HIV & The Treatment of Depression II: Antidepressant Selection Part 1

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I have no conflicts of interest or relationships to disclose
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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

<table>
<thead>
<tr>
<th>SSRIs</th>
<th></th>
<th>SNRIs</th>
<th></th>
<th>Atypicals</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Fluoxetine</td>
<td>•</td>
<td>Venlafaxine</td>
<td>•</td>
<td>Bupropion</td>
<td>•</td>
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<tr>
<td>Sertraline</td>
<td>•</td>
<td>Desvenlafaxine</td>
<td>•</td>
<td>Mirtazapine</td>
<td>•</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>•</td>
<td>Duloxetine</td>
<td>•</td>
<td>Vortioxetine</td>
<td>•</td>
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<tr>
<td>Fluvoxamine</td>
<td>•</td>
<td>Levomilnacipran</td>
<td>•</td>
<td>Vilazodone</td>
<td>•</td>
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<tr>
<td>Escitalopram</td>
<td>•</td>
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<td></td>
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<tr>
<td>Citalopram</td>
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</tbody>
</table>
Selective Serotonin Reuptake Inhibitors

- Generally recognized as first-line medications for
  - Unipolar Depression
  - Anxiety Disorders
  - PTSD
  - OCD

- As a class, generally well tolerated (esp. compared to MAOIs and TCAs)

- Anxiety, PTSD, and especially OCD often require higher doses to treat than Depression
  - Start low and go slow as there can be worsening anxiety with initiation of treatment
  - Initial anxiety likely represents an akathisia syndrome, but is generally transient
SSRI Class-Specific Side Effects

• Initial Increase in Anxiety
  - Mitigate by starting low and going slow
  - Likely represents a transient akathisia-like syndrome

• Nausea
  - Start low and go slow
  - Gets better in the vast majority of patients

• Sexual Dysfunction
  - Decreased libido (up to 50%)
  - Delayed orgasm or anorgasmia (up to 35%)
  - Erectile dysfunction (up to 35%)
  - Typically improves for people over time
  - If persists, consider switching to better tolerated medication or dose reduce
  - Can augment with PDE inhibitors (men and women), Bupropion, Buspirone, Mirtazapine
SSRI Class-Specific Side Effects

- **Bleeding Risk**
  - SSRIs inhibit SERT on platelets thereby reducing intracellular 5HT which prevents platelet aggregation
  - GI bleed
    - SSRI pts are 55% more likely to experience a UGI bleed than non-SSRI pts
    - Concomitant use of NSAIDs quadruples the risk of GI bleed
    - Warfarin and other anticoagulants also increase the risk (3-4x) of GI bleed independent of changes in INR
  - Intracerebral Hemorrhage
    - SSRIs increase the lifetime likelihood of ICH
    - Do not initiate w/in 1 month of an ICH
    - For those already on an SSRI, the risk of repeat hemorrhage must be weighed against the risk of psychiatric decompensation following an ICH if the SSRI is discontinued
  - Post-operative bleeding risk is increased, but guidelines do not suggest discontinuing an SSRI prior to surgery
SSRI Class-Specific Side Effects

• Hyponatremia
  - Highest risk is within the 1st 30-days of starting a medication
  - Not related to dose
  - Highest risk groups are older individuals (esp. older women)
  - Likely due to SIADH
  - Risk of hospitalization from hyponatremia in AD-treated patients is 5x that of the general population
  - Consider closer sodium monitoring in the following:
    • Individuals >60 yo
    • Those on more than 1 diuretic
    • Those with a history of hyponatremia/SIADH
<table>
<thead>
<tr>
<th>Drug</th>
<th>Dosing Range</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
<tbody>
<tr>
<td>Citalopram</td>
<td>10mg to 40mg; Legacy patients may be on up to 80mg</td>
<td>Well tolerated</td>
<td>QTC prolongation (black box warning)</td>
</tr>
<tr>
<td>(Celexa)</td>
<td></td>
<td>Minimal P450 interactions</td>
<td>Max dose in ≥60 is 20mg</td>
</tr>
<tr>
<td>Escitalopram</td>
<td>5mg to 20mg; May go to 30mg if needed</td>
<td>Well tolerated</td>
<td>Minimal P450 interactions</td>
</tr>
<tr>
<td>(Lexapro)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sertraline</td>
<td>25mg to 200mg; May go to 300mg if needed</td>
<td>Large dosing range makes it useful for those sensitive to</td>
<td>May have more sexual side effects than others (save</td>
</tr>
<tr>
<td>(Zoloft)</td>
<td></td>
<td>dose adjustment side effects, dopamine re-uptake inhibition</td>
<td>Paroxetine)</td>
</tr>
<tr>
<td>Fluoxetine</td>
<td>10mg to 80mg; 90mg weekly</td>
<td>Long t½, activation may help atypical depression</td>
<td>Can be activating and worsen anxiety initially more</td>
</tr>
<tr>
<td>(Prozac)</td>
<td></td>
<td></td>
<td>than others, long t½ limits utility in elderly and</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>medically complex patients</td>
</tr>
<tr>
<td>Paroxetine</td>
<td>IR: 10mg to 60mg; CR: 12.5mg to 75mg</td>
<td>Sedating, may be beneficial for severe anxiety, useful in</td>
<td>Sedating, short t½ causes significant withdrawal</td>
</tr>
<tr>
<td>(Paxil)</td>
<td></td>
<td>PTSD and anxious/irritable depression</td>
<td>symptoms, worst sexual side effects, anticholinergic</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(caution in elderly)</td>
</tr>
<tr>
<td>Fluvoxamine</td>
<td>25mg to 300mg (total daily)</td>
<td>Has FDA indication for OCD, Sedating</td>
<td>Sedating, worst for GI side effects, significant drug-</td>
</tr>
<tr>
<td>(Luvox)</td>
<td></td>
<td></td>
<td>drug interactions</td>
</tr>
</tbody>
</table>
Interactions with Antiretroviral Drugs

- **Fluoxetine**
  - Clinically insignificant dose reductions in Ritonavir and Cobicistat
  - Increases Delavirdine by 50%; however, no dose changes have been recommended
  - Is significantly decreased by Nevirapine
  - Case reports of Serotonin Syndrome with Ritonavir (doses 400-1200mg/d) and Efavirenz
  - Cardiac and neurologic events have been reported when co-administered with Ritonavir

- **Fluvoxamine**
  - Can decrease clearance of Nevirapine
  - May alter protease inhibitor and Elvitegravir concentrations

Interactions with Antiretroviral Drugs

- **Paroxetine**
  - Is significantly decreased by Ritonavir-boosted Darunavir and Fosamprenavir
  - Can increase toxicity of protease inhibitors

- **Sertraline**
  - Is significantly decreased by Ritonavir-boosted Darunavir and Fosamprenavir as well as Efavirenz

- **Citalopram**
  - Recommended not to exceed 20mg per day if co-administered with 2C19 inhibitors such as Efavirenz and Etravirine

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Serotonin-Norepinephrine Reuptake Inhibitors

- Can be considered equivalent to SSRIs as a first-line treatment for:
  - Unipolar Depression
  - Anxiety Disorders
  - PTSD
  - OCD

- As a class, they shine in modulating pain response, so consider for those with comorbid:
  - Fibromyalgia
  - Complex Regional Pain Syndrome
  - Pelvic Floor Dysfunction/Chronic Urogenital Pelvic Pain Syndrome
  - Migraine Headache
  - Cluster Headache
  - Neuropathic Pain
SNRI Class-Specific Side Effects

- Hypertension
- Urinary Hesitancy/Retention
- Diaphoresis
- SSRI Side Effects
  - Initial Anxiety
  - Nausea
  - Sexual Dysfunction
  - Bleeding Risk
  - Hyponatremia
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<th>Drug</th>
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<tr>
<td>Venlafaxine (Effexor)</td>
<td>ER 37.5mg to 225mg, May consider 300mg for select patients</td>
<td>Can be helpful for those with co-morbid ADHD, &amp;/or pain conditions, few drug-drug interactions, may be good for atypical depression, Venlafaxine + Mirtazapine = California Rocket Fuel</td>
<td>SSRI at doses less than 100mg/day, short t½ causes significant withdrawal symptoms including electrical zap sensations, dose-dependent HTN. An IR formulation exists, but should only be used for those with NG-tube, PEG, etc.</td>
</tr>
<tr>
<td>Desvenlafaxine (Pristiq)</td>
<td>25mg to 100mg, Most studies suggest that 100mg does not offer any benefit over 50mg</td>
<td>More stable plasma concentrations than Venlafaxine, Seems to lack withdrawal effects of Venlafaxine</td>
<td>Coverage Issues</td>
</tr>
<tr>
<td>Duloxetine (Cymbalta)</td>
<td>20mg to 120mg</td>
<td>SNRI at all doses, 60mg is sweet spot for pain conditions, may have less rates of HTN than other SNRIs, often considered second line for peripheral neuropathy after gabapentinoids but could easily be first line</td>
<td>So-so as a primary antidepressant, 2D6 inhibitor, contraindicated in those with hepatic impairment, urinary retention</td>
</tr>
<tr>
<td>Levomilnacipran (Fetzima)</td>
<td>20mg to 120mg</td>
<td>May be good for those experiencing poop out on other SNRIs</td>
<td>Coverage issues, high rates of urinary hesitancy/retention, elevated BP can be problematic</td>
</tr>
</tbody>
</table>
Interactions with Antiretroviral Drugs

- **Venlafaxine / Desvenlafaxine**
  - Theoretically may decrease the plasma concentration of protease inhibitors via P-glycoprotein induction
  - Only really been shown to occur with Indinavir, though

- **Duloxetine**
  - Plasma concentrations may be increased by Ritonavir, unclear significance
  - Use with caution with PIs and older NRTIs/NNRTIs, especially in those with comorbid HCV due to potential hepatotoxicity

- **Levomilnacipran**
  - 3A4 substrate, use with caution in patients on boosted regimens as much higher rates of hypertension and urinary retention at baseline

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