ToxTalks:

A Bulletin for Healthcare Professionals Who Manage Poisoned Patients

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Serotonin Neurotoxicity

Serotonin neurotoxicity, also known as serotonin syndrome, represents a range of clinical manifestations due to increased serotonin activity in the central nervous system. It is a spectrum disorder, with signs and symptoms ranging from mild to life-threatening.

Clinical Spectrum

The milder signs of serotonin neurotoxicity typically include anxiety, tremors, tachycardia, hyperreflexia, and clonus. While clonus can occasionally be seen in other conditions, it is highly specific to serotonin neurotoxicity. It is noteworthy that patients taking therapeutic doses of SSRIs may exhibit 1 or 2 beats of ankle clonus without having serotonin syndrome. The most severe signs include seizures, muscle rigidity, hyperthermia, and acidosis, warranting immediate and aggressive management.

Common Medications Leading to Serotonin Neurotoxicity

Serotonin neurotoxicity is precipitated by pharmacological agents. Common culprits include:

Selective Serotonin Reuptake Inhibitors (SSRIs)
Serotonin-Norepinephrine Reuptake Inhibitors (SNRIs)
Monoamine Oxidase Inhibitors (MAOIs)
Certain antibiotics such as linezolid
Cyclic antidepressants
Certain analgesics like fentanyl, tramadol and meperidine
Over-the-counter drugs such a dextromethorphan
Illicit substances such as “Molly” (MDMA) and LSD

Fentanyl is particularly notable as an iatrogenic cause of serotonin neurotoxicity. Fentanyl infusions for sedation should be avoided in patients on SSRIs or in cases of overdose of unknown substances, due to its potential to exacerbate serotonin toxicity.

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Management Strategies

The first line of treatment for serotonin neurotoxicity involves benzodiazepines and other GABA agonists. These are used to manage autonomic instability, increased muscle tone, and seizures. The effectiveness of benzodiazepines in controlling agitation and muscle rigidity is well-documented, making them a cornerstone in the management of serotonin syndrome. Dexmedetomidine, an alpha-2 agonist, can be used as an adjunct.

Cyproheptadine, an antagonist at the 5-HT2A serotonin receptor, is often taught as a potential antidote due to its mechanism of action. However, its use in clinical practice is limited. This limitation is due to several factors, including its anticholinergic side effects, limited efficacy, oral administration route, and the effectiveness of other supportive measures. Instead, emphasis is placed on discontinuing the offending agent and providing supportive care, including fluid resuscitation, GABA agonists, cooling measures for hyperthermia, and seizure management. In some cases, patients will require intubation and even paralysis to facilitate control of spontaneous clonus and increased muscle tone.

Conclusion

Understanding the spectrum of serotonin neurotoxicity is crucial for timely diagnosis and management. While there are specific pharmacological interventions, the mainstay of treatment lies in supportive care and the use of benzodiazepines for symptomatic control. Awareness of medications that can precipitate this condition, especially in the context of polypharmacy, is essential for prevention and early intervention.

For any further assistance or to discuss complex cases of serotonin neurotoxicity, healthcare providers are encouraged to contact the Blue Ridge Poison Center at 1-800-222-1222. Healthcare providers may call the dedicated HCP line: 1-800-451-1428.