

The Serotonin Syndrome

Boyer EW, Shannon M. *N Engl J Med* 2005;352:1112-20

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 (41.1C)
- 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_{2A} receptors appear to be most important in syndrome
- 5HT_{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 – 5HT_{1A} antagonist
 - May cause hypotension in unstable pts
- Bromocriptine
 - Implicated in SS – can worsen Sx
- Dantrolene
 - No effect on survival in animal models

