SEROTONIN SYNDROME

HOW DOES SEROTONIN WORK?

• Serotonin (5-hydroxytryptamine) is a neurotransmitter that is synthesized from the amino acid tryptophan in serotonergic mid-brain and medulla cells.
• Serotonin acts at least at 14 receptors subtypes in the CNS (mostly) and periphery.
  • CNS activity include cerebral vasoconstriction, modulating mood, anxiety, aggression, sleep
  • Peripheral activity includes increased GI motility, increased vasodilatation and cardiovascular
tropetry and chronotropy.

WHAT IS THE SEROTONIN SYNDROME? Hyperstimulation of serotonin receptors

• Typical clinical presentation of fever, altered mental status, neuromuscular hyperactivity and autonomic dysfunction
  • AMS ranging from agitation, confusion, delirium, drowsy and coma
  • N-M activity ranging from restlessness, tremor, myoclonus and hyporeflexia
  • AD ranging from labile blood pressure, tachycardia, tachypnea, mydriasis, nausea, vomiting, tearing, salivation, abdominal pain and diarrhea
• Onset usually hours after increase in dose or addition of another medication that increases serotonin levels. Clinical course without complications after stopping offending drug s is 24-48 hours. Associated with 10-20% mortality in severe cases.
• Complications include hyperthermia, lactic acidosis, rhabdomyolsis, renal failure, liver failure, ARDS and DIC.

WHAT MEDS PREDISPOSE YOU TO THIS? Usually combinations of the following

• Increased presynaptic release due to speed, cocaine, MDMA, codeine, reserpine and MAOI’s
• Decreased reuptake due to SSRI’s, TCA’s, MAOI’s, ergot derivatives, sumitriptan and ergots.
• Decreased metabolism due to cocaine and MAOI’s
• Post synaptic serotonin agonist such as bromocriptine, buspar, trazadone, lithium, levodopa
• Others such as bupropion, remeron, effexor, atypical antipsychotics

WHAT ELSE IS ON THE DDX? Remember this is an uncommon condition.

• Other hyperthermic syndromes (increased body temp with normal hypothalamic thermoregulator set point, overwhelming the body’s inability to dissipate heat)
  • Heat stroke (exertional and non-exertional)
  • Drug induced (speed, cocaine, MAOI’s, anticholinergics, TCA’s,
  • Neuroleptic malignant syndrome
  • Malignant hyperthermia
  • Endocrinopathies (thyrotoxicosis, pheochromocytoma)
• Febrile illnesses (increased body temp due to an increase in the hypothalamic set point by pyrogens)
  • CNS infection, bleed or trauma
  • Infection (systemic or local)
  • Inflammatory conditions
  • Neoplasms

How to distinguish from NMS?

• NMS is an idiosyncratic drug reaction to antipsychotic medications resulting in DA depletion.
  • Clinically, muscle rigidity (lead pipe) more than muscular hyperactivity, associated with dyskinesia, dystonia, dysphagia and incontinence, lasts days to weeks.
• NMS is treated with dantrolene and bromocriptine.
WHAT TO DO?
• Call POISON control!
• GI decontamination with charcoal
• Cooling blankets for hyperthermia (NSAIDS and tylenol will not work)
• BDZ for agitation and muscle hyperactivity (DO NOT use haldol)
• Serotonin receptor antagonist (many case reports, no trials)
  • Ciproheptadine (periactin) antihistamine, 4-8 mg PO Q 2-4 hrs (NTE 32 mg/24hr)
  • Chlompromazine (thorazine) D2 antagonist, 50-100 mg IV/IM, (DO NOT use if suspect NMS)
• Supportive/ vigilance for end organ dysfunction.
• If not clinically improving within 24 hours, look for other DX!