Antiviral Medications, Part 2: HIV Antiretroviral Therapy

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Medical-surgical nurses in collaboration with an interprofessional team play an integral role in optimizing adherence and outcomes for patients with human immunodeficiency virus (HIV). Knowledge of antiretroviral medications and regimens is essential for medical-surgical nurses to help achieve treatment goals of individuals infected with HIV.

TABLE 1. Stages of HIV

<table>
<thead>
<tr>
<th>Stage</th>
<th>Symptoms</th>
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</thead>
<tbody>
<tr>
<td>Stage 1 - Acute Stage</td>
<td>Flu-like symptoms lasting several weeks; very contagious</td>
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<tr>
<td>Stage 2 - Dormant Stage</td>
<td>Symptoms subside; some patients may remain in this stage many years or may progress rapidly through this stage; at the end of stage 2, CD4 counts begin to decrease and viral load increases.</td>
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<tr>
<td>Stage 3 - AIDS</td>
<td>Most severe stage due to severe damage to immune system; patients acquire opportunistic illnesses, especially infection and cancers; persons with AIDS live an average of 3 years.</td>
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</tbody>
</table>

Source: CDC, 2016a

Treatmen Goals for HIV

Clinical care for HIV/AIDS has improved substantially with increased knowledge of the disease and medications, best practices, and enhanced primary care. HIV now is treated primarily with a class of medications called antiretroviral therapy (ART). In combination with other antiretroviral (ARV) medications, ART is part of an HIV regimen (AIDSinfo, 2016). When taken appropriately, ART can extend significantly lives of people infected with HIV, help keep them healthy, and decrease the chance of their infecting others. These medications, however, cannot cure HIV (AIDSinfo, 2016; CDC, 2016a). Part 1 of this ARV medications series focused on treating herpes and influenza viruses (Felicilda-Reynaldo, Patterson, & Gloe, 2017). In Part 2, indications, contraindications, untoward effects, and nursing implications for administration of ART in the treatment of HIV are presented.

Medical-surgical nurses in collaboration with an interprofessional team play an integral role in optimizing adherence and outcomes for patients with human immunodeficiency virus (HIV). Knowledge of antiretroviral medications and regimens is essential for medical-surgical nurses to help achieve treatment goals of individuals infected with HIV.
2016; U.S. Department of Health and Human Services [DHHS], 2016a, 2016b). When deciding to start ART, practitioners must consider the individual’s comorbid conditions. ART should be considered on a case by case basis (DHHS, 2016a). Although ART is recommended for all individuals, it is recommended urgently for people with a history of an AIDS-defining illness, HIV/hepatitis B (HBV) co-infection, HIV/hepatitis C (HCV) co-infection, acute opportunistic infections, lower CD4 counts, HIV-associated neuropathy, and pregnancy, as well as patients at risk for transmitting HIV to sexual partners (Raper & Dobbs, 2016).

Risks and benefits should be evaluated consistently for each patient. In particular, providers must consider the difficulty of a patient in adhering to a complicated drug regimen. Potential benefits for early ART include maintaining a higher CD4 T-cell count to help reduce irreversible immune system damage; decrease risk of complications; and decrease risk of co-morbid medical conditions, such as cardiovascular disease, renal disease, liver disease, and non-AIDS-associated infections and malignancies. Risks of taking ART early include side effects and toxicity development; development of viral resistance to medications; less time to prepare for therapy and the need for adherence, and shorter time to learn about HIV; long exposure time to ART with increased chance of treatment fatigue; potential transmission of medication-resistant viruses; and use of current ART regimens before development of potentially less toxic and more effective antiretroviral medications (Raper & Dobbs, 2016).

**Antiretroviral Medications**

Over 30 medications within six classes are available for ART. The six classes of ARV agents include nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), integrase strand transfer inhibitors (INSTIs), fusion inhibitor (FI), and chemokine receptor antagonist (CCR5 antagonist) (Raper & Dobbs, 2016; U.S. Food and Drug Administration [FDA], 2016). ART generally consists of three medications from at least two different classes: two NRTIs plus one drug from either NNRTI, PI (boosted with ritonavir), INSTI, or a CCR5 antagonist (AIDSinfo, 2016; Raper & Dobbs, 2016). Numerous medications exist within the six classes, with even more combinations possible for ART.

**Nucleoside Reverse Transcriptase Inhibitors**

NRTIs include abacavir (Ziagen®), lamivudine (Epivir®), zidovudine (Retrovir®), didanosine (Videx®), emtricitabine (Emtriva®), tenofovir (Vemlidy®), Viread®), and stavudine (Zerit®) (AIDSinfo, 2016; FDA, 2016). Their primary mechanism of action is inhibition of retrovirus replication, including HIV, interfering with viral RNA-directed DNA polymerase, also known as reverse transcriptase. This class of medications decreases the ability of DNA chains to lengthen, preventing viral reproduction; it also inhibits viral insertion into the host DNA (Karch, 2017; Raper & Dobbs, 2016).

Renal function must be monitored during use of NRTIs because these drugs are eliminated via the kidneys (Raper & Dobbs, 2016). Raper and Dobbs also identified the risk for life-threatening lactic acidosis. Treatment for lactic acidosis should start with identification of cause, and additional treatment with intravenous fluids and supplemental oxygen. If severe, mechanical ventilation may be required (Lloyd, 2016). Common untoward effects include anemia, bone marrow suppression, headache, myopathy, dry mouth, nausea, vomiting, constipation, diarrhea, flatulence, renal issues, and rash (Karch, 2017; Raper & Dobbs, 2016).

**Non-Nucleoside Reverse Transcriptase Inhibitors**

NNRTIs include rilpivirine (Edurant®), etravirine (Intelence®), delavirdine (Rescriptor®), efavirenz (Sustiva®), and nevirapine (Viramune®) (AIDSinfo, 2016; FDA, 2016). Acting as specific noncompetitive reverse transcriptase inhibitors, NNRTIs prevent the transfer of information that allows the virus to continue formation of viral DNA; the virus becomes unable to take control of the cell and reproduce (Karch, 2017). Additionally, NNRTIs disrupt the catalytic site of the enzyme (Raper & Dobbs, 2016). When combining this class of medications with other ARTs, Raper and Dobbs noted providers must be aware that clinically significant drug interactions may occur. These interactions could include drug toxicity, risk of resistance, hyperlipidemia, hepatotoxicity, myopathy, rhabdomyolysis, and renal failure (Foy, Sperati, Lucas, & Estrella, 2014). Because liver problems could be severe and life-threatening with NNRTIs, providers must monitor liver function (Raper & Dobbs, 2016). Common untoward effects with NNRTIs include headache, fatigue, dizziness, drowsiness, vivid dreams, liver problems, dry mouth, nausia, vomiting, diarrhea, constipation, flatulence, and rash (Karch, 2017; Raper & Dobbs, 2016).

**Protease Inhibitors**

Atazanavir (Reyataz®), darunavir (Prezista®), fosamprenavir (Lexiva®, Telzir®), indinavir (Crixivan®), lopinavir and ritonavir combination (Kaletra®), nelfinavir (Viracept®), saquinavir (Invirase®, Fortovase®), and tipranavir (Aptivus®) are PIs (AIDSinfo, 2016; FDA, 2016). They act uniquely as selective and competitive inhibitors of HIV protease; this class plays an important role in preventing cleavage of protein precursors essential for HIV maturation, infection of new cells, and replication (Raper & Dobbs, 2016). As a result, the HIV particle remains immature and non-infective with the inability to inject itself into a cell (Karch, 2017). PIs also may be prone to drug interactions with other medications that use the cytochrome P450 pathway (Raper & Dobbs, 2016). A list of cytochrome P450 drug interactions can be found through the Indiana University School of Medicine (2016).

Unlike NNRTIs, PIs are eliminated in the feces and do not require renal monitoring. However, liver problems could be severe and liver function monitoring is necessary (Raper & Dobbs, 2016). Many of the medications within this class are not recommended in patients with severe hepatic impairment (Karch, 2017). Common untoward effects
for PIs are hyperglycemia, hyperlipidemia, lipodystrophy, diarrhea, other gastrointestinal disturbances, liver problems, rashes, and bleeding problems (Karch, 2017; Raper & Dobbs, 2016).

**Integrase Strand Transfer Inhibitors**

INSTIs include dolutegravir (Tivicay®), elvitegravir (Vitekta®), and raltegravir (Isentress®) (AIDSinfo, 2016; FDA, 2016). Their primary mechanism of action is blocking the integrase enzyme, which HIV needs to make more virus (Raper & Dobbs, 2016). This class should be monitored (Karch, 2017). Common untoward effects include headache, myopathy, pyrexia, edema, sleep disorders, somnias, rhinitis, cough, URTI, rash, diarrhea, and urinary problems (Raper & Dobbs, 2016).

**Fusion Inhibitor**

Only one fusion inhibitor medication is available: enfuvirtide (Fuzeon®), also known as T-20 (AIDSinfo, 2016a; FDA, 2016). Its primary mechanism of action is blocking fusion, an important step in the process of HIV entry into CD4 cells (Raper & Dobbs, 2016). Common untoward effects with the FI include injection site reactions (swelling and pain), skin itchiness, insomnia, fatigue, dizziness, nausea, diarrhea, and numbness in feet and legs (Karch, 2017; Raper & Dobbs, 2016).

**CCR5 Antagonist**

Maraviroc (Selzentry®) is the only available CCR5 antagonist (AIDSinfo, 2016; FDA, 2016). This drug blocks CCR5, a molecule found on the surface of CD4 cells, to prevent HIV from entering the cell (Raper & Dobbs, 2016). Because severe hepatotoxicity has been reported, liver function must be monitored (Karch, 2017). Common untoward effects are dizziness, paraesthesia, rhinitis, cough, URTI, pyrexia, edema, sleep disorders, rash, diarrhea, and urinary problems (Raper & Dobbs, 2016).

**ART Combination for Treatment-Naïve HIV Patients**

Medications used to treat HIV usually are given as a combination of three drugs. For adults and adolescents, the preferred first-line combination includes two NRTIs plus efavirenz. However, the decision regarding specific medications depends on if the individual is treatment-naïve or has other viral illnesses (Gunthard, Aberg, & Eron, 2014). Each of the ART medications has unique characteristics and should be used based on the patient's individual circumstances. ART combination options for first-line treatment and alternatives for adults and adolescents are summarized in Table 2.

**Nursing Implications**

Nurses play a very important role in managing care of patients receiving ART. Essential nursing considerations include thorough assessment through a complete history and physical (Karch, 2017). Patient education must be specific to the ART regimen, but should include regular medical care, strict adherence to the regimen (e.g., when to take the medications), periodic blood testing (especially renal and hepatic function tests), and education regarding potential treatment side effects (Karch, 2017).

A meta-analysis of 85 trials showed text messaging was more effective than standard of care in improving patient adherence to ART (Kanters et al., 2017). Furthermore, patients who underwent cognitive behavioral therapy and supportive interventions had improved viral suppression than those treated with standard of care. The study also found using multiple interventions to promote adherence to ART and viral suppression is superior to implementing single interventions.

In a systematic review and meta-analysis of 125 studies, Shubber and colleagues (2016) found multiple barriers reported by patients with HIV regarding adherence to ART. Barriers included forgetfulness, a major change in their daily routines, depression, alcohol/substance misuse/abuse, and secrecy or stigma. For maximum efficiency, authors concluded healthcare providers should use a triaged approach to identify...
patients at risk for poor adherence and establish interventions to help these patients overcome multiple barriers they may face.

Cost may be a concern for many patients with these expensive medications. Coverage can vary greatly among insurance providers. Programs such as Medicaid, Medicare, drug assistance programs, state AIDS Drug Assistance Programs, or resources in the community, often pay the majority of medication costs (Raper & Dobbs, 2016). Assistance should be provided to individuals and their families to find additional resources to help offset the costs.

**Special Considerations for Pregnant Women Taking ART**

The Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission suggested multiple considerations when determining ART use (DHHS, 2016b). These include convenience, adverse effects, drug interactions, resistance testing results, pharmacokinetics, and experience with use in pregnancy. The same ART regimen recommended for non-pregnant adults generally can be used if appropriate in pregnant women, if there are no known adverse effects in women, fetuses, or infants that would outweigh the benefits of ART (DHHS, 2016b).

**ART Failure**

Although ART often is very successful, the potential for failure exists. Factors that may increase the risk for failure include AIDS diagnosis, patients’ co-morbid conditions, higher pretreatment HIV RNA level, lower pretreatment CD4 T-cell count, presence of pretreatment drug-resistant virus, prior ART failure, adverse effects or toxicity to ARTs, non-adherence, and suboptimal potency and effects of ARTs due to pharmacokinetic factors in the HIV reservoir (Raper & Dobbs, 2016). Identifying potential causes of ART failure is essential, according to Raper and Dobbs. Nurses play an integral role in assisting clinicians in determining an individual’s risk for ART failure, including non-adherence to ART.

Nurses can assist with determining risks for ART failure by having effective communication with the patient and examining pharmacy records for treatment adherence (Raper & Dobbs, 2016). No standard exists for assessing patient adherence to ART; however, some validated tools have been helpful in the clinical setting, such as viral load tests and patient self-report of adherence. Additional tools include patient pharmacy record and pill counting (AIDSinfo, 2014).

When available, viral load tests should be performed every few months during ART. Viral load tests measure the effectiveness of ART to control viral replication (measurement of CD4 count). If the treatment is working, the viral load will drop to less than 50 copies/mL (Raper & Dobbs, 2016). Viral load suppression is a reliable indicator and has been used to encourage continuous adherence among patients. Patients who have not achieved viral suppression after 24 weeks of ART have high risk for suboptimal adherence.

Patient self-report of adherence is another common way of evaluating medications use. Patient self-reports need to be assessed carefully as patients may overestimate their adherence to treatment. Usually self-report is paired with other objective tests such as viral load suppression (AIDSinfo, 2014). Additional measures of adherence include pharmacy records and pill counts. Pharmacy records are valuable if patients retrieve their medication from one source. According to AIDSinfo, however, pill count could be inaccurate as this may be altered by patients.

Strict adherence to ART is crucial not only to decrease risk of HIV transmission, but also to sustain HIV suppression, reduce risk of drug resistance, and improve patients’ overall health, quality of life, and survival (DHHS, 2016a). Poor adherence is a major cause of therapeutic failure; achieving adherence to ART is a critical factor of long-term outcome in patients with HIV (Aidsinfo, 2014). When ART is discontinued or interrupted, effects could include HIV viral rebound, loss of virologic control, resistance to treatment, and loss of alternative treatment options, resulting in impaired clinical progression (Raper & Dobbs, 2016).

**Viral rebound** is defined as having a detectable viral load after a period of undetectable viral load. Major causes of viral rebound include medication resistance and poor adherence (AIDSinfo, 2017). Unplanned interruption of treatment may be necessary for illness, toxicity, surgery, or if medication is not available (Raper & Dobbs, 2016). Providers must assess continually for potential for interruption and risks versus benefits (Raper & Dobbs, 2016).

Standard monitoring for patients undergoing ART should include mental health conditions, alterations in metabolism of glucose or lipids, cardiovascular risks, co-infection with HBV or HCV, any high-risk behaviors, patients’ immunization history, hepatic and renal function, sexually transmitted infections, any somatic signs and symptoms, and tobacco, alcohol, and substance use (Raper & Dobbs, 2016). This allows healthcare providers to determine other potential causes of non-adherence, development of co-morbid conditions, and poor clinical progression in case of treatment failure.

Patients who are changing their ART treatment after failure should consult infectious disease providers. These providers will need to consider individualized patient characteristics in determining new medication combinations to ensure effective ongoing treatment and reduce the development of drug resistance (Gunthard et al., 2014). Providers also will need to determine if new combinations are part of resistance patterns in the specific geographic location where treatment is provided (Huang et al., 2016).

**Conclusion**

Medical-surgical nurses in collaboration with an interprofessional team play an integral role in optimizing adherence and outcomes for patients with HIV. Knowledge of ART medications and regimens is essential for medical-surgical nurses. Interventions include formulating attainable treatment plans adapted to the individual patient,
Instructions For Continuing Nursing Education Contact Hours

Antiviral Medications, Part 2: HIV Antiretroviral Therapy

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Learning Outcome

After completing this learning activity, the learner will be able to discuss antiviral medications used to manage human immunodeficiency virus.

Learning Engagement Activity

Review the resources available from the FDA on antiretroviral drugs used in the treatment of HIV infection at https://www.fda.gov/ForPatients/Illness/HIVAIDS/Treatment/ucm118915.htm

Fees — AMSN Member: FREE Regular: $20

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identifying barriers with ART, surveilling ART routinely, noting predictors of success, and identifying potential adverse effects of medications (Raper & Dobbs, 2016).

REFERENCES


