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Original research article

Study on the factors affecting the need for invasive ventilation in patients of neurotoxic snake bite at a tertiary care center of Bihar

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Abstract

Twelve patients with severe neuroparalytic snake envenomation were admitted to the intensive care unit with respiratory failure over one year period. Initially, ptosis and ophthalmoplegia, followed by bulbar palsy and respiratory muscle weakness were the common sequelae. All of them received cardio-respiratory support with mechanical ventilation, anti-snake venom (median dose of 20 vials), and anticholinesterase therapy. Most survived with complete neurological recovery. So, good outcome in such cases is related to early cardiorespiratory support and anti-venom therapy.

Keywords: anticholinesterase, envenomation, polyvalent anti-snake venom

Introduction

Snakebites remain a public health problem in many countries even though it is difficult to be precise about the actual number of cases. According to toxicity, they are categorized as hematotoxic, neurotoxic, and myotoxic. Among the neurotoxic group, the majority of bites are due to Naja naja (common cobra), Ophiphagus Hannah (king cobra), and Bungarus Caeruleus (Krait) in India. The snake venom consists of different enzymatic and nonenzymatic components loosely categorized as neurotoxins and hemorrhagens. In our ICU, most of the cases admitted are neurotoxic snakebites from the above-mentioned three commonest varieties. Neurotoxic envenomation has the potency to cause a broad spectrum of presentations starting from ptosis and ophthalmoplegia to respiratory arrest. Timely administered anti-snake venom and ventilatory assistance can prevent the mortality and morbidity of the victims [1-5].

Methodology

In our ICU, all the patients (from Southern Bihar) of neurotoxic envenomation presented with neuromuscular involvement with respiratory paralysis from March 2020 to March 2021. They were received in the emergency where they were resuscitated and shifted to ICU as early as possible. Detailed history and systemic examination, site of the bite, any local reaction at the site of the bite was recorded. Routine laboratory investigations including arterial blood gases and a complete hemogram with coagulation profile were sent at the time of admission. APACHE-II scoring was done for every patient at the time of admission.

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TABLE 293-2 Calculation of Acute Physiology and Chronic Health Evaluation II (APACHE II) Score[a]									
Acute Physiology Score									
SCORE	**4**	**3**	**2**	**1**	**0**	**1**	**2**	**3**	**4**
Rectal temperature (°C)	≥41	39.0–40.9		38.5–38.9	36.0–38.4	34.0–35.9	32.0–33.9	30.0–31.9	≤29.9
Mean blood pressure (mmHg)	≥160	130–159	110–129		70–109		50–69		≤49
Heart rate (beats/min)	≥180	140–179	110–139		70–109		55–69	40–54	≤39
Respiratory rate (breaths/min)	≥50	35–49		25–34	12–24	10–11	6–9		≤5
Arterial pH	≥7.70	7.60–7.69		7.50–7.59	7.33–7.49		7.25–7.32	7.15–7.24	<7.15
Oxygenation If FIo_2 >0.5, use (A – a) Do_2 If FIo_2 ≤ 0.5, use Pao_2	≥500	350–499	200–349		<200 >70	61–70		55–60	<55
Serum sodium (meq/L)	≥180	160–179	155–159	150–154	130–149		120–129	111–119	≤110
Serum potassium (meq/L)	≥7.0	6.0–6.9		5.5–5.9	3.5–5.4	3.0–3.4	2.5–2.9		<2.5
Serum creatinine (mg/dL)	≥3.5	2.0–3.4	1.5–1.9		0.6–1.4		<0.6		
Hematocrit (%)	≥60		50–59.9	46–49.9	30–45.9		20–29.9		<20
WBC count (10^3/mL)	≥40		20–39.9	15–19.9	3–14.9		1–2.9		<1
Glasgow Coma Score[b,c]									
Eye Opening	*Verbal (Nonintubated)*			*Verbal (Intubated)*			*Motor Activity*		
4—Spontaneous	5—Oriented and talks			5—Seems able to talk			6—Verbal command		
3—Verbal stimuli	4—Disoriented and talks			3—Questionable ability to talk			5—Localizes to pain		
2—Painful stimuli	3—Inappropriate words			1—Generally unresponsive			4—Withdraws from pain		
1—No response	2—Incomprehensible sounds 1—No response						3—Decorticate 2—Decerebrate 1—No response		
Points Assigned to Age and Chronic Disease									
Age, Years	*Score*								
<45	0								
45–54	2								
55–64	3								
65–74	5								
≥75	6								
Chronic Health (History of Chronic Conditions)[d]						*Score*			
None						0			
If patient is admitted after elective surgery						2			
If patient is admitted after emergency surgery or for reason other than after elective surgery						5			

All the patients were ventilated [Table 1] initially in synchronized intermittent mechanical ventilation.

Table 1: Indications for mechanical ventilation

Acute ventilatory failure	pH <7.30, $PaCO_2$>50 mmHg, apnea
Impending ventilatory failure	
Tidal volume	< 3-5 ml/kg
Resp. rate and pattern	>25-30/min, labored and irregu lar pattern
Minute ventilation	>10 L/min
$PaCO_2$ trend	Increasing to over 50 mmHg
Vital signs	Increase in heart rate and blood pressure
Severe hypoxemia	PaO_2 - <60 mmHg at FiO_2 - >50% or PaO_2 - <40 mmHg at any FiO_2 Severe cyanosis
Prophylactic ventilatory support	To reduce pulmonary complications To avoid hypoxia

With the improvement of neuromuscular paralysis, weaning was implemented through CPAP mode. If successfully tolerated, they were put on a T-piece trial. Extubation was done after assessing clinically and arterial blood gas parameters [Table 2].

Table 2: Criteria for extubation

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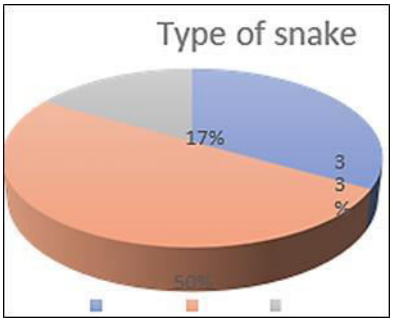
Criteria	Methods of assessment
Rapid breathing index	Respiratory rate/tidal volume in liter-<100 min/L
Blood gases	Acceptable blood gases on FiO_2 less than 40% and spontaneous minute ventilations less than 10 L/min PaO_2/FiO_2 more than 300 mmHg
Cardiopulmonary assessment	Absence of cardiopulmonary problems (e.g., CHF, pulmonary edema, pneumonia, tachycardia, arrhythmia, chest retractions, distended stomach.)

Polyvalent anti-snake venom (ASV) started as a loading dose (50 ml over two hours) and maintenance infusion (50 ml every six hourly). We have also used anticholinesterase (i.e., neostigmine started at a rate of 25 mcg/kg/hour) and anticholinergic (glycopyrrolate) combination as an infusion to reverse the neuromuscular blockade till ptosis was improved in every case [6]. Bomb BS *et al*. in 1996 showed that anticholinesterases are the cornerstone of neurotoxic bites, even in the absence of anti-snake venom. The outcome measure studied were survival, duration of ventilation, and requirement of ASV and anticholinesterase.

Results

Out of 12 patients [Table 3], 4 were bitten by a cobra, 6 were bitten by krait and for 2 patients the type of snake could not be determined. Neuroparalytic symptoms started within an hour of bite in four individuals. The site of the bite has been localized from history as well



as the bite mark. One patient has developed local cellulitis at the site of the bite for which higher antibiotic coverage and low molecular weight dextran were given.

Signs and symptoms	No. of patients
Pain and mild swelling	12 (100%)
Ptosis	12 (100%)
Diplopia	9 (75%)
Dysphagia and dysphonia	7 (58%)
Flaccid paralysis	2 (16%)
Coma and seizures	0

In all patients, anti-snake venom was given within a short period of the onset of symptoms and continued till significant recovery was regained in the power of all four limbs and intercostal muscles. ASV

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requirement was varying from 10 vials to 30 vials maximum up to 48 hours of the bite. (mean ASV administered 18 vials) No patient in our series demonstrated hypersensitivity reaction to anti-snake venom. Anticholinesterase therapy was continued till the improvement of the ptosis [Figure 1].

We have started Ceftriaxone and Metronidazole on an empirical basis in all the patients on admission to prevent soft tissue infection at the site of the bite. Most of them recovered uneventfully. No patients presented with any bleeding episode or renal involvement or any cardiac injury. No patient needed reintubation in our series. Mean duration of ICU stay 5 days.

Table 3: List of the patients

Age (years)	Sex	Site of bite	Type of snake	Onset of symptoms	APACHE II	Treatment started after	Total ASV doses received	Duration of the stay in the ICU
42	F	Left hand	Cobra	30 minutes	19	3 hours	20	9 days
32	F	Left leg	Krait	2 hours	15	7 hours	18	4 days
50	M	Right leg	Krait	2 hours	19	12 hours	20	5 days
28	M	Right ear	Cobra	45 minutes	13	4 hours	18	6 days
34	M	Left thigh	Krait	3 hours	17	7 hours	20	5 days
36	F	Right elbow	Krait	4 hours	17	9 hours	20	4 days
25	M	Left great toe	?	4 hours	13	12 hours	16	3 days
28	M	Right hand	Krait	3 hours	11	8 hours	14	3 days
19	F	Left leg	Cobra	1 hour	9	4 hours	16	5 days
46	F	Right shoulder	Krait	2 hours	17	8 hours	20	4 days
39	M	Right foot	Cobra	30 minutes	19	4 hours	20	7 days
36	M	Right thigh	?	3 hours	15	6 hours	18	3 days

Discussion

Ophitoxemia (clinical spectrum of venomous snake bite) starts with the onset of local changes within six to eight min of snakebite. Local pain, tenderness and reddish wheal followed by edema, swelling, and appearance of bullae are a feature common to all snakes. Cobra and Kraits usually produce early wet gangrene whereas vipers produce a slower onset dry gangrene. Apart from fright and psychological shock, cobra bites can produce symptoms as early as 5 - 30 minutes or they may be delayed up to 10 hours. They selectively produce a flaccid type neuromuscular paralysis. Muscles innervated by cranial nerves are involved earlier. While ptosis and ophthalmoplegia are among the first symptoms (found in all cases), the pupils and diaphragm are the most resistant to toxins. But pupillary changes (found dilated in affected patients) can occur earlier as a consequence of respiratory arrest and hypoxia-as was evident in our cases. Cardiotoxic features include tachycardia, hypotension, and ECG changes.

Pre-synaptic as well as postsynaptic neurotoxins of cobra and krait affect mainly muscles of the eye, tongue, throat, and chest causing respiratory failure [7]. The severity of envenomation and respiratory paralysis is related to - dose of venom injected, the potency of venom, anatomic location of the bite, age, health and immune status of the victim, and timely medical intervention [8]. In all patients, timely administration of ASV and cardiorespiratory support was led to a favorable outcome.

Immediate endotracheal intubation is necessary in patients with bulbar involvement to protect the airway. Weaning from mechanical ventilation is relatively easy as the patients are otherwise healthy and usually

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responsive to ASV within a short period as shown in several studies. The duration of mechanical ventilation in our patients is shown in [Figure 2].

In our study, we have used a lower loading dose of ASV and maintenance infusion through a syringe pump [9]. Anticholinesterase therapy was administered to all patients to combat postsynaptic toxins as most of them reached us very early (median duration of two hours).

Conclusion

From our study, we can conclude that administration of anti-snake venom with anticholinesterase therapy and cardio-respiratory support is the mainstay of therapy in neurotoxic envenomation with respiratory failure. The outcome is excellent if management is started early and before irreversible hypoxic insult.

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