

Serotonin Syndrome

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THE STORY IN ONE SENTENCE

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“Too much serotonin makes your heart race, your muscles shake and lock up, and your thinking confused and wild.”

Normal anatomy — the body's job

Normally the brain keeps serotonin—a messenger chemical—at a steady, balanced level so mood stays even, thinking stays clear, body temperature stays normal, and muscles move smoothly without shaking or locking up.

BODY'S JOB

Serotonin is made by neurons (nerve cells) in the brainstem (the base of your brain where it meets your spine). Those neurons send serotonin up to the cortex (the thinking part of your brain) to help you focus and stay calm, down to the spinal cord to control muscle tone and reflexes, and out to the hypothalamus (the brain's thermostat) to keep your body temperature in the safe range of about 98–99°F. After serotonin delivers its message, pumps on the nerve cell suck it back in and break it down so the signal stops cleanly.

1. Serotonin is released from brainstem neurons when you need alertness or mood support.
2. It travels to receptors (docking spots) all over the brain, spinal cord, and gut to deliver its calming, focusing message.
3. Pumps called SERT (serotonin transporters) pull leftover serotonin back into the nerve cell.
4. Enzymes (especially MAO, monoamine oxidase) inside the cell break down the serotonin so the signal ends.
5. This cycle keeps serotonin rising and falling gently, never flooding the system.

What breaks

When you take two drugs that both raise serotonin—like an SSRI (which blocks the pump that sucks serotonin back in) plus an MAOI (which blocks the enzyme that breaks serotonin down)—the serotonin piles up with nowhere to go, flooding every receptor and locking the brain's alert and movement circuits wide open.

CLINICAL TERM

Excessive serotonergic agonism at central and peripheral 5-HT_{1a} and 5-HT_{2a} receptors caused by additive or synergistic drug effects (SSRI, SNRI, MAOI, tramadol, linezolid, methylene blue, dextromethorphan, MDMA, or St. John's wort) results in hyperactivation of the sympathetic nervous system, neuromuscular excitation, and altered mental status.

How the body compensates

At first your body tries to cope with the serotonin flood by sweating to cool down, trembling to burn off the overactive signals, and pumping adrenaline to keep blood pressure stable—but these workarounds only mask the danger for a short window before the system breaks.

1. {'what': 'Sweating and skin flushing', 'why': 'The hypothalamus (brain's thermostat) senses rising core temperature from muscle overactivity and opens skin blood vessels and sweat glands to dump heat—but if serotonin keeps flooding in, sweating cannot keep up and fever spikes above 104°F (40°C).'} }
2. {'what': 'Tremor and restlessness', 'why': 'Spinal motor neurons fire too fast, causing fine trembling and an urge to move constantly—your muscles are trying to discharge the excess nerve signals, but this only generates more heat and lactic acid.'} }
3. {'what': 'A fast heart rate (Tachycardia) (fast heart) and high blood pressure', 'why': 'The sympathetic nervous system releases norepinephrine and adrenaline to try to stabilize circulation against the chaos—but this drives heart rate above 100-120 and blood pressure dangerously high, straining the heart.'} }
4. {'what': 'Agitation and confusion', 'why': 'The cortex (thinking brain) is flooded with serotonin signals it cannot process, so attention fragments, thinking becomes muddled, and the person may hallucinate or become combative as the brain tries to make sense of the overload.'} }
5. {'what': 'Dilated pupils (Mydriasis) (wide pupils)', 'why': 'Excess serotonin stimulates the sympathetic nerves to the iris (the colored ring in your eye), forcing the pupils to dilate (open wide) as if you are in danger—even in bright light.'} }

Domino effect

1. Two serotonin-boosting drugs are taken together (or one drug is started before the other has cleared from the body). — Each drug blocks a different step in serotonin cleanup—one stops the reuptake pump (SERT), the other stops the breakdown enzyme (MAO)—so serotonin cannot escape the synapse and floods every serotonin receptor in the brain, spinal cord, and gut.
2. Within 6–24 hours, serotonin receptors in the brainstem and spinal cord lock into continuous firing. — The raphe nuclei (serotonin-making cells in the brainstem) and the spinal interneurons (which control muscle tone) are overwhelmed by serotonin, so they send non-stop excitatory signals down to muscles and up to the cortex, unable to reset.
3. The sympathetic nervous system (fight-or-flight) turns on full blast: heart rate jumps to 100–140, blood pressure climbs, pupils dilate, and sweating pours out. — Serotonin overstimulates 5-HT_{2a} receptors in the hypothalamus and brainstem, which command the adrenal glands to dump adrenaline and norepinephrine into the blood—your body thinks it is in mortal danger and cannot turn off the alarm.
4. Muscles begin to shake, jerk rhythmically (clonus), and stiffen, especially in the legs; reflexes become hyper-jumpy. — Spinal motor neurons, flooded with serotonin, fire too fast and cannot relax, so muscles contract repeatedly and rigidly—this uncontrolled muscle work generates huge amounts of heat and breaks down muscle fibers, releasing myoglobin and creatine kinase into the blood.
5. Core body temperature spikes above 104°F (40°C), and the person becomes confused, agitated, or delirious. — The hypothalamus (brain's thermostat) loses control as serotonin jams its temperature sensors; meanwhile the cortex (thinking brain) cannot filter the flood of serotonin signals, so thinking fractures into confusion, hallucinations, or combative agitation.
6. Muscle breakdown (rhabdomyolysis) clogs the kidneys with myoglobin, lactic acid builds up from overworked muscles, and clotting proteins activate (disseminated intravascular coagulation, DIC). — Destroyed muscle fibers dump myoglobin (a large protein) into the bloodstream; the kidneys try to filter it but the tubes clog, leading to acute kidney injury. High fever and too much acid in the blood (acidosis) (too much acid in the blood) damage blood vessel linings, triggering runaway clotting that uses up all the clotting factors and causes bleeding.
7. Without rapid cooling, sedation, and stopping all serotonergic drugs, multi-organ failure (kidneys, liver, heart, brain) occurs within 24–48 hours. — Sustained hyperthermia (high fever) denatures (cooks) proteins in every cell, blood clots choke off oxygen to organs, and too much acid in the blood (acidosis) poisons cellular enzymes—once multiple organs fail, the mortality rate climbs above 10–15% even with intensive care.

8. If the serotonergic drugs are stopped immediately, the patient is cooled (ice, fans, sometimes paralytics and intubation), and cyproheptadine (a serotonin blocker) is given, serotonin levels drop within hours and most symptoms resolve in 24–72 hours with full recovery. — Serotonin has a short half-life (it breaks down quickly once new drug dosing stops), so halting the flood lets the reuptake pumps and MAO enzymes catch up and clear the excess—cooling and muscle relaxation prevent irreversible organ damage while the brain resets.

Symptoms · what the patient feels, and why

- Agitation or restlessness: Too much serotonin (a brain messenger that affects mood and movement) over-revs parts of the brain that control behavior and alertness, making you feel jumpy, on-edge, or unable to stay still.
- Fast heart rate (tachycardia): Excess serotonin spills over onto the sympathetic nervous system (the body's gas pedal), speeding up the heart as if you're in danger even when you're not.
- Dilated pupils (mydriasis): The flood of serotonin pushes the sympathetic nervous system into overdrive, telling the muscles in the iris to pull the pupil wide open—like the body thinks it needs to see in the dark or prepare for a threat.
- Muscle twitching or jerking (myoclonus): Serotonin receptor 5-HT_{2A} (a docking site for serotonin on nerve cells) gets overstimulated in the spinal cord and brain stem, causing the muscles to fire off little jerks and twitches that you can't control.
- Rigid or stiff muscles (especially in the legs): Too much serotonin locks up the motor neurons (the nerve cells that tell muscles to move), making muscles clench tight—often worse in the lower body because those motor pathways run through the lumbar spinal cord where serotonin receptors are dense.
- Sweating more than usual (diaphoresis): The sympathetic nervous system, revved up by serotonin overload, orders sweat glands all over the body to open up—your body thinks it's overheating or under stress.
- Confusion or trouble thinking clearly: Excess serotonin floods the cerebral cortex (the outer thinking part of the brain), scrambling signals and making it hard to focus, remember, or make sense of things around you.
- High fever (hyperthermia): Severe serotonin overload disrupts the hypothalamus (the brain's thermostat) and cranks up muscle activity so much that the body generates more heat than it can shed—like an engine running too hot.
- Shivering or tremor: Serotonin overstimulates reflexes in the spinal cord that normally help you keep warm, so your muscles start shaking rapidly even if you're not cold.

- **Diarrhea:** About 95 percent of the body's serotonin sits in the gut, where it tells the intestines to squeeze and push. Too much serotonin makes the bowel speed up, flushing out watery stool.

Focused exam

- **Core body temperature $\geq 38.5^{\circ}\text{C}$ (101.3°F), often climbing fast:** Too much serotonin hijacks the hypothalamus (the brain's thermostat), making muscles fire nonstop and produce runaway heat. High fever in serotonin syndrome can trigger blood clots forming inside vessels (disseminated intravascular coagulation) and organs shutting down within hours.
- **Overactive reflexes (Hyperreflexia)** (reflexes jump too hard when you tap the tendon) and **rhythmic muscle jerking (clonus)** (the foot or knee bounces on its own after one tap): Excess serotonin floods receptors in the spinal cord, making nerves fire over and over without control. Rhythmic muscle jerking (Clonus)—especially in the ankles—is the single most specific sign that separates serotonin syndrome from other drug reactions and infections.
- **Muscle rigidity worse in the legs than the arms, plus tremor:** Serotonin overdrive hits the lower spinal cord harder, so the legs stiffen more. This lower-body pattern is the opposite of Parkinson rigidity (which spreads evenly) and helps confirm serotonin syndrome.
- **Agitation, confusion, and disorientation appearing suddenly** (within hours to 1 day, not slowly over weeks): Serotonin floods the prefrontal cortex (the front of the brain that organizes thoughts and controls impulses) and the limbic system (the emotion and alertness centers). Mental status change happening in the first 24 hours after starting or raising a serotonin drug is the key timing clue.
- **Blood pressure elevated, heart rate fast** (usually >100 beats per minute), and **pupils dilated** (wide open): Excess serotonin turns on the sympathetic nervous system (the body's gas pedal for fight-or-flight), releasing norepinephrine (the chemical that speeds the heart and squeezes blood vessels). These vital-sign changes mean the whole body is locked in overdrive.
- **Recent start of an SSRI, SNRI, MAOI, tramadol, linezolid, methylene blue, or MDMA within 1–2 weeks—or combining two serotonin drugs:** Serotonin syndrome does not happen spontaneously; it only appears when serotonin-boosting drugs stack up or when a single strong serotonin drug is started. Matching the timeline of symptoms to the drug timeline makes the diagnosis.

Diagnostics · every test answers a question

- **Creatine kinase (CK)** → Are the muscles breaking down from nonstop firing and heat?
- **Basic metabolic panel** (sodium, potassium, creatinine, bicarbonate) → Are the kidneys failing, and is the blood turning acidic from muscle breakdown?

- Complete blood count (CBC) with platelets → Is the blood clotting system breaking down from high heat and inflammation?
- Liver enzymes (AST, ALT) → Is the liver being damaged by high fever and poor blood flow?
- Urinalysis and urine myoglobin → Is muscle protein spilling into the urine and threatening the kidneys?
- Electrocardiogram (ECG) → Is the heart rhythm becoming unstable from the serotonin overdrive and electrolyte shifts?
- CT head (non-contrast) or lumbar puncture if diagnosis is uncertain → Could this be a brain bleed, stroke, or infection instead of serotonin syndrome?

Treatment logic

- Stop all serotonin-raising medicines immediately (SSRIs, SNRIs, MAOIs, tramadol, linezolid, methylene blue, MDMA, St. John's wort) → Removes the source driving serotonin levels too high, so the brain's serotonin receptors stop being overstimulated. This is the only way to stop the cascade at its root.
- Cool the body aggressively if temperature $\geq 39^{\circ}\text{C}$ (102.2°F): ice packs to the groin and armpits, cold IV saline, and cooling blankets → High fever itself damages brain cells, triggers blood clots inside vessels (DIC), and breaks down muscle (rhabdomyolysis). Bringing the temperature below 38.5°C protects organs and slows the runaway muscle firing that generates more heat.
- Give lorazepam 1–2 mg IV (or diazepam 5–10 mg IV) and repeat every 10–15 minutes until the person is calm and muscles relax → Benzodiazepines boost GABA (the brain's main calming signal), which quiets overexcited neurons in the cortex, limbic system, and spinal cord. This lowers agitation, reduces muscle rigidity, slows the heart rate, and brings down blood pressure.
- Give cyproheptadine 12 mg by mouth as the first dose, then 2 mg every 2 hours (maximum 32 mg in 24 hours) if symptoms persist → Cyproheptadine is a serotonin receptor antagonist (it blocks 5-HT_{1A} and 5-HT_{2A} receptors), directly stopping serotonin from activating nerve cells. It is the only drug that reverses the receptor-level cause of serotonin syndrome.
- Give IV fluids (normal saline) rapidly—start with 1–2 liters over the first hour, then continue at 200–300 mL/hour—to flush myoglobin out of the kidneys → Aggressive hydration dilutes the muscle protein (myoglobin) in the urine and keeps it from crystallizing and blocking kidney tubules. This prevents acute kidney injury when CK is elevated.

- Do NOT give antipsychotics (haloperidol, risperidone, olanzapine) because they block dopamine and can worsen rigidity and fever → Avoiding antipsychotics prevents serotonin syndrome from escalating into a neuroleptic malignant syndrome-like crisis (where muscle rigidity and fever spiral out of control and become lethal). Some antipsychotics also have mild serotonin effects that can add fuel to the fire.
- Move to the ICU if fever stays $\geq 39^{\circ}\text{C}$ after 1 hour of cooling, rigidity does not improve with benzodiazepines, heart rhythm becomes irregular, or confusion deepens → ICU monitoring allows minute-by-minute tracking of vital signs, rapid response to dangerous heart rhythms, and intubation with mechanical ventilation if muscles are so rigid the person cannot breathe safely. Paralytic drugs and deep sedation may be needed in the sickest cases to stop the muscle activity generating heat.

Medications

Stop all serotonin-boosting drugs immediately · First-line intervention (withdrawal of causative agents)

The body has too much serotonin (a brain messenger that controls mood, movement, and body heat) because of the medicines the person is taking. Stopping those drugs lets serotonin levels fall back to safe levels. Most people start feeling better within 24 hours after the last dose leaves the body.

1. You identify and stop every drug that raises serotonin: SSRIs (like sertraline, fluoxetine), SNRIs (like venlafaxine), MAOIs (like phenelzine), tramadol, ondansetron, linezolid, dextromethorphan, MDMA, and St. John's wort.
2. Once the drug is stopped, the body breaks down the leftover medicine over hours to days (depending on the drug's half-life).
3. As drug levels drop, serotonin levels in the brain and body fall back toward normal.
4. Symptoms like muscle jerking, fever, fast heart rate, confusion, and sweating begin to resolve—usually within 24 hours, but can take longer if the drug stays in the body a long time.

SAFETY WATCH

Never stop an MAOI and immediately start an SSRI or SNRI—you must wait at least 2 weeks (5 weeks for fluoxetine) to let the MAOI fully leave the body, or serotonin syndrome can come roaring back. · If the person was taking the drug for depression or pain, stopping it suddenly can cause withdrawal symptoms (anxiety, dizziness, flu-like aches)—but serotonin syndrome is life-threatening, so you stop the drug first and manage withdrawal separately. · Watch for return of the original psychiatric or pain condition once the drug is stopped; plan safe follow-up care and alternative treatment.

Aggressive cooling (ice packs, cooling blankets, cold IV fluids) · Supportive care (temperature control)

Serotonin syndrome causes dangerously high body temperature (hyperthermia) because too much serotonin makes muscles contract rapidly (like shivering on overdrive) and disrupts the hypothalamus (the brain's thermostat). Cooling from the outside and inside lowers core body temperature and prevents organ damage from the heat.

1. You apply ice packs to the neck, armpits, and groin (areas where big blood vessels run close to the skin).
2. You use cooling blankets or misting fans to lower skin temperature.
3. You give cold IV saline (salt water) to cool the blood directly as it flows through the body.
4. As core temperature drops below 39°C (102.2°F), the risk of seizures, kidney failure, and muscle breakdown (rhabdomyolysis) falls.

SAFETY WATCH

Monitor core temperature (rectal or esophageal probe) every 15–30 minutes—cooling too fast can cause shivering, which generates MORE heat and makes things worse. · Stop cooling once temperature reaches 38–38.5°C (100.4–101.3°F) to avoid overcooling (hypothermia). · Watch for rhabdomyolysis (muscle breakdown that releases toxins into the blood)—check creatine kinase (CK) levels and urine color (dark brown means muscle protein is spilling into urine and can clog the kidneys).

Lorazepam or diazepam · Benzodiazepine (sedative and muscle relaxant)

Lorazepam and diazepam boost GABA (the brain's main calming signal) in the brain and spinal cord. This calms the overactive nerves that are firing too fast because of excess serotonin, relaxes stiff muscles, lowers agitation, and helps control fever by reducing muscle activity.

1. You give lorazepam 1–2 mg IV every 5–10 minutes or diazepam 5–10 mg IV every 5–10 minutes until the person is calm and muscles are loose.
2. The benzodiazepine locks onto GABA-A receptors and makes them more sensitive to GABA.
3. GABA then opens chloride channels in nerve cells, which slows down electrical firing.
4. Muscle stiffness, tremor, and agitation decrease; heart rate and blood pressure drop; fever often improves because muscles stop generating excess heat.

SAFETY WATCH

Watch breathing closely—high or repeated doses can slow or stop breathing, especially if the person already took opioids or alcohol; be ready to support breathing with a bag-mask or ventilator. · Give doses slowly and titrate to effect (calm but still awake and breathing well); do NOT give a fixed large dose all at once. · Lorazepam is preferred in liver disease because the liver does not need to process it before it works; diazepam lasts longer and is better for prolonged agitation but requires a healthy liver.

Cyproheptadine · Serotonin receptor antagonist (5-HT_{2A} blocker) and antihistamine

Cyproheptadine blocks serotonin from locking onto 5-HT_{2A} receptors (the serotonin docking sites that drive fever, muscle stiffness, confusion, and agitation when overstimulated). By blocking these receptors, it directly reverses the core problem in serotonin syndrome—too much serotonin activity.

1. You give an initial dose of 12 mg by mouth (crushed and given through a feeding tube if the person cannot swallow safely).
2. Cyproheptadine molecules travel to the brain and spinal cord and sit on 5-HT_{2A} receptors, blocking serotonin from attaching.
3. With receptors blocked, serotonin cannot trigger the cascade that causes fever, muscle rigidity, tremor, and altered mental status.
4. If symptoms persist after 2 hours, you give 2 mg every 2 hours (maximum 32 mg in 24 hours) until symptoms resolve.

SAFETY WATCH

Cyproheptadine causes heavy sedation (extreme sleepiness)—monitor breathing and be ready to support the airway if the person becomes too drowsy to protect it. · It can cause dry mouth, blurry vision, and urinary retention (trouble peeing) because it also blocks acetylcholine receptors (anticholinergic effect). · No IV form exists—if the person cannot take pills or liquid by mouth, crush the tablet and give it through a nasogastric or orogastric tube. · Do NOT confuse serotonin syndrome with neuroleptic malignant syndrome (NMS)—cyproheptadine helps serotonin syndrome but does NOT help NMS.

AVOID antipsychotic drugs (e.g., haloperidol, olanzapine, chlorpromazine) · Contraindicated in serotonin syndrome

Antipsychotic drugs block dopamine receptors (the brain's movement and reward control system) and can also block receptors that help cool the body. In serotonin syndrome, giving an antipsychotic worsens muscle stiffness, raises body temperature even higher, and can trigger

neuroleptic malignant syndrome (NMS)—a similar but distinct life-threatening reaction. They do NOT help serotonin syndrome and actively make it more dangerous.

1. If mistakenly given, the antipsychotic blocks dopamine receptors in the basal ganglia (the brain's movement control center), worsening muscle rigidity.
2. It also disrupts the hypothalamus (the brain's thermostat), making it even harder for the body to cool down.
3. Fever climbs, muscles stiffen further, and the person may develop NMS on top of serotonin syndrome—a deadly combination.

SAFETY WATCH

NEVER give antipsychotics (especially haloperidol, droperidol, chlorpromazine, or olanzapine) if you suspect serotonin syndrome—use benzodiazepines instead for agitation.

· If an antipsychotic was already given by mistake, stop it immediately and monitor closely for worsening fever and rigidity. · Learn to distinguish serotonin syndrome (rapid onset, overactive reflexes (hyperreflexia), tremor, dilated pupils, often diarrhea) from NMS (slow onset over days, lead-pipe rigidity, normal or small pupils, no diarrhea)—treatment differs.

Intubation, mechanical ventilation, and ICU-level supportive care · Advanced life support

In severe serotonin syndrome, the person may become so confused or sedated (from benzodiazepines and cyproheptadine) that they cannot protect their airway, or muscles may be so rigid that breathing becomes too hard. Intubation (placing a breathing tube) and mechanical ventilation (a machine that breathes for the person) keep oxygen flowing to the brain and organs while the serotonin clears. ICU monitoring catches and treats complications like seizures, heart rhythm problems, kidney failure, and dangerously low blood pressure.

1. You move the person to the ICU if they have severe hyperthermia ($>41^{\circ}\text{C}$ or 105.8°F), altered mental status (confusion, unresponsiveness), severe muscle rigidity, unstable vital signs, or rhabdomyolysis.
2. You give sedation (often propofol or more benzodiazepines) and insert a breathing tube to protect the airway and ensure oxygen delivery.
3. The ventilator takes over breathing while you continue cooling, give cyproheptadine through a feeding tube, and give IV fluids to support blood pressure and flush toxins from muscle breakdown through the kidneys.
4. You check labs every 4–6 hours: creatine kinase (muscle breakdown marker), creatinine and BUN (kidney function), potassium and calcium (can spike dangerously when muscles break down), lactate (sign of poor oxygen delivery), and complete blood count.

SAFETY WATCH

Watch for ventilator-associated pneumonia (lung infection from the breathing tube)—keep the head of the bed elevated and suction secretions regularly. · Monitor for acute kidney injury from rhabdomyolysis—if creatine kinase climbs above 5,000–10,000 U/L or urine turns dark brown, give aggressive IV fluids (often 200–300 mL/hour or more) to flush myoglobin (muscle protein) out before it clogs the kidney's filters. · Watch for compartment syndrome (swelling inside muscle compartments that cuts off blood flow)—if limbs become swollen, tight, and painful, measure compartment pressures and consider emergency fasciotomy (surgical release of pressure). · Track for disseminated intravascular coagulation (DIC)—severe cases can trigger widespread clotting and bleeding; check PT, PTT, fibrinogen, and D-dimer if bleeding or bruising appears.

Red flags

- High fever above 104°F (40°C)—this means the body is overheating dangerously and can damage organs.
- Seizures (sudden shaking you can't stop)—the brain is firing out of control.
- Very stiff muscles that won't bend (severe rigidity)—this can break down muscle tissue and poison the kidneys.
- Fast, confused thinking that gets worse quickly—sign the brain is overwhelmed.
- Low blood pressure or trouble staying awake—means the body is starting to shut down.

Nursing priorities

1. Stop all serotonin-raising medicines immediately and hold them until a doctor reviews the case. — Serotonin syndrome is caused by too much serotonin flooding the brain, so the first step is to remove the source. Continuing SSRIs, MAOIs, tramadol, linezolid, or other culprits will keep poisoning the nervous system and make symptoms worse.
2. Check temperature every 15 minutes, and if it is 102.2°F (39°C) or higher, start aggressive cooling right away with ice packs to the groin and armpits, cold IV saline, and a cooling blanket. — High body temperature (hyperthermia) damages organs, breaks down muscle tissue (rhabdomyolysis), and can cause kidney failure and death. Cooling the body quickly lowers the temperature and prevents permanent harm.
3. Give lorazepam (Ativan) 1 to 2 mg IV or diazepam (Valium) 5 to 10 mg IV, and repeat every 10 to 15 minutes until the patient is calm and muscles relax. — Benzodiazepines calm the overactive nervous system, stop seizures, reduce muscle rigidity, and lower heart rate and blood pressure. Relaxing the muscles also reduces heat production and prevents rhabdomyolysis (muscle breakdown that poisons the kidneys).

4. Monitor heart rate, blood pressure, and oxygen levels continuously, and place the patient on a cardiac monitor. — Serotonin syndrome causes a fast heart rate (tachycardia) (fast heart rate), high or dangerously low blood pressure, and arrhythmias (irregular heartbeats). Continuous monitoring catches life-threatening changes early so the team can treat them before the heart or brain fails.
5. If the patient is confused, agitated, or having seizures, protect the airway and keep suction and intubation equipment at the bedside. — Severe serotonin syndrome causes altered mental status and seizures, which can block the airway or cause the patient to vomit and breathe it into the lungs (aspiration). Being ready to intubate (place a breathing tube) protects the airway and keeps oxygen flowing to the brain.
6. Draw blood to check creatine kinase (CK, a marker of muscle breakdown), kidney function (creatinine and BUN), liver enzymes, and electrolytes, and send a urine sample to check for myoglobin. — Severe muscle rigidity breaks down muscle tissue (rhabdomyolysis), releasing toxins like myoglobin and creatine kinase into the blood. Myoglobin clogs the kidneys and causes acute kidney injury. Early detection allows the team to give IV fluids to flush the kidneys and prevent permanent damage.
7. Start two large-bore IV lines and give normal saline at 200 to 300 mL per hour if the patient is sweating heavily, has a fever, or has signs of muscle breakdown. — Sweating (diaphoresis) and high fever cause dehydration. Aggressive IV fluids replace lost water, support blood pressure, and help the kidneys flush out muscle toxins (myoglobin) to prevent kidney failure.
8. If agitation, fever, and muscle rigidity do not improve with benzodiazepines and cooling, prepare to give cyproheptadine (Periactin) 12 mg by mouth or feeding tube, then 2 mg every 2 hours, as ordered by the doctor. — Cyproheptadine is an antihistamine that blocks serotonin receptors in the brain and reverses serotonin syndrome. It is used in moderate to severe cases when stopping the drugs and giving benzodiazepines are not enough to control symptoms.

Sources

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