

A Study to Correlate Elevated Creatinine Phosphokinase with Snake Bite and Acute Kidney Injury

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Abstract:

CONTEXT

Hemotoxic snake bite is associated with acute kidney injury in around two thirds of cases. This study is to establish the relation between elevated CPK values with acute kidney injury and reversibility with alkaline diuresis in snake bite patients of Government Rajaji Hospital, Madurai.

AIM OF THE STUDY

To establish the correlation between creatinine phosphokinase with hemotoxic snake bite and acute kidney injury.

To find out the benefit of sodium bicarbonate infusion in preventing creatinine elevation in such cases.

SETTING AND DESIGN

Prospective Cross sectional study

MATERIALS AND METHODS

STUDY POPULATION:

Patients with history of snake bite who fulfill the inclusion and exclusion criteria getting admitted in General Medicine wards of GOVT RAJAJI HOSPITAL, MADURAI, during the period of JANUARY 2016 TO JUNE 2016.

STATISTICAL ANALYSIS

Mean, standard deviation

RESULTS

The CPK values tend to correlate with the incidence of acute kidney injury and it can be prevented with soda bicarbonate infusion.

CONCLUSIONS:

This study correlates one of the factors in the prevention of AKI, but there are more than 10 mechanisms attributed to the cause of renal failure in snake bite patients. So this intervention may be in addition to the other treatment with IVF, anti-venom, antibiotics and prevention of dehydration. The CPK values tend to correlate with the incidence of renal failure and it can be prevented with soda bicarbonate infusion. Other factors like NGAL levels were not measured to assess for the incidence of renal failure. So all these are to be considered in treating a patient with hemotoxic snake bite with elevated CPK values.

Keywords: Snake bite, creatinine phosphokinase (CPK), acute kidney injury (AKI)

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I. Introduction

India, similar to global incidence in estimation to have the highest snakebite mortality. WHO estimated the number of bites to be 83,000 with 11,000 deaths per annum. Much of the fatalities are due to the victims not reaching the primary care in time where treatment can be administered. Venomous snake has specialized venom synthesizing apparatus and fangs, favoring effective venom delivery. Venom producing snakes come from family of Elapidae, Viperidae, Colubridae, and Atractaspididae. But most of the burden is caused by bites of vipers and elapids. Much commonly, vipers significantly causes coagulopathy, renal failure when compared with elapids which causes neurotoxicity. It is mainly observed in snakes which belong to the viperidae group and it is seen less with sea snake bites and bites of colubridae group. Most of the Indians are victims of Russell's viper or echiscarinatus bites, which causes AKI.

It is an important complication of snake bite and a proper supportive management after the antivenom administration is of utmost importance for a good patient outcome.

Tubular necrosis and cortical necrosis are the important causes of renal failure. The renal failure after bite is usually reversible, but if acute cortical necrosis occurs, it may lead to an incomplete recovery.

The main cause of this “unacceptable incidence” of snake bite fatalities is because people try out bizarre remedies initially instead of going to a primary health care. There are very less number of studies on the development and outcome of AKI following snake bite in India.

The exact pathogenesis for ARF is not well established. However a number of factors contribute like

- Bleeding causing hypotension
- Circulatory collapse
- Disseminated intravascular coagulation
- Intravascular hemolysis
- Nephrotoxicity of the venom
- Nephrotoxic drugs in treatment
- Cellulitis causing myoglobinuria and tubular necrosis
- Acute interstitial nephritis is also described

Albuminuria can be present in most of the cases. This shows that the toxin induced breakdown of the renal filtration barrier. However, this finding is more useful in followup of these patients as a persistent albuminuria can serve as a marker of residual renal dysfunction after recovery from acute kidney injury.

Other common findings would be thrombocytopenia, metabolic acidosis and coagulopathy is itself an independent marker since it is an indirect marker for damaged renal vasculature. Rhabdomyolysis and its link with elevated CPK :

- The sarcolemma contains numerous pumps that regulate cellular electrochemical gradient.
- This gradient maintains electronegativity within cell, for which ATP is used as an energy source.
- Rhabdomyolysis causes ATP depletion disrupts cellular transport leads to elevated intracellular calcium level, activation of proteases and leakage of CREATININE KINASE, potassium, phosphate, and myoglobin

Muscle damage is further amplified by infiltration of neutrophils

Ferrihemate produced from myoglobin at acidic pH produces free radicals and direct nephrotoxicity.

These proteins may enhance vasoconstriction through interactions with nitric oxide and endothelin.

Thereby causing AKI

Tubules showed an intact basement membrane surrounding degenerating epithelium, erythrocytes, and leukocytes. Endothelial swelling of small arterioles and necrosis of peritubular capillaries also were evident in this patient. In the second patient, the biopsy was performed 31 days after the bite. The urinary space contained unidentified cells with large cytoplasmic vacuoles but no erythrocytes. The cortical tubules were lined by flattened epithelium with large nuclei and a dilated endoplasmic reticulum. The tubular basement membrane was thickened, and fibroblastic proliferation was seen in the interstitium. Sitprija and Boonpucknavig have found electron-dense mesangial deposits by electron microscopy even in the absence of renal failure in patients bitten by cobras and green pit vipers. In green pit viper envenoming, fibrin thrombi and degenerating platelets have been observed in the glomerular capillaries. Immunofluorescence data are scanty; Sitprija and colleagues demonstrated granular deposits of C3 without any immunoglobulins in the glomerular mesangium and arterial walls in 2 patients with acute renal failure following Russell's viper bite.

II. Materials And Methods

Study Population:

Patients with history of snake bite who fulfill the inclusion and exclusion criteria getting admitted in General Medicine wards of GOVT RAJAJI HOSPITAL, MADURAI, during the period of JANUARY 2016 TO JUNE 2016.

Inclusion Criteria:

All patients with history of snake bite with signs of envenomation aged 15 to 60 years of both sexes admitted in general medicine wards of Government Rajaji Hospital, Madurai.

Exclusion Criteria:

Patients with pre existing renal diseases and ischemic heart diseases with present history of snake bite. Patients with the risk of developing renal diseases due to underlying diseases like hypertension, diabetes, connective tissue diseases and chronic infection. Patients with history of medications (steroids, nephrotoxic drugs) within last 10 days, before the snake bite. Neurotoxic snake bites were not included Patients referred after 3 days of snake bite.

Ethical Committee Approval: Obtained.

Study Protocol:

Data will be collected using a pretested proforma meeting the objectives of the study. Detailed history, physical examination, and necessary investigations will be undertaken. The purpose of the study will be explained to the patient and informed consent obtained.

Using noninvasive methods acute kidney injury in snake bite patients who fulfill the inclusion criteria is assessed. The analysis of the data will be done using appropriate statistical methods.

LABORATORY INVESTIGATIONS:

Complete haemogram, Whole blood clotting time, Bleeding time, Blood urea and serum creatinine, CREATINE PHOSPHO KINASE (CPK), USG abdomen and pelvis, Prothrombin time.

PARTICIPANTS:

Patients admitted with history of snake bite with signs of envenomation in General Medicine wards of Government Rajaji Hospital, Madurai from January 2016 to June 2016.

METHODS

Around 250 patients admitted to medicine department with history of snake bite with features of hemotoxicity was tested for serum CPK levels, routine blood investigations and USG abdomen and pelvis was also done to rule out chronic kidney disease.

First and third day creatinine values were measured and the patients were divided into cases and controls for intervention with sodium bicarbonate (1 ampoule in 500 ml NS over 1 hour) with serial monitoring for hypokalemia

The patients were later followed up with repeat renal function tests to assess the need for hemodialysis.

STATISTICAL ANALYSIS:

Mean and standard deviation for continuous variables and proportions for categorical variables are reported .Data analysis was done with the help of computer by using SPSS 16 software and Sigma Stat 3.5 version (2012).

Using this software mean, standard deviation and „p“ value were calculated and P value of < 0.05 was taken as significant.

III. Results

Around 250 patients 85% were males and 15% were females with most of the males within 35-45 working population. Around 15% are less than or equal to 25 years, 27% are between 25-35 years of age, 31% between 35-45 years and 27 % are 45 and above years.

More than 90% patients with cellulitis or with history of hemotoxicity developed CPK elevations of more than 150 which was significant First day creatinine values were higher in the non intervention group than in the intervention groups by around 45% Third day creatinine values were also greater in the non intervention than post soda bicarbonate infusion group. And 28% were requiring hemodialysis in the non-intervention group. But around 12% in the intervention group were requiring hemodialysis.

	No Intervention		Intervention	
	n=125		n=125	
	Mean ± SD	(min, max)	Mean ± SD	(min, max)
CPK	344.5 ± 240.0	(38, 955)	405.8 ± 147.5	(167, 784)
p-value	0.016 (Significant)			

TABLE 1 shows that cases with CPK elevation were mainly included under study

	Group			
	No Intervention		Intervention	
	n=125		n=125	
	Mean ± SD	(min, max)	Mean ± SD	(min, max)
3 rd day Creatinine	2.4 ± 1.3	(1.0, 6.5)	2.5 ± 1.3	(0.8, 6.3)

TABLE 2:
This chart shows that there was less increase in third day creatinine values in the cases group post soda bicarbonate infusion than in the controlgroup.

IV. Discussion

In our study around 250 patients were analysed after applying inclusion and exclusion criteria, clinical examination were done for all of them. Later first and third day urea and creatinine values were done with CPK values and other routine investigations were also done.

The observations made in the study were males formed most of the study population around 75-80% and most of them were within the age group of 35-45 years with around 15% are less than or equal to 25 years, 27% are between 25-35 years of age, 31% between 35-45 years and 27% are 45 and above years.

And it was also found out that the higher the value of CPK in these patients the more the patients go into to develop AKI. So intervention group was tried with sodium bicarbonate because one of the mechanisms attributed is precipitation of myoglobin in the distal tubules thereby leading to acute tubular necrosis.

It was found that the intervention group had much lesser incidence of dialysis requiring creatinine levels with statistical significance. Around 85% of cases recovered following soda bicarbonate infusion without dialysis whereas those without infusion only 67% recovered.

V. Conclusion

This study correlates one of the factors in the prevention of AKI, but there are more than 10 mechanisms attributed to the cause of renal failure in snake bite patients. So this intervention may be in addition to the other treatment with IVF, anti-venom, antibiotics and prevention of dehydration. The CPK values tend to correlate with the incidence of renal failure and it can be prevented with soda bicarbonate infusion. Other factors like NGAL levels were not measured to assess for the incidence of renal failure. So all these is to be considered in treating a patient with hemotoxic snake bite with elevated CPK values.

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