

# Side Effects of Psychiatric Medications and Serotonin Syndrome

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Benefis Health System

# Research Validated Factors for Suicide Risk Assessment [1]

- Males (4X as likely to complete, but F 4X as likely to attempt)
- Age: Men >45, women >55
- White males (but in younger ages NA also have high suicide rate)
- Divorced, decease spouse, or never married

# Suicide Risk Factors

- Chronic pain
- Poor Health/loss mobility/disfigurement
- Poor Social Support
- Doctors and Lawyers have high rates
- High social status (and a fall in social status)

# Suicide Risk Factors

- Hx of mental illness or psych hospitalization for any reason
  - Schizophrenia
  - Mood disorders
  - Personality disorders
  - Anxiety disorders (social phobia and panic disorder)
- Hx impulsivity
- Substance abuse

# Suicide Risk Factors

- Hx of a suicide attempt (especially in past 3 months)
- Fam Hx of suicide
- Hx of self-injurious behaviors (cutting)
- Access of Lethal Means
- Hopelessness, being a burden

# Protective Factors

- Employed
- Religious Aversion to Suicide
- Removal of lethal means
- Good social support/Sense of responsibility to others

## Medications to Reduce Suicide Risk, [2] [3]

- Lithium
- Clozaril

# Lithium <sup>[4]</sup>

- Areas with higher natural Li in water supply have lower suicide rates <sup>[2]</sup>
- Wt gain
- Sedation
- Tremor
- Polyuria (nephrogenic DI)



# Lithium [4]

- Hypothyroidism
- Acne/psoriasis/hair loss
- Seizures

# Lithium Toxicity <sup>[1]</sup>

- Caused by dehydration, overdose, low salt intake
- Also NSAIDs, ACE inhibitors, thiazide diuretics, metronidazole

# Lithium Toxicity <sup>[1]</sup>

- Vomiting, abd pain
- Ataxia, lethargy, AMS
- Clonus, fasciculations, hyper-reflexia
- coma

# Treatment <sup>[1]</sup>

- d/c Li
- Aggressive Hydration
- Trend Li level, electrolytes and renal function
- Dialysis for Li >4 or serious clinical symptoms

# Clozaril (Clozapine)

- Refractory schizophrenia
- Can decrease suicide risk in psychotic disorders
- LOTS of side effects

## Clozaril (Clozapine) [4]

- Trend CBC weekly for 6 mo; then biweekly for 6 months, then monthly thereafter
- Agranulocytosis

## Clozaril (Clozapine) [4]

- Anti H1: sedation
- Anti Alpha 1: dizziness/hypotension
- Anti M1: dry mouth, constipation, paralytic ileus
- Wt gain, DM, HLD

# Clozaril (Clozapine)

- Seizures
- Myocarditis



# Serotonin Syndrome <sup>[1]</sup>

- Potentially fatal
- History or recent med changes is key for distinguishing from other similar presentations

# Serotonin Syndrome <sup>[1]</sup>

- Symptoms in order of appearance:
  - Diarrhea
  - Restlessness
  - Agitation/hyperreflexia/clonus
  - Autonomic instability (usually HTN and tachycardia)

# Serotonin Syndrome [1]

- Diaphoresis
- Myoclonus/SZ/hyperthermia
- Delirium/coma/Status Epilepticus

# Serotonin Syndrome <sup>[1]</sup>

- possibly
  - Leukocytosis
  - Rhabdo
  - hyponatremia

# Serotonin Syndrome [1]

- Treatment:
  - Stop offending agents
  - Cooling
  - Cyproheptidine (serotonin receptor antagonist)
  - Benzos (for myoclonus or agitation)
  - Paralytic agents (fever in SS is muscular in origin)
  - IVF to support renal fxn

# Serotonin Syndrome

- MAOIs and other serotonergics
- Tramadol
- DXM
- Triptans
- Lithium
- Selegiline

# Trazodone [4]

- Priapism
- 1:8,000
- Can occur at any dose
- Intracavernosal epinephrine injection

# Clinical Question 1

- Which antidepressant has a specific FDA warning for QTc prolongation and specific max dosing guidelines in patients over age 60?
  - A: Sertraline (Zoloft)
  - B: Bupropion (Wellbutrin)
  - C: Mirtazapine (Remeron)
  - D: Citalopram (Celexa)
  - E: Duloxetine (Cymbalta)



# Citalopram (Celexa) [5]

- 2011FDA prescriber warnings for Citalopram for a max recommended dose of 40mg daily due to dose dependent risk of QTc prolongation and increased risk of fatal arrhythmia.
- “not recommended” for patients with a history of congenital long QT syndrome, bradycardia, hypomagnesemia, hypokalemia, recent MI and uncompensated heart failure.
- Max recommended dose of Citalopram in patients over age 60 (or with hepatic impairment) is 20mg daily.
- “Not recommended” in patients taking other QTc prolonging medications.

## Clinical Question 2

- A female patient of child bearing age has Bipolar Disorder. She is stable and regularly compliant with medications. She takes an oral contraceptive regularly but becomes pregnant anyway. Which psychiatric medication could explain this?
  - A: Valproic Acid (Depakote)
  - B: Carbamazepine (Tegretol)
  - C: Lithium
  - D: Lamotrigine (Lamictal)
  - E: Oxcarbazepine (Trileptal)

# Carbamazepine [1]

- Carbamazepine is a CYP 3A4 inducer.
- It can induce oral contraceptive metabolism leading to uncertain contraceptive efficacy.
- autoinduce can itself and potentially its clinical effect could wane over time requiring higher dosing.

# Neuroleptic Malignant Syndrome [6]

- Again med hx is important, recent antipsychotic changes/initiation
- More common with high potency older antipsychotics
- Can happen with newer atypical antipsychotics as well

# Neuroleptic Malignant Syndrome [6]

- Hyperthermia
- Muscle rigidity (“lead pipe”)
- AMS (mutism, stupor, agitation)
- Tachycardia
- HTN or hypotension

# Neuroleptic Malignant Syndrome [6]

- Tachypnea/hypoxia
- Diaphoresis
- Sialorrhea
- Tremor
- Incontinence
- CPK elevations/myoglobinuria

# Neuroleptic Malignant Syndrome [6]

- Leukocytosis
- Metabolic acidosis
- NI head imaging and CSF

# NMS Treatment <sup>[6]</sup>

- d/c dopamine blocker (metoclopramide)
- IVF hydration
- Cooling
- Anticoagulation
- Antihypertensives/pressors depending on presentation



# NMS Treatment [6]

- IV Ativan effective in 75% cases
  - Up to 20mg daily in divided doses
- If Ativan doesn't work, emergent ECT

# NMS Treatment [6]

- Less evidence for dantrolene or adding a dopamine agonist (amantadine, bromocriptine)
  - But evidence of decreasing mortality
- Levodopa/carbidopa

## Lamictal (lamotrigine) [4]

- Na channel blocker used as mood stabilizer
- 1:10 develop benign rash
- Rare Stevens-Johnson Syndrome

# Lamictal (lamotrigine) [4]



Fig. 9. Leukoplakia of mouth mucosa. Painful on the contact with the tongue.

# Lamictal (lamotrigine) [4]



# Lamictal (lamotrigine) [4]

- Benign rash:
  - Spotty/non-confluent
  - Nontender
  - NI lab tests
  - No systemic effects
  - Can decrease dose, wait one week, then resume titration in slower increments

# Lamictal (lamotrigine) [4]

- SJS:
  - Highest risk is first 6-8 week titration period
  - 1:3000 pts on lamictal

# Lamictal (lamotrigine) [4]

- Confluent, widespread, rapidly progressing
- Itching
- Tenderness; appears red and swollen
- Prominent neck/upper trunk
- Eyes/lips/mouth/GU
- Non-blanching



# Lamictal (lamotrigine) [4]

- SJS
  - Fever/flu like symptoms
  - Pharyngitis
  - Lymphadenopathy
  - Abnl CBC
  - Stop lamictal without a taper if any of aforementioned findings are present

# Lamictal (lamotrigine) [4]

- Minimizing risk (also minimize chance benign rash)
  - Slow titration
    - 2mg daily for 2 weeks, then 50mg daily for 2 weeks, then 100mg daily for one week, then up to 200mg daily
  - Stress importance of not missing doses and restarting at a high dose

# Common Antipsychotic Side Effects [6]

- Acute Dystonia
- Younger patients, soon after initiation
  - Less risk with atypical antipsychotics
  - Tx: Cogentin (benztropine) or Trihexyphenidyl (artane)
    - Anticholinergics- decrease excess acetylcholine caused by dopamine blockade
    - Can also treat tremor and bradykinesia
  - Benadryl

# Common Antipsychotic Side Effects [6]

- Akathisia

- Tx with propranolol (10-20mg up to QID) or klonopin/valium
- Propranolol can also treat tremor from Li

# Common Antipsychotic Side Effects [6]

- Parkinsonism
- Can Tx with Cogentin or Artane
- Can also use amantadine 100mg BID or TID

# Tardive Dyskinesia

- Usually after 6 months of treatment
- Less risk with atypical antipsychotics but can still happen
- Elderly higher risk, especially women
  - So don't over treat mild depression in elderly by adding abilify or rexulti

# Tardive Dyskinesia

- Can be permanent
- AIMS scale for monitoring for TD movements
- TX Valbenazine (Ingrezza), Duetetrabenazine (Austedo)

# References

- [1] Kaplan and Sadock's Synopsis of Psychiatry. 10<sup>th</sup> edition
- [2] Baldessarini et al. Decreased risk of suicides and attempts during long term lithium treatment. Bipolar Disord 2006; 8, pgs 625-39.
- [3] Wagstaff A, et al. Clozapine: in prevention of suicide in patients with schizophrenia or schizoaffective disorder. CNS Drugs 2003; 17: 273:80.
- [4] Stahl's Essential Psychopharmacology, Prescriber's Guide. Stahl, Steven. 6<sup>th</sup> Ed, 2017.
- [5] <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-revised-recommendations-celexa-citalopram-hydrobromide-related>
- [6] Massachusetts General Hospital Handbook of General Hospital Psychiatry, 6<sup>th</sup> ed. Stern et al. 2010