Utility of Serum Creatinine, Creatine Kinase and Urinary Myoglobin in Detecting Acute Renal Failure due to Rhabdomyolysis in Trauma and Electrical Burns Patients

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Abstract Rhabdomyolysis due to trauma and burns is an important cause of acute renal failure (ARF) secondary to myoglobinuria. To prevent morbidity and mortality from ARF due to rhabdomyolysis, early detection of ARF by monitoring the biochemical parameters such as serum creatinine, serum creatine kinase (CK), and urinary myoglobin (UM) can be helpful. The aims of the study were (1) to detect ARF due to rhabdomyolysis using serum creatinine, serum CK, and UM in trauma and electrical burn patients (2) to compare utility of these parameters in early prediction of ARF in patients of rhabdomyolysis. A total of 50 patients with trauma and electrical burns were included in the study. Serum creatinine, serum CK, and UM measurements were done at the time of admission and after 48 h. Diagnosis of ARF was made in the patients by Rife's criteria. The presence of significant elevation of creatinine, serum CK, and UM at the time of admission and after 48 h was compared in patients developing ARF by Fisher's exact test. Fifteen of the 50 patients developed ARF as per the defined criteria. Of

these, 9 patients (60%) had raised level of serum creatinine above 1.4 mg% at admission and 14 patients (93.33%) had CK level >1250 U/L at admission, whereas UM was positive in 6 (40%) patients. Serum creatinine was significantly raised in all of the 15 ARF patients (100%) after 48 h of admission and serum CK was raised in 14 of the 15 ARF patients (93.33%). UM was negative in all the patients after 48 h of admission. Statistical analysis showed that rise in serum CK on admission was significantly increased in patients developing ARF as compared with serum creatinine and UM ($P<0.0001$). On admission, CK is a better predictor of ARF due to rhabdomyolysis than creatinine and UM. Initial creatinine is a better predictor of ARF due to rhabdomyolysis than UM. UM assay is not a good investigation for early prediction of ARF in rhabdomyolysis.

Keywords Creatine kinase · Urinary myoglobin · Serum creatinine · Acute renal failure · Rhabdomyolysis

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Introduction

Rhabdomyolysis due to massive breakdown of skeletal muscles can lead to acute renal failure (ARF) secondary to myoglobinuria [1]. It is commonly seen in trauma and electrical burns patients. To prevent morbidity and mortality from ARF due to rhabdomyolysis, early detection of ARF by monitoring the biochemical parameters such as serum creatinine, serum creatine kinase (CK), and urinary myoglobin (UM) can be helpful [2]. We performed this study in trauma and electrical burns patients to evaluate the use of these biochemical parameters for early prediction of high-risk patients who tend to develop ARF.

Patients and Methods

This was a prospective observational study done during the period of July 2007 to December 2008. The study was approved by the Institutional Ethical Committee. A total of 50 patients with acute trauma including extremity fractures, vascular injuries, crush injuries, high tension electrical burns (>1000 volts) presenting within 24 h of injury were included in the study. On admission, a detailed history was taken and a thorough physical examination of the patients was done and recorded as per the proforma. Serum creatinine was done on admission and after 48 h by Jaffe's kinetic method. Serum creatinine >1.4 mg% was considered significantly raised. Serum CK was done on admission and at after 48 h by CK NAC-activated method. Serum CK >1250 U/L (5 times the higher normal range of serum CK) was considered significantly raised. Similarly, UM was done on admission and after 48 h by myoglobin immunochromatographic rapid test. This test detects urinary myoglobin if its level is >100 ng/mL. Urine output was recorded every hour and the patients who had output less than 0.3 mL/kg/h for 24 h were defined as having ARF as per RIFLE criteria. The patients were treated conservatively with fluid resuscitation and supportive measures during initial period. Nephrology opinion was taken for the patients not responding to conservative treatment and decision of renal dialysis was taken as per the consulting nephrologists' opinion. Statistical analysis was done by Fischer's exact test by using SPSS statistical software.

Results

A total of 50 patients ($n=50$) of trauma and electric burns were included in the study. There were 44 males and 6 female patients. The mean age of the patients was 33.3 years (range 10–58 years). Of the 50 patients, 26 (52%) patients were of trauma and 24 (48%) patients of electrical burns.

UM was tested positive in 22 patients (44%) on admission, and after 48 h of admission it was found to be negative in all of the 50 patients (100%). The mean value of serum

creatinine on admission and after 48 h was 1.32 mg% and 1.85 mg%, respectively, whereas the mean value of CK at admission and after 48 h was 4003.8 U/L and 7586.9 U/L, respectively.

Fifteen patients (30%) had serum creatinine level above 1.4 mg% on admission and serum CK ≥ 1250 U/L was present in 32 patients (64%). After 48 h of admission, serum creatinine was raised above 1.4 mg% in 18 patients (36%), whereas serum CK >1250 U/L was seen in 31 patients (62%). Fifteen (30%) patients had urinary output less than 0.3 mL/kg/h for 24 h. So, they were diagnosed as having ARF. In the patients who developed ARF, the mean values of serum creatinine on admission and after 48 h were 1.48 mg/dL and 3.55 mg/dL, respectively ($P<0.0001$). Similarly, the mean values of CK on admission and after 48 h in the patients developing ARF were 7502.4 U/L and 20,255.3 U/L, respectively ($P=0.0004$).

Table 1 shows the comparison between the ARF and non-ARF patients. Of the 15 patients with ARF, 9 patients (60%) had raised level of serum creatinine above 1.4 mg% at admission and 14 patients (93.33%) had CK level >1250 U/L at admission, whereas UM was positive in 6 (40%) patients. Serum creatinine was significantly raised in all of the 15 ARF patients (100%) after 48 h of admission and serum CK was raised in 14 of the 15 ARF patients (93.33%). UM was negative in all the patients after 48 h of admission.

The comparison of serum creatinine, CK, and UM on admission and after 48 h in the patients who developed ARF is shown in Table 2. It shows that in the patients with ARF, admission CK was significantly raised in 14 patients (93.33%) and creatinine was significantly raised in 9 patients (60%). Thus, raised admission value of CK (P value <0.0001) is a better predictor of ARF due to rhabdomyolysis than serum creatinine. Similarly, UM was positive in 6 of the 15 (40%) patients with ARF on admission. Thus, on comparing UM and CK level, admission value of CK is a better predictor than UM in detecting ARF ($P<0.0001$) due to rhabdomyolysis. On comparison of serum creatinine and UM at admission, it was observed that serum creatinine is a better predictor than UM in detecting ARF ($P<0.0071$). On comparison of all the same above parameters at 48 h of

Table 1 Comparison between ARF and non ARF patients

Parameters	ARF (n)	No ARF(n)	<i>p</i> value ^a
No. of patients	15	35	
Age (yrs)	32.8 $\pm$ 11.2	33.57 $\pm$ 10.85	0.82
Elevated serum creatinine (> 1.4 mg/dL) on admission	9	6	0.005
Elevated serum creatinine (> 1.4 mg/dL) at 48 hrs	15	3	<0.0001
Urinary myoglobin test positive on admission	6	16	0.764
Urinary myoglobin test positive at 48 h	0	0	–
Elevated CK (>1250 U/L) on admission	14	20	0.018
Elevated CK (>1250 U/L) at 48 hrs	14	18	0.0046

^aFischer's exact test

Table 2 Comparison of serum creatinine, creatine kinase and urinary myoglobin on admission and after 48 h in patients who developed ARF

Parameters	Number of patients with ARF (<i>n</i> =15)		<i>p</i> value ^a			<i>p</i> value ^a
	Significant values on admission	Non significant values on admission		Significant values at 48 h	Non significant values at 48 h	
Serum creatinine ^b	09	06	<0.0001	15	0	0.014
Creatine kinase level ^c	14	1		14	01	
UM test positive	06	09	0.0071	0	15	<0.0001
Serum creatinine	09	06		15	0	

^a Fishers exact test^b Significant value >1.4 mg/dL^c Significant value >1250 U/L

UM urinary myoglobin

admission, results showed that serum creatinine done after 48 h of admission was elevated in all the 15 patients (100%) and CK was raised further with a peak in 14 patients (93.33%) ($P=0.0140$). However, UM test was negative in all the 15 patients (100%) with ARF at 48 h of admission. Thus, after 48 h of admission, CK and serum creatinine are better predictor of ARF due to rhabdomyolysis than UM ($P<0.0001$). Renal dialysis was required in 5 (3 electric burns and 2 trauma) of the 15 patients with ARF.

Simple linear regression analysis showed a significant negative correlation between CK levels at admission with urine output at 24 h and after 48 h of admission ($r^2=0.221$ and 0.219, respectively). Similarly, the simple regression analysis showed a significant negative correlation between serum creatinine levels at admission with urine output after 48 h of admission ($r^2=0.11$) (Fig. 1).

An ROC curve was constructed to identify the cutoff values of serum creatinine and serum CK that provided the best diagnostic accuracy to predict ARF. A cutoff value of admission serum creatinine of 1.5 mg% yielded a sensitivity of 58.8% and a specificity of 90.9%. Similarly, a cutoff value of admission serum CK of 3805 U/L yielded a sensitivity of 76.5% and specificity of 87.9%.

Discussion

Rhabdomyolysis accounts for an estimated 8–15% of cases of ARF. The overall mortality rate for patients with rhabdomyolysis is approximately 5% [3]. It also accounts for up to 28% of the causes of posttraumatic ARF requiring dialysis. Clinically significant rhabdomyolysis is poorly characterized biochemically and is difficult to diagnose [4].

A study done by Sharp et al. [4] showed that sequential addition of admission laboratory values of

serum creatinine >1.5 mg%, base deficit <−4, serum CK level >5000 U/L, and myoglobinuria increases the

Fig. 1 Simple linear regression analysis between CK level at admission with urine output at 24 h **a**, CK level at admission with urine output at 48 h **b** and Serum creatinine level at admission with urine output at 48 h **c**

ability to predict which patients will develop dialysis requiring ARF after an episode of rhabdomyolysis [4]. The present study also shows that the presence of significant level of serum creatinine, serum CK, and myoglobinuria are the most important factors in predicting ARF due to rhabdomyolysis.

CK is the most reliable diagnostic indicator for rhabdomyolysis [5, 6]. This assay is widely available and is supposed to be 100% sensitive [7]. CK levels peak within 24–36 h postinjury, about the time the patient usually arrives at a medical office or emergency department. Levels in the range of 10,000–3,00,000 U/L are not uncommon in patients who have rhabdomyolysis; however, concentrations below 20,000 U/L are unlikely to be associated with a risk of renal impairment, unless there are other contributing risk factors [8, 9]. Unfortunately, no standard CK level is diagnostic for rhabdomyolysis, although most authors consider CK levels five times normal or greater to be diagnostic. Our study identified a cutoff value of CK 3805 U/L to be 76.5% sensitive and 87.9% specific in predicting ARF after 48 h of injury.

In a study done by de Meijer et al. [10], 26 patients with severe rhabdomyolysis were taken into the study and their clinical and laboratory data were reviewed. It was found that mean CK level was $38,351 \pm 34,354$ U/L on admission and rose further in all patients (mean $59,147 \pm 67,514$ U/L). Renal failure developed in 17 patients (65%). Serum CK levels correlated with the onset of ARF, as these patients had significantly higher admission and peak CK concentrations. The conclusion of the study was that level of CK predicted the development of ARF in patients with severe rhabdomyolysis [10]. The finding was similar to our study, which showed that the initial value of CK predicted the development of ARF in patients with rhabdomyolysis.

Myoglobinuria does not occur without rhabdomyolysis, but rhabdomyolysis not necessarily results in visible myoglobinuria [9]. Myoglobin is rapidly and unpredictably eliminated by hepatic metabolism. Therefore, tests for myoglobin in plasma or urine are not unique diagnostic procedures. The overall degradation and removal of CK are slow, so its concentration remains elevated much longer and in a more consistent manner than that of myoglobin. Thus, CK is more reliable than myoglobin in assessing the presence and intensity of damage to muscles [11].

Pigmenturia will be missed in rhabdomyolysis if the filtered load of myoglobin is insufficient or has largely resolved before the patient seeks medical attention. Myoglobin is cleared from plasma more rapidly than CK. Thus, it is not unusual for CK levels to remain elevated in the absence of myoglobinuria [12]. In our study, we also found that after 48 h of admission, serum CK was elevated in 14 patients (93%) with a peak as compared with UM, which was negative in all the patients ($P < 0.0001$).

Fernandez et al. [13] found that the only variable that was predictive of both ARF and need for hemodialysis in

separate multivariate regression models was initial serum creatinine. No patient developed ARF with initial creatinine less than 1.7 mg/dL [13]. On the other hand, the present study showed that only 9 of the 15 (60%) patients who developed ARF had significantly raised initial creatinine.

In our study we found that in the patients who had developed ARF, the 48 h serum creatinine rose further in all patients with a mean value of 3.546 mg/dL along with CK, which also rose with a peak mean value of 20,255.3 U/L in 14 patients. However, UM was negative in all these patients.

On comparing serum CK and UM after 48 h it was found that serum CK was raised in 14 patients (93%) and UM was negative in all the patients (0%). Thus, CK is a better marker than UM ($P < 0.001$). On comparing serum creatinine and serum CK after 48 h in patients who developed ARF, serum creatinine was raised in all the 15 patients as compared with serum CK, which was raised in 14 patients ($P = 0.0140$).

Of the 15 patients who developed ARF, 5 (33.33%) patients required hemodialysis, rest of the patients recovered with conservative treatment. In our study, we found that serum CK level at admission above 7502.3 U/L followed by a peak is a good predictor of ARF due to rhabdomyolysis. The present study also demonstrated a significant negative correlation with CK level at admission with urine output.

Our study has certain limitations. First, the number of patients included in the study is small. Second, we could not measure the exact level of myoglobin in urine and only identified its presence or absence by a rapid chromatography test.

Finally, we conclude that on admission, CK is a better predictor of ARF due to rhabdomyolysis than creatinine and UM. Initial creatinine is a better predictor of ARF due to rhabdomyolysis than UM. UM is a weak predictor for early prediction of ARF in rhabdomyolysis. Serum CK, serum creatinine, and UM should be done routinely in all trauma and electrical burn patients. The patients with admission CK above 3805 U/L should be considered at high risk for developing ARF and resuscitation should be started immediately.

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