Pathophysiology of dilatation of pupils due to scorpion and snake envenomation and its therapeutic value: Clinical observations

Himmatrao S Bawaskar, Parag H Bawaskar[1], Pramodini H Bawaskar

Dilated nonreacting pupils are routinely taken as a sign of irreversible brain damage. Alpha-receptor stimulation (scorpion sting) and presynaptic acetylcholine receptor blocker (krait bite) may result in dilation of pupils without involvement of the brain. This study was aimed to clinically evaluate the response of pupils in scorpion sting and krait bite. Victims of scorpion sting and krait bite were chosen from Raigad district. Scorpion sting and krait bite cases were admitted to hospital and were clinically evaluated in detail regarding neurological manifestations. Both cases had nonreacting dilation of pupils, complete neurological recovery accompanied with reverse of pupillary size and its response to light. In scorpion sting and krait bite poisoning, dilated nonreacting pupils are not the signs of irreversible brain damage.

Key words: Acetylcholine receptors, alpha-1 receptors, anticholinesterase, krait, scorpion

Scorpion and snake toxins do not cross the blood brain barrier. Autonomic nervous system plays an important role in the pathophysiology of maintaining the size of pupils in the eyes. Dilator pupillary muscle is rich in alpha-1 (sympathomimetic) receptors, whereas the constrictor pupillary muscle is rich in acetylcholine receptors. Scorpion venom evokes autonomic storm as a result of delayed closing of neuronal sodium channel. Alpha-1 receptor stimulation plays an important role in the pathogenesis of scorpion envenoming. Beta-bungarotoxin content of krait venom blocks the presynaptic acetylcholine receptors. We report pupillary dilatation in scorpion sting and krait bite cases irrespective of different pathophysiologies. These clinical observations can be utilized for a new therapeutic approach.

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Bawaskar Hospital and Clinical Center, Mahad Raigad, [1]Department of Cardiology, Topiwala National Medical College and BYL Nair Hospital Mumbai, Maharashtra, India

Correspondence to: Dr. Himmatrao S Bawaskar, Bawaskar Hospital and Clinical Research Center, Mahad, Raigad, Maharashtra, India. E-mail: himmatbawaskar@rediffmail.com

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Case Reports

Case report (krait bite)

On October 12, 2008, at 7.30 a.m., an 8-year-old female was admitted at a general hospital in Mahad with a complained of heaviness in the eyelids and unable to open the eyes, blurred vision, and difficulties in deglutition. She had nasal twang voice, body ache, heaviness, and tingling numbness sensation over the back of nape. She woke up at 3.30 a.m. due to pain in abdomen and experienced some pricking sensation over the back of nape. Nearly 2.5 feet long krait was seen lying in her bedding [Fig. 1]. On clinical examination she had—myasthenic face, whole cornea covered with eyelids, external ophthalmoplegia, and unable to protrude the tongue beyond the teeth margins. She could count up to twenty in one breath. Her expiratory nasal blow was good in intensity. Both pupils were dilated, fixed, and not reacting to light [Fig. 2]. There were no fang marks or swelling at the site of bite (back of nape of neck); pulse was regular and good in volume. Her blood pressure was 100/70 mmHg, and oxygen saturation (SpO_2) was 93%. Muscle power was Grade 5/5 in all limbs; her speech slurred with nasal sound. She can easily lift the head

Figure 1: Krait (*Bungarus caeruleus*)

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from pillow. Deep tendon reflexes were present. She was investigated and her hemoglobin was 8.8 g/dl, total white cell count was 4200, serum urea was 25 mg/dl, serum creatinine was 0.9 mg/dl, random blood sugar was 95 mg/dl, serum sodium was 138 mEq, and potassium was 3.4 mEq.

Nasal oxygen was given to her in semiprone position. Polyvalent antisnake venom (ASV) of 100 ml added to 250 ml of normal saline was given intravenously over 30 minutes; ASV 20 ml, neostigmine 25 μg/kg was preceded by intravenous 0.06 mg atropine which is called an elapid cocktail administered over 4 h interval and was continued for the next 24 h. Bulbar palsy was recovered at the end of 12 h [Fig. 3] and ptosis persisted for 36 h. She was discharged on the 3rd day.

Case report (scorpion sting)

On October 21, 2008, at 3.30 p.m., a 55-year-old male had vomiting and profuse sweating literally flowing all over his body [Fig. 4]. He gave a history of scorpion sting on his right index finger at 2.00 p.m. while he was harvesting the grass on the farm. The scorpion was red [Fig. 5]. Soon after stinging, he experienced mild pain at the stung site which is attributed to vasoconstriction as a result of excessive catecholamines. On arrival at the hospital, he was sweating profusely all over his body; he changed his cloths twice. Extremities were cold; blood pressure was 180/110 mmHg. Grade 3/6 systolic murmur of mitral regurgitation heard over apex; there was loud S3 gallop. Respiratory rate was 18/min and no rales were audible in the chest. Electrocardiograph showed tented T-waves. Pupils were dilated and not reacting to light [Fig. 6]. Echocardiography showed poor myocardial contraction with left ventricular ejection fraction of 33%. He was closely monitored, SpO_2 was 94%. He was investigated and white cell count was 9000/mm^3 and creatine phosphokinase-MB was 66.4 (normal: l0–20).

He was given nasal oxygen, intravenous crystalloid solution, scorpion antivenin 50 ml, and oral prazosin 1 mg, repeated at 3 h interval. Sweating persisted for 2.5 h. Blood pressure gradually reduced to 96/68 at the end of 3 h of admission, and pupils became to normal size reacting to light [Fig. 7]. Ejection fraction was 56% on the 3rd day. He was discharged on the 3rd day.

Discussion

Envenoming by krait bite is associated with a syndrome of neuromuscular paralysis that falls into rapid-onset phase leading to profound paralysis within 30–60 min, stable phase of deep paralysis lasting for 2–3 days, and recovery phase of 2–3 weeks. Circulating venom can be neutralized by early reporting the victim to hospital and administration of an

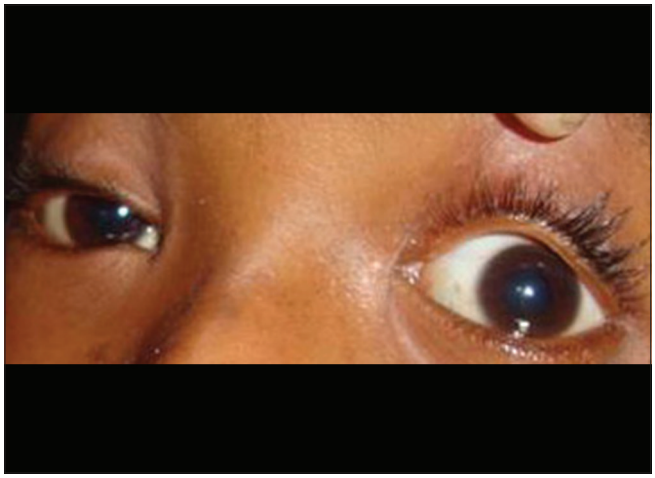

Figure 2: Dilated nonreacting pupils in krait bite victim - Case 1

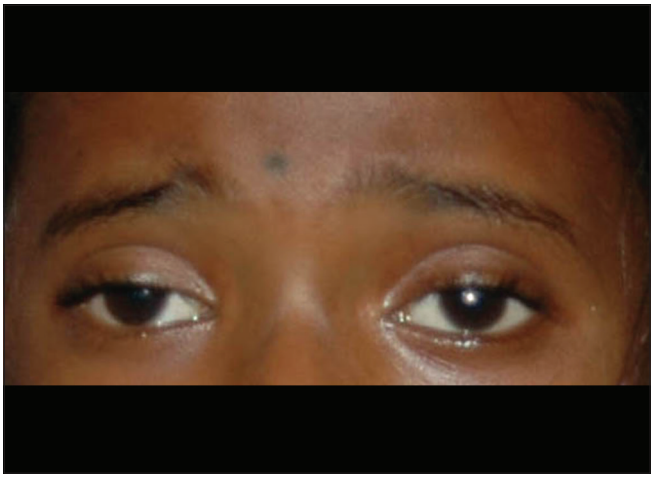

Figure 3: Recovery

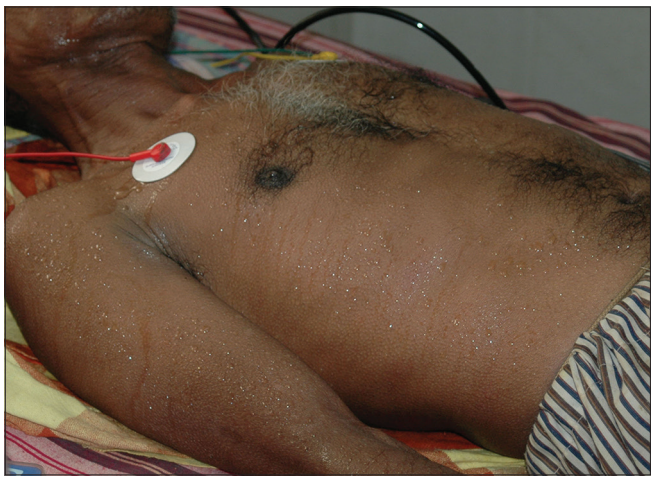

Figure 4: Profuse sweating due to scorpion sting

Figure 5: Red scorpion (*Mesobuthus tamulus*)

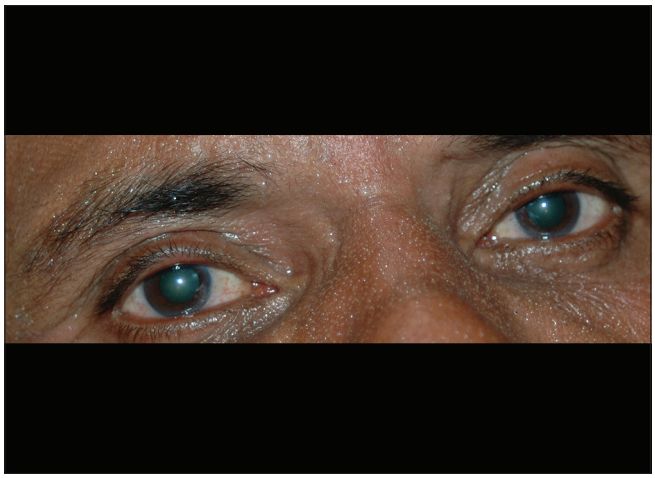

Figure 6: Dilated nonreacting pupils

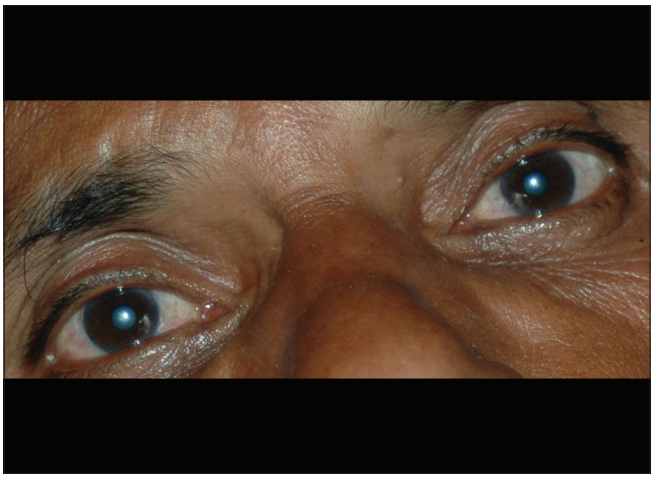

Figure 7: Recovery with normal-sized pupils

appropriate dose of ASV. Complete recovery is accompanied with regeneration of destroyed neuromuscular junction. While during the recovery phase as neuromuscular contacts are restored or receptors are regenerated. While, at present, there is no treatment or preventive measures once the degeneration of receptors occurred.[1] Sphincter pupillae is rich in acetyl choline concentration, maximum venom reach to sphincter pupillae because of abundant of micro vascular circulation, because of this maximum concentration venom reach to sphincter pupillae, krait venom irreversible block the acetyl choline receptor ,result in long standing dilated non reacting pupils [Fig. 2].

Dilatation of pupils is due to paralytic action of krait venom on cholinergic receptors.[2] Dilated nonreacting pupils do not indicate the irreversible brain damage in elapid bite.[3,4] Krait venom blocks the presynaptic receptors and resistance to acetyl cholinesterase inhibitor (ACHEI). In 2014 we from India first reported 15 patients out of 16 coppery color (kokan krait) victims respond to ACHEI.[5] However, we have reported in India species of krait venom has properties to block both pre- and post-synaptic receptors did response to ACHEI.[3,4] An indication of ACHEI in krait bite victim depends on the positive response to short-acting ACHEI (Tensilon test).[6] However, edrophonium is expensive and not available in rural India. In such situation, pupillary response to the pilocarpine eye drop is a simple scientific, inexpensive clinical bedside test which can be easily performed at primary health centers.

Pilocarpine is a parasympathomimetic agent that acts directly to the sphincter pupillae through the muscarinic receptors.[7] Till date, there is no published study of the use of pilocarpine test for the premonitory positive response to ACHEI in elapid poisoning or improvement of ptosis by putting ice-cold water in gloves over ptosis eyelid. Hypothermia sensitizes the receptors to the existing acetylcholine. Sphincter pupillae is rich in cholinergic muscarinic M3 receptors. Dilator (radiating) pupillary muscle is supplied by sympathomimetic alpha-1 receptors.[8]

Neurotoxin content of venom prevents the release of acetylcholine at sphincter pupillae resulting in paralysis of antagonism to the dilator pupillae. Neurotoxin of Indian red scorpion venom delays the closing of neurogenic sodium channels resulting in pouring excessive catecholamine into circulation. Autonomic storm is characterized by transient short cholinergic action (vomiting, sweating, salivation, and bradycardia) and prolonged sympathetic (hypertension, tachycardia, pulmonary edema, hypotension cold extremities, and death) stimulation.[9] Excessive sweating with dilatation of pupils is suggestive of alpha-1-receptor stimulation as a result of preganglionic release of acetylcholine and postsympathetic stimulation.[10]

Krait venom has action similar to botulinum toxin; thus, it can be utilized for the cure of dystonia.[11] Brugada syndrome is due to the deficiency of sodium current in the myocardium; drug derived from scorpion toxin could increase the sodium current and treat Brugada syndrome.[12] Ion channel scientists might usefully explore the possibility of using the analyzed scorpion venom fraction, the irreversible block caused by bungarotoxin.[8,13] Charybdotoxin, a calcium-activated potassium channel blocker, is found in the venom of the Israeli scorpion *Leiurus quinquestriatus*, an iberiotoxin from *Mesobuthus tamulus* venom may have similar effects.[14] The beta-bungarotoxin of krait venom does not block calcium-activated potassium channel.[14]

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Conflicts of interest

There are no conflicts of interest.

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