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Serotonin Syndrome

Serotonin syndrome results from excessive central and peripheral serotonergic activity. It can be caused by one or more of the following factors: decreased serotonin breakdown (methylene blue, monoamine oxidase inhibitors [MAOIs]), decreased reuptake of serotonin (selective serotonin reuptake inhibitors [SSRIs], cocaine, dextromethorphan, tramadol, meperidine, methadone), an increase in serotonin precursors or agonists (L-tryptophan, LSD), and an increase in release of serotonin (amphetamines, buspirone).

The syndrome occurs most frequently in overdoses of single agents or in therapeutic dosing of more than one proserotonergic drug. Symptoms usually begin within 24 hours after the addition of an agent that increases the activation of serotonin receptors and may go unrecognized in individuals experiencing mild clinical effects. It presents with a rapid onset of a triad of symptoms consisting of altered mental status and CNS changes (anxiety, agitation, confusion, hallucinations, mydriasis), neuromuscular hyperactivity (clonus, myoclonus, tremors, sweating, hyperreflexia, ocular clonus, muscular rigidity), and autonomic instability (flushing, diaphoresis, shivering, hypertension/hypotension, hyperthermia, tachycardia, tachypnea). Patients will often also experience gastrointestinal symptoms of nausea, vomiting, diarrhea and abdominal pain. Severe cases require ICU admission, often presenting with profound hyperthermia (temperatures >41.1°C), acidosis, delirium, rigidity (mostly in the lower extremities), rhabdomyolysis, seizures, and coma.

The diagnosis of serotonin syndrome is based upon clinical presentation and drug history. There are no laboratory tests that confirm the diagnosis, but elevated WBC count, increased CPK, and mild metabolic acidosis may be seen. Treatment involves discontinuing any and all agents that may contribute to the syndrome. In mild to moderate toxicity the primary treatment is benzodiazepines to help reduce anxiety, agitation, and neuromuscular hyperactivity. The antihistamine cyproheptadine, used for its serotonin antagonist effects, has also shown efficacy. In severe toxicity, sedation, intubation and neuromuscular paralysis may be necessary.

Elizabeth McCormick, PharmD
PGY-2 Pediatric Pharmacy Resident
University of Maryland School of Pharmacy

***DID YOU KNOW THAT…** it was in 1982 that the term "serotonin syndrome" first appeared in the literature?*

In 1982, Insel et al reported on two patients with adverse effects from a combination of clomipramine and a monoamine oxidase inhibitor (MAOI). An earlier description of the syndrome had been published in 1955 in which a patient receiving iproniazid for pulmonary TB died after receiving meperidine. The patient was diagnosed with "toxic encephalitis" at the time. In the 1960's, a similar illness with significant hyperactivity was reported following the concurrent use of l-tryptophan and MAOI's.

Maryland Poison Center
University of Maryland School of Pharmacy