ORIGINAL ARTICLE

Cardiotoxicity Profile of Snake Bite

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Abstract

The present study was conducted in 80 cases of snake bite to understand their possible, biochemical and electrical cardio toxic effects. All patients were subjected to routine and specific investigation (ECG, X Ray, SGOT, CPK, CPK - MB, Troponin levels). Subjects were included in three groups, haemotoxic, neurotoxic and non - envenomed group. They were subjected to investigations at the time of admission, 24 hours and 72 hours after the admission. No significant statistical change occurred in cardiac enzymes in all groups at the time of admission. Significant statistical change occurred in LDH, CPK-MB at 24 hours and 72 hours after admission in haemotoxic group. Significant statistical change occurred in Troponin levels and CPK and SGOT at 24 hours after admission but no statistical change occurred at 72 hours after admission. But there was no statistical significant change in biochemical parameters in a neurotoxic group. At admission, there was tachycardia in 29 cases (53.7%) in haemotoxic group and in 16 cases (29.7%) at 24 hours which was statistically significant. At admission there was bradycardia in 10 cases (18.5%). In neurotoxic group there was tachycardia in 6 (60%) cases at admission and in 2 cases (20%) at 24 hours. There was bradycardia in 1 case in neurotoxic group. No significant change occurred in all groups at 72 hours. The present study showed significant statistical ECG changes at admission in the non - envenomated, neurotoxic and hemotoxic groups in the form of tachycardia or bradycardia. Also significant statistical ECG changes in the form of tachycardia was observed 24 hours after admission in hemotoxic group. It could be concluded that snake bites especially haemotoxic group carry the risk of inducing cardio toxic effects but these effects are not fatal.

Key Words

Cardiotoxicity, Snake Bite, Hemotoxic

Introduction

The history of reptiles dates back to as long as 250 million years and snake bites in human beings seem to be taking place since the time of appearance of humanity on this planet. With its surrounding seas, India is inhabited by more than 60 species of venomous snakes - some of which are abundant and can cause severe envenomations. Spectacled cobra (Naja naja),common krait (Bungarus caeruleus), saw-scaled viper (Echis carinatus) and Russell's viper (Daboia russelii) have long been recognised as the most important, but other species may cause fatal snakebites in particular areas, such as the central Asian cobra (Naja oxiana) in the far north-west, monocellate cobra (N. kaouthia) in the north-east,greater black krait (B. niger) in the far north-east, Wall's and Sindkraits (B. walli and B. sindanus) in the east and west and humpnosed pit-viper (Hypnale hypnale) in the south-west coast and Western Ghats.

The state of Jammu & Kashmir has a distinct zoogeographical importance in that it lies at the junction of 2 major faunal regions : the plearctic and the oriental, and thus harbours many interesting groups of fauna.

Snake bites, both poisonous and nonpoisonous, are frequent in both the hilly and plain areas of Jammu region especially during summer and rainy seasons. In Jammu region, the majority of snake bites occur between May and October, the peak incidence being in rainy season Lahori *et al* (1) . The region harbours various types of poisonous snakes mainly belonging to families Elapidae and Viperidae. Snakes belonging to these two families are the commonest encountered species in the rest of

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the country also. Snakes belonging to family Elapidae are mainly neurotoxic, though some hemotoxic and cardiotoxic effect, have also been reported. Those belonging to family Viperidae are mainly hemotoxic and is the most common species encountered in our region (2). Snakebite remains an important cause of accidental death in modern India, and its public health importance has never been fully appreciated. The deaths due to snake bite account for 5% of all accidental deaths and nearly 0.5% of all deaths in India. (45,900 snakebite deaths in 2005 in India) (3).

Snake venom has a very complex heterogeneous composition, containing enzymes, lethal peptides, nonenzymatic proteins, metals, carbohydrates, lipids, biogenic amines, free amino acids and direct hemolytic factors. As little data is available regarding the cardiotoxic effects of snake bite, the current study was carried out to evaluate the possible bio-chemical and electrical effects of venoms leading to cardiotoxicity.

Material & Methods

This study was jointly carried out over a period of 6 months in 80 patients with history of a snake bite who presented in emergency departments of GMC hospital, Jammu and ASCOMS Hospital Sidhra, both being tertiary care centers in the city.

The subjects in this work were divided into 3 groups -

Group I (Non Envenomed Group): with history of snake bite but without any local or systemic signs, or laboratory findings, suggestive of envenomation (except for the bite marks). They were put under observation for at least 24 hours, with an hourly check of their vital signs and any symptoms or signs of envenomation.

Group II (neurotoxic group): who presented with symptoms and signs of envenomation.

Group III (hemotoxic group): who presented with symptoms and signs of envenomation

In patients presenting with bleeding from mucocutaneous sites, systemic bleeding, intravascular hemolysis, or a deranged laboratory coagulation profile anytime during hospital stay, were indicators of hemotoxicity If frank evidence of hemotoxicity was evident, the evaluation was extended to assess for possible intracranial, intraperitoneal, gastro-intestinal hemorrhage, excessive mens-trual loss and intramuscular haemorrhage, which may present as compartment syndrome.Clinically, neurotoxicity was assessed by testing for muscle power and for adequacy of ventilatory function. At the bedside, if patient can cough forcibly and the forceful blow is perceived at one meter, then venti-latory function is presumed to be adequate. Neuro-neurotoxic manifestations were recorded including sensory or motor paralysis in the form of paresthesias, taste and smell abnormalities, ptosis, general flaccidity, respiratory paralysis and cranial nerve palsies e.g. diplopia, dysphagia and dysphonia. Cardiotoxicity was assessed by changes in heart rate, blood pressure, dysrhythmias,conduction defects on ECG monitoring.

II. Biochemical Parameters assessed in this study were

1. Creatinine Phosphokinase
2. Creatinine Phosphokinase MB
3. Lactate Dehydrogenase
4. Troponin (I & T) levels
5. SGOT

Results

No significant statistical change occurred in cardiac enzyme LDH in all groups at time of admission. Significant statistical elevation of LDH was observed in hemorrhagic group 24 hr and 72 hrs after admission in comparison to non envenomed bite and neurotoxic groups. However the elevation in LDH value in hemorrhagic group 72 hr after admission was much lesser that that occurred 24 hr after admission. No significant change occurred with non envenomed bite and neurotoxic group 24 hr and 72 hr after admission. The CPK enzyme showed no statistically significant changes in all groups at time of admission. Elevation in CPK occurred 24 hrs after admission in hemorrhagic group in comparison to non envenomed and neurotoxic groups while no change occurred with non envenomed bite and neurotoxic groups. No significant changes occurred 72 hrs after admission in all groups.

The CPK enzyme showed no statistically significant changes in all groups at time of admission. Elevation in CPK occurred 24 hrs after admission in hemorrhagic group in comparison to non envenomed and neurotoxic groups while no change occurred with non envenomed bite and neurotoxic groups. No significant changes occurred 72 hrs after admission in all groups.

The SGOT enzyme showed no statistically significant changes in all groups at time of admission. Elevation in SGOT occurred 24 hrs after admission in hemorrhagic group in comparison to non envenomed and neurotoxic groups while no change occurred with non envenomed bite and neurotoxic groups. No significant changes occurred 72 hrs after admission in all groups.

The Troponin level enzyme showed no statistically significant changes in all groups at time of admission. Elevation in troponin occurred 24 hrs after admission in hemorrhagic group in comparison to non envenomed and neurotoxic groups while no change occurred with non envenomed bite and neurotoxic groups. No significant changes occurred 72 hrs after admission in all groups.

Table 1. Enzyme Changes in 3 Groups

Enzyme	Time Since Admission(hrs)	Group		
		Non envenomated (n=16) Mean ± SD	Neurotoxic (n=10) Mean ± SD	Hemotoxic (n=54) Mean ± SD
LDH	0	253 ± 9.9	258 ± 14	264 ± 13.5
	24	252 ± 11	256 ± 12	385 ± 25
	72	250 ± 12	253 ± 11.5	303 ± 15
CPK	0	32 ± 5.2	32.4 ± 5	33.2 ± 5.4
	24	31.3 ± 4.8	31.6 ± 4.5	39 ± 3.2
	72	30.5 ± 4	31.2 ± 3.5	34 ± 4
CPK-MB	0	13.5 ± 3.8	13.8 ± 4.3	13.6 ± 4.5
	24	13.5 ± 3.4	13.8 ± 4	24 ± 5
	72	13.5 ± 2.9	13.7 ± 3.8	19.5 ± 3
SGOT	0	28 ± 5	28.5 ± 4	28.2 ± 5
	24	28 ± 4.8	28.6 ± 4.8	29 ± 4.5
	72	28 ± 4.6	29 ± 4.6	28 ± 4.7
TROPONIN-T	0	0.01 ± 0.004	0.01 ± 0.005	0.01 ± 0.002
	24	0.01 ± 0.003	0.01 ± 0.007	0.01 ± 0.003
	72	0.01 ± 0.003	0.01 ± 0.004	0.01 ± 0.004
TROPONIN-I	0	2.8 ± 0.7	2.6 ± 0.4	2.5 ± 0.6
	24	2.8 ± 0.5	2.6 ± 0.5	2.5 ± 0.8
	72	2.7 ± 0.8	2.6 ± o.9	2.5 ± 0.7

The cardiac enzyme CPK-MB showed no significant statistical change in all groups at time of admission. Significantly statistically elevation occurred in hemorrhagic group 24 hr and 72 hr after admission in comparison to other groups. However the elevation in CPK-MB value in hemorrhagic group 72 hr after admission was much lesser than that occurred 24 hr after admission. No change occurred with non envenomed bite and neurotoxic groups 24 hr and 72 hr after admission.

Electrocardiographic Changes (ECG)

At admission there were tachycardia in 9 cases (56.3%) of non envenomed bite group, in 6 cases (60%) of neurotoxic group and in 29 cases (53.7%) of hemorrhagic group. There were bradycardia in 1 (10%) of neurotoxic group and in 10 cases (18.5%) of hemorrhagic group. There was tachycardia 24 hr after admission, in 2 cases (20.0%) of neurotoxic group and in 16 cases (29.7%) of hemorrhagic group)

Discussion

In the Jammu region, snake bites are very common during the summer and rainy seasons. Majority of our patients (80%) reported within 24hrs of the bite.

After the bite 60% of our patients experienced local pain of variable intensity. Pain however was never so severe as to be the main concern of the patients. Russel (4) recorded pain in 65% and tingling & numbness in 57% cases of rattle snake venom poisoning in United States.

Hydrolase enzymes such as metalloproteinases, phospholipases A2 and possibly hyaluronidases are mostly responsible for the local damage frequently observed in snake bite .

Regarding the systemic manifestations, neurotoxic manifestations were evident in 10 patients (12.5%), while haemotoxic manifestations were evident in 54 patients (67.5%). This was in accordance with findings of Lee *et al* (5) who demonstrated that the neurotoxic paralysis may begin within the first hour of snake bite and is seen first as ptosis, then blurred vision and diplopia, followed by facial weakness and dysarthria.

In severe cases, weakness of the limbs, paralysis of respiration, and fixed and dilated pupils may be observed. The systemic effects of elapid venoms are predominantly neurotoxic causing a selective neuromuscular block, affecting mainly the muscles of the eyes, tongue, throat and chest, leading to respiratory failure in severe poisoning. Haemorrhagic manifestations were a result of disturbance of normal coagulation process. Fear and palpitation were due to autonomic dysfunction which is common in patients with snake bites.

Table 2 . ECG Changes in 3 Groups

ECG Changes		Groups (n=80)		
		Nonenvenomated n(%)=16(20%)	Neurotoxic n=10(12.5%)	Hemotoxic n=54(67.5%)
Admission	Normal	7(43.7)	3(30)	15(27.8)
	Tachycardia	9(56.3)	6(60)	29(53.7)
	Bradycardia	0(0)	1(10)	10(18.5)
24 hrs	Normal	16(100)	8(80)	38(70.3)
	Tachycardia	0(0)	2(20)	16(29.7)
	Bradycardia	0(0)	0(0)	0(0)
72 hrs	Normal	16(100)	10(100)	54(100)
	Tachycardia	0(0)	0(0)	0(0)
	Bradycardia	0(0)	0(0)	0(0)

The main pattern of toxicity was haemotoxic (n=54; 67.5%) that was caused by snake bite of Viperidae family followed by neurotoxicity (n=10; 12.5%) that was due to Elapidae family. This observation was in accordance with Akbar *et al* (6) who observed that the major pattern of toxicity was hemotoxicity(52%) followed by neurotoxicity (22%).

Regarding cardiac function, no significant statistical change occurred in cardiac enzyme LDH in all groups at time of admission. Significant statistical elevation of LDH was observed in haemotoxic group 24hrs (F-stat=979.39, p=0.000000, ANOVA) and 72hrs (F-stat=200.20, p=0.000000, ANOVA) after admission. However, the elevation in LDH value in haemotoxic group 72hrs after admission was much lesser than that occurred 24hrs after admission. No significant change occurred with neurotoxic bite and non envenomated group 24hrs and 72hrs after admission. These findings were in agreement with Gonca *et al* (7) , who documented that there was raised LDH above normal ranges in haemotoxic group.

The CPK enzyme showed no statistically significant changes occurring in all three groups at time of admission. Statistically significant elevation in CPK occurred 24hrs after admission in haemotoxic group (F-stat=46.11, p=0.000000, ANOVA), while no change occurred with neurotoxic and non envenomated groups at the same time. No significant change was seen in all three groups after 72 hrs. This finding was in agreement with Cupo *et al* (8), who observed that the CPK values are raised in patients with envenomation. Elevated CPK indicates that some muscle damage was present (rhabdomyolysis) as emzymes is liberates from inside damaged muscle cells secondary to the rhabdomyolytic activity of certain venom constituents and it does not necessarily indicate myocardial damage.

In addition, the cardiac enzyme CPK-MB showed no significant statistical change in all groups at time of admission. Significantly statistical elevation occurred in haemotoxic group 24hrs (F-stat=129.07, p=0.000000, ANOVA) and 72hrs (F-stat=64.26, p=0.000000, ANOVA) after admission. However, the elevation in CPK-MB value in haemotoxic group 72hrs after admission was much lesser than that occurred 24hrs after admission. No change occurred in neurotoxic and non envenomated groups 24hrs and 72hrs after admission. This finding was in agreement with Cupo *et al* (8) who observed that the CPK-MB values are raised in patients with envenomation.

Troponin -T showed no statistically significant changes occuring in all three groups at the time of admission. Elevation in Troponin-T occurred 24hrs after admission in haemotoxic group, while no change occurred with neurotoxic and non envenomated groups at the same time. No significant change occurred 72hrs after admission in all groups.

Troponin-I showed no statistically significant changes occurring in all three groups at time of admission. Elevation in Troponin-I occurred 24hrs after admission in haemotoxic group, while no change occurred with neurotoxic and non envenomated groups at the same time. No significant change occurred 72hrs after admission in all groups. SGOT showed no statistically significant changes in all three groups at the time of admission. Elevation in SGOT occurred 24hrs after admission in haemotoxic group, while no change occurred with neurotoxic and non envenomated groups at the same time. No significant change occurred 72hrs after admission in all groups.

In haemotoxic group, 29 cases (53.7%) showed tachycardia at admission whereas 16 cases (29.7%)

showed tachycardia at 24hrs. This finding was statistically significant (p=0.011). In neurotoxic group, 6 cases (60%) showed tachycardia at admission whereas 2 cases (20%) showed tachycardia at 24hrs. This finding was statistically insignificant (p=0.17). At 72hrs tachycardia was not observed in haemotoxic , neurotoxic and non-envenomated groups.

In haemotoxic group, 10 cases (18.5%) showed bradycardia at admission and none at 24hrs and 72hrs. In neurotoxic group, 1 case (10%) showed bradycardia at admission and none at 24hrs and 72hrs.

Warrel *et al* (9) making observations on E.carinatus bite noted tachycardia in 43% cases partly due to anxiety but subsequently consistent with the level of fever and blood loss. Circulatory effects of E.carinatus venom observed in experimental animals include hypotension and bradycardia due to myocardial depression or to mesenteric vasodilatation (10) or to release of histamine (11).

Electrocardiographic abnormalities following snake bite may be due to direct cardiotoxic action of venom, hypotension or electrolyte disturbances.

Present in cobra venom cardiotoxin inhibits direct and indirect stimulation of skeletal muscle, decrease the acetylcholine release at the nerve endings and blocks axon conduction (12,13). Some effects of cardiotoxin resemble those of digitalis in that it can cause cardiac arrest in systole (14,15).

The present study showed significantly statistical ECG changes at admission in the nonenvenomated, neurotoxic and haemotoxic groups in the form of tachycardia or bradycardia. Also, significantly statistical ECG change in the form of tachycardia was observed 24hr after admission in the haemotoxic group. Nayak *et al* (16) , had documented ECG abnormalities which included sinus tachycardia and arrhythmia, bradycardia, tall T-waves and abnormalities suggestive of myocardial ischemia and non specific T-wave abnormalities. Atrioventricular blocks were also seen. However, Agarwal *et al* (17) , in a retrospective series of 55 patients with severe neurotoxic snake envenoming secondary to elapid snake bites, found no clinically significant cardiac involvement. Tachycardia and bradycardia in this study may be due to autonomic nervous system dysfunction where tachycardia occurred due to sympathetic stimulation as a result of severe fear and bradycardia occurred due to parasympathetic stimulation, also as a result of severe fear.

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