Admission Creatine Phosphokinase in Acute Poisoning: Is it a Predictive Factor for the Treatment Outcome?

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Abstract

Background: Poisoning has reported to be a major cause of death and burden of disease in low- and middle-Income countries . Rhabdomyolysis is a common consequence of many poisoning cases and serum creatine phosphokinase (CPK) is a marker for it. The aim of the study was to assess whether the admission creatine phosphokinase in comatose patients with acute poisoning is a predictive factor for the treatment outcome.

Methods: In this prospective observational study, eighty poisoned comatose patients who were admitted with a serum CPK> 250 IU/L (not due to muscular trauma in accidents, myocardial ischemia and infarction, infections, hyperthermia, electrolytic disorders and diabetic ketoacidosis) were included. The severity of poisoning was assessed using Poisoning Severity Score. The admission CPK level; and outcome (survived with and without complication and death) for all patients were recorded. Patients were divided based on CPK levels into three categorizes: Low, medium and high.

Results: Seventy five percent of the patients in high CPK level group, 29.5% in medium CPK level group and 35% in low CPK level group developed complications or death. Binary logistic regression results indicated that the chance of complications is much higher for patients with high admission CPK levels (more than 10000 IU/L) [OR, 5.57; 95% CI (1.29 - 23.93)] than whom with low levels.

Conclusion: We concluded that the admission serum CPK level for a poisoned patient, seems to be an acceptable predictor for the outcome in poisoned patients. Further studies are still needed.

Keywords: Coma, Intoxication, Creatine phosphokinase, Rhabdomyolysis, Treatment outcome (JPMA 62: S-67; 2012).

Introduction

Poisoning has reported to be the 7th leading cause of death and 10th leading topic for burden of diseases in low- and middle-Income countries of Europe and central Asia in 2001.[1] Chemicals involved in acute poisonings ended in 240,000 deaths worldwide in the year 2004.[2] In some studies in Iran drug use was the most common cause of adult intoxications and majority of cases occurred intentionally.[3-5] Poisonings comprised 5.40% of total admissions to a university hospital in Tabriz, another city of Iran, from 2003 to 2005 and 90.2% of them were advertent.[6] In Mashhad, main groups of poisons in admitted patients during 1993-2000 were pharmaceuticals (61.4%), chemicals (22.8%), and natural toxins (16.6%).[7] A study in Sari, Northern Iran, concluded that notable prevalence of intentional poisoning and its mortality among young adults requires considerable attention.[8]

Rhabdomyolysis which means destruction of skeletal muscle cells, is a common consequence of many poisoning cases in emergency departments.[9,10] Poisoning with antidepressants, anticholinergics, narcotics (morphine & heroine), cocaine, lysergic acid diethylamide (LSD), phencyclidine, carbon monoxide, isoniazid, olanzapine, paraphenylenediamine (PPD), clenbuterol (misused for body building), lipid-lowering drugs, antihistamines and even theophylline is previously reported to cause rhabdomyolysis.[11-33] There are different proposed mechanisms including prolonged immobilisation and muscle Compression, general circulatory failure and muscle hypoxia, hyperthermia and muscle damage, drug-induced delirium, choreoathetosis, dystonic reactions and seizures and direct muscle injury.[34,35]

Acute poisoning and long-term intoxication with alcohol is also a well known issue for emergency medicine physicians and can induce rhabdomyolysis.[34,36,37]

Diagnosis of rhabdomyolysis is possible by measuring serum creatine phosphokinase (CPK) and myogloboline level in the serum and urine.[38] Rhabdomyolysis is frequently accompanied by myoglobinuria and the two terms are often used interchangeably.[39] Serum CPK level measurement is not reported as a routine laboratory test for poisoned patients.[40] On the other hand, unexplained serum CPK elevation is not a rare

clinical problem, especially in emergency diseases.[41]

This study aimed to evaluate the frequency distribution of admission CPK level in patients presenting with coma due to acute poisoning and to assess the relation between this variable and toxic agent ingested, patient's age and gender, time from ingestion to admittance to the emergency room and relation between CPK level and patient's outcome.

Methods

This prospective cohort study was performed in Noor and Ali Asghar [PBUH] general teaching hospital, Isfahan University of Medial sciences (IUMS), Isfahan, Iran. The project was approved by the research ethics committee of IUMS (Research Project Number 385553) and regarding to the patients clinical condition, legally eligible companion has filled a written informed consent form for the participation in the study.

All of the poisoned comatose patients who were admitted with a serum creatine phosphokinase level of more than 250 IU/L which was not due to muscular trauma in accidents, myocardial ischemia and infarction, infections, hyperthermia, electrolytic disorders and diabetic ketoacidosis, were included in the study.

All subjects were checked for relevant laboratory tests such as complete blood count (CBC), blood urea nitrogen (BUN), serum creatinine (Cr), blood sugar (BS), serum sodium (Na+), serum potassium (K+), urinalysis (U/A) and serum creatine phosphokinase (CPK) based on the standard laboratory methods. They all received the standard and supportive therapy[30] by the attending clinical toxicologists of the poisoning emergency department. Patients' data including age, gender, ingested drug/poison, time elapsed from ingestion to emergency department admission, poisoning severity and result of the laboratory tests were collected with a check list. Patients were followed until any of these situations occurred: recovering without complications, recovering with any complication (acute renal failure, aspiration pneumonitis) and death. The outcome was recorded and then grouped in two major categories: survival without complications group and complications and/or death group. Since seven patients died and all of them had complications, they included in the complication group. The severity of poisoning was assessed using Poisoning Severity Score (PSS).[42] Patients were divided with respect to their initial serum CPK level into 3 groups: low level CPK (250U/L < CPK level ≤ 1500U/L), medium level CPK (1500 < CPK level ≤ 10000), high level CPK (> 10000 U/L). Daily CPK measurement was done for all subjects during their stay in the ward (until discharged or dead).

Statistical Analysis:

Data were analyzed using the Statistical Package for the Social Sciences version 17.0 (SPSS Inc, Chicago, IL, USA). Descriptive data were presented as mean± SE or n (%) where appropriate. Kruskal-Wallis test was used to compare outcome between different baseline CPK levels and CPK levels frequency in respect to ingestion time. One Way Analysis of Variance (ANOVA) was performed to compare mean CPK level with respect to different variables. Logistic regression was applied to calculate odds ratio (OR) with 95% Confidence Interval (CI) to show how predictive is the CPK level. P value less than 0.05 was considered significant.

Results

There were 80 eligible poisoned comatose patients during the investigation time including 59 (73.8%) men and 21 (26.2%) women. Patients were divided into 3 subgroups based on their age: age less than 20 years; 20 ≤ age ≤ 40 years; and age more than 40 years. Most of the patients were in the second subgroup (73.3%). The frequency distribution of ingested toxin emphasized on high rate of poisoning by narcotics abuse (25%) (Table-1).

Seventy percent of the patients presented within eight hours and 27.5% presented between eight to 24 hours after ingestion. Only two patients arrived after 24 hours. 55% of the patients had moderate, 25% low and 20% high admission CPK level. The mean (SE) CPK level in comatose patients was 7796.95±1239.76 IU/Lit (95% Confidence Interval, 5329.25-10264.64) (minimum, 414; maximum, 74520). The CPK level with respect to different variables has been shown in Table-1. Regarding to outcome most of the patients (60%) survived without complications (Table-1).

75% of the patients in high CPK level group, 29.5% in medium CPK level group and 35% in low CPK level group developed complications or death (Table-2).

Binary logistic regression results indicated that the chance of complications is 5.57 times higher for patients with

Table-1: Baseline Creatine phosphokinase (CPK) level with respect to different variables.

Variable	Number of patients (%)	CPK level (IU/L) Mean ± SE	P value
Toxic agent			
CO	4 (5)	13848.75 ± 5351.69	
Alcohol	3 (3.75)	10430.67 ± 2087.36	< 0.000
TCA	3 (3.75)	43060.67 ±16590.50	
Mixed ingestion	12 (15)	6886.75 ± 2051.63	
Narcotics (Opioids)	20 (25)	6098.65 ± 1405.42	
Insecticides	18 (22.5)	5782.33 ± 2318.51	
BZD	11 (13.75)	5523.09 ± 2132.98	
Anticonvulsants	8 (10)	4659.87 ± 638.72	
Unknown	1 (1.25)	11580	
Time from ingestion to presentation			
< 4 hours			
4-8 hours	19 (23.75)	9100.78 ± 2292.84	0.8
> 8-24 hours	37 (46.25)	8166.81 ± 2219.14	
> 24 hours	22 (27.5)	6511.04 ± 1628.98	
	2 (2.5)	2713.00 ± 1593.00	
Outcome			
Survived without complications	48 (60)	5233.70 ± 795.98	0.01
Complication or death	32 (40)	11641.81 ± 2748.92	

TCA: Tricyclic Antidepressant; BZD: Benzodiazepine; CO: Carbon Monoxide.

Table-2: CPK serum levels with respect to different variables.

Variables	CPK level (IU/L) Low >250-1500	Moderate >1500 - 10000	High More than 10000	P value
Total patients	20 (25)	44 (55)	16 (20)	
Time from ingestion to presentation				
< 4 hours	3 (15.8)	11 (57.9)	5 (26.3)	
4-8 hours	8 (21.6)	21 (56.8)	8 (21.6)	0.3
>8-24 hours	8 (36.4)	11 (50.0)	3 (13.6)	
> 24 hours	1 (50.0)	1 (50.0)	0 (0)	
Outcome				
Survived without complications	13 (65)	31 (70.5)	4 (25)	
Complication or death	7 (35)	13 (29.5)	12 (75)	

The results are expressed as n (%). CPK: Creatine Phosphokinase.

Table-3: Prognostic value of CPK level for outcome prediction.

Variable	β	SE	P value	OR (95% CI)
CPK level:				
High (more than 10000 IU/L)	1.71	0.74	0.02	5.57 (1.29 – 23.93)

CPK: Creatine phosphokinase; OR, Odds Ratio; SE: Standard error; β: Estimated coefficient.

Table-4: CPK level in respect to different outcomes.

Variable	Number of patients (%)	CPK level Mean±SE (IU/L)	P value
Without complications	48(60)	5233.70 ± 795.98	
Complications			
Renal Failure	3 (3.75)	8590 ± 3090	
Other complications			
(Aspiration pneumonitis)	22 (27.5)	9591.80 ± 2166.57	0.007
Death	7 (8.8)	20950.85 ± 10514.33	
Total	80 (100)	7796.95±1239.76	

CPK: Creatine phosphokinase.

CPK level more than 10000 IU/L in comparison with Low CPK level (>250-1500 IU/L) (Table-3).

There was also a significant difference between mean admission CPK level of different outcome groups. (Table-4).

Discussion

There were 80 poisoning patients in this study arrived in coma signs, who showed high levels of CPK (>250 IU/Lit) in primary medical experiments. The patients consisted of 59 (73.7%) men and 21 (26.3%) women. This distribution may be caused by different roots like higher rate of addiction in men and more decisive men attempting suicide. In studies done by Talaie et al. the gender intricate is nearly like ours.[9,43]

In present study the largest age group was 20-40 years old with a percentage of 76.3% while the smallest one was <20 years old people group. The patients' average age in those studies was 32 years old with a range of 13-78.[9,43]

We found that the most frequent increased CPK grade was the moderate one (55%) while the least one was the high grade (20%). In Jankovic study the most frequent grade was the low one (59%).[10] This difference can be caused by our study inclusion criterion, choosing patients arriving in coma.

In our study poisoning by narcotics had the most frequency (25%). While Talaie et al, introduced opium as the most common cause of rhabdomyolysis in poisoning, too[9] Jankovic reported that in his study population poisoning by medicinal drugs occurred mostly and the least frequent situation was using narcotics and then alcohol.[10] These differences can be caused by narcotics easy accessibility in Iran.

There are results emphasizing on the link between CPK increased level and poisoning type. In present study the highest mean CPK level occurred in poisoning with TCAs while the least one aroused with anti-seizure drugs.

Investigated endpoints in this study included recovering without complication, complications development or death. The most frequent outcome was complete recovery (60%) whereas the least one was possessed by acute renal failure (3.75%).

In Jankovic et al. study 16% of patients suffered from acute renal failure and in the Talaie research, 6%.[9,10] As they have concluded, in addition to direct effects of toxins on kidneys, renal complications of rhabdomyolysis complicating intoxications, is a matter of concern, which worsens the clinical course, sometimes leading to death.

Though not always, in poisoned patients with elevated CPK levels whom are at risk for rhabdomyolysis, early treatment including fluid therapy, alkalizing urine or hemdialysis when needed can reduce the rate of ARF. This can also decrease death rate caused by secondary renal failure and electrolyte abnormalities.

We have concluded that the serum CPK level, which is an indicator of muscle damage and a product of it, may give clues to the poisoned patient's outcome, if measured at the admission time. We observed that the severity of its highness is important in this regard. In high grade elevations, the risk of complications and death becomes highly increased. Although other investigators to our best of knowledge, have not focused on this issue which makes it a new concept, our study has its own limitations including as small sample size and the missing the

study of poisoned patients with normal serum CPK levels at the time of addmission. So, further studies are recommended.

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Conflict of Interest:

Authors declared no conflict of interest.

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