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Maryland Poison Center
UNIVERSITY OF MARYLAND SCHOOL OF PHARMACY

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The Maryland Poison Center's Monthly Update: News, Advances, Information

Pediatric aripiprazole ingestions

Clinical courses have been described in pediatric patients with overdoses of aripiprazole that differ from overdose of other antipsychotic agents. These cases describe prolonged periods of sedation that wax and wane with alternating periods of sedation, altered mental status and normal sensorium. Aripiprazole possesses unique pharmacokinetic and pharmacodynamic properties that may, in part, describe the reason behind these unique presentations.

Aripiprazole is metabolized via cytochrome P450 (CYP) enzymes 3A4 and 2D6 to an active metabolite, dehydroaripiprazole. There is genetic variability in the activity of CYP2D6 including rapid metabolizers (normal), ultrarapid metabolizers (fast), and poor metabolizers (slow). The elimination half-lives of aripiprazole and dehydroaripiprazole are estimated to be 75 and 95 hours, respectively. However, in individuals with poor CYP2D6 activity, the half-life of aripiprazole can be prolonged up to 146 hours (*Drug Metab Pharmacokinet*. 2007; 22(5):358-66). Unlike most antipsychotics that are antagonists, aripiprazole functions as a partial agonist at post-synaptic D2 receptors. Furthermore, aripiprazole is thought to exhibit variable effects on dopamine receptors ranging from full agonism to antagonism. These unique effects on dopamine receptors can result in a wide variety of pharmacological effects depending on dopamine concentrations and may contribute to the fluctuations in neurological status that have been described in pediatric patients.

Two cases highlight variability in clinical courses. One case described a 2-year-old female that developed lethargy within an hour of ingesting an estimated 195 mg aripiprazole. She progressed to unconsciousness and remained profoundly sedated during the 24 hours following the ingestion. Sedation and truncal ataxia continued for the 3 days following ingestion requiring four days hospitalization until her symptoms resolved and she was discharged (*Clin Toxicol*. 2005;43(3):193-5). Gupta and colleagues published a separate case describing a 3-year-old who developed lethargy shortly after ingesting 200 mg of aripiprazole tablets. He became increasingly arousable over the 16-hour period following the ingestion, but experienced acute recurrent sedation (responsive only to sternal rub) as well as extrapyramidal symptoms including rhythmic jaw movements and tongue twitching. He slowly became more alert and returned to baseline 72 hours after the ingestion (*Pediatr Emerg Care*. 2019; 35(8):e145-e146).

Young children who have taken excessive doses of aripiprazole and experience significant lethargy should be brought to an emergency department for further observation and symptomatic treatment. Aripiprazole may cause mild or overt hypotension, which often responds to intravenous fluid administration. Patients may be safely discharged if they are hemodynamically and neurologically intact. Parents/caregivers should be counseled to closely monitor the child for changes in neurological status in the 1-2 days following the ingestion and to return to the emergency department if significant central nervous system depression occurs.

Did you know?

The most common symptom of second-generation antipsychotic overdose is sedation. In addition, these agents can cause QTc prolongation through their blockade of cardiac hERG potassium channels. Alpha-1 antagonism may cause softer blood pressures, which often results in a reflex tachycardia. Some of these agents (most notably quetiapine) also possess anti-cholinergic properties.

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