Central Nervous System Toxicity

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KEYWORDS

• Agitated delirium • Altered mental status • CNS toxicity • CNS depression
• Drug-induced seizures

KEY POINTS

- Central nervous system (CNS) toxicity may manifest as a depressed level of consciousness, agitation, confusion, seizures, or psychosis; each existing along a spectrum, coexisting, or waxing and waning.
- History may be valuable in elucidating the cause of CNS toxicity but can often be misleading; the clinician must maintain skepticism when considering the history and place at least equal emphasis on physical findings when determining the cause of illness and managing patients.
- Identification of toxidromes, when present, or smaller constellations of physical and electrocardiographic findings may allow the identification of a toxicant or class of toxicants, aiding in management.
- Patients for whom there is any concern for nonconvulsive status epilepticus, such as those with a prolonged period of unconsciousness following a generalized seizure, sudden unexpected deterioration in level of consciousness, or motor activity of unclear significance, may benefit from electroencephalogram evaluation.

INTRODUCTION

Central nervous system (CNS) toxicity may result from exposure to a vast array of xenobiotics. The term *xenobiotic* describes any substance that is foreign to the human body. Sources of exposure may be medicinal, recreational, environmental, or occupational; the means of exposure may be intentional or unintentional. Whether toxic effects result from an exposure depends on the dose to which one is exposed. However, other factors may influence the development of toxicity, such as chronicity of exposure, the pharmacokinetics of the particular agent, genetic polymorphisms that may influence the pharmacokinetics, and concomitant exposure to other toxicants.

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Clinical manifestations of CNS toxicity are diverse. Patients may present with CNS depression, agitation, confusion, psychosis, or seizures. *Altered mental status* is a vague term that is often used to describe disturbances in consciousness. Xenobiotic toxicity may manifest as altered thought content, resulting in psychosis or confusion; may vary the level of arousal, resulting in agitation, lethargy, stupor, or coma; or may affect both elements of consciousness.[1]

The goal of this article is to provide a rational approach to the assessment, diagnosis, and management of patients presenting with CNS toxicity resulting from xenobiotic exposure. CNS toxicity is categorized as CNS depression, indicating a decrease in the level of alertness, and agitated delirium, indicating a state of restlessness or excitation with confusion. Seizures are considered separately. The focus is on the more common causes of CNS toxicity that emergency health care providers are most likely to encounter in their practice because a comprehensive list and description of toxicants is beyond the scope of this article.

PATIENT HISTORY

In assessing patients with potential CNS toxicity, the history is a valuable component of the evaluation. Occasionally, history alone can provide a diagnosis and allow anticipation of the clinical course. However, the history may be limited, unavailable, or, in some cases, misleading because patients, friends, families, and caregivers may erroneously misattribute symptoms to an inconsequential agent or cause. It is not unusual for patients to present with an empty pill bottle, which may have been used to store a completely different medication than that listed on the label. Thus, although it is important to gather as much information as possible from patients, families, friends, bystanders, and prehospital personnel, it is equally important to maintain a degree of skepticism and to place more value on physical examination findings if they are inconsistent with the history provided.

Box 1 lists the historical elements to consider when assessing patients with possible CNS toxicity. The clinician should inquire about symptoms observed before the health care presentation, such as hallucinations, seizures, or confusion. The timing of the symptom onset may differentiate an acute overdose (with sudden development of symptoms) from chronic toxicity resulting from the gradual increase of a drug concentration to a toxic range. The use of new medications, whether over the counter or prescription, might point toward a drug interaction. Recent discontinuation of medications might suggest a withdrawal syndrome. Information regarding the availability of nonpharmaceutical toxicants, such as ethylene glycol or methanol, in addition to medications and illicit substances should be sought. Potential environmental

Box 1
Important historical information

- Symptoms before health care presentation
- Timing of onset of symptoms (sudden, gradual)
- Recent initiation or discontinuation of medications
- Availability of pharmaceutical and nonpharmaceutical toxicants
- Number and type of pills present in available containers
- Medical history of patient, relatives, and housemates
- Review of systems (ie, recent illnesses or complaints, suicidality)