

COMMENT

MANAGEMENT OF HIV

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In the early 1980s, a number of homosexual men in New York, San Francisco and other areas of USA began to develop Pneumocystis pneumonia, Kaposi's sarcoma and other opportunistic infections. All of those people were immuno-deficient and that was the beginning of Acquired Immunodeficiency Syndrome (AIDS) epidemic. In 1983, Human Immunodeficiency Virus (HIV) was first detected in a patient with AIDS. Presently more than forty million people are HIV positive in the world and HIV-1 is responsible for most of the cases.

There are various modes of transmission of HIV including sexual contact, contamination of blood and blood products, intravenous drug abuse, accidental inoculation and vertical transmission. Perinatal transmission can be reduced by elective cesarean section and antiretro viral therapy (ART) especially with zidovudine (AZT)^{1,2}. Transmission also depends on the viral load. The lower the viral load the less infectious the patient and vice versa. Prevention is better than cure and primary prevention can be done by using barrier methods of contraception, routine blood screening and encouraging IV drug abuser not to share needles. This golden rule of primary prevention is especially important for HIV and AIDS. Various trials are also being done around the world to develop a vaccine for HIV.

HIV can be diagnosed by detecting anti-HIV antibodies in the serum. Enzyme-linked immunosorbant assay (ELISA) is commonly used for screening purpose but these days rapid test is also widely available. Rapid HIV tests demonstrate sensitivities and specificities comparable to those of ELISA. More than 60 rapid HIV tests have been developed and are used in various countries. The main advantage of rapid test is its low cost and the results are available on the same day^{3,4}.

In the early part of HIV sero-conversion, the features are non-specific and resemble flu or glandular fever. Patient may complain of fever, weakness, muscle aches, rash, pharyngitis or lymphadenopathy. The CD4 count

continuously drops and when it is below 200 cells/ μ L, the patient is more likely to develop different opportunistic infections including Kaposi's sarcoma, Non-Hodgkin's lymphoma, Tuberculosis, Pneumocystis pneumonia, esophageal candidiasis, cerebral toxoplasmosis and Cryptococcus meningitis⁵. Opportunistic infections are a major cause of morbidity and mortality in HIV positive patients and Pneumocystis pneumonia is the most common opportunistic infection in patients with AIDS^{6,7}. The recommended treatments of some of the opportunistic infections are shown in table I.

Table I :Common opportunistic infections and recommended treatment in patients with AIDS.

INFECTION	TREATMENT
Mycobacterium tuberculosis	First line: Isoniazid, Streptomycin, Rifampicin, Amikacin, Pyrazinamide, Kanamycin, Ethambutol and Capreomycin. Second line: Ofloxacin, Aminosalicyclic acid, Ciprofloxacin, Clarithromycin, Cycloserine, Azithromycin, Ethionamide
Mycobacterium avium	Clarithromycin+Ethambutol+Rifabutin or Rifampicin+/-Ciprofloxacin
Pneumocystis pneumonia	Co-trimoxazole or Pentamidine isetionate 2nd Line: Primaquine+Clindamycin, Trimetrexate+Calcium folinate, Atovaquone
Candidiasis	For local infection: Nystatin; systemic treatment: Fluconazole or Amphotericin B.
Toxoplasmosis	Sulfadiazine or Clindamycin + Pyrimethamine
Cryptococcal meningitis	Amphotericin B and Flucytosine or Fluconazole
Cytomegalovirus	Ganciclovir or Foscarnet. Alternate: Valganciclovir or Cidofovir

The treatment was revolutionized when Highly Active Anti retroviral Therapy (HAART) was introduced in 1996. AIDS is still a major cause of death in parts of Africa, South East Asia and other developing countries as the treatment is very expensive and majority of people in these countries cannot afford it. ART suppresses viral load to such low levels that virus is unable to generate drug-resistance mutation⁸. The target is to achieve a viral load of <50 HIV RNA copies/ml within three to six months of starting treatment.

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The treatment should be started when CD4 count is between 200 and 350 cells/ μ L. According to British HIV Association (BHIVA), the treatment should commence with two nucleoside reverse transcriptase inhibitors (NRTI) with either a non- nucleoside reverse transcriptase inhibitor (NNRTI) or ritonavir boosted protease inhibitor (PI). Before beginning the treatment, resistance testing should be done of all patients. Where treatment is widely available, ten percent of newly diagnosed patients are at least partially resistant to drugs^{9,10}.

HLA B5701 status of patient should be tested if the treatment includes abacavir as five percent of abacavir-treated patients develop hypersensitivity which can be life-threatening and is more common in HLA B5701 positive patients^{11,12}. If patient is co-infected with hepatitis B, then the treatment should include lamivudine. Asymptomatic patients, whose viral load is undetectable and CD4 count is stable, are usually followed-up every three months.

After the commencement of HAART, patient may get immune-reconstitution syndrome which is characterized by the paradoxical worsening and flaring up of pre-existing infections including Mycobacterium tuberculosis, Mycobacterium avium complex, Pneumocystis jirovecii pneumonia, toxoplasmosis, hepatitis B and C, CMV, toxoplasmosis, Varicella zoster virus infection, cryptococcal infection and progressive multi-focal leukoencephalopathy caused by JC virus. Immune reconstitution syndrome can be treated with non-steroidal anti-inflammatory drugs or steroids to reduce inflammation along with management of opportunistic infection. Immune reconstitution syndrome is more common in patients with a CD4 count of less than 50 cells/ μ L¹³.

Patients sometime also complain of abnormal fat redistribution with Cushingoid features which is more common with stavudine and zidovudine. All nucleoside and nucleotide RTIs are associated with hepatic steatosis and lactic acidosis. Patients can develop other side-effects like peripheral neuropathy and pancreatitis with didanosine, nephropathy with tenofovir and indinavir and rash with delavirdine and nevirapine.

Various trials are being done all over the world and many drugs are in the pipeline and will be available in near future. AIDS, which was a fatal disease in early 1980s, has now become a chronic manageable disease. The treatment has improved drastically in the last twenty-five years especially in the developed countries and will improve further with the availability of new drugs.

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