Combating HIV & AIDS – A Review on Drug Side-Effect Profile

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World AIDS Day is distinguished on 01st December every year to increase awareness about HIV/AIDS and to demonstrate international unity in the face of the endemic. The day is an occasion for communal and private partners to disseminate information about the status of the pandemic and to encourage progress in HIV/AIDS prevention, treatment and care around the world, predominantly in high prevalence countries.

Key facts:

1. HIV continues to be a major global public health issue, having claimed more than 25 million lives over the past three decades.
2. There were approximately 35.3 [32.2– 38.8] million people living with HIV in 2012.
3. HIV infection is usually diagnosed through blood tests detecting the presence or absence of HIV antibodies.
4. There is no cure for HIV infection. However, effective treatment with antiretroviral drugs can control the virus so that people with HIV can enjoy healthy and productive lives.
5. In 2012, more than 9.7 million people living with HIV were receiving antiretroviral therapy (ART) in low and middle-income countries.

Between 2011-2015, WHO World AIDS Day has the theme: "Getting to zero: zero new HIV infections. Zero discrimination. Zero AIDS-related deaths".

Antiretroviral therapy (ART) is cure of people infected with human immunodeficiency virus (HIV) using anti-HIV drugs. The standard treatment consists of a combination of at least three drugs (often called “highly active antiretroviral therapy” or HAART) that hold back HIV replication. Three drugs are used in order to diminish the probability of the virus emergent resistance. ART has the prospective both to lessen mortality and morbidity rates among HIV-infected community, and to recover their quality of life.

There are diverse classes of anti-retroviral drugs aimed at preventing replication of HIV at various points of the life cycle:

1. Nucleoside or nucleotide reverse transcriptase inhibitors - abacavir, didanosine, emtricitabine, lamivudine, stavudine, and tenofovir.
2. Non-nucleoside reverse transcriptase inhibitors - efavirenz, etravirine, and nevirapine.
3. Protease inhibitors - atazanavir, indinavir, lopinavir, nelfinavir, ritonavir, saquinavir.
4. Integrase inhibitors - raltegravir.
5. Fusion inhibitors - enfuvirtide.
6. CCR5 antagonists - maraviroc.

Antiretroviral medicines work by stopping the HIV from making copies of itself. The amount of virus in the body (viral load) is decreased. This gives immune system some time to become strong again and allows the body to make more CD4 T cells. The aim of treatment is to reduce the viral load to very low levels for as long as possible, and to increase the number of CD4 T cells to a normal level. This in turn means that the patient is less likely to get infections.

The medicines in each class work in slightly different ways, but all work to stop the HIV from replicating itself. They work best when they are prescribed in combination.

Side Effects of HAART (refer the Table)

Side effects are a secondary, typically undesirable effect of a drug or medical treatment.

Antiretroviral medicines can have many side effects. Some can be very serious, even life-threatening, such as liver failure or inflammation of the pancreas (pancreatitis). Most are not serious but may reduce the quality of life.

Because highly active antiretroviral therapy (HAART) requires the use of 3 or more antiretroviral medicines, some side effects are likely to occur, including: nausea or vomiting, diarrhea, abdominal pain, severe fatigue, muscle aches, rash and fever.

HIV medications can induce anemia, neutropenia, and idiopathic thrombocytopenic purpura.

Other adverse systemic affects of HAART include an increased risk of hyperglycemia and dyslipidemia associated with metabolic syndrome. Abdominal obesity and insulin resistance or glucose intolerance are the main risk factors for dyslipidemia associated with metabolic syndrome. These patients are at a greater risk for Type 2 diabetes mellitus and cardiovascular disease. Therefore, it is important to be aware of these additional systemic effects and monitor patients' sugar and cholesterol levels accordingly.

Name	Adverse Events
Nucleoside reverse transcriptase inhibitors (NRTIs): NRTIs are associated with lactic acidosis, hepatic steatosis, and body fat redistribution (lipodystrophy)	
Abacavir	Hypersensitivity reaction (may include fever, rash, nausea, vomiting,diarrhea, malaise, shortness of breath, cough, pharyngitis); patients positive for HLA-B*5701 are at highest risk for hypersensitivity (perform HLA screening before initiating)
Didanosine	Peripheral neuropathy, pancreatitis, nausea, lactic acidosis
Emtricitabine	Minimal toxicity, hyperpigmentation
Lamivudine	Minimal toxicity, severe acute exacerbation of hepatitis may occur with Hepatitis B Virus (HBV) co-infection upon discontinuation
Stavudine	Peripheral neuropathy, pancreatitis, lactic acidosis, lipoatrophy, hyperlipidemia
Tenofovir	Nausea, vomiting, diarrhea, headache, asthenia (weakness), renal insufficiency
Zalcitabine	Peripheral neuropathy, pancreatitis, lactic acidosis, stomatitis (inflammation of the mucous membrane of the mouth)
Zidovudine	Nausea, vomiting, headache, asthenia, anemia, neutropenia
Non-nucleoside reverse transcriptase inhibitors (NNRTIs): NNRTIs are associated with rash, and may cause Stevens-Johnson syndrome and toxic epidermal necrolysis	
Efavirenz	Rash, CNS (eg, somnolence, vivid dreams, confusion, visual hallucinations), hyperlipidemia
Nevirapine	Rash, hepatitis
Protease Inhibitors: All PIs are associated with metabolic abnormalities including dyslipidemia, hyperglycemia, insulin resistance, and lipodystrophy. (Atazanavir is less likely to cause dyslipidemia.)	
Atazanavir	Indirect hyperbilirubinemia, prolonged PR interval, skin rash(20%),
Fosamprenavir	Rash, nausea, vomiting, diarrhea,
Indinavir	Nephrolithiasis, nausea, indirect hyperbilirubinemia
Lopinavir/ritonavir	Nausea, vomiting, diarrhea, asthenia,
Nelfinavir	Diarrhea
Ritonavir	Nausea, vomiting, diarrhea, asthenia, oral paresthesias
Saquinavir	Nausea, diarrhea, headache, PR and QT interval prolongation

Integrase inhibitor (II)	
Raltegravir	Nausea, diarrhea, headache, Creatine Kinase elevations, myopathy / rhabdomyolysis (rare)
Chemokine receptor antagonist (CCR5 antagonist)	
Maraviroc	Constipation, dizziness, infection, rash
Fusion inhibitor (FI)	
Enfuvirtide	Injection-site reactions (eg, pain, erythema, induration, nodules), Neutropenia

Lipodystrophy, metabolic acidosis, new-onset diabetes mellitus and dyslipidemias are common co-morbidities that occur with the use of ART. The development of these complications, especially if patients are not informed in advance, may lead to non-adherence to medication regimens.

ROLE OF PHARMACIST

Pharmacists can contribute to the careful pharmacologic and dietary management that is required for the treatment of multiple diseases and disorders and can work with prescribers on the prevention and management of ART-related morbidity.

Pharmacists play an important role in the out-patient care of HIV-infected patients by ensuring patient adherence to complex treatment regimens and providing pharmaceutical care.

DEFINITIONS:

Neutropenia *is defined as an absolute neutrophile count (ANC) of less than 1,500 cells/mm3of blood. Neutropenia is commonly related with HIV and its frequency increases with the progression of HIV to AIDS. Patients have an increased risk of infection when ANC values drop below 1,500 cells/mm*^{3}

Idiopathic thrombocytopenic purpura (ITP), *is defined as isolated low platelet count (thrombocytopenia) with normal bone marrow and the lack of other causes of thrombocytopenia. It causes a characteristic purpuric rash and an increased tendency to bleed.*

Lipoatrophy *is the term telling the localized loss of fat tissue.*

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