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PREVENTION OF ACUTE KIDNEY INJURY IN VASCULOTOXIC SNAKE BITE WITH FORCED ALKALINE DIURESIS

General Medicine

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ABSTRACT

Snake bite is the one of the common health hazards since centuries, specially faced by rural population in tropical and subtropical countries with heavy rainfall and humid climate. Though snakebite is a life-threatening centuries old condition, WHO has included it in neglected tropical diseases in the year 2009(1). Acute kidney injury is among the common complication after vasculotoxic snake bite which is the cause for significant morbidity and mortality.

KEYWORDS

Acute kidney injury, forced alkaline diuresis, vasculotoxic snake bite

BACKGROUND

Snake bite envenomation is a common acute life-threatening medical emergency. Worldwide about 1.2 million to 5.5 million cases of snake bite occurs and about 20 to 94 thousand estimated deaths occurs because of it[2]. In India alone about 1300 to 50,000 deathsoccur because of snake bite, & it is found that Majority of snake bite deaths go unreported[3]. In India, only 7.23% cases of snake bite related death gets reported, as many victims go to traditional healers and many deaths occur before reaching hospital. Survey of 1.1 million homes in India, in 2001–03, the study found 562 deaths (0.47% of total deaths) were assigned to snakebites, mostly in rural areas, and more commonly among males. it is found that 65.7% death occurs because of common Krait bite. mostly in month of June to September4.

Overall about 20% of patients with snake bite, develops acute kidney injury leading to significant morbidity and mortality because of snake bite[5].Annual snakebite deaths were greatest in the states of Uttar Pradesh (8,700), Andhra Pradesh (5,200), and Bihar (4,500). Other Indian states with high incidence of snakebites cases are Tamil Nadu, West Bengal, Maharashtra and Kerala. Because a large proportion of global totals of snakebites arise from India, global snakebite totals might also be underestimated[6].

INTRODUCTION

There are about 216 species of snakes identifiable in India, Fortunately, only a few of them are known to be of medical importance. The major families of poisonous snakes in India are Elapid which includes common cobra (naja naja), king cobra and common krait which are generally neurotoxic. Viperidae includes Russell's viper, Echis carinatus (saw scaled or carpet viper), and pit viper which are vasculotoxic. Hydrophidae (sea snakes) are myotoxic[7]. Renal lesions have been associated with bites from members of the last 3 families, including the Russell's viper, Echis carinatus, pit viper. Acute kidney injury is mostly associated with bites of Russell's Viper[8,9], saw-scaled Viper[10], Puff Adder[11], Pit Viper, Sea snake[12] and Tiger snake[13]. AKI and rhabdomyolysis have also been reported following wasp and bee stings[14,15]. So, the renal injury from the vasculotoxic snake bite is the most significant reason for the morbidity and mortality associated with the snake bite. These renal manifestations have been reported with varying frequency in different studies. Information on the precise incidence in different geographic regions is lacking but obviously varies with the distribution of the viperlike snakes.

VENOMS AND CLINICAL MANIFESTATIONS

Snake venoms are highly variable and complex mixtures of enzymes, low-molecular-weight polypeptides, glycoproteins, and other constituents. Among the deleterious components are haemorrhagins that promote vascular leakage and cause both local and systemic bleeding. Proteolytic enzymes cause local tissue necrosis, affect the coagulation pathway at various steps, and impair organ function. Hyaluronidases promote the spread of venom through connective tissue. Myocardial depressant factors reduce cardiac output, and bradykinins cause vasodilation and hypotension. Neurotoxins act either pre- or postsynaptically to block transmission at the neuromuscular junction, causing muscle paralysis. Most snake venoms have multisystem effects on their victims. After a venomous snakebite, the time to symptom onset and clinical presentation can be quite variable and depend on the species involved, the anatomic location of the bite, and the amount of venom injected. Envenomation by most viperids and some elapids with necrotizing venoms cause progressive local pain, swelling, ecchymosis, and (over a period of hours to days) haemorrhagic or serum-filled vesicles and bullae. In serious bites, tissue loss can be significant. Systemic findings are extremely variable and can include tachycardia or bradycardia, hypotension, generalized weakness, changes in taste, mouth numbness, muscle fasciculations, pulmonary edema, renal dysfunction, and spontaneous haemorrhage[2].

Among systemic manifestations 20 to 40% of cases subsequently develop anuria, oliguria, and acute renal failure. Renal angle tenderness is most important clinical sign for early diagnosis. There is serial rise in blood urea level and serum creatinine with acidosis and hyperkalaemia, tubular damage by Venom itself, interstitial nephritis, haemoglobinuria, hypotension and microthrombi in the kidney contribute to acute tubular necrosis. Acute tubular necrosis and cortical necrosis are the common causes for renal failure in snake bite[18].

Acute interstitial nephritis is also documented as cause for AKI[19]. Another reason for the significant morbidity is coagulation dysfunction because of Venome and its effect on the coagulation cascade.

simple bedside test 20-minute whole blood clotting test (20 WBCT) if impaired will give the clue of Impeding coagulation dysfunction.

Aim of the study: Effectiveness of Forced alkaline diuresis to prevent AKI in vasculotoxic snake bite.

METHODOLOGY

Study design: Prospective observational study in patients of vasculotoxic snake bites in the month from April 2017 to October 2017, in government medical college and hospital.

Inclusion criteria: we labelled them as study group.

1. Definitive history of snake bite by presence of fang marks consistent with a snake bite at the alleged site of bite; Identification of snake if possible, either as per patient's history or if a dead snake was brought by the patient.
2. Evidence of local toxicity in form of swelling, cellulitis, gangrene, ecchymosis, blisters, blebs, or bleeding at the site of bite and area proximal to it and the evidence of coagulation disturbances in form of local or systemic bleeding.
3 Patients in whom 20 minutes' whole blood clotting test was impaired.
4 Patients whose urine sample was positive for RBCs.
5 AKI was defined as an abrupt (within 48 hours) absolute increase in the serum creatinine concentration of ≥ 0.3 mg/dL from

baseline value measured after admission in our hospital or measured elsewhere after the history of snake bite; or a percentage increase in the serum creatinine concentration of ≥ 50% above baseline after snake bite; or urine output less than 0.5 mL/kg per hour for more than 6 hours[17].

Exclusion criteria:

1.Known case of past renal disease or ultra-sonographic evidence of bilateral small kidney; or patients whose baseline creatinine was more than 1.5 mg on any previous medical records before snake bite. We also excluded the patients who are known cases of diabetes or hypertension or those who have been exposed to the nephrotoxic drugs in last one week depending on the history on previous medical records.

MATERIALS AND METHODS:

A total of 69 patients who were admitted in government medical college and hospital, with a definite history of snakebite were evaluated by history, clinical examination and investigating that includes Bleeding time, clotting time, PT INR, urinary RBCs, serum creatinine, blood urea level, and complete blood count and platelet count.

Those patients who falls in inclusion criteria received alkaline diuresis in treatment along with standard treatment with anti-snake venom.

METHOD FOR FORCED ALKALINE DIURESIS

Inj. frusemide 20 mg iv bolus (injection frusemide should not be given at the beginning of the cycle if the patients clinical status showing the signs of dehydration, as frusemide will worsen the dehydration and will enhance the process of acute tubular necrosis, in this case it should be given after fluids and loading of sodium bicarbonate, physician has to make this judgment on seeing the patient.



Inj sodium bicarbonate 40 meq in 500 ml of normal saline over 30 min.



Another 40meq of inj. Sodium bicarbonate in 500 ml of ringer lactate over 30min followed by



Inj KCL 20meq in 500ml of D5 over 90min.



Inj. Mannitol 100cc over 30min

INJ. Mannitol should be given very cautiously with strict urine output monitoring as the drug has a renal excretion, can further compromise the renal function in case of toxicity. Urine output of 3ml/kg/ min should be present, in any case of established oliguria or deranged renal function test, in such cases mannitol better to be avoided.

MONITORING

Patient was under strict monitoring for the urine output and we expected urine output of 3 ml/kg/hr those who did not meet this criterion were loaded with another 20 mg of iv Inj of frusemide.

Urinary PH should be maintained above 7.5, ideally 8.0-8.5.

Serum electrolytes should be checked at 4 hr interval, and any evidence of hypokalaemia should be corrected for effective alkalinisation of urine. ideally potassium level should be above 3.5.

Serum level of sodium for hypernatremia and serum calcium every 4 hourly should be checked to detect any hypocalcaemia because of sodium bicarbonate loading.

Those who did not respond, we repeated the cycle thrice.

How does FAD help in preventing the Acute Kidney Injury :

Forced alkaline diuresis will decrease the passive reabsorption from the proximal renal tubules, thereby increasing the clearance of many nephrotoxic contents such as haemorrhagins, myoglobin's because of rhabdomyolysis from cellulitis, help in preventing the acute tubular necrosis caused by theses agents.

Results of study:

we studied total number of 69 patients of vasculotoxic snake bites in medical college and hospital and following observations were noted.

Table no. 1

Total	69
Asymptomatic	37
Symptomatic	32
Falling in inclusion criteria (study group)	13
Forced alkaline diuresis	13
AKI	0

We studied total 69 patients admitted in our hospital with definite history of snake bite, and we noticed that 37 patients i.e. about 53.62% of the total were asymptomatic who did not require any treatment except observation for 24 hours. Rest 32 patients developed some signs and symptoms of snake envenomation. As this study is related to renal manifestations of vasculotoxic snake bites, we are not commenting on the symptoms of neurotoxic snake bite among these 32. Out of these, a total of 13 patients who were falling in the inclusion criteria for the study had received forced alkaline diuresis 2 or 3 cycles; and it is found that none of the patients who received forced alkaline diuresis developed acute kidney injury shown by rise in serum creatinine level or decreased urine output.

After this significant finding of the study regarding the effectiveness of forced alkaline diuresis we did the comparative study from retrospective data among the total 50 patients admitted in our hospital with definite history of snake bite in last year, in the hospital.

Table no.2

Total	50
Asymptomatic	32
Symptomatic	18
falling in inclusion criteria (study group)	10
Forced alkaline dieresis	0
AKI	2

In this group that we studied, we noticed that out of 50 patients 32 patients i.e. about 64% of the patient did not develop any signs or symptoms of vasculotoxic snake envenomation after 24 hours of observation. A total of 18 patients who developed some signs of snake envenomation, 10 patients were falling in the inclusion criteria, (study group). These 10 study patient were treated with standard treatment of anti-snake venom and conservative management, but they did not receive forced alkaline diuresis.

At the end of this study of this retrospective data, it was found that 2 patients among 10 i.e. about 20% developed acute kidney injury due to snake bite, in the form of rising creatinine and decreased urine output; and these eventually required haemodialysis for the further management

DISCUSSION:

Acute kidney injury, is one of the most common cause for morbidity and mortality related to vasculotoxic snake bite.

The study was aimed at to see the effectiveness of forced alkaline diuresis in preventing the AKI, in vasculotoxic snake bite.

It consists of two aspects first the overall prevalence of AKI in vasculotoxic snake bite, and then prevalence in patients who were treated with forced alkaline diuresis.

The study consists of 69 patients of snake bite, in which a total 32 patients were showing signs of envenomation of vasculotoxic snake bite,13 patients who were falling in the inclusion criteria (study group) were treated with forced alkaline diuresis, and we observed that none of the patient developed AKI.

This was in agreement with the study shown in table no 3

TABLE NO. 3

STUDY	study group	FAD	AKI	AKI
OUR STUDY	13	13	0	0%
DR Mohammed Shahed et al20	10	10	0	0%

patients in the study who received forced alkaline diuresis as a treatment modality, 0% percent patient developed AKI.

Comparable study done by DR Mohammed Shahed et al[20] in the table no 4, also shows the similar results.

AKI in patients who did not receive forced alkaline diuresis.
In our retrospective study of 50 patients of snake bite,10 patients who were falling in inclusion criteria but did not receive forced alkaline diuresis as treatment modality AKI developed in 2 patients i.e. 20% This was in agreement with the studies in the table 4.

Table 4

Study name	ARF
OUR STUDY	20%
P Mukhopadhyay et al[21]	44.13%
Tushar B Patil et el[22]	20.48%

The percentage of AKI in vasculotoxic snake bite who did not receive FAD in the treatment 20 to 44% from above studies.

CONCLUSION:

Snake bite induced acute kidney injury can be prevented with effective use of forced alkaline diuresis as a treatment modality.

Without FAD in the treatment the incidence of AKI is higher in vasculotoxic snake bite patients than who receive it in the management.

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