



The Blue Ridge Poison Center

Tox Talks

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DRUG AND TOXIN INDUCED SEIZURES

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MEDICINE? The Blue Ridge Poison Control Center offers CME-accredited toxicology lectures through telemedicine. To request a topic, schedule a lecture for your staff, or more information contact Heather Collier: 434-924-5185 or HLC8E@virginia.edu.

THE UVA CENTER OF CLINICAL TOXICOLOGY associated with the Blue Ridge Poison Center manages over 500 patients each year on site in the University of Virginia Health System - from outpatient clinic visits to critically ill inpatients managed in our pediatric and adult intensive care units. In addition, over 2,000 requests are made each year for consultation with our Boarded Medical Toxicologists from other healthcare facilities by phone or telemedicine. Call 1-800-222-1222 24 hours a day, every day. [Cell users: 1-800-451-1428]

IN CHARLOTTESVILLE

Reminder: At University of Virginia Hospital, the first Wednesday of every month features toxicology Grand Rounds. For more information, contact Heather Collier: 434-924-5185 or HLC8E@virginia.edu
Register to receive this newsletter via email: Kristin Wenger: klw2s@virginia.edu

Case: A three-year-old boy was brought to the emergency room for recurrent seizures. He had been reportedly well with no history of seizure disorder. The patient was treated aggressively with repeated doses of lorazepam, followed by phenytoin and phenobarbital. None of these interventions were successful in stopping his seizures. As the healthcare provider caring for this child, what additional questions should be asked and what other treatments can be considered?

Discussion: Numerous toxins can potentially cause seizures. Some agents cause seizures primarily, or directly, by altering the balance between inhibitory (i.e. GABA and adenosine) and excitatory neurotransmission. Some of these agents and their mechanism of action are listed in Table 1. Many other agents cause seizures secondarily by causing profound systemic derangements such as hypoglycemia, hemodynamic collapse, or hypoxia. These abnormalities are responsible for the patient's seizures and treatment is aimed at correcting the metabolic abnormalities.

In general, toxin induced seizures are treated in a similar fashion to other seizures. Clinicians should assure the patient maintains a patent airway and the blood glucose should be measured. Most toxin induced seizures will be self-limited. However, for seizures requiring treatment the first line agent should be parenteral benzodiazepines. If benzodiazepines are not effective at controlling seizures a second line agent such as phenobarbital should be employed. In cases of toxin induced seizures, phenytoin is generally not recommended. It is usually ineffective and may add to the underlying toxicity of some agents. If a poisoned patient requires intubation, it is important to avoid the use of long acting paralytic agents as these agents may mask seizures if they develop.

TABLE 1: AGENTS AND MECHANISM OF ACTION		
Category	Specific agents	Mechanism
Analgesics	Propoxyphene Tramadol Meperidine	Unclear
Antimicrobials	Isoniazid	GABA depletion
	Penicillin	GABA antagonism
Drugs of abuse	Amphetamines Cocaine Phencyclidine	Adrenergic agonism
Psychiatric Medications	Cyclic antidepressants	GABA antagonism
	Venlafaxine Bupropion	Unclear
Pesticides	Organophosphate	Cholinergic excess
	Organochlorine (lindane)	GABA antagonism
Plants/Mushrooms	Gyrometra esculenta	GABA depletion
	Water hemlock	GABA antagonism
Over the Counter	Anti-histamines	Histamine antagonism
	Caffeine	Adenosine antagonism
Withdrawal	Ethanol	GABA receptor downregulation and NMDA receptor upregulation
	Benzodiazapines	GABA receptor down regulation
Others	Camphor	Unclear
	Carbamazepine Theophylline	Adenosine antagonism
	Lidocaine	Sodium channel blockade
	Baclofen	GABA _b agonism

Several toxins have unique treatments that should be employed in addition to standard treatment.

TABLE 2: SEIZURE CAUSING AGENTS REQUIRING SPECIFIC TREATMENTS	
Agent	Treatments
Isoniazid <i>Gyrometra esculenta</i> mushroom	Pyridoxine
Theophylline	Barbiturates reportedly more effective than benzodiazapines. Hemodialysis may be required to speed drug elimination.
Organophosphates Nerve Agents	Atropine must be used in addition to benzodiazepines

Case continued: On further questioning it was revealed that the child's mother was taking isoniazid for tuberculosis and the patient had been found with the bottle several hours before the seizures began. Isoniazid, *Gyrometra* mushrooms (false morels) and hydrazine (found in rocket fuel) can cause seizures refractory to treatment by inhibiting pyridoxine phosphokinase which leads to a depletion of GABA. The treatment initially involves administration of benzodiazepines, fluid resuscitation, and correction of acidosis. However, due to GABA depletion, benzodiazepines and barbiturates will typically be ineffective. Patients will require administration of pyridoxine in order restore GABA synthesis. Pyridoxine administration will also correct confusion and coma caused by isoniazid poisoning. The recommended dose for pyridoxine is 1 gram of pyridoxine for every gram of isoniazid ingested. An empiric dose of 5 gms or 70 mg/kg (up to 5 gms) in children is recommended if the exact amount of the ingestion is not known. Give slowly over 5-10 minutes. This dose can be repeated if seizures do not resolve or mental status remains altered. Avoid giving doses in excess of 10 gms of pyridoxine as this can result in severe peripheral neuropathy.

After determining that isonizid may have been responsible for the patient's seizures he was given a dose of pyridoxine, soon after which his seizures abated and the child made a full recovery.

~Dr. David Lawrence, D.O., is completing his second year of Fellowship with the Division of Medical Toxicology, University of Virginia.

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