Psychiatry in Medical Settings
Pharmacology Challenges in Consultation Psychiatry

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Disclosure

Relevant Financial Relationships
None

Off-Label/Investigational Uses
The off-label use of antipsychotic medications in the treatment of agitated delirium will be discussed
Learning Objectives

• Increased understanding of factors influencing the choice of psychotropic medications in a patient with complex medical co-morbidities
Altered Mental Status in a Young Patient with Cancer

• 34 year old SWF diagnosed 6 months ago with aplastic anemia, admitted after BIB EMS to ED for after “found down” outside her apartment by a neighbor. AMS upon arrival to ED.

• Consultation Question: Management of Agitated Delirium
History

• Psych Hx: Depression and inpatient treatment for an eating disorder

• Medical Hx:
  • Multiple childhood admissions for recurrent pneumonias
  • Seen in ED 6 months ago for fatigue – viral syndrome? Pancytopenic. Bone marrow bx: hypocellularity (5%)
Exam

• T 38.5.  P 112 RR 12  BP 98/62

• Yelling and pulling at restraints, attempting to strike staff, demanding to leave

• Waxing and waning LOC, attention and concentration

• AVH, PI

• Oriented only to self

• Labs:  WBC 1.7, Hgb 8.2, Plts 3,000

• ECG:  QTc 515 msec
Antipsychotics with Higher Risk for Causing QTc Prolongation

- IV Haloperidol > PO or IM
- Ziprasidone
- Chlorpromazine
- Thioridazine
- Droperidol
- Pimozide
- Iloperidone

Resource for Medications to Avoid with Prolonged QTc:
Crediblemeds.org

Credible Meds. Drugs to be avoided by congenital long QT patients. Available at: http://crediblemeds.org; Dietle A, QTC Prolongation With Antidepressants and Antipsychotics. US Pharm. 2015; 40(11): HS34-HS40
Antipsychotics that do not cause QTc Prolongation

• Aripiprazole
• Lurasidone
• Clozapine
• Loxapine
• Brexpiprazole

Dietle A, QTC Prolongation With Antidepressants and Antipsychotics. US Pharm. 2015; 40(11): HS34-HS40
Management of Psychosis and Agitation in Medically Ill Patients with (or at Risk for) Prolonged QTc

- For patients with risk factors, but no prolonged QT:
  - First Tier Choice: Olanzapine po or IM, Aripiprazole po
  - Second Tier Choice: Risperidone, Quetiapine, po or IM Haloperidol

- If the QTc is 450 – 499 msec
  - Aripiprazole, Olanzapine, Risperidone, Quetiapine

- If the QTc is 500 msec +
  - Aripiprazole, Valproate, Trazodone*, Benzodiazepines

General Considerations

• If risk factors, baseline and intermittent ECG, Quetiapine and olanzapine – sedating meds may make lower doses possible

• Avoid polypharmacy, combination with others that prolong QTc, monitor electrolytes

• FDA recommends cardiac monitoring for all patients receiving IV haloperidol

Antipsychotics that do not cause QTc Prolongation

- Aripiprazole
- Lurasidone
- Clozapine
- Loxapine
- Brexiprazole

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Consult # 2

• Four days later, she has been treated for bacteremia/sepsis and her mental status has cleared. She is A&O X 4, cooperative and has insight that she was confused. She has reported SI to the staff.

• Consultation Question: Evaluate for depression
History and ROS

• FHx: Depression in 3 maternal relatives. No bipolar illness or psychosis

• Psych Hx: No suicide attempts, mania, psychosis, SIB. Inpatient X 2 for depression and anorexia nervosa, binge-eating/ purging type. No h/o mania/ hypomania

• Social History:
  • No EtOH, rx or illicit substance abuse hx.
Exam

- PHQ -9 = 27
- Depressed mood, hopeless re her prognosis and future, feels helpless and unworthy of treatment, no appetite, anergic, no motivation, hypersomnia, no libido, can’t concentrate. No psychosis.
- + SI with plan to ingest “poison”
- Affect: tearful, distraught, depressed
What’s All the Fuss?

• SSRI’s are associated with a dose-dependent MODEST (+6.10 msec), but statistically significant, increase in QTc interval compared with placebo.
What’s All the Fuss?

• “A comprehensive review of the published literature has concluded that there is little evidence that psychotropic drug – associated QTc interval prolongation *by itself* is sufficient to predict TdP.”

• At least one additional risk factor in 92% of cases

• In TdP cases
  - 20% had QTc < 500 msec
  - 75% at therapeutic drug doses

Other Risk Factors

- Congenital Prolonged QTc
- Female
- Hypomagnesemia
- Hypokalemia
- Bradycardia
- Recent MI
- Co-administered QTc-prolonging meds

Antidepressants with Higher Risk for Causing QTc Prolongation

- Amitriptyline, amoxapine, clomipramine, desipramine, doxepin, imipramine, nortriptyline
- Citalopram, escitalopram, fluoxetine, paroxetine, sertraline
- Mirtazapine, trazodone, venlafaxine

Credible Meds. Drugs to be avoided by congenital long QT patients. Available at: http://crediblemeds.org; Dietle A, QTC Prolongation With Antidepressants and Antipsychotics. US Pharm. 2015; 40(11): HS34-HS40
Antidepressants and QTc

- No QTc Prolongation:
  - Cymbalta (duloxetine)
  - Pristiq (desvenlafaxine)
  - Fetzima (levomilnacipran)

- No clinically significant QTc Prolongation at Therapeutic Doses:
  - Viibryd (vilazodone)
  - Desyrel (trazodone)
  - Wellbutrin (bupropion)
  - Trintellix (vortioxetine)

Dietle A, QTC Prolongation With Antidepressants and Antipsychotics. US Pharm. 2015; 40(11): HS34-HS40
Which would be the SAFEST antipsychotic medication for the management of her agitation?

1. Intravenous haloperidol
2. Oral quetiapine
3. Intramuscular olanzapine
4. Oral aripiprazole
5. Oral risperidone
What would be the SAFEST antidepressant choice?

1. Sertraline
2. Nortriptyline
3. Desvenlafaxine
4. Mirtazapine
5. Bupropion
Thank You!
Low-dose IV Haloperidol in the ICU

- 34 patients. Baseline QTc < 500 msec. Delirium, in ICU. Other risk factors not excluded.

- 1 mg IV q6h vs placebo, double blind. Telemetry + q 12h ECG.

- No significant difference in average rate of change of QTc over time, proportion of patients who developed QTc prolongation (8/34 H vs 14/34 P), a QTc > 500 msec (4/34 H vs 3/34 P) or increase QTc by > 60 msec 6/34 H vs 14/34 P)

- Need to study larger numbers and higher doses
Saphris (asenapine): Sublingual

• Mild effect on QTc, comparable to quetiapine
  • 2 to 5 msec compared to placebo. No QTc increases ≥60 msec, no prolongation to QTc to ≥500 msec.

• 10 mg SL acute agitation in ER. Well tolerated. NNT comparable to IM ziprasidone 10-20 mg, IM olanzapine 10 mg, IM aripiprazole 9.75 mg, haloperidol 6.5 – 7.5 mg, IM lorazepam 2 mg