

Serotonin Syndrome



Overview:

If you are wondering about the serotonin syndrome, it probably means that you or someone you know is taking a medication that could cause this syndrome.

Serotonin is an important chemical in the blood, gastrointestinal tract, and brain. It directly affects sleep, appetite, mood, learning, sex, and body temperature.

The most likely cause of the serotonin syndrome is an interaction between two medications, both of which

have potent effects on serotonin in the brain. It can sometimes result from overdoses of single medications that affect brain serotonin. Taking a single medication that affects serotonin at a regular dose is an exceptionally rare¹ cause of serotonin syndrome.

The serotonin syndrome varies from being very mild to potentially fatal. The seriousness of the syndrome primarily depends on which medications are being combined. This can lead to confusion and inconsistent

advice from health professionals. Some warn never to combine 2 medications with potent effects on brain serotonin while others allow for many of these combinations and reserve this warning for only the most concerning medication combinations.

You should ask your physician or pharmacist if the combination of medications that you are concerned about is considered a “low risk” or “high risk” combination.

Signs & symptoms:

The signs & symptoms of a serotonin syndrome occur quickly (minutes to hours) after ingesting the medications at fault. Severity ranges from mild to severe. The person experiencing the syndrome may be very confused and unable to understand or tell what is happening to them. A severe serotonin syndrome is a potentially fatal medical emergency. Immediate treatment is essential.

Mild

Rapid onset of:

- jitteriness, restlessness, or anxiety
- irritability, feeling on edge
- tremor
- diarrhea
- mild shivering
- mild confusion
- difficulty communicating

Severe

Rapid onset of:

- high fever
- sweating
- severe shivering
- confusion
- agitation
- incoordination
- muscle twitching, contractions, and spasms of the legs, feet, or eyes
- muscle stiffness
- racing heart rate
- high blood pressure
- seizures
- dilated pupils

Having only one of these signs or symptoms does not indicate presence of the serotonin syndrome. Several must occur at the same time.

Medicines that can cause the serotonin syndrome

Combining 2 medications (but not more than 2) in column B usually causes no problems or, very unusually², results in a milder form of serotonin syndrome. Severe side effects are very rarely³ associated with medications in column B, whether taken alone or when combining 2 of them. **Do not** combine medications in column A with each other or with medications in column B due to the risk of a severe serotonin syndrome.

Column A	Column B
Monoamine oxidase inhibitors Isocarboxazid (Marplan) Linezolid (Zyvox) Methylene blue Moclobemide (Manerix) Phenelzine (Nardil) Selegiline (Deprenyl, Emsam) Tranlycypromine (Parnate)	Antidepressants: Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline Desvenlafaxine, duloxetine, venlafaxine Mirtazapine, trazodone Tricyclic antidepressants (especially clomipramine, imipramine) Narcotics, anti-migraine, & other pain medications: Fentanyl, meperidine, methadone, pentazocine, propoxyphene, tramadol ⁴ , triptans (sumatriptan, etc.) Cough suppressants: Dextromethorphan (“DM”) Natural health products: St. John’s wort, L-tryptophan Street drugs: Cocaine, Ecstasy (MDMA) Miscellaneous: Amphetamine, buspirone, dexfenfluramine, lithium, metoclopramide, sibutramine

**Strictly avoid:
Column A + Column A
or
Column A + Column B**

¹ “Exceptionally rare” means less than 1 in 10,000.

² “Very unusually” indicates less than 1 in 100. ³ “Very rarely” indicates less than 1 in 10,000. ⁴ There are other concerns with tramadol; it should not be combined with column A medications and several in column B.

What to do

When a concerning combination is identified:

The most important step is to avoid a serious serotonin syndrome by making sure your physician(s) and pharmacist(s) know ALL the medications you take (non-prescription, prescription, natural medicines, street drugs). If they identify 2 or more medications that may cause a serious serotonin syndrome when combined you must not take these medications. Your physician(s) and pharmacist(s) can help to find a safer combination. If they find 2 medications that are thought to cause a milder serotonin syndrome on occasion then you have 2 options: i) to discuss options for alternatives that do not have the same risk; or, if this is not a good option, ii) to create a plan for monitoring for signs and symptoms of serotonin syndrome.

When signs & symptoms are observed:

Based on the signs & symptoms, if you suspect a mild case of serotonin syndrome contact a physician or pharmacist immediately. You will need their help in finding safer medications that do not cause this problem and advice as to whether a visit to the closest Emergency Department is needed.

If you suspect that someone you know is experiencing a serious case of serotonin syndrome you must consider it a medical emergency. Contact 911 or get the person to a hospital Emergency Department immediately.

After effects

Mild to moderate cases generally resolve without any after effects within 1-3 days (depending on the properties of the medications involved) of stopping the medicines involved. Serious cases often require several days of intensive care in a hospital.

Suggested resources for patients and clinicians

Free

Mayo Clinic: Serotonin syndrome

<http://www.mayoclinic.com/health/serotonin-syndrome/DS00860>

Medline Plus: Serotonin syndrome

<http://www.nlm.nih.gov/medlineplus/ency/article/007272.htm>

Patient.co.uk: Serotonin syndrome

<http://www.patient.co.uk/doctor/Serotonin-Syndrome.htm>

PsychoTropical Research: Serotonin Toxicity/Serotonin Syndrome

www.psychotropic.com/1_st_intro.shtml

Arora B, Kannikeswaran N. The serotonin syndrome—the need for physician's awareness. *Int J Emerg Med* 2010; 3(4): 373-7.

<http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3047867/?tool=pubmed>

Not free

Boyer EW, Shannon M. The serotonin syndrome. *N Engl J Med*. 2005 Mar 17; 352(11): 1112-20.



What you need to know about your medications
and the

Serotonin Syndrome

Clinic/Pharmacy Information: