

Psychopharmacology and the HIV-Positive Patient

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 - Memory changes
 - Substance abuse

Course Objectives

- Understanding the effects of HIV and HIV-related medications on mental health
- Appreciation for the myriad of drug-drug interactions, and those to avoid
- Familiarity with applying the biopsychosocial model in treating the HIV-positive patient
- Knowledge about drugs of abuse in HIV

HIV

HIV

- Rapidly-mutating retrovirus contracted through exchange of bodily fluids (blood, semen, mother's milk, vaginal secretions)
- Compromises human immune system, notably through destruction of CD4+ t cells, creating vulnerability to viral, fungal, and parasitic infections

HIV and the Brain

HIV enters CNS early, via macrophages;
Macrophages and microglial cells
responsible for CNS replication
Subcortical structures targeted

CNS Implications of CD4 Count

- >500 lymphocytes/microliter
 - Acute retroviral syndrome (ARS)
 - Persistent generalized lymphadenopathy (PGL)
 - Aseptic meningitis

CNS Implications of CD4 Count

- 200-500 lymphocytes/microliter
 - Pneumonia - bacterial
 - Kaposi's Sarcoma (KS)
 - B-cell lymphoma
 - Anemia

CNS Implications of CD4 Count

- <200 lymphocytes/microliter
 - *Pneumocystis Carinii* Pneumonia (PCP)
 - Disseminated Histoplasmosis and Coccidioidomycosis
 - Extrapulmonary tuberculosis
 - Progressive Multifocal Leukoencephalopathy (PML)
 - Wasting
 - Neuropathy
 - HIV Dementia
 - Non-Hodgkin's Lymphoma (NHL)

CNS Implications of CD4 Count

- <100 lymphocytes/microliter
 - Toxoplasmosis
 - Cryptococcosis

CNS Implications of CD4 Count

- <50 lymphocytes/microliter
 - Disseminated Cytomegalovirus (CMV)
 - Disseminated Mycobacterium avium complex (MAC)
 - CNS Lymphoma

Treatment

- Interrupts the HIV lifecycle by introducing drugs into vulnerable points (mainly enzymes) in the viral replication system
 - reverse transcriptase
 - protease
 - fusion

Nucleoside-Analogue Reverse Transcriptase Inhibitors

- Includes AZT(Retrovir™), ddI(Videx™), ddC(Hivid™), d4T(Epivir™), ABC(Ziagen™)
- Primarily eliminated by the kidneys
- CNS Penetration 10-40% (AZT 60%)

Non-Nucleoside Reverse Transcriptase Inhibitors

- Includes NVP(Viramune™), DLV(Rescriptor™), EFV(Sustiva™)
- Many interactions possible due to CYP450 metabolism: substrates, inhibitors, and inducers
- Mental status changes possible

Considerations with Sustiva™

- Most severe side effects occur during first month
- Generally subside by the end of 4 weeks
- Include nervousness, dizziness, depression, mania, psychosis, suicidality, insomnia

Nucleotide Reverse Transcriptase Inhibitors

- Tenofovir (Viread™)
 - renally eliminated; possibility of competition for active tubular secretion

Protease Inhibitors

- Includes IDV(CrixivanTM), RTV(NorvirTM), SQV (InviraseTM, FortovaseTM), NFV(ViraceptTM), APV(AgeneraseTM), LPV/RTV(KaletraTM)
- Poor-Moderate CNS penetration
- Many serious drug interactions possible, especially involving CYP450

Fusion Inhibitors

- T20 (Fuzeon™)
 - bid subcutaneous injections
 - peptide; metabolism likely not an issue

Other HIV-related medications to consider

- Antifungals
 - very potent 3A4 inhibitors
- IFN- α (Hepatitis treatment)
 - mental status changes possible

Standard of Care - Lab Data

- Routine
 - Viral load
 - CD4+ T cells count (absolute and percent)
 - Liver function tests
 - Renal function, electrolytes
 - Complete blood cell count
- Specialized
 - Resistance testing
 - Therapeutic Drug Monitoring - Investigative

HIV and Mental Illness

HIV and Mental Health

- Incidence of mental illness in HIV -- before and after infection
- Incidence of substance abuse in HIV
- Mental health considerations in the selection of antiretrovirals
 - some antiretrovirals have potentially severe CNS side effects, including suicidality
- Non-Adherence
 - risk factors predominately psychosocial

Special Topics in HIV Relevant to Mental Health and Psychopharmacology

- Lipodystrophy
 - Disturbing body changes may occur, including deformation of face, limbs, trunk
- Metabolic abnormalities
 - May include insulin resistance, lipid elevations
- Disconnect Syndrome
 - Viral load and CD4 no longer maintain an inverse relationship -> implications for elevated CNS burden of virus and cognitive decline

Drug-Drug Interactions

Drug Metabolism in HIV

- Cytochrome P450 System
 - Most major isoenzymes potentially involved in metabolism of HAART
 - 3A4 involved in most serious drug-drug interactions
 - Some antiretrovirals less predictable (e.g., efavirenz both inhibits and induces 3A4)

Drug Metabolism in HIV

- UGT (uridine diphosphate-glucuronosyltransferase)
 - Consider when prescribing protease inhibitors with some opiate analgesics, tricyclics, lamotrigene, olanzapine, and 3-hydroxysubstituted benzodiazepines

Drug Metabolism

- Alcohol Dehydrogenase
 - e.g., interaction between abacavir and chloral hydrate
- Renal Elimination
 - consider with tenofovir, nucleoside analog reverse transcriptase inhibitors
- P-Glycoprotein
 - extent of involvement not entirely clear

Psychotropic Cautions

Antidepressants

Review P450 of psychotropic(s) and HIV-related medications

Anticonvulsants

Caution with those that induce P450; immune function considerations

Anxiolytics; sedative-hypnotics

P450 and UGT interactions

Antipsychotics

Caution with cardiac conduction and immune function

Herbal Medication Cautions

St John's Wort

Garlic Capsules

Milk Thistle

Cat's Claw (Uña de Gato)

Psychiatric Assessment and Management

General Assessment for all HIV Psychiatric Patients

- Review current medications: side effects and interactions. Adherence?
- Review physical health. Check labs for abnormalities (in addition to standard of care): thyroid, testosterone, and others as indicated
- Explore substance abuse and STD exposure
- Taking herbals?
- Consider CNS workup if symptoms are new and $CD4 < 200$ (I.e., imaging, EEG, LP, additional labs)

Assessment - Psychosocial

- Psychological
 - Defenses employed
 - Flexibility; resiliency
- Socioeconomic
 - Finances
 - Current relationships
 - Losses
 - Supports
 - Housing situation

Treatment Approach - Depression

- Biological
 - Screen for bipolar disorder
 - Antidepressants
 - Other pharmacotherapy
 - Substance Abuse treatment
 - Changing HAART
- Psychological Issues
 - Individual, group psychotherapy
 - Supportive versus insight-oriented
- Socioeconomic Issues
 - address losses, finances, employment, housing

Treatment Approach - Anxiety

- Biological
 - SSRIs
 - Anxiolytics: Benzodiazepines and others
 - Substance Abuse Treatment
 - Changing HAART
- Psychological
 - Individual, Group
 - CBT, supportive, insight-oriented
- Socioeconomic
 - address losses, finances, employment, housing

Treatment Approach - Insomnia, Vivid Dreams

- Assure patients that vivid dreams very common
- Avoid attempting to interpret dreams
- Review sleep hygiene. Substance abuse?
- Selection of sleep medications depends on etiology of insomnia and concurrent HIV-related medications
 - sedating antidepressants
 - anxiolytics, sedative-hypnotics
 - neuroleptics
 - Other, including changing HAART

Treatment Approach- Memory Changes

– Biological

- Maximizing HAART for CNS penetration
- Assure adherence to HAART
- Antidepressants
- Stimulants
- Transdermal Selegeline (clinical trial stage)

Treatment Approach- Memory Changes

– Psychological

- Individual therapy aimed at helping patient cope with losses

– Socioeconomic

- Assistance at home; making lists
- Consider safety at work and driving
- Family involvement
- Conservatorship if indicated

Treatment Approach - Agitation, Mood Lability

- Neuroleptics
 - newer atypical preferable due to HIV effects on basal ganglia
- Benzodiazepines
 - caution with interactions, substance abuse, severely medically ill
- Anticonvulsants
- Lithium
 - toxicity may occur rapidly
- Changing HAART if all else fails

Substance Abuse in HIV

- Alcohol
 - liver disease
- Club Drugs - Methamphetamine, Ketamine, GHB, Ecstasy
 - potentially deadly interactions with HAART
- Cocaine
 - leads to dramatically increased viral load
- Opiates
 - interactions with HAART

Review Questions

- 1) What are the five major classes of antiretroviral medications?**
- 2) What is the significance of the CD4 count? Of the viral load?**
- 3) Which benzodiazepines would be safest for someone taking a potent 3A4 inhibitor?**
- 4) A patient on HAART is recreationally taking crystal methamphetamine. What is your advice?**
- 5) Primary care MD approaches you, “I want to start Charlie on Sustiva™.” What would you want to know about Charlie, and how would you advise this doctor?**