Carbamazepine-induced Seizure in a Nonepileptic Child

Sir,

Seizure-inducing effects of antiepileptic drugs (AEDs) are known in epileptic patients even at normal therapeutic doses.[1] AED-induced seizure exacerbation in patients of epilepsy is well known which may have a number of reasons including inappropriate choice of AEDs (e.g., aggravation of seizures and myoclonus in juvenile myoclonic epilepsy due to carbamazepine), paradoxical effects, AED-induced encephalopathy, or unmasking of seizures. Few cases can be due to indirect effects such as hyponatremia due to drugs such as carbamazepine or oxcarbazepine.[2]

Carbamazepine is one of the most widely used anticonvulsant drugs. Severe carbamazepine toxicity (which is aggravated by its metabolite carbamazepine-10, 11-epoxide) causes hypotension, cardiac dysrhythmias, respiratory depression, coma, and rarely seizures. In general, serum levels of carbamazepine are used to assess or predict toxicity. Carbamazepine levels <30 μg/mL are associated with mild to

moderate toxicity and serum levels >40 μg/mL are associated with major toxicity symptoms such as apnea, coma, and seizures.[3]

The overdose cases are not infrequent in children with seizure disorders, but there is very little literature available on effects of carbamazepine overdose in young healthy children. In one such article, the author has found that carbamazepine toxicity in young children commonly presents as nystagmus, ataxia, and drowsiness. In all those cases, the children accidentally took carbamazepine prescribed for a family member.[4]

The mechanism of most of the drug poisoning cases could be due to nonspecific manifestation of drugs mechanism of action. Overdose-related symptoms can lead to sedation or sleep disturbances, and true proconvulsant effect appears at toxic doses. The latter mechanism is more relevant in our case of carbamazepine toxicity.[5] We present the case of a previously healthy, nonepileptic child who presented with generalized tonic–clonic status following accidental overdose of carbamazepine tablets.

A 5-year-old boy weighing 10 kg with no known comorbidity presented to the hospital casualty with generalized tonic–clonic status. As a part of emergency management, the child was treated with injection midazolam followed by intravenous valproic acid. His father gave a history of consumption of 5 tablets of carbamazepine (of 200 mg each; which were prescribed to his grandfather). As the child was drowsy, he was electively intubated to protect his airway. As he continued to be in status epilepticus, he was started on midazolam drip at 1.5 μg/kg/min. He was also given gastric lavage after collecting blood for carbamazepine level and other routine laboratory parameters. His carbamazepine level was found to be 20 μg/mL. Therapeutic range for carbamazepine (on treatment) is 4–12 μg/mL. He was also evaluated for other factors that may have precipitated the seizure, including metabolic parameters, magnetic resonance imaging of brain (which was normal), and electroencephalogram (EEG), which revealed diffuse slowing. His seizures stopped in 6 h, and his sensorium improved over the next 24 h. The midazolam drip was gradually tapered, and the child was discharged after 5 days.

Carbamazepine is a very well-recognized AED in the management of epilepsy. At the same time, it is also reported as a cause of paradoxical reactions such as seizure in patients with epilepsy. Even at normal doses, it is known to provoke complex focal seizures in adults, focal status epilepticus in children, and myoclonic status in those with juvenile myoclonic epilepsy. This phenomenon has EEG correlation with increased generalized spike and wave activity.[6] This is similar to new-onset arrhythmias seen in patients treated with antiarrhythmic agents due to effects on automaticity, the intrinsic firing rate of autonomic tissue, or the heart's resting membrane potential.[5]

Stremski *et al*. evaluated 61 pediatric patients with carbamazepine toxicity (>12 μg/mL). Dystonic reactions, apnea, and coma were seen more frequently in those with carbamazepine toxicity. They however did not find any relation of seizure occurrence in this cohort and peak carbamazepine level.[7]

Our case, however, presented with generalized tonic–clonic seizures due to carbamazepine toxicity. This aspect of carbamazepine toxicity in healthy nonepileptic children is not routinely seen in clinical practice. There are sparse reports of the proconvulsant adverse effects of carbamazepine in those without prior seizure disorder.[8]

All reported cases of normal children with carbamazepine overdose or toxicity are found to be accidental in nature, and it puts a question about safe storage of medication that should be out of reach of children. In this reported case, the drug was prescribed for a family member. It is still imperative to rule out any familial type of undiagnosed epilepsy in the child which might get unmasked in such accidental cases of AED poisoning.[9]

Population-based data regarding carbamazepine or other AED toxicity causing seizures in normal individuals are scanty. However, it is clear that some AEDs such as carbamazepine have the potential to cause aggravation of existing condition and even development of new episode of seizure in neurologically normal children.

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Conflicts of interest

There are no conflicts of interest.

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