Caring for Hospitalized HIV-Positive Patients from Admission to Discharge: Factors to Consider

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Objectives

- Describe the most frequently encountered antiretroviral-related errors in hospitalized, HIV-positive patients.
- List strategies to avoid antiretroviral-related medication errors.

Introduction

- Antiretroviral therapy (ART) has drastically decreased HIV-related morbidity and mortality
- As of March 27, 2012, DHHS HIV Guidelines recommend ART for all HIV-infected patients
- > 20 FDA-approved agents comprising six different classes
  - Combination ART consists of:
    - At least 3 antiretroviral agents with 2 different mechanisms of action

HIV-Related Errors

- Studies have demonstrated error rates of 5-84% in hospitalized HIV-infected patients
- Oftentimes despite availability of CPOE and targeted electronic decision support programs
- Majority of errors occur within the first 24 hours of hospital admission

Types of HIV-Related Errors

- Incorrect antiretroviral (ART) or opportunistic infection (OI) prophylactic regimens
  - Omission
  - Substitution
- Dosing errors
- Administration errors
  - Timing
  - Food requirements
- Drug interactions
- Therapeutic duplication

Initial Rx

- IM is a 34 y/o M who presents to the ED with a non-productive cough, fever, and dyspnea for the last three weeks. His past medical history is consistent with HIV/AIDS (dx 2 years ago) and Pneumocystis jiroveci (PJP) pneumonia. He is being admitted for suspected pneumonia.
  - NKDA
  - T 38.5°C, WBC 6.5, Est CrCl 82 ml/min
  - Last CD4 count 24 (4%); VL > 100,000 c/ml (4 months ago)
  - CXR: ground glass appearance
  - Blood and sputum cultures pending
- Physician orders:
  - Tenofovir/emtricitabine 300/200mg 1 tablet PO Q12h
  - Sulfamethoxazole/trimethoprim 800/160mg 1 tablet PO daily
  - Ceftriaxone 1g IVPB Q24h, azithromycin 500mg IVPB daily
Admission: First Steps

- Assess the appropriateness of all medications ordered including ART
  - Perform a medication history
    - Call patient’s pharmacy to verify medication history and adherence
  - Refer to the most recent DHHS HIV Guidelines

ART: Treatment Naïve Patients

- **2 Nucleos(t)ide Reverse Transcriptase Inhibitors (NRTI)**
  - Tenofovir/emtricitabine

- **Non-nucleoside Reverse Transcriptase Inhibitor (NNRTI)**
  - Efavirenz

- **Integrase Inhibitor**
  - Raltegravir

Preferred agent selected based on efficacy, adverse effect profile, drug interactions, comorbidities, ease of administration/pill burden, and resistance profile


Medication Reconciliation/Order Verification

- The patient and the pharmacy confirm the following:
  - Truvada/emtricitabine 300/200mg – 1 tablet PO daily
  - Atazanavir 300mg – 1 capsule PO daily
  - Ritonavir 100mg – 1 capsule PO daily
  - Sulfamethoxazole/trimethoprim 800/160mg – 1 tablet PO daily
  - Azithromycin 600mg – 2 tablets PO once weekly

- All prescriptions were last filled 4 months ago

Back to IM...

- Physician ordered:
  - Tenofovir/emtricitabine 300/200mg 1 tablet PO Q12h
  - Sulfamethoxazole/trimethoprim 800/160mg 1 tablet PO daily
  - Ceftriaxone 1g IVPB Q24h
  - Azithromycin 500mg IVPB Q24h

  What prescribing errors occurred?

IM Prescribing Errors

- **Tenofovir/emtricitabine 300/200mg** should be once daily versus Q12h (dosing error)
- Atazanavir 300mg and ritonavir 100mg once daily (omission error)
- Sulfamethoxazole/trimethoprim 800/160mg should be dosed for PJP treatment versus prophylaxis
- May consider changing azithromycin to MAC prophylactic dose (1200mg once weekly)
- Reassess need for antimicrobial therapy for CAP versus PJP

Formulary Substitution

- The pharmacy has tenofovir, lamivudine, and lamivudine/zidovudine on formulary but not, tenofovir/emtricitabine. Atazanavir and ritonavir are on formulary and available in the pharmacy.

Which one of the following options is the best ART regimen for IM while hospitalized?

A. Substitute tenofovir/emtricitabine with lamivudine/zidovudine; continue atazanavir/ritonavir
B. Continue tenofovir and substitute emtricitabine with lamivudine; continue atazanavir/ritonavir
C. Order tenofovir/emtricitabine; continue atazanavir and ritonavir in the meantime
D. Order tenofovir/emtricitabine and hold atazanavir and ritonavir until regimen can be restarted together
NO Formulary Substitutions Please

- Higher rates of errors observed
- Not recommended to split combination products
- Conversions to formulary agents frequently lead to errors of omission or dosing errors and potential for errors at discharge
- Formulary should be assessed based on
  - Patient population and incidence of HIV
  - Commonly used ART
- Other benefits to adding ART to formulary improved drug interaction monitoring

Patients Own Medications

- Depends on hospital policy
- Should be verified by pharmacist
- Pros
  - Correct therapy
  - Minimal delays in therapy
  - Improved patient satisfaction
  - Improved discharge medication reconciliation
  - Reduced risk of administering part of a regimen
- Cons
  - "Non-formulary" listing with limited drug interaction evaluation

Administration Errors

- IM is receiving tenofovir/emtricitabine, atazanavir, and ritonavir. The medications are scheduled daily at 2100.

Which one of the following is a potential error?

A. tenofovir/emtricitabine needs to be administered with food
B. atazanavir/ritonavir needs to be administered with food
C. tenofovir/emtricitabine, atazanavir, and ritonavir all need to be administered with food
D. No potential errors identified

Administration Errors Continued

- IM now requires emergent intubation due to respiratory failure. He has subsequently been diagnosed with PJP and is receiving adequate treatment.

How should his ART be administered?

A. Hold ART
B. Switch ART to oral solutions
C. Crush tenofovir/emtricitabine and open atazanavir and ritonavir capsules
D. Crush tenofovir/emtricitabine, open atazanavir capsules, and give ritonavir as an oral solution

Crush or Not to Crush

<table>
<thead>
<tr>
<th>Drug</th>
<th>Okay to Crush or Sprinkle</th>
<th>Solution or Suspension Available</th>
<th>Food Considerations</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir/emtricitabine</td>
<td>No information</td>
<td>No</td>
<td>Without regard to meal</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>No PK studies, no enteric coating or sustained release, degrades in water, grape or orange juice, moisture sensitive and must be consumed immediately after meal</td>
<td></td>
</tr>
<tr>
<td>Atazanavir</td>
<td>No</td>
<td>No</td>
<td>Absorption increases with food</td>
<td></td>
</tr>
<tr>
<td>Ritonavir</td>
<td>No</td>
<td>10mg/ml solution (peppermint or orange flavored)</td>
<td>Should be taken with food</td>
<td></td>
</tr>
</tbody>
</table>

Drug Interactions

- IM has been on pantoprazole 40mg daily for stress ulcer prophylaxis since intubation. He has now been extubated and his ART (tenofovir/emtricitabine, atazanavir, and ritonavir) is being restarted. The team wants to continue stress ulcer prophylaxis.

Which one of the following options is the best strategy to manage the potential drug interaction between pantoprazole and atazanavir? Continue:

A. ART and pantoprazole
B. Pantoprazole and change atazanavir to darunavir
C. ART and pantoprazole; separate the doses by 12 hours
D. ART and change pantoprazole to famotidine 40mg Q12h
Drug Interaction Review

NRTI Drug Interactions

<table>
<thead>
<tr>
<th>NRTI</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tenofovir (TDF)</td>
<td>Lamivudine (3TC)</td>
</tr>
<tr>
<td>Viracept®</td>
<td>Zidovudine (ZDV)</td>
</tr>
<tr>
<td>Viread®</td>
<td>Abacavir (ABC)</td>
</tr>
<tr>
<td>Indinavir (IDV)</td>
<td>Tandemvir® (ATV)</td>
</tr>
<tr>
<td>Kaletra®</td>
<td>Emtricitabine (FTC)</td>
</tr>
<tr>
<td>Atripla®</td>
<td>—</td>
</tr>
</tbody>
</table>

NNRTI Drug Interactions

<table>
<thead>
<tr>
<th>NNRTI</th>
<th>Drug Interactions</th>
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</thead>
<tbody>
<tr>
<td>Efavirenz (EFV)</td>
<td>Nevirapine (NVP)</td>
</tr>
<tr>
<td>Sustiva®</td>
<td>Viramune®</td>
</tr>
<tr>
<td>—</td>
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</tbody>
</table>

PI Drug Interactions

<table>
<thead>
<tr>
<th>PI</th>
<th>Drug Interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ritonavir (RTV)</td>
<td>Lopinavir (LPV)</td>
</tr>
<tr>
<td>—</td>
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</tbody>
</table>

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Infection (Opportunistic) Prevention

<table>
<thead>
<tr>
<th>Infection/OI</th>
<th>Indication Criteria</th>
<th>First Choice</th>
<th>Alternative</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pneumocystis jiroveci pneumonia</td>
<td>CD4 count &lt; 200 cells/mm³</td>
<td>Sulfamethoxazole/trimethoprim (1 tablet po Q12h daily)</td>
<td>Then add azithromycin 1 tablet po weekly</td>
</tr>
<tr>
<td>Toxoplasmosis</td>
<td>Toxoplasma IgG titer ≥ 1:64</td>
<td>Sulfamethoxazole/trimethoprim (1 tablet po daily)</td>
<td>Then add pyrimethamine 1 tablet po weekly</td>
</tr>
<tr>
<td>Mycobacterium avium complex (MAC) CD4 ≤ 50 cells/mm³</td>
<td></td>
<td>Rifabutin, Itraconazole</td>
<td>Boceprevir, Omeprazole</td>
</tr>
<tr>
<td>Malaria</td>
<td>CD4 count &lt; 200 cells/mm³</td>
<td>Atovaquone/proguanil + pyrimethamine (1 tablet po daily)</td>
<td>Then add sulfadoxine/pirimethamine (1 tablet po weekly)</td>
</tr>
<tr>
<td>Aspergillus</td>
<td></td>
<td>Amphotericin B liposomal, voriconazole</td>
<td>Voriconazole</td>
</tr>
<tr>
<td>Coccidioidomycosis</td>
<td></td>
<td>Amphotericin B liposomal, voriconazole</td>
<td>Voriconazole</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td></td>
<td>Fluconazole</td>
<td>Voriconazole</td>
</tr>
<tr>
<td>Polyoma Kaposi’s sarcoma</td>
<td>CD4 count &lt; 50 cells/mm³</td>
<td>Ganciclovir or Cidofovir</td>
<td>Foscarnet</td>
</tr>
<tr>
<td>Cytomegalovirus retinitis</td>
<td>CD4 count &lt; 50 cells/mm³</td>
<td>Ganciclovir or Cidofovir</td>
<td>Foscarnet</td>
</tr>
</tbody>
</table>

IM is Ready for Discharge

- IM is being discharged from the hospital after 26 days. He will be going home on the following:
  - Truvada/emtricitabine 300/200mg – 1 tablet PO daily
  - Atazanavir 300mg – 1 capsule PO daily
  - Ritonavir 100mg – 1 capsule PO daily
  - Sulfamethoxazole/trimethoprim 800/160mg – 1 tablet PO daily
  - Azithromycin 600mg – 2 tablets PO once weekly

What are the steps involved in the discharge process?

Discharge: First Steps

- Perform discharge medication reconciliation
- Discharge counseling is key
  - Stress patient adherence
  - Reduce readmission potential
- Ensure patient is able to access medications and follow-up
  - Insured/no insurance?
  - Utilize Care Managers/Coordinators
  - Many Patient Assistance Programs and rebates available through manufacturers

Strategies to Prevent Errors in HIV-Positive Hospitalized Patients

- Heelon and colleagues significantly reduced the time until an error was rectified in hospitalized HIV-positive patients
  - Pharmacist reviewed all patients who had ART ordered for HIV
- Create a checklist and reassess regularly
- Consider the most common types of errors and address for ART and/or OI treatment/prophylaxis
Strategies to Prevent Errors in HIV-Positive Hospitalized Patients

- **ART/OI**: Does the regimen seem appropriate? Does it contain all components? No formulary substitutions? Are there duplications? Does the patient require OI prophylaxis?

- **Dosing errors**: Are all doses appropriate? Do the medications need to be renally or hepatically dose adjusted?

- **Administration errors**: Are there specific timing or food requirements? Is the patient temporarily NPO?

- **Drug interactions**: ALWAYS double-check. Keep the most common in mind.

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Summary

- More patients will be receiving ART

- High potential for a variety of errors

- Errors in this patient population have devastating consequences

- Pharmacists play a large role in error prevention

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Strategies to Prevent Errors in HIV-Positive Hospitalized Patients

- ART should be considered a team
  - “Hold one, hold all”

- Perform medication reconciliation at admission and discharge

- If possible no formulary substitutions

- Ensure access to medications prior to discharge

- Know when to ask for help and consult an expert