
Serotonin Syndrome: Diagnosis and Treatment

Last updated October 2023

Introduction: Serotonin syndrome is a rare but potentially life-threatening medical emergency that occurs in patients on medications that affect serotonin levels. Be particularly vigilant when patients are on high doses or multiple serotonergic agents.

Causes

A variety of substances can trigger serotonin syndrome, including OTC medications and supplements:

- **Selective Serotonin Reuptake Inhibitors (SSRIs):** The most common offenders, often in overdose or when used in combination with other serotonergic agents.
- **Monoamine Oxidase Inhibitors (MAOIs):** Can cause severe or fatal serotonin syndrome when combined with SSRIs or foods high in tyramine.
- **Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs):** Another class to be cautious of, particularly when used in combination with other serotonergic medications.
- **Recreational Drugs:** Substances like MDMA ("Ecstasy") can lead to acute serotonin syndrome.
- **OTC Medications and Herbal Supplements:** Keep an eye out for over-the-counter drugs like dextromethorphan and herbal supplements such as St. John's Wort.
- **Other Medications:** Some antipsychotics (e.g., risperidone), antiemetics (e.g., ondansetron), and even certain antibiotics (e.g., linezolid) can contribute.

Diagnosis:

Suspect serotonin syndrome if a patient on a serotonergic medication exhibits any of the following:

- **Spontaneous clonus:** Rhythmic muscle contractions and relaxations occurring spontaneously without any provocation. This is a strong clue pointing towards serotonin syndrome. It's most easily observed at the ankle but can be present in other muscle groups.
- **Inducible clonus:** Like spontaneous clonus but occurs upon stimulation, like suddenly dorsiflexing the foot.
- **Ocular clonus:** Rhythmic, involuntary oscillations of the eyes.
- **Elevated body temperature**
- **Autonomic nervous system overactivity:** tachycardia, hypertension, diaphoresis, tachypnea
- **Hyperreflexia**
- **Agitation**

Differential Diagnosis

- **Neuroleptic Malignant Syndrome (NMS):** Often mistaken for serotonin syndrome, NMS typically features "lead-pipe" rigidity rather than hyperreflexia.
- **Anticholinergic Toxicity:** Similar in presentation to serotonin syndrome but generally lacks neuromuscular symptoms like clonus.
- **Sepsis and other Systemic Infections:** Fever and altered mental status in these conditions can be misleading, but lab findings and clinical presentation help distinguish these scenarios.

Laboratory Work-up

Although there is no definitive laboratory test to diagnose serotonin syndrome, certain evaluations help in ruling out other conditions and assessing the severity of symptoms. These include:

- Complete Blood Count (CBC): to explore infectious etiologies.
- Serum Electrolytes: to evaluate for electrolyte imbalances, like hyperkalemia, that can happen secondary to rhabdomyolysis (the breakdown of muscle tissue).
- Renal and Liver Function Tests: to assess for serotonin syndrome-induced organ damage.
- Creatine Kinase Levels: To evaluate for rhabdomyolysis.
- Blood Cultures and Lumbar Puncture: To exclude infectious etiologies

Pathophysiology

Elevated levels of serotonin in the central and peripheral nervous system precipitate the syndrome.

Treatment

- Discontinue all serotonergic medications immediately
- Supportive Care:
 - Administer intravenous fluids
 - Provide oxygen
 - Control agitation with benzodiazepines
- Temperature Control: Reducing body temperature is critical. Hyperthermia can lead to multi-organ failure and even death.
 - Use physical cooling methods like cooling blankets and cold water immersion.
 - Antipyretics are ineffective for serotonin syndrome.
- Prescribe cyproheptadine, an H1-antagonist with antiserotonergic properties, although evidence supporting its effectiveness is limited.
 - Initial dose is 8-12 mg administered orally, followed by 2 mg q2 hours or 8 mg q6 hrs as needed.
- ICU Admission
 - Severe cases necessitate admission to an intensive care unit