Review Article

HIV Infection: A Review

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ABSTRACT

HIV infection/Acquired immune deficiency syndrome (AIDS) is a condition where CD4+ cell count falls below 200 cells/µl and immune system begins to fail in humans. AIDS is transmitted by sexual contact, exposure to infected body fluids or tissues and from mother to child during pregnancy, delivery or breast feeding. Therefore the effort for prevention and management of AIDS is essential. The management of HIV infection can be controlled by antiretroviral therapy, alternative medicine, use of condoms etc. In present review is gives an about stages of HIV infection, HIV transmission and approaches for prevention and management of AIDS.

Keywords: HIV infection, CD4+, Antiretroviral therapy.

INTRODUCTION

AIDS/HIV infection is one of the most dangerous and a pandemic[1] disease which is spreading over a large demographic area of the world. It impacts on society such as an illness, a source of discrimination and economic condition of people. Human immunodeficiency virus infection is a disease of human immune system caused by infection with human immune deficiency virus. It is called AIDS when a person infected with HIV has a CD4+ count of less than 200cells/µL. HIV destroys the immune system by attacking and killing CD4 cells.HIV uses the machinery of the CD4 cells to multiply (make copies of it) and spread throughout the body. Prevention[2] of HIV infection primarily through safe sex, male circumcision, use of diaphragms, substance abuse treatment, condom use, use needle exchange programs are key strategies to control the spread of disease and may lead to a near normal life expectancy. Antiretroviral treatment reduces the risk of death and complications from the disease these medications. The present review gives idea about HIV transmission, stages of HIV infections and approaches for prevention and treatment of AIDS.

HIV Transmission

HIV is transmitted principally in three ways: by sexual contact, by blood (through transfusion, blood products, or contaminated needles), or by passage from mother to child. Although homosexual[3] and, heterosexual[4] transmission is the most important means of HIV spread worldwide today. Treatment of blood products and donor screening has essentially eliminated the risk of HIV from contaminated blood products in developed countries, but its spread continues among intravenous drug users who share needles. Breast milk from infected mothers has been observed high levels virus. HIV is not spread by the fecal-oral route; aerosols; insects; or casual contact, such as sharing household items or hugging.

Discovery of HIV

AIDS was first recognized in the United States in June 5,1981. There was rare opportunistic infections observed unusual clusters of Pneumocystis pneumonia (PCP) caused by a form of Pneumocystis carinii(now recognized as a distinct species Pneumocystis jirovecii) in five homosexual men in Los Angeles. PCP clusters were found among healthy men in cities throughout the country along with other opportunistic diseases such as kaposi's sarcoma and persistent generalized

lymphadenopathy. It was reported among gay men in Southern California in 1982 that a sexually transmitted infectious agent might be the etiological agent. The syndrome was initially termed as GRID or gay related immune deficiency. It was identified by health authorities that some people with the syndrome were not homosexual men. The same opportunistic infections were found among hemophiliacs heterosexual intravenous drug users. The disease was named by CDC as AIDS by august 1982.A new retrovirus[5] from lymphoid ganglions was isolated by doctor's from Dr. Luc Montagnier's team at the Pasteur Institute in France in May 1983.It was suspected that the virus was the cause of AIDS. The virus was later named lymphadenopathy associated virus(LAV).Robert Gallo et.al[6] of United States confirmed the discovery of the virus,but they called it as human T lymphotropic virus type III (HTLV-III) in May 1984.The International Committee on Taxonomy of Viruses named the virus as HIV(Human Immunodeficiency Virus) in May 1986.Francoise Barre Sinoussi and Montagnier were awarded Nobel Prize in Physiology or Medicine for their discovery of human immunodeficiency virus in 2008.There are two types of HIV that cause AIDS such as HIV type1(HIV-1) and HIV-2[7].The modes of transmission of both types are similar and are associated with the same opportunistic infections, but HIV-2 appears to progress slowly.

Stages of HIV Infection[8]

The Centers for Disease Control and Prevention (CDC) has identified the stages of a typical HIV infection: Categories A, B and C.

Category A stage

Category A stage can be known by performing a blood test. While at least half of infected individuals will develop a mononucleosis-like illness (headache, muscle ache, sore throat, fever, and swollen lymph nodes) within three weeks of exposure. Swollen lymph glands and malaise can persist for years through Category A HIV. In this stage CD4 count is greater or equal to 500 cells/µl and no AIDS defining conditions

Category B stage

Category B stage indicates of immune system failure. Persistent infections such as yeast infections, shingles, diarrhea, and certain cancerous conditions of the cervix are apparent. In this stage CD4 count is between 200 to 500 cells/µl and no AIDS defining conditions.

Category C stage

Category C is synonymous with AIDS. Category C HIV (clinical AIDS) occurs once CD4 numbers have fallen substantially (to 200/mm^3 from the normal level of 800–1200 cells/ mm^3). In this stage the opportunistic infections associated with AIDS appear. The patient may observe yeast infections of the esophagus, bronchi, and lungs; *Pneumocystis* pneumonia (a fungal infection); toxoplasmosis (caused by a protozoan that is spread by cats); Kaposi's sarcoma (a rare cancer of the skin caused by a virus); cytomegalovirus (CMV) infections; and tuberculosis.

Approaches for prevention of AIDS

- **Antiretroviral therapy (HAART)**

Beginning in the mid-1990s, an increasing number of HIV-infected individuals began a drug regime called highly active antiretroviral therapy (HAART) a combination of three or more anti-HIV drugs taken at the same time[9]. With the advent of HAART[10, 11] deaths from HIV began to decline in various countries.

- **Vaccine Development[12]**

It may be possible to enhance the immunogenicity of adenovirus vaccines by boosting them with naked DNA containing antigens similar to those delivered by the viral vector. In addition, some of the newer vaccine trials are considering whether people who become infected after receiving the vaccine are better able to control HIV infection. This would allow the person to stay healthier for a longer period of time and may make the people who receive the vaccine less infectious to future partners.

Table 1: FDA approved Entry inhibitors for antiretroviral therapy (HAART)

Generic Name	Adult dose(mg)/day	Brand Name	Manufacturer	FDA Approval Date
Enfuvirtide	90(2) Subcutaneously	Fuzeon	Hoffmann La Roche	March 13,2003
Maraviroc	400(2)	Selzentry	Pfizer	Aug.6,2007

Table 2: FDA approved Integrase inhibitors (IIs) for antiretroviral therapy (HAART)

Generic name	Adult dose(mg)/day	Brand name	Manufacturer	FDA approval date
Raltegravir	400(2)	Isentress	Merck	Oct.12,2007

Table 3: FDA approved Nucleoside Reverse Transcriptase Inhibitors (NRTIs) for antiretroviral therapy (HAART)

Generic name	Adult dose(mg)/day	Brand name	Manufacturer	FDA approval date
Zidovudine	200(3)	Retrovir	GlaxoSmithKline	March19,1987
Abacavir	300(2)	Ziagen	ViiV Healthcare	Dec.17,1998
Lamivudine	150(2)	Epivir	GlaxoSmithKline	Nov.17,1995
Stavudine	30-40(2)	Zerit	Bristol Meyers Squibb	June 24,1994
Zalcitabine	0.75(3)	Hivid	Hoffmann La Roche	Mar.19,1992
Didanosine	200(2)	Videx Videx EC	Bristol Meyers Squibb	Oct.9,1991
Tenofovir disoproxil fumarate	300(1)	Viread	Gilead Sciences	Oct.26,2001
Emtricitabine	200(1)	Emtriva	Gilead Sciences	July 2,2003

Table 4: FDA approved Non-nucleoside Reverse Transcriptase Inhibitors (NNRTIs) for antiretroviral therapy (HAART)

Generic name	Adult dose(mg)/day	Brand name	Manufacturer	FDA approval date
Delavirdine	400(3)	Rescriptor	ViiV Healthcare	April4,1997
Efavirenz	600(1)	Sustiva	Bristol-Myers Squibb	Sept.17,1998
Etravirine	200(2)	Intelence	Tibotec	Jan18,2008
Nevirapine	200(1)first 14days then 2 times daily	Viramune	Boehringer Ingelheim	June21,1996
Rilpivirine	25-150(3)	Edurant	Janssen Pharmaceuticals,Inc	May 20,2011

Table 5: FDA approved Protease inhibitors (PIs) for antiretroviral therapy (HAART)

Generic name	Adult dose(mg)/day	Brand name	Manufacturer	FDA approval date
Atazanavir	300(1)	Reyataz	Bristol Meyers Squibb	June20,2003
Indinavir	800(3)	Crixivan	Merck	March13,1996
Darunavir	600(2)	Prezista	Janssen Cilag Pty Ltd.	June 23,2006
Fosamprenavir	1400(2)	Lexiva	ViiV Healthcare	Oct.20,2003
Nelfinavir	1250(2)	Viracept	ViiV Healthcare	March14,1997
Ritonavir	600(2)	Novir	Abbot Laboratories	March1,1996
Tipranavir	500(2)	Aptivus	Boehringer Ingelheim	June 20,2005
Saquinavir	1200(3)	Invirase	Hoffmann La Roche	Dec.6,1995

Table 6: Nucleotide Reverse Transcriptase Inhibitors (NRTIs) for antiretroviral therapy (HAART)

Generic Name	Brand Name	Manufacturer
Tenofovir disoproxil fumarate	Viread	Gilead Sciences

Table 7: FDA approved Fixed dose combinations for antiretroviral therapy (HAART)

Generic name	Brand name	Manufacturer	FDA approval date
Zidovudine+Lamivudine	Combivir	GlaxoSmithKline	Sept.26,1997
Abacavir+Lamivudine	Epzicom(USA), Kivexa(Europe)	GlaxoSmithKline	Aug.2,2004
Abacavir+Zidovudine +Lamivudine	Trizivir	GlaxoSmithKline	Nov.15,2000
Lopinavir+ritonavir	Kaletra	Abbot Laboratories	Sept.15,2000
Tenofovir+Emtricitabine	Truvada	Gilead Sciences	August 2,2004
Efavirenz+Tenofovir +Emtricitabine	Atripla	Gilead Sciences and Bristol Meyers Squibb	July 12, 2006
Rilpivirine+Tenofovir +Emtricitabine	Complera	Gilead Sciences and Tibotec	August 10,2011
Elvitegravir+Cobicistat +Tenofovir/emtricitabine	Stribild	Gilead Sciences	August 27.2012
Dolutegravir +Abacavir/Lamivudine	Triumeq	ViiV Healthcare	August 22,2014

Table 8: Antiviral for HIV infection

Product name	Sponsor	Development phase
Apricitabine	Avexa	Phase III
Reformulated raltegravir	Merck	Phase III
F/TAF(emtricitabine/tenofovir alafenamide fixed dose combination)	Gilead Sciences	Phase III
Cobicistat/elvitegravir/emtricitabine/tenofovir alafenamide fixed dose combination	Gilead Sciences	Phase III
Cobicistat/darunavir/emtricitabine/tenofovir alafenamide fixed dose combination	Gilead Sciences	Phase II
Amdoxovir	RFS Pharma	Phase II
MK-1439 (doravirine)	Merck	Phase II

Table 9: Cell therapy for HIV infection

Product name	Sponsor	Development phase
Cal-1(blood stem cell therapy)	Calimmune	Phase I/II
MazF gene therapy	Takara Bio	Phase I
SB-728-T(CCR5 receptor modulator)	Sangamo Bio Sciences	Phase II

Table 10: Vaccines development for HIV-1 infections

Product name	Sponsor	Development phase
AGS-004(personalized immunotherapy)	Argos Therapeutics	Phase II
GOVXB11(DNA/MVAvaccine)	Geo Vax Labs	Phase II
HIV recombinant vaccine	GlaxoSmithKline	Phase II
HIV Vaccine	Novartis	Phase I
HIV Vaccine(Ad4-mGag)	PaxVax	Phase I
HIV Vaccine(Ad4-EnvC150)	PaxVax	Phase I
HIV Vaccine(SAV001)	Sumagen Canada	Phase I
Pennvax-B(DNA vaccine)	InovioPharmaceuticals	Phase I
Pennvax-G (DNA Vaccine clades A,C,D)	InovioPharmaceuticals	Phase I
Remune (HIV Vaccine)	Immune Response BioPharma	Phase III
RemuneX(HIV combination vaccine)	Immune Response BioPharma	Phase III
Vacc-4x(Intradermal vaccine)	Bionor Pharma	Phase II
PBSVax(HIV-MAG DNA vaccine)	Profectus Bio Sciences	Phase I

Alternative medicine for AIDS

Herbal medicines[13] provide rational means for the treatment of many diseases that are obstinate and incurable in other systems of medicine. These are gaining popularity because of several advantages such as often fewer side effects, better patient tolerance, relatively less expensive and acceptance due to long history of use. Medicinal effects of plants tend to normalize physiological function and correct the underlying cause of the disorder.

Topical protection

Topical microbicides are products that may be formulated as gels, sponges, films, or rings that can be applied to vaginal or rectal mucosa with the goal of preventing or significantly reducing the risk of acquiring HIV. A topical microbicide, the spermicidal agent[14] Nonoxynol-9 (N-9) was shown safe and effective.

Male circumcision[15]

Male circumcision can provide as an HIV-prevention strategy among heterosexual men. Male circumcision significantly reduced the risk of HIV acquisition by approximately 50 percent among uninfected men.

Use of diaphragms[16]

The Methods for improving Reproductive Health in Africa (MIRA) trial examined the effectiveness of using a diaphragm with lubricant to prevent the acquisition of HIV among women in Zimbabwe and South Africa. The trial found that the use of diaphragms and lubrication over and above the provision of condoms did not afford woman added protection from HIV acquisition.

Substance abuse treatment[17]

Substance abuse treatment is an important HIV-prevention strategy because people in treatment are less likely to engage in risky sexual behaviors and inject drugs or share needles. Substance abuse interventions that impact HIV prevention in the U.S. include pharmacotherapy (e.g. opoid substitution).

The role of alcohol and other drug use in HIV prevention[18]

Alcohol consumption is linked to decreased inhibition and impaired judgment and in light of contradicting data on the relationship between alcohol consumption and sexual risk behavior. The effect of consuming alcohol while taking antiretroviral has been shown to be less dangerous but may promote resistance and ultimately compromise the efficacy of the medications over time.

Counselling /intervention to promote condom use[19, 20]

Condom use protects from sexually transmitted infections (STIs) and unwanted pregnancies. The use of condom depends on the knowledge and attitude of users towards condom. Knowledge of condom is universal, but there are rural-urban differences observed. Reason for choosing condoms over other spacing family planning methods includes the fear of side effects of other modern spacing methods. Female condoms help protect against sexually transmitted infections, including HIV**.** Condoms are the only contraceptive method that can protect against both pregnancy and sexually transmitted infections.

CONCLUSION

AIDS is a pandemic disease which spreads globally in human society. Hence there is need for effective treatment for controlling HIV infection. There is control in the mortality and morbidity of HIV infected individuals by the implementation of various approaches. It is better to control AIDS by taking preventive measure, awareness among people regarding AIDS.

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