HIV & The Treatment of Depression III: Antidepressant Selection Part 2

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Data in this presentation offer a limited perspective of how systemic, social, and economic factors impact health. We recognize that racism, not race, creates and perpetuates health disparities.

To Learn More:
https://www.cdc.gov/minorityhealth/racism-disparities
Objectives

• List the first line FDA approved medications for major depressive disorder
• Discuss relevant drug-drug interactions between common antidepressants and antiretroviral drugs
First Line Antidepressant Agents

**SSRIs**
- Fluoxetine
- Sertraline
- Paroxetine
- Fluvoxamine
- Escitalopram
- Citalopram

**SNRIs**
- Venlafaxine
- Desvenlafaxine
- Duloxetine
- Levomilnacipran

**Atypicals**
- Bupropion
- Mirtazapine
- Buspirone
- Vortioxetine
- Vilazodone
Bupropion

- **Wellbutrin®, Zyban®, Forfivo®**
- **Dosing Formulation:**
  - IR (TiD dosing), SR (BID dosing), XL (daily dosing)
- **Dosing Range (XL):** 150mg, 300mg, 450mg
- Can be utilized alone or as an augmentation agent
- Can offset the sexual side effect of an SSRI/SNRI
- **Targets**
  - Atypical Depression
  - ADHD
  - Stimulant Use Disorder
  - Smoking Cessation
  - Weight Loss
  - SSRI/SNRI-induced sexual dysfunction
- **Cons**
  - Can cause increased anxiety
  - Can cause insomnia
  - Lowers the seizure threshold (IR>SR>XL)
  - Contraindicated in those with h/o seizure, eating disorders, and AUD (if h/o DTs/complicated w/d)
- **Pearls**
  - SR dosing has long enough t1/2 to support daily dosing in augmentation
  - Substituted cathinone which means it is a true stimulant and a relative of the “bath salts”
  - Abusible, can be crushed and snorted
  - Cathinones have a significant risk of lowering seizure threshold and leading to status epilepticus in overdose setting
  - Overdose can be fatal
Bupropion Interactions with Antiretroviral Drugs

• Bupropion is a 2B6 substrate and strong 2D6 inhibitor

• Ritonavir, Lopinavir, Nevirapine, and Efavirenz can all decrease plasma concentration of Bupropion by 50%  
  - Dose increases may be required, but still important not to exceed 450mg total daily dose
Mirtazapine

- Remeron®
- Dosing Range: 7.5mg to 45mg; doses up to 60mg to 90mg may be considered
- 7.5mg and 15mg are generally more sedating than doses above 22.5mg; however, it is difficult to predict if 7.5mg will be more sedating than 15mg or vice-versa
- Multiple receptor targets:
  - H1 antagonist – sedation and appetite stimulation
  - 5HT2A – antidepressant effect
  - 5HT2C antagonist – antidepressant effect & weight gain
  - 5HT3 antagonist – antiemetic
  - Alpha-2 antagonist – boosts serotonin and norepinephrine release
Mirtazapine

**Pros**
- Can be a useful agent for helping medically ill individuals with multi-modal action
  - Think those with hospital insomnia, failure to thrive, chronic nausea, cancer, AIDS
- Few drug-drug interactions
- Oral disintegrating tablet formulation available
- Alpha-2 antagonist activity essentially supercharges SSRIs/SNRIs and making this an ideal augmentation agent for other antidepressants
  - Venlafaxine + Mirtazapine combination may be as effective as tranylcypromine but with less side effects
- Antidepressant least likely to induce hyponatremia
- Can be useful in helping with Cannabis Use Disorder and Stimulant Use Disorder

**Cons**
- Can be overly sedating with hangover effect possible
  - Mitigate by pushing dose to 30mg
- Weight gain limits use
- Weight gain is more problematic in younger and less so in older patients
  - Up to 15lbs may be common
  - No direct insulin resistance, just increased caloric intake
- May not be as effective as other antidepressants for severe depression in monotherapy
Mirtazapine Interactions with Antiretroviral Drugs

- Likely minimal, though may compound some neuropsychiatric effects of Efavirenz such as ataxia and vivid dreams
Buspirone

- **Buspar®**

- **Dosing Range**
  - 10mg TID to 20mg TID, OR
  - 15mg BID to 30mg BID

- **Uses**
  - For generalized anxiety disorder, it may be used as monotherapy and help with symptoms faster than an SSRI; however, it is not a PRN medication
  - Shines as an augmentation agent to other antidepressants (especially 2D6 inhibitors which decrease plasma clearance of Buspirone)
  - Boosts the effect of the antidepressant
  - Can offset sexual side effects of SSRIs/SNRIs

- **Cons**
  - Short t1/2 (2-3hrs) makes dosing adherence problematic
  - TID dosing is ideal and should be utilized in monotherapy
  - Active metabolite has a t1/2 of about 6hrs, which supports BID dosing if using it as an augmentation agent
  - Dizziness
  - Sedation
Buspirone Interactions with Antiretroviral Drugs

- Buspirone is a 3A4 substrate
- Boosted regimens may increase plasma concentrations of Buspirone
- This could be a good thing given the short t1/2

Trazodone

• Desyrel ®

• Dosing Range
  - Insomnia: 25mg – 200mg
  - Depression: 300mg-600mg

• Uses
  - Mainly used as a soporific agent, as better antidepressants exist
  - Can boost the antidepressant effects of other antidepressant agents

• Cons
  - Hangover effect: sedation, ataxia possible
  - Priapism
    • Penile and Clitoral possible
  - Orthostatic hypotension
  - Serotonergic agent: Serotonin Syndrome possible
Trazodone Interactions with Antiretroviral Drugs

- Trazodone is a 3A4 and 2D6 substrate
- Increased sedation, fatigue, hypotension, and syncope reported when co-administered with Ritonavir and Cobicistat
- Use with Saquinavir is not recommended given risk of cardiac arrhythmia
Newer Antidepressants

Vortioxetine (Trintellix)

• Dosing Range: 5mg to 20mg
• Pros
  - May have less sexual side effects than SSRIs at low doses
  - Pro-cognitive, can increase focus and concentration
  - Somewhat activating
• Cons
  - $$$
  - Not very good for anxiety
  - Significant nausea as side effect

Vilazodone (Viibryd)

• Dosing Range: 10mg to 40mg
• Pros
  - May have less sexual side effects than SSRIs at low doses
  - Maybe better for anxiety than Vortioxetine
• Cons
  - $$$
  - Must be taken with food
  - Can cause nausea (less so than Vortioxetine)
Newer Antidepressants

Bupropion-Dextromethorphan (Auvelity)

- **Typical Dose**: Dextromethorphan 45 mg/Bupropion 105 mg twice daily
  - Start at once daily in the morning then increase to BID

- **Pearls**
  - Mixed activity of both Bupropion and Dextromethorphan results in rapid reduction in depressive symptoms
  - Not associated with psychotomimetic effects

- **Cons**
  - $$$ - Approved 2022
  - Dizziness, nausea, dry mouth, decreased appetite, and anxiety

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Newer Antidepressants Interactions with Antiretroviral Drugs

- Vortioxetine & Vilazodone
  - No significant interactions expected

- Bupropion/Dextromethorphan
  - Protease Inhibitors will decrease reduction of Bupropion by inducing 2B6

Questions?
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