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

Samuel Jackson, MD (he/him)
Acting Assistant Professor
University of Washington
Department of Psychiatry and Behavioral Science

Last Updated: 2/1/2024

Disclosures

I have no conflicts of interest or relationships to disclose

Disclaimer

Funding for this presentation was made possible by U1OHA29296 from the Human Resources and Services Administration HIV/AIDS Bureau. The views expressed do not necessarily reflect the official policies of the Department of Health and Human Services nor does mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. *Any trade/brand names for products mentioned during this presentation are for training and identification purposes only.*

AETC AIDS Education & Training Center Program Mountain West

Data Considerations

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

MWAETC

First Line Antidepressant Agents

SSRIs	SNRIs	Atypicals
• Fluoxetine • Sertraline • Paroxetine • Fluvoxamine • Escitalopram • Citalopram	• Venlafaxine • Desvenlafaxine • Duloxetine • Levomilnacipran	• Bupropion • Mirtazapine • Vortioxetine • Vilazodone

MWAETC

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

MWAETC

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

MWAETC

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

MWAETC

Drug	Dosing Range	Pros	Cons
Citalopram (Celexa)	10mg to 40mg; *Legacy patients may be on up to 80mg*	Well tolerated Minimal P450 interactions	QTc prolongation (black box warning) Max dose in ≥60 is 20mg
Escitalopram (Lexapro)	5mg to 20mg May go to 30mg if needed	Well tolerated Minimal P450 interactions	
Sertraline (Zoloft)	25mg to 200mg May go to 300mg if needed	Large dosing range makes it useful for those sensitive to dose adjustment side effects, dopamine re-uptake inhibition may help with treatment-refractory & atypical depression	May have more sexual side effects than others (save Paroxetine)
Fluoxetine (Prozac)	10mg to 80mg 90mg weekly	Long t½, activation may help atypical depression	Can be activating and worsen anxiety initially more than others, long t½ limits utility in elderly and medically complex patients
Paroxetine (Paxil)	IR: 10mg to 60mg CR: 12.5mg to 75mg	Sedating, may be beneficial for severe anxiety, useful in PTSD and anxious/irritable depression	Sedating, short t½ causes significant withdrawal symptoms, worst sexual side effects, anticholinergic (caution in elderly)
Fluvoxamine (Luvox)	25mg to 300mg (total daily)	**Has FDA indication for OCD,** Sedating	Sedating, worst for GI side effects, significant drug-drug interactions

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

Goodlet, K. J., Zmarlicka, M. T., & Peckham, A. M. (2019). Drug–drug interactions and clinical considerations with co-administration of antiretrovirals and psychotropic drugs. CNS spectrums, 24(3), 287-312.

MWAETC

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

Goodlet, K. J., Zmarlicka, M. T., & Peckham, A. M. (2019). Drug–drug interactions and clinical considerations with co-administration of antiretrovirals and psychotropic drugs. CNS spectrums, 24(3), 287-312.

MWAETC

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

MWAETC

Drug	Dosing Range	Pros	Cons
Venlafaxine (Effexor)	ER 37.5mg to 225mg May consider 300mg for select patients	Can be helpful for those with co-morbid ADHD, &/or pain conditions, few drug-drug interactions, may be good for atypical depression, Venlafaxine + Mirtazapine = California Rocket Fuel	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.
Desvenlafaxine (Pristiq)	25mg to 100mg Most studies suggest that 100mg does not offer any benefit over 50mg	More stabile plasma concentrations than Venlafaxine Seems to lack withdrawal effects of Venlafaxine	Coverage Issues
Duloxetine (Cymbalta)	20mg to 120mg	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	So-so as a primary antidepressant, 2D6 inhibitor, contraindicated in those with hepatic impairment, urinary retention
Levomilnacipran (Fetzima)	20mg to 120mg	May be good for those experiencing poop out on other SNRIs	Coverage issues, high rates of urinary hesitancy/retention, elevated BP can be problematic

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

Goodlet, K. J., Zmarlicka, M. T., & Peckham, A. M. (2019). Drug–drug interactions and clinical considerations with co-administration of antiretrovirals and psychotropic drugs. CNS spectrums, 24(3), 287-312.

Acknowledgment

This Mountain West AIDS Education and Training (MWAETC) program is supported by the Health Resources and Services Administration (HRSA) of the U.S. Department of Health and Human Services (HHS) as part of an award totaling $3,333,289 with 0% financed with non-governmental sources.

The content in this presentation are those of the author(s) and do not necessarily represent the official views of, nor an endorsement by, HRSA, HHS, or the U.S. Government.

AETC AIDS Education & Training Center Program Mountain West