Antiretroviral Overview and Medication Adherence

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After completing this session, participants will be able to

- Identify common barriers to ART adherence
- Learn about specifics of adherence promotion in correctional settings
- Assess/enhance ART adherence
- Cite available antiretrovirals and their classifications
- Discuss current treatment guidelines/recommendations for HIV management
Primary Goals of ART

- Maximal and durable viral suppression
- Restoration and preservation of immune function (CD4 count)
- Improved quality of life
- Reduced HIV-related opportunistic infections (OIs)
- Reduced morbidity and mortality

New York City Department of Health

- **Antiretroviral Therapy - 2011**
  The Health Department now recommends offering antiretroviral treatment (ART) to any person living with HIV, regardless of the person’s CD4 cell count. The recommendation is based on evidence that ART can improve the health of people living with HIV and that ART can prevent transmission of HIV from an HIV-infected person to an uninfected sexual partner.

- San Francisco department of health issued similar guidance in 2010
Recommendations for Initiation of Therapy in Antiretroviral Naïve HIV-infected Patients

- Patients initiating antiretroviral therapy should be willing and able to commit to lifelong treatment and should understand the benefits and risks of therapy and the importance of adherence.

- Patients may choose to postpone therapy, and providers may elect to defer therapy, based on clinical and/or psychosocial factors on a case-by-case basis.

Significance of Adherence in HIV

- > 95% adherence required.

- To achieve maximal suppression of viral replication & preserve immune function by slowing the destruction of CD4+ cells.

- Ultimate goal: 100% adherence with all doses all of the time & improved quality of life and survival.

- To prevent viral resistance to drug therapy.
Defining Adherence

- **Compliance** - patient *passively* conforms to a provider prescribed treatment plan

- **Adherence** -
  - Patient takes an active role in implementing the plan (collaborative process)
  - Patient shares responsibility
  - Involves progression through various stages

Factors that Influence Adherence

- **Patient-related factors**
  - Alcohol/substance abuse – provide treatment prior to initiating ART
  - Psychiatric needs – utilize mental health consultation to identify
  - Correct misconceptions about HIV and ART which are common among inmates and may adversely affect adherence
  - Use teaching tools that are appropriate in language and reading level
  - Encourage participation in peer support groups
Factors that Influence Adherence

- **Consistently predictive of non-adherence**
  - Symptoms and side effects/disease state
  - Negative life events/stress
  - Complexity of regimen
  - History of reasons for non-adherence
  - History of missed medical appointments

- **Consistently predictive of adherence**
  - Family or social support
  - Self-efficacy

Assessing Progression Toward Adherence to ART

1. **Acceptance of ART (Readiness)**
   - **barriers:**
     - recent HIV diagnosis
     - denial of diagnosis
     - lack of knowledge
     - lack of trust in provider
     - lack of trust in medications
     - beliefs

2. **Ability to take ART**
   - **barriers:**
     - motivation, skills

3. **Maintenance of adherent behavior**
Adherence assessment

- Assess the determinants of adherence
  - prior to initiation of ART
  - within first few days of initiation of ART
  - at each visit to assess any change in determinants

Adherence screening questions

- It’s OK to stop taking HIV medications once I feel better.
  - True  False  Don’t know
- The viral load test measures how much HIV there is in my blood.
  - True  False  Don’t know
- If my viral load is undetectable, it means I no longer have HIV
  - True  False  Don’t know
- To control the virus, I should take all the medications I have been told to take. Not just some of them.
  - True  False  Don’t know
Adherence screening questions

- How important is it for you to be able to identify your medications?
  - Very important
  - Not important
  - Not sure

- How important is it for you to keep medical appointments?
  - Very important
  - Not important
  - Not sure

- How important is it for you to take your medications?
  - Very important
  - Not important
  - Not sure

Patient Readiness for HAART

- Health Belief Model can be used to assess readiness and likelihood of adherence to Highly Active Antiretroviral Therapy (HAART)
Health Belief Model and Adherence

Individual Factors
- Demographics, lifestyle, social support, mental health, substance use
- Perceived susceptibility of HIV disease progression
- Perceived severity of HIV disease progression
- Perceived benefits and barriers of ART
- Perceived threat of non-adherence
- Cues to action
- Likelihood to engage in adherence behavior
- Self-efficacy for adherence

Health Belief Model: Concepts (1)

- **Perceived susceptibility**: the individual’s belief that she is susceptible to HIV disease progression

- **Perceived severity**: the individual’s belief that HIV disease progression has serious consequences
Health Belief Model: Concepts

- **Perceived benefits**: the individual’s belief that adherence to ART would reduce susceptibility to HIV disease progression or disease severity.

- **Perceived barriers**: the individual’s belief that the materials, physical and psychological costs of adhering to ART outweigh the benefits.

Strategies to Promote Adherence

- **Perceived barriers**
  - Address patient questions and concerns with specific information and strategies to address barriers (e.g., regimen complexity, dietary restrictions, short and long term side effects).
  - Provide incentives for adherence.
  - Provide ongoing support and reassurance.
  - Provide and instruct patient how maintain a daily pill diary to identify barriers to adherence.
Strategies to Promote Adherence

- Perceived barriers (cont.)
  - Anticipate and discuss potential side effects, their duration and management
  - Simplify regimens, dosing and food requirements
  - Include patient in development of plan of care/decision-making process
  - Establish readiness to start therapy

- Perceived benefits
  - Provide specific information re dose, schedule and dietary requirements of ART and potential benefits of adherence
  - Graph patient’s viral load and CD4+ count before and throughout treatment to trend response for reinforcement of benefits of adherence
  - Utilize team approach with nurses, physicians, pharmacists and peer counselors
Health Belief Model: Concepts

- **Cues to action**: the individual’s exposure to factors that prompt adherence to ART
- **Self-efficacy**: the individual’s confidence in her ability to successfully adhere to ART

Strategies to Promote Adherence

- **Cues to action**
  - Provide detailed, specific, easily understood information re when and how to take medication
  - Provide and instruct patient in the use of tools to foster and reinforce adherence
    - beepers, watches, pill organizers, stickers, telephone reminders, medication planner, written instructions, instruct to place medications in location where they will be seen
  - Utilize educational aids including charts, cartoons, written information
Strategies to Promote Adherence

**Cues to action (cont.)**
- Provide adherence assessment and counseling at routine medical visits
- Enlist friends/family/partner to provide motivation and remind patient to take medications
- Collaborate with patient to choose a regular daily activity as a cue to take medication (getting out of bed, making breakfast or dinner)

**Self-efficacy**
- Provide skill building for adherence
  - role-playing (e.g. patient-provider communication skills; use of jelly beans to practice taking medications on schedule)
  - problem solving (what to do for late or missed dose)
  - planning ahead for refills
  - management of medications during changes in daily schedule
  - potential side effects, self-management strategies, when to call the health care provider
Strategies to Promote Adherence

**Self-efficacy (cont.)**
- Collaborate with patient on potential solutions for patient-identified barriers to adherence.
- Provide positive reinforcement for adherence.
- Contract with patient for adherence.
- Utilize role models with adherent behavior
- Utilize the problem-solving process (e.g. ask the patient “Think of a time when you might miss a dose of your medication. What would you do then?”)

Evaluation of Adherence

- Adherence tends to decline over time
- Ask questions in a way that gives permission for missed doses.
  - “Which doses are the hardest to remember to take?” “Which doses did you miss?”
- Use open-ended questions.
  - “Can you tell me about how you take your medicines on a typical weekday?”
  - “How do you take your medicines on a weekend day?”
Evaluation of Adherence

- Communicate the understanding that problems with adherence are expected.

- Normalization of adherence problems opens door for honest communication.
  - “Many people have difficulty sticking to their medication schedule. What problems have you had with taking your medications?”

- When providing information, keep it simple.

- Stress and anxiety lower the ability to assimilate new information.

- Assess understanding of new information by asking patients to repeat it in their own words.
Factors that Influence Adherence

- **Medication-related factors**
  - Complex regimens
  - Drug/drug interactions
  - Misconceptions
  - Side effects
  - Complexity of regimen (pill burden, dosing frequency, food requirements)
  - Difficulty taking meds (swallowing pills, daily scheduling issues)
  - Food requirements
  - DOT vs. KOP

Methods for Dispensing Medications

- Two ways of dispensing in prison settings: keep-on-person (KOP) & directly observed therapy (DOT).
- With KOP, inmates are issued a day's or week's worth of medications to keep in their cells & take at the appropriate times.
- DOT - the inmates must stand in a pill line & be observed taking medications.
DOT - pros & cons

**Advantages:**
- Less medication waste
- Increased adherence rates (assures dosage)
- More contact with medical (SE’s/education)
- Favorable outcome clearly documented

**Disadvantages:**
- Lockdowns or other circumstances make it impossible
- Increased staffing
- Potential loss of confidentiality
- Teaches inmate nothing (passive)
- May increase NON-adherence r/t time demands
- Lack of once a day regimens make it cumbersome

K.O.P. - pros & cons

**Advantages:**
- Confidentiality
- Decrease in staffing
- Empowerment

**Disadvantages:**
- Medication Waste
- Potential Non-adherence
- Less interface with medical
- Inaccurate adherence assessment
- Prison schedule may not allow for appropriate meals or fluids
- Medications may be stolen for re-sale to other inmates.
Approach to Inmate Adherence in a Correctional Setting

- Assess inmate readiness
- Simplify medication regimens
- Assess medication adherence at each encounter
- Use all medical staff to aid in adherence monitoring
- Consider DOT only after unsuccessful education attempts

Fostering Adherence - Inmate

- Thorough, holistic assessment before starting HIV medications
- Prompt, frequent, follow-up once treatment begins (ongoing)
- Provide language appropriate educational tools
- Assure inmate has tools to adhere- clock, water, food
Approach to Inmate Adherence in a Correctional Setting

- Implement programs for continuity of care
  - Entering prison
  - Intra-prison movement
  - Release from prison
- Tailor medications to prison life
  - Work release
  - Lock up/segregation (detailed info in Handout)
- Monitor for active depression and/or substance abuse
- Consider stopping ART (if interventions fail) to avoid resistance

Develop long-term, trusting relationships

- Deal with inmate’s mistrust of authority & unfamiliarity with health care providers/services
- Be clear & open about the reality of HAART therapy
- Be clear about the consequences of missing doses
- Have a liaison between inmate & medical
Fostering Adherence - TEAM

- Provider(s) approach and attitude
- Multi-disciplinary approach
- Pharmacy involvement & management
- Calculate adherence on all encounters
- Peer Support (individual/groups)
- Multidisciplinary case review
- Monitor progress!!!
For successful adherence.....

**Patient Must:**
- Make a choice & be ready
- Believe they can adhere
- Understand the regimen and the illness
- Integrate regimen into their lifestyle

**Provider Must:**
- Involve Client in process
- Teach problem solving skills
- Teach behavioral skills
- Use positive reinforcement
- Omit Barriers
- **Empower not enable!**

Clinical Evaluation of Adherence

- Level of HIV RNA in plasma
- CD4+ lymphocyte count
- Clinical condition of patient
- Resistance testing
Resistance

- The ability of HIV to enter the cell and replicate despite presence of antiretroviral drugs
- Can lead to increasing viral load, ongoing damage to immune system, progression of HIV disease

Adherence/Resistance Relationship

(Harrigan et al., 2005)
Condition Recommendation

- **In presence of**
  - AIDS-defining illness
  - Pregnancy
  - HIV-associated nephropathy
  - HBV co-infection when HBV therapy is indicated and/or
  - CD4 count <350 cells/mm³

  **Start ART**

<table>
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<tr>
<th>CD4 count</th>
<th>Recommendation</th>
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<tr>
<td>350-500 cells/mm³</td>
<td>ART is recommended</td>
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<tr>
<td>&gt;500 cells/mm³</td>
<td>ART is recommended or optional</td>
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DHHS 2011 Guidelines

Recommendations for Initiation of Therapy in Antiretroviral Naïve HIV-infected Patients

DHHS Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents. 2011.
Available at: http://www.aidsinfo.nih.gov.

Is the question when to treat?

or

Is the question when NOT to treat?
Studies That Informed Guidelines on When to Start

- SMART trial[1]
  - Reduced risk of both opportunistic disease and serious non-AIDS events observed in patients who initiated and remained on antiretroviral therapy at CD4+ cell counts > 350 cells/mm³

- ART-CC[2]
  - Smaller absolute risk of AIDS or death seen for patients starting ART at CD4+ cell counts > 350 cells/mm³ vs ≤ 350 cells/mm³

- NA-ACCORD[3]
  - Survival benefit with earlier vs deferred ART
    - Risk of death 69% higher for patients deferring ART until CD4+ cell count ≤ 350 cells/mm³ vs 351-500 cells/mm³
    - Risk of death 94% higher for patients deferring ART until CD4+ cell count ≤ 500 cells/mm³ vs > 500 cells/mm³

Antiretroviral Treatment Guidelines “Basic Concepts”

- Combination antiretroviral therapy continues to be standard of care:
  - Use at least 3 active agents together

- Goals of antiretroviral therapy
  - Undetectable viral load (VL < 50/40 copies/mL)
  - CD4 restoration
  - Clinical success

Starting Antiretroviral Therapy

- What do you need to know?
  - Are they a candidate?
  - Are they going to take therapy?
  - How do their co-morbidities fit with the medications available
    - Drug side effect concerns
  - What medications is their virus sensitive to?

Antiretroviral Rules
(almost full-proof)

- If patient is not taking at least 2 active agents - then it’s a good idea to question the situation
- If patient decides to stop one agent, they should stop them all (contact prescriber)
- Watch carefully for drug-drug interactions when adding or subtracting medications
- Adherence the greatest key to therapy success!
Five classes of antiretroviral medications available

1. Nucleoside Reverse Transcriptase Inhibitors (NRTI’s)
   - Nucleotide RTI’s (tenofovir)

2. Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI’s)

3. Protease Inhibitors (PI’s)

4. Fusion Inhibitors: enfuvirtide, CCR5 antagonists

5. Integrase Inhibitors

Viral Load / CD4 testing

- Viral loads:
  - Baseline
  - 2-8 weeks post therapy commencement
  - Every 3-6 months

- CD4 counts:
  - Every 3-6 months at first
  - In clinically stable patients with suppressed viral load, CD4 count can be monitored every 6–12 months

Drivers of Therapy

- Therapy simplification and improved tolerability
- Drug resistance

STR

“The new term in HIV”
Single Tablet Regimens

STR options

- **Atripla** (efavirenz/tenofovir/emtricitabine)
- **Complera** (rilpivirine/tenofovir/emtricitabine)
- **Stribild** (elvitegravir/cobicistat/tenofovir/emtricitabine)
Summary

- Assessing for adherence is complex
- Involves frequently assessing for:
  - acceptance of treatment
  - barriers to adherence
  - motivation and behavioral skills for adherence
  - stage of behavioral change
- Collaborative efforts- patient, provider, pharmacists & support networks.
- Preventative, multifaceted & repetitive interventions work best.

Summary

- Antiretroviral treatment recommendations continue to evolve
  - Starting patients sooner
  - Prefer newer agents
- Once you start, you shouldn’t stop
- Side effects continue to be an important consideration but drugs are getting safer
- Adherence is everything!
Thank You

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