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Snake Bite - Translating Protocols into Practice

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Abstract: *There are many protocols available for treating poisonous snake bites and every treating physician thinks that he is always right. We submit a prospective study done over a period of seven months in a tertiary care hospital in Tamil Nadu. This study emphasizes on low dose ASV as a measure for better clinical response and reducing the morbidity and mortality.*

Aim of the Study: *The aim of the study is to prove that low dose ASV can reduce morbidity and mortality, if the guidelines given by state/ national/ WHO are followed on the basis of individual requirements.*

Material And Methods: *This is a prospective observational study in a tertiary medical care hospital, Dharmapuri, Tamil Nadu, south India, between Jan 2016 to July 2016 with 545 patients all are presented with history of snake bite and285 patients with signs of envenomation exclusion criteria all patients with pre existing renal disease, those who are on drugs like aspirin and clopidogrel, and patients with previous history of bleeding diathesis are excluded from this study*

Results: *Totally we encountered 2295 snake bite patients over a period of 3 years from 2013 – 2015. Among them, 112 (4.88%) patients died of snake bite related AKI. Average number of ASV vials used per patient ranged from 9.27 to 14.83, thus showing the efficacy of low dose ASV regimen.*

Conclusion: *Our study shows that when the signs and symptoms are carefully and constantly observed, low dose ASV is not inferior to high dose ASV in effectively treating snake bite patients as ASV neutralizes only unbound, free flowing venom.*

Keywords: *Low dose ASV, snakebite, envenomation,*

I. Introduction

World Health Organization estimates the number of poisonous snake bites to be 83,000 per annum with 11,000 deaths[1] in India Most of the fatalities are due to the victim not reaching the hospital in time where definite treatment can be administered. In addition, the community is also not well informed about the occupational risks and simple measures like wearing protective shoes while working in the fields which can prevent the bite. Multiple protocols are being followed for polyvalent anti-snake venom (ASV) administration which has given mixed results in different localities.

There are 13 known species that are poisonous and of these four, namely common cobra (Naja naja), Russell's viper (Dabiola russelii), saw-scaled viper (Echis carinatus) and common krait (Bungarus caeruleus) are highly venomous and believed to be responsible for most of the poisonous bites in India. A single bite of cobra contains venom capable of killing 15 to 20 persons. When 13 mg of venom is fatal for an average man, it can inject 12 to 20 times such dose and that is why serious cobra bite cases may not reach hospital live.

Krait bites often outnumber cobra bites and krait can inject larger than fatal dose in successful bites. Banded Krait bites rarely and it is to be noted that Indian antivenom has no neutralizing effect in this snakebite

Large number of Russell's viper bite cases comes with severe local pain at the site of bite with bleeding from the site, with bleeding from gum margins. Sometimes the non-poisonous snakebite causes alarm reactions in a patient like palpitation and restlessness. A venomous snakebite is diagnosed from the symptoms suggestive of systemic envenomation. Haemostatic abnormalities are prima facie evidence of viperidae bite. All viperidae bites can cause renal failure. Neurotoxic symptoms like ptosis can also be seen in a Russels viper bite.

Total Number Of Patients Encountered

	2013	**2014**	**2015**
Male	401	370	847
Female	48	252	377
Total	449	622	1224
ASV	6660	5765	11443
Average ASV used	14.83	9.27	9.34

Mortality Due To Snake Bite With Aki

	2013	**2014**	**2015**
Male	15	36	23
Female	9	20	9
Total	24	56	32
Percentage	5.34%	9%	2.6%

Signs & symptoms suggesting a viperidae bite:

- Local pain, swelling and erythema at the bite site.
- Tender enlargement of lymph nodes draining the bitten part since the larger molecular weight venom fractions enter into the lymphatics causing local necrosis and/or blistering.
- Nausea, vomiting, abdominal pain and abdominal tenderness which suggest a gastro-intestinal or retro-peritoneal bleed.
- Hypotension resulting from hypovolemia or direct vasodilatory effects of venom fractions
- Low back ache or loin pain which suggest of the likelihood of developing renal failure, retroperitoneal bleed passage of reddish or dark brown colored urine, reduction in the amount of urine output lateralizing neurological signs indicative of an intracranial bleed muscle pain indicating rhabdomyolysis are some of the manifestations.
- Bilateral parotid enlargement (viper head appearance).
- Conjunctival edema and sub-conjunctival haemorrhage
- Dysgeusia with a metallic taste
- Confusional state
- Ptosis
- Jaundice - the victims could bleed internally from any organ or mucosal surface.
- Hemoptysis, epistaxis,hematuria, hematemesis & melena,chemosis, macular bleed, excessive menstrual bleed, bleeding from the bite site or cannula, bleeding into the muscles, gingival bleed, bleeding into the skin and mucous membranes showing as purpura or petechia.

Indications for administration of asv in hemotoxic bites:

- Deranged haemostatic profile, suggested by either or all of An abnormal WBCT, PT / APTT above 1.5 times normal.
- The presence of a significant local inflammation at the bite site by way of severe pain, swelling and erythema or cyanosis.
- Tender enlargement of draining lymph nodes.
- Abdominal pain, Recurrent nausea and vomiting. Acute abdominal tenderness which may suggest gastrointestinal bleeding or retroperitoneal bleeding.
- Bleeding manifestation such as hemoptysis, epistaxis, hematuria, hematemeses, malena,macularbleed, petechial skin haemorrhage, bleeding from bite site, or cannula.
- BLOOD PARAMETERS a) Crenated RBC in peripheral blood smear b) Rise in serum creatinine of >30% of base line value c)Proteinuria >2+ d)Raised D dimer value e)Low platelet value REPEAT DOSE IN HEMOTOXIC BITES.

As already mentioned after the initial 10 vials of ASV no additional ASV is given for the next 6 hours as the liver is unable to replace the clotting factors in under 6 hours. After 6 hrs the 20 min WBCT is repeated and a repeat dose of ASV is given if there is an abnormality in the clot formation. Another 5-10 vials are administered over 1 hour depending on the degree of coagulation abnormality. The 20 min WBCT is repeated at 6 hourly intervals until coagulation is restored. In the majority of cases of hemotoxic bites a dose of 20 vials of ASV suffices.

The available polyvalent ASV does not neutralize the venom of the pit viper species namely - Hump nosed, Malabar and green pit vipers. Use of ASV is not advocated in Pit viper bites, if the snake is identified as belonging to the pit viper species. Swelling, local necrosis and blistering suggests a cobra bite, associated with descending paralysis. Initially muscles innervated by cranial nerves, commencing as a ptosis, diplopia or an ophthalmoplegia occurs. The patients complain of a difficulty in focusing and the eyelids feel heavy. Dysphagia, dysgeusia (tingling sensation in the tongue with a loss of taste), diaphoresis, circumoral pallor and paresthesia. Profound thirst, miosis, abdominal pain, vomiting Painful lymphadenopathy Palpitation, breathlessness, chest pain are other associated manifestations.

Neurotoxic bites, signs & symptoms:

- Paralysis of jaw and tongue may lead to upper airway obstruction and aspiration. Pooling of salivary secretions occurs as the patient is unable to swallow. Bulbar paralysis and respiratory failure follow.
- Hypoxia due to inadequate ventilation can cause cyanosis, altered sensorium and coma. This is a life threatening situation and needs urgent intervention.
- Paradoxical respiration as a result of intercostal muscle paralysis. Krait bite often presents in the early morning with paralysis that can be mistaken for a stroke
- Late Onset Envenoming – the patient should be kept under close observation for at least 24 hours. Many species especially the krait and the hump nosed pit viper are known for the length of time that can take for symptoms to manifest. Often this can take between 6 -12 hours.
- In the case of elapidae bites there may be very little local reaction at the bite site. Local pain develops by 30 minutes.
- The usual systemic signs and symptoms suggesting envenomation are ptosis, blurring of vision, tinnitus, double vision, difficulty in swallowing etc. The patient may feel sleepy and the head droops. There is slurring of speech and the voice may become indistinct and breathing becomes shallow. Death is usually due to acute respiratory failure.

Neurotoxic bites - signs & symptoms of neurotoxic bite which may be used as an indication for asv administration:

- Swelling, necrosis and local pain
- Descending Paralysis- Ptosis, diplopia, or ophthalmoplegia
- Respiratory paralysis
- Dysphagia
- Painful regional lymphadenopathy
- Paradoxical respiration resulting from the paralysis of the intercostal muscles

Treat the case with 10 vials of ASV initially as was mentioned with haemotoxic bites. If the Neostigmine test is positive, 0.5 mg of Neostigmine is injected intravenous with 0.6 mg of iv atropine. The same is repeated at half hourly intervals to a total of 5 doses. This is followed up by repeat injections at increasing intervals of 2 to 12 hours. Initial dose of 10 vials is given and if symptoms persist or worsen or in respiratory failure, repeat 10 more vials of ASV after 1-2 hours as a second dose and discontinue ASV. 20 vials is the maximum dose of ASV that should be given in an elapidae bite victim. Once the patient in respiratory failure has received 20 vials of ASV and is supported on a ventilator ASV should be stopped.

This is under the assumption that all circulating venom would be either fixed or neutralized by this point. Further doses of ASV do not serve any useful purpose then LAB TESTS Haematological -Hb, PCV,TLC,DC,ESR Peripheral smear for crenated red cells, schistocytes, platelet count which is repeated at 6 hour interval for the first 24 hours Coagulation work up -CT,BT, APTT, PT DIC work up - d –Dimer, FDP, fibrinogen which is repeated on Day 3 Renal function - Urea, creatinine Liver function – AST, ALT,ALP, S bilirubin, protein, albumin Muscle enzyme – CPK Biochemistry – S Na, K+, sugars Urine is checked for protein, haemoglobin, myoglobin. Blood group and Rh typing at the earliest ABG Test repeated on a daily basis are Hb, PCV,Urea, creatinine, platelets, urine-protein The coagulation profile normalizes within 24-48 hours of treatment in most cases.

HYPOTENSION

Hypotension is one of the important causes of renal failure in snakebite. Bleeding either into tissues or externally and loss of plasma into the bitten extremity can produce hypotension and circulatory collapse.

ACUTE KIDNEY INJURY

Acute kidney injury (AKI) is one of the most significant complications developing due to snake bite. AKI is associated with bites of Russell's Viper, saw-scaled Viper, Puff Adder, Pit Viper and Sea snake.

HEMODYNAMIC CHANGES

- Haemodynamic changes in snakebite vary among snakes involved.
- In a study of Russell's viper envenomation in canines, initially the cardiac output was decreased,
- systemic vascular resistance (SVR) and renal vascular resistance (RVR) was increased;
- the renal blood flow (RBF) and the glomerular filtration rate (GFR) were decreased.
- . 6 HOURS AFTER ENVENOMATION
- cardiac output was increased;

- SVR was decreased
- RVR was markedly increased;
- RBF and GFR further decreased.

MANAGEMENT OF SNAKE BITE

- RIGHT APPROACH
- *Reassure*
- *Immobilize*
- *Get to Hospital*
- Initial victim evaluation include state of airway, breathing, circulatory status, and consciousness.
- Urgent resuscitation is prerequisite in victim with shock, respiratory failure and cardiac arrest. It may include:-
- (A) Oxygen therapy and intravenous access with a large-bore intravenous catheter are a priority. A bolus of normal saline or Ringer's lactate should be given to all patients with suspected envenomation.
- (B) Tourniquets though no more recommended, are still used extensively because of lack of awareness. Sudden removal of tourniquet leads to a massive surge of venom.
- Check for pulse distal to tourniquet.
- Apply BP cuff with pressure and slowly release it to prevent sudden release of high dose of venom in circulation and its complications
- (C) If the victim has brought the snake, try identifying the species carefully, since crotalids can envenomate even when dead.
- Considering the high chance of developing kidney impairment after snakebite, the immediate care must include patient's adequate hydration, aiming at a maximum renal protection.
- However, the most important treatment to prevent AKI is early and specific anti-venom application at the recommended doses.

DOSE OF ASV

S. No.	ASV	Systemic	Local	Hemorrhagic	Neurological	Mixed
1.	Stat	5	5	5	5	5
2.	1st hour	5	5 Next Joint	2	2 (hourly)	2
3.	2nd hour	-	5 Next Joint	2	2 (hourly)	2
4.	6TH hour	5	5 Next Joint + FFP	2	2 (hourly)	2
5.	Total	15	15	11	11	11

SCORING SYSTEM FOR STARTING ASV

S. No.	SYMPTOMS, SIGNS, LAB PARAMETERS	SCORE
1	HR> 175/min, hypotension, hypertension, malignant arrythmyias, cardiac arrest (major)	5
2	Signs of impending respiratory failure/ tachypnoea, head lag, paralysis (major)	5
3	Systemic bleeding (gastro-intestinal or retroperitoneal bleeding. intra-cranial bleeding gingival bleeding, epistaxis, ecchymotic patches, hemoptysis, subconjunctival hemorrhages, continuous bleeding from the bite site, bleeding from pre-existing conditions e.g. haemorrhoids, (major)	5
4	Progressive painful swelling /early compartment syndrome(major)	5
5	Consumption coagulopathy detectable by 20WBCT (major)	5
6	Myotoxic- Muscle aches, muscle swelling, involuntary contraction of muscles,myoglobinuria (major)	5
7	Progressive painful swelling /early compartment syndrome (major)	5
8	Severe confusion, lethargy, seizure, coma, psychosis, generalised fasiculation (major)	5
9	Acute abdominal pain, repeated vomiting, diarrhoea	3
10	Tender enlargement of local draining lymph node.	3
11	Petechiae, purpura, ecchymoses, blebs and gangrene, Bleeding or ecchymosis at the injection site	3
12	Dysphonia, dysarthria, diplopia, dysphagia,ptosis	2
13	Local swelling, local pain, bleeding, blistering and necrosis (non progressive)	2

1. Start ASV if the score is 5 or above.
2. High dose regimen may be followed if patient presents with major features as depicted in scoring system.
3. Low dose regimen may be followed if patient presents with minor features as depicted in scoring system

FOR VASCULOTOXIC BITES
HIGH DOSE INTERMITTENT BOLUS THERAPY
10 vials of polyvalent ASV stat over 30 minutes as infusion, followed by 6 vials 6 hourly as bolus therapy till clotting time normalizes and /or local swelling subsides.

LOW DOSE INFUSION THERAPY
10 vials for Russel's viper or 6vials for Saw scaled viper as stat as infusion over 30 minutes followed by 2 vials every 6 hours as infusion in 100 ml of normal saline till clotting time normalizes or for 3 days, whichever is earlier. If 30 vials of ASV have been administered reconsider whether continued administration of ASV is serving any purpose, particularly in the absence of proven systemic bleeding.
If large doses have been administered and the coagulation abnormality persists, give fresh frozen plasma (FFP) or cryoprecipitate (fibrinogen, factor VIII), fresh whole blood, (if FFP not available) or platelet concentrate.

FOR NEUROTOXIC BITES
ASV 10 vials stat as infusion over 30minutes later followed by 2nd dose of 10 vials after 1 hour if no improvement within 1st hour.
Repeat ASV when there is worsening neurotoxic or cardiovascular signs even after 1–2 h. Maximum dose 20vials of ASV for neurologically envenomed patients.

- Dose of ASV does not vary with age of victim. ASV should ideally be administered within 4 hours of bite, but is effective even if given within 24 hours.
- ASV neutralizes only unbound, free flowing venom.
- If severe cellulitis is present ASV should be given within two hours which will prevent compartment syndrome ,tissue necrosis, gangrene ,acute kidney injury,
- If the cellulitis cross one major joint 5 vials of ASV should be given (two joints 10, three 15 immediately).
- The hitch with determining the optimum ASV dose is that the quantity of venom injected at a bite is very variable, depending on the species and size of the snake, the mechanical efficiency of the bite, whether one or two fangs penetrated the skin and whether there were repeated strikes.
- Furthermore, neutralization by antivenin must occur almost immediately after venom enters the circulation to significantly impact on recovery time of the coagulopathy due to envenomation
- The correction of coagulopathy is the most important criteria to continue the ASV treatment.
- After the first dose of bolus ASV, it should be repeated after 6 hours depending on the coagulation profile and may be repeated till the coagulation profile is corrected.
- In snake bite with neurotoxic poisoning after the first dose has been given, another dose may be repeated after 1 hr provided the patients have not improved, or worsened
- the supportive drugs like atropine and neostigmine should be administered according to signs and symptoms to buy time till ASV acts and neutralizes the venom with ventilator support
- As it carries risk of anaphylaxis, epinephrine should thus be kept ready always
- The suggestion of the total requirement of dosages lies between 10 and 30 vials of ASV
- The presently available polyvalent ASV, one effective against bites due to common neurotoxic and haemoto toxic snakes
- It is expensive and scarce-especially in high-risk areas. Although ASV has been used for many years, there is no universal consensus in many centers on the optimal dose and protocol of its administration.
- Theoretically, it would appear that patients with more severe envenomation need higher doses of ASV for effective neutralization of circulating snake venom.

GENERAL MANAGEMENT

- Early fluid resuscitation
- local wound care,
- Low dose ASV and other supportive measures were followed as a protocol in all these patients. .
- There is an increasing shortage of ASV in several developing countries and important incentive for a regulated dosing protocol would be to prevent the crisis of ASV availability and supply.
- In this era of rising medical expenditure and most of the countries facing shortage of ASV, further randomized trials are to be encouraged to determine lower and appropriate doses of ASV in management of snake bite cases.

II. Conclusion

Our study shows carefully observing the signs and symptoms, low dose ASV is non inferior to high dose ASV in effectively treating snake bite patients as ASV neutralizes only unbound, free flowing venom. The Indian National Snakebite Protocol may also need to be reviewed taking into consideration these newer developments average ASV administered was 10-15 vials that is much less than the prescribed maximum dose of 30 vials.

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