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BRIEF REPORT

Rhabdomyolysis and Acute Poisoning; a Brief Report

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Abstract: **Introduction:** Some studies have reported creatinine phosphokinase (CPK) as a new emerging way in predicting the outcomes of poisoned patients. This study aimed to evaluate the association of serum CPK level in the first 24 hours with outcomes of poisoned patients. **Methods:** This retrospective cross-sectional study was performed using the medical profiles of poisoned patients aged between 13 and 70 years old who were referred to the emergency department of a big referral medical toxicology center during 6 years and whose necessary data for this study was available. **Results:** 318 patients with the mean age of 34.9±14.5 years were studied (77.1% male). The mean serum CPK level of patients was 4693.1 ± 10303.8 (35–89480) IU/L. There was no significant correlation between serum CPK level and cause of poisoning (r= 0.16; p=0.51), age (r = -0.021; p = 0.651), sex (r = 0.131; p = 0.281), seizure (r = -0.022; p = 0.193), level of consciences (r = -0.138; p = 0.167), and duration of hospital stay (r= 0.242, p = 0.437). The mean serum CPK level was significantly higher in ICU admitted (p<0.0001), AKI (p<0.0001), hyperkalemia (p<0.0001), hypophosphatemia (p=0.045), and hypocalcaemia (p=0.008) cases. The best cut off point of serum CPK level in predicting acute kidney injury (AKI) was estimated to be 10000 IU/L (sensitivity = 83.8% and specificity = 68.8%). **Conclusion:** It seems that CPK could be considered as a candidate tool for screening the intoxicated patients in need for ICU admission and at risk for AKI.

Keywords: Poisoning; creatine kinase; rhabdomyolysis; patient outcome assessment

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1. Introduction

Acute poisoning is a major and common cause of mortality worldwide, especially in developing and low income countries (1). Based on World Health Organization (WHO) reports, poisoning is responsible for 45000 deaths per year in people younger than twenty years old (available on: http://www.who.int/violence_injury_prevention/child/injury/world_report/Poisoning_english.pdf). Developing outcome prediction tools for screening and disposition of these patients is one of the interesting fields of research. Some studies have reported that serum creatine phosphokinase (CPK) level may become a newly emerging way in prediction of poisoning severity and outcome (1-4). It has been shown that CPK more than 10000 IU/L in poisoned patients could be associated with more complications (3, 5). CPK increase occurs in acute muscle necrosis and rhabdomyolysis. There are some possible mechanisms for increase of serum CPK in poisoning patients (6, 7). Toxic serum level of any drug, muscle necrosis following substance overdose, seizure and serotonergic and neuroleptic syndromes may be possible causes of increase in the CPK level in poisoned patients (8, 9). This study aimed to evaluate the association of serum CPK level in the first 24 hours with outcomes of poisoned patients.

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2. Methods

2.1. Study design and setting

This retrospective cross-sectional study was performed on medical profiles of poisoning patients who were referred to emergency department (ED) of Loghman Hakim Educational Hospital, Tehran, Iran, between July 2011 and July 2017. Loghman Hakim Hospital is a big referral toxicology center in the Middle East. This study was approved by Research Ethics Committee of Shahid Beheshti University of Medical Sciences and Health Services.

2.2. Participants

Using census sampling, patients who were at least 13 years old and were referred to the mentioned ED and whose necessary data for this study was available (e.g.: serum CPK level of the first 24 hours of admission) were evaluated. Patients with recent trauma, myocardial infarction (MI), cerebrovascular accident (CVA), cardiopulmonary resuscitation (CPR) or surgery in the past 6 months, pregnancy or lactation, renal or hepatic diseases, and history of substance or fitness drug use were excluded. Creatinine ≥ 1.8 mg/dl was considered as acute kidney injury (AKI).

2.3. Data gathering

Data gathering was performed using a checklist that consisted of demographic variables, consciousness level based on Glasgow coma scale (GCS), history of hematuria and seizure, urinary output, serum CPK level, blood urea nitrogen (BUN), creatinine level in the first 24 hours of admission, and outcomes (disposition, need for dialysis, acute kidney injury (AKI), mortality, need for intubation and need for ICU admission). A trained toxicology resident was responsible for gathering data from the patients' profiles.

2.4. Statistical analysis

Data were analyzed using IBM SPSS statistical software (Chicago, USA) version 22 and t- test and chi square tests. P< 0.05 was considered significant. Findings were presented using mean ± standard deviation or frequency and percentage. Chi square, Fisher's exact, and student t tests were used for comparisons. Area under the receiver operating characteristic (ROC) curve was used for estimating the best cutoff point of serum CPK in predicting the occurrence of AKI.

Table 1: Baseline characteristics of studied patients

Variable	Values
Sex	
Female	72 (22.9)
Male	243 (77.1)
Age group (year)	
< 18	19 (6.0)
18 - 35	163 (51.4)
35- 60	102 (32.2)
≥60	33 (10.4)
Seizure	
Yes	51 (18.7)
No	222 (81.3)
Hematuria	
Yes	2 (0.8)
No	260 (99.2)
GCS	
Mild (14- 15)	56 (21.0)
Moderate (9- 13)	102 (38.4)
Severe (3- 8)	105 (39.6)
Vital signs	
Systolic blood pressure (mmHg)	107.67 ± 21.50
Pulse rate (/minute)	97 ± 26
Respiration rate (/minute)	19 ± 4
Oxygen Saturation (%)	88.6 ± 12.3
Urinary Output (ml)	
1^{st} day	1856.9 ± 1533.9
2^{nd} day	2832.2 ± 2462.1
3^{rd} day	2941.4 ± 1768.7
4^{th} day	3316.4 ± 2009.6
Creatine phosphokinase (IU/L)	
<1000	150 (50.5)
1000- 5000	74 (24.9)
5000- 10000	36 (12.1)
10000-15000	12(4.0)
15000-20000	6 (2.4)
>20000	19 (6.4)

Data are presented as mean ± standard deviation or number (%). There is missing data in some variables.

Table 2: Causes of poisoning in the studied patients

Cause	Number (%)
Neuropsychiatric drugs	135 (42.4)
Acetaminophen	70 (22.1)
Alcohol	63 (19.8)
Opium	29 (9.1)
Carbone monoxide	7 (2.2)
Other	14 (4.4)

3. Results:

3.1. Baseline characteristics

318 patients with the mean age of 34.9±14.5 (13-85) years were studied (77.1% male). Baseline characteristics of participants are shown in table 1. The most important cause of poisoning were benzodiazepines (24.6%) and acetaminophen (22.1%), respectively (table 2). Mean serum blood urea nitrogen (BUN) and creatinine levels of the studied patients were 52.89 ± 46.1 mg/dl and 1.7 ± 1.2 mg/dl, respectively. Patients

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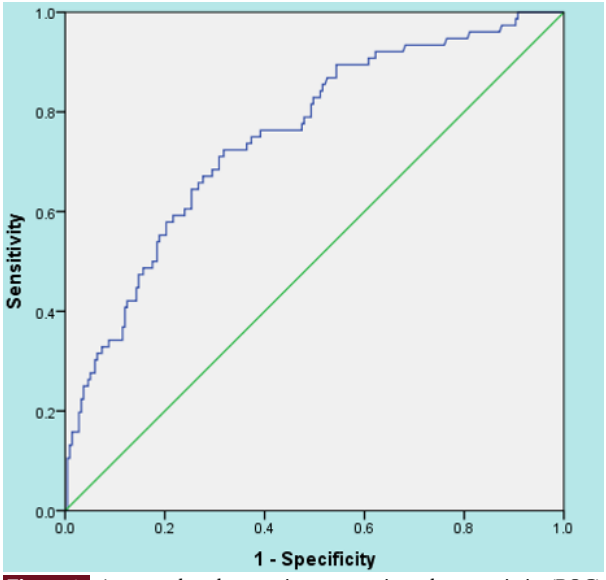

Figure 1: Area under the receiver operating characteristic (ROC) curve of serum creatine phosphokinase (CPK) level of poisoned patients on the first day in predicting acute Kidney injury (p< 0.0001).

were hospitalized for 12.74 ± 12.05 (1-72) days on average. The mean serum CPK level of studied patients was 4693.1 ± 10303.8 (35–89480) IU/L. There was no significant correlation between serum CPK level and cause of poisoning (r= 0.16; p=0.51), age (r = -0.021; p = 0.651), sex (r = 0.131; p = 0.281), seizure (r = -0.022; p = 0.193), level of consciences (r = -0.138; p = 0.167), and duration of hospital stay (r= 0.242, p = 0.437).

3.2. Outcomes

37 (11.6%) cases were admitted to intensive care unit (ICU), 83 (26.1%) died, and 198 (62.3%) were discharged from hospital. AKI was developed in 79 (26.5%) cases out of which 14 (17.7%) needed dialysis. Table 3 compares the mean serum CPK level of patients based on the studied outcomes. The mean serum CPK level was significantly higher in ICU admitted (p<0.0001), AKI (p<0.0001), hyperkalemia (p<0.0001), hypophosphatemia (p=0.045), and hypocalcaemia (p=0.008) cases. Figure 1 shows the area under the ROC curve of first day serum CPK level in predicting AKI (AUC= 0.752, 95%CI: 0.688-0.815; p< 0.0001). The best cut off point of serum CPK level in this regard was estimated to be 10000 IU/L based on the ROC curve analysis (sensitivity = 83.8% and specificity = 68.8%).

4. Discussion

Based on the results of the present study, there was a significant correlation between serum CPK level of poisoned patients and need for ICU admission and AKI development. The best CPK cut off point in predicting AKI was 10000 IU/L. There was no significant correlation between serum CPK level and age, sex, level of conciseness, seizure, need for intubation, duration of hospital stay, and mortality. Some of the patients that survive poisoning face mortality due to other side effects. Rhabdomyolysis and its side effects including AKI should be counted as common complications in these patients. If the definition of rhabdomyolysis is considered CPK level over 1000 IU/L, the prevalence of rhabdomyolysis in the patients studied in the present research will be about 50% and this emphasizes the necessity of paying attention to this matter. Mild and moderate rhabdomyolysis by itself is a curable and self-limiting problem but there is controversy regarding the level of CPK that is associated with nephrotoxicity and kidney failure. This level was estimated at 15000 IU/L and higher in patients with traumatic rhabdomyolysis following Bam earthquake (10-12). It seems that the cause of rhabdomyolysis affects the toxic level of this enzyme. What can be concluded from the findings of the present study is that poisoned patients with serum level of 10000 IU/L and higher are at a significant risk of nephrotoxicity and AKI due to it. Eizadi et al. (2012) study showed that higher levels of serum CPK level correlated with a higher risk of developing complications, increased need for dialysis and mortality (13). Our findings were similar regarding the increasing risk of complication development such as AKI but we had different findings regarding the correlation of serum CPK levels and need for dialysis and mortality. Dadpour et al. (2017) showed that, about 80% of patients with serum CPK level > 10000 IU/L, were in need of dialysis (14). In the present study, there was no significant correlation between CPK level and need for dialysis. Only 22.2% of cases in need of dialysis had CPK > 10000 IU/L in this study. Nevertheless, it should be noted that rhabdomyolysis is not the sole cause of AKI in poisoning patients and unlike traumatic rhabdomyolysis cases in which CPK nephrotoxicity could be considered the cause of AKI with higher confidence, here more caution should be taken while interpreting the findings. It seems that when facing this type of patients, screening cases with a higher level of muscular enzymes, as well as considering other conditions, is a wise thing to do for referring them to more advanced centers with better treatment equipment.

5. Limitations

The limitation of this study was performing it in a retrospective manner and having missing data.

6. Conclusion

Based on the results of the present study, there was a significant correlation between serum CPK level of poisoned pa-

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Table 3: Outcomes of studied patients and its relation with serum creatine phosphokinase (CPK) levels in the first 24 hours

Outcome	Number (%)	CPK level	P value
Treated and discharged			
Yes	196 (61.6)	4296.8±9240.5	0.323
No	122 (38.4)	5636.4±10288.3	
Intubation			
Yes	98 (30.8)	5385.8±9719.9	0.216
No	193 (66.2)	3975.7±8369.8	
ICU admission			
Yes	37 (11.6)	21519.9±17582.8	<0.0001
No	281 (88.4)	2246.9±3798.9	
Acute kidney injury			
Yes	76 (25.9)	11731.6±15406.2	<0.0001
No	217 (74.1)	2222.9±4274.5	
Dialysis			
Yes	29 (9.1)	7968.1±12763.4	0.062
No	289 (90.9)	4338.2±9202.8	
Mortality			
Yes	83 (26.1)	4524.9±9168.0	0.873
No	235 (73.9)	4732.5±9798.8	
Hyperkalemia			
Yes	76 (23.9)	8930.3±14716.6	<0.0001
No	242 (76.1)	1796.7±5782.9	
Hyperphosphatemia			
Yes	31 (27.4)	8663.2±13855.8	0.045
No	82 (72.6)	4036.7±9243.1	
Hypocalcemia			
Yes	69 (56.6)	8170.3±12647.8	0.008
No	53 (43.4)	2797.1±7855.1	

tients and need for ICU admission and AKI development. The best CPK cut off point in predicting the AKI was 10000 IU/L. There was no significant correlation between serum CPK level and age, sex, level of conciseness, seizure, need for intubation, duration of hospital stay, and mortality.

7. Appendix

7.1. Acknowledgements

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7.2. Author contribution

None.

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7.3. Conflict of interest

The authors declare that there is no conflict of interest.

7.4. Funding

None.

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