The Serotonin Syndrome


LLSA Review
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Serotonin Syndrome

- Predictable consequence of excess 5HT
- Syndrome can range from mild to lethal
  - Mild – moderate cases easy to treat
  - Avoid adding other proserotonergic drugs
  - Most famous case – Libby Zion
    - Severe unrecognized toxicity and death
    - 93 Deaths reported in 2002
Serotonin Syndrome

- Many drugs/combinations associated with syndrome
  - Non-selective/irreversible MAOIs
    - Subtype A
  - Meperidine, dextromethorphan, SSRIs, ecstasy
  - Combinations of above are associated with severe toxicity

- Clinical Triad -
  - Mental status changes
  - Autonomic hyperactivity
  - Neuromuscular disorders
Clinical Features

- Serotonergic Agent administered in past 5 weeks
- Fast Onset, increased bowel sounds
- Tremor, hyperreflexia
- Spontaneous clonus
- Muscle rigidity, T > 38, + ocular or inducible clonus
- Clonus + agitation or diaphoresis
Clinical Features

- **Mild**
  - Tachycardia, mydriasis, shivering
  - Myoclonus, hyperreflexia

- **Moderate**
  - Hypertension, hyperthermia (40 C)
  - Clonus - > LE than UE
  - Mild agitation, hypervigilance, neck extension
Clinical Features

- Severe
  - Hyperpyrexia (41.1°C)
  - Shock
  - Agitated delirium
  - Rigidity
  - Seizures
Laboratory Features

- Metabolic Acidosis
- Rhabdomyolysis
- Transaminitis
- DIC
- Renal Failure
Pathophysiology

- Serotonin important in wakefulness, thermoregulation, mood, motor tone, vascular tone and GI motility
- Excess serotonin = Agonism at 5-HT\textsubscript{2A} receptors appear to be most important in syndrome
- 5HT\textsubscript{1A} and NE may also play critical role
Differential Dx

- Anticholinergic
  - Dry skin
  - Normal muscle tone
  - Decreased bowel sounds
  - Urinary Retention
- Malignant Hyperthermia- inhalational anesthetics
  - Skin mottling
  - Rigidity
  - Hyporeflexia
- NMS– dopamine antagonists
  - Slow onset 1-3 days
  - Normal pupils
  - Bradyreflexia
  - Bradykinesia
Management

- Mild – Hyperreflexia + Tremor
  - Supportive care, BZD
- Moderate
  - Supportive Care, BZD
  - Cyproheptadine
    - 12 mg PO, 2 mg Q 2 hr if symptomatic
    - Maintenance 8 mg Q 6 hr
Management

□ Severe

■ Direct acting vasopressors
■ Benzodiazepines
■ Non-depolarizing paralytics
■ Consider IM chlorpromazine 50 -100 mg
Pitfalls

- Propanolol – $5\text{HT}_{1A}$ antagonist
  - May cause hypotension in unstable pts
- Bromocriptine
  - Implicated in SS – can worsen Sx
- Dantrolene
  - No effect on survival in animal models