliemia, metabolic acidosis, hypocalcemia, hyponatriemia, hyperphosphatemia, cardiac dysrhythmia, changes in mental status, hypotension and shock (2, 3, 7-10). Definitive diagnosis of rhabdomyolysis should be made upon laboratory tests that include serum CK, urine and serum myoglobin. In addition, skeletal muscle biopsy can be used to confirm the diagnosis, but it is not necessary (2, 3). The value of elevation of CK is rather arbitrary and there is no cut-off value that conclusively diagnoses rhabdomyolysis. Myoglobinuria may resolve early in the course of rhabdomyolysis and make this parameter less sensitive.

2. THE AIM

The aim of this study is to detect the incidence of rhabdomyolysis in critically ill patients in the surgical ICU and to raise awareness of this medical condition and its treatment among the clinicians.

3. MATERIAL AND METHODS

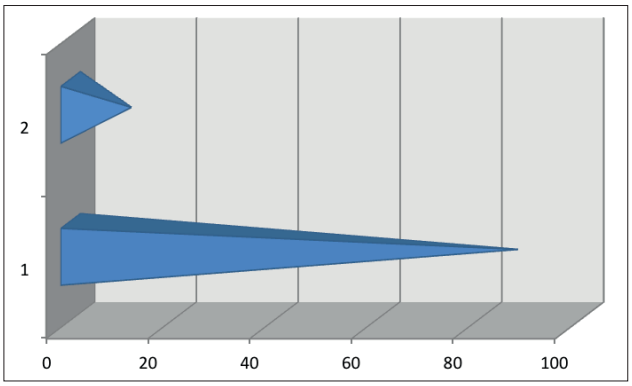
A retrospective review of all surgical, trauma and burn patients admitted to surgical ICU of the University Surgical Clinic "Mother Teresa" in Skopje, Macedonia, from January 1st till December 31st 2015 was performed. Medical records were examined to identify patients with diagnosis of rhabdomyolysis. The records were screened for available serum creatine kinase (CK) with level > 200 U/l, available myoglobin in the serum with level > 80 ng/ml, or if they had a clinical diagnosis of rhabdomyolysis by an attending doctor. Variables extracted included demographic data, highest CK and myoglobin levels, and occurrence of acute kidney injury (AKI) that required dialysis. Patients were excluded if they had preexisting renal insufficiency. Data collected on patients with rhabdomyolysis included diagnosis on admit ion in the ICU, maximum laboratory values for serum CK and myoglobin, number of dialysis for each patient with AKI and outcomes. Descriptive statistical methods were used to analyze the collected data.

4. RESULTS

Totally 110 surgical, trauma and burn patients out of 1084 patients hospitalized in the ICU from January 1st till December 31st 2015, were screened for elevated serum myoglobin and CK under suspicion of rhabdomyolysis. 93 patients proved positive for elevated levels of myoglobin above 80 ng/ml and CK levels above 200 U/l. Out of total amount, 73 patients were male, while 20 were female. Average age of the patients was 43 (range 16-72 years). 82 (88%) patients were trauma patients, mostly traffic traumatism victims (73 patients), with severe fractures of the limbs, multiple ribs fractures, thoracic concussions and blunt force abdominal trauma. Other 9 trauma patients were crush syndrome or fall from heights victims 11 (12%), were surgical non trauma patients. Distribution of trauma and non trauma patients diagnosed with rhabdomyolysis is presented in Graph 1. Average values of serum myoglobin levels were 230 ng/ml, with highest values of > 5000 ng/ml. Patients who developed AKI had serum myoglobin levels above 2000 ng/ml. Average values of serum CK levels were 400 U/l, with highest value of 21600 U/l. Patients who developed AKI had serum CK levels above 3000 U/l. 7 (7.5%) patients developed acute kidney injury (AKI) that required dialysis. After average 4 dialysis, kidney function was restored in 6 patients, and the levels of serum CK and myoglobin dropped rapidly, except in one patient who died after the second dialysis. Diagnosis upon ICU admission of the patients who developed rhabdomyolysis are presented in Table 1.

Diagnosis	Number of patients who developed rhabdomyolysis	Percentage
Trauma patients	82	88%
Acute abdominal event, sepsis	6	6 %
Burns	2	2 %
Spinal cord injury	1	1 %
Ruptured aorta	1	1 %
Acute adrenal crisis, sepsis	1	1 %

Table1. Admission diagnosis of the ICU patients who developed rhabdomyolysis



Graph 1. Distribution of trauma and non trauma patients diagnosed with rhabdomyolysis. Legend: 1) Trauma patients diagnosed with rhabdomyolysis; 2) Surgical non trauma patients diagnosed with rhabdomyolysis

5. DISCUSSION

Most of the available literature about rhabdomyolysis are review articles, retrospective studies of medical records and case reports. Demographic profile of the patients with rhabdomyolysis in our study, 78 % men, average age 43 is similar to the demographic profile of the study of Sharp et al., (11) - 80.2 % male, average age 41.2

		sensitivity	specificity	PPV	NPV	Overall accuracy
FNAB	4cm	78.57%	94.11%	84.61%	91.42%	89.58%
	≥4cm	71.4%	100%	100%	92%	93.33%
	total	76.19%	96.49%	88.88%	91.66%	91.02%

Table 1. Sensitivity, specificity, PPV, NPV, and overall accuracy of FNAB based on final pathology

years. The demographic profile suggests that rhabdomyolysis occurs predominantly in male population, who have more lean muscle body mass than female, making them more prone to this complication. In our study, direct muscle injury by severe trauma was the main cause for developing rhabdomyolysis in 88% of the patients, while in the study of Sharp et al, (11) direct muscle injury was the cause of rhabdomyolysis in 56 % of the patients. Hypoxic injury, sepsis, infections and other miscellaneous causes were the cause of rhabdomyolysis in only 12 % of the patients in our study, while Sharp et al (11) found that these causes were present in almost half of the patients (44%) who developed rhabdomyolysis. Taking into consideration the fact that these are retrospective studies of medical records with available CK and myoglobin plasma levels, the big differences in the percentages of causes of rhabdomyolysis between these two studies can be explained by low suspicion of attending doctors of rhabdomyolysis in non trauma patients in our ICU. In our study, acute kidney injury requiring dialysis occurred in 7.5% of the patients, while in the Sharp et al. study, that percentage was 9,5 %. Talving et al, reported occurrence of acute kidney injury in 13% of pediatric (< 18 years) trauma patients with rhabdomyolysis (12). According to Chan et al, patients with body mass index 25 kg/m^2 or greater are at a significant higher risk for rhabdomyolysis after trauma (13). Number of authors proposed prediction models for development of acute kidney failure caused by rhabdomyolysis, mainly focusing on CK levels and myoglobin levels. Talving et al, conclude that CK values of 3000 U/L or higher pose significant risk for acute kidney injury (12). According to Sharp and colleagues, plasma CK levels of 5000 U/L or higher present risk of persistent kidney insufficiency (11). El-Abellati et al, conclude that serum CK levels higher than 773 U/L, and myoglobin levels higher than 368 mg/L are cut off values for prediction of AKI (7). According to Premru et al, serum myoglobin levels > 15 000 mg/L were most significantly related to the development of AKI. Patients who developed AKI in our study had serum CK levels above 3000 U/L (14). Regardless the cause, the treatment of rhabdomyolysis is identical, and the treatment goals are directed towards maintaining adequate tissue perfusion and oxygenation, thus preventing hypo perfusion and hypoxia, eliminating the products of rhabdomyolysis and maintaining urine output, preventing acute kidney injury, as well as eliminating the primary cause of rhabdomyolysis (2, 3, 10, 15). Main goal of the treatment is to prevent acute kidney failure by maintaining urine output of 200-300 ml/hour (3). It is suggested to initiate aggressive fluid resuscitation by using normal saline, and to avoid potassium and lactate rich solutions because of the increased risk of hyperkalemia and lactate acidosis that accompany rhabdomyolysis (2, 3, 15). Diuretics are recommended, as well as alkalization of urine by adding sodium bicarbonate into normal saline solutions in order to decrease the cast formation and minimize the toxic effect of myoglobin on the renal tubules. New therapeutic strategies that include antioxidant and anti inflammatory agents (Iron helators, Acetaminophen, N- acetylcysteine, Vitamin E, Vitamin C, flavonoids, L- carnitine, Suramine, Pentoxifylline and Mesenchymal stem cells) have shown efficiency in animal models in neutralizing the effect of myoglobin on kidneys (16). Controlled clinical trials are needed to evaluate potential benefits of these agents for prevention and treatment of rhabdomyolysis induced AKI.

6. CONCLUSION

Regular monitoring and early detection of elevated serum CK and myoglobin levels in critically ill surgical and trauma patients is recommended in order to recognize and treat rhabdomyolysis in timely manner and thus prevent development of AKI.

• Conflict of interest: none declared.

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