AIDS: Treatment Strategies for AIDS Patients

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ABSTRACT

Initial cases of acquired immune deficiency syndrome were identified among homosexuals in 1981 in the United States. The human immunodeficiency virus was identified in 1983, and in 1984, it was linked to AIDS. There are two strains, HIV-1 HIV-2, HIV-1 is more common in humans. Antiretroviral therapy is the primary treatment used for AIDS. There are 23 antiretroviral drugs currently available with different modes of action. These drugs are categorized based on the stage of viral life cycle that they hinder. Non-nucleoside reverse transcriptase inhibitors and nucleoside reverse transcriptase inhibitors are the two distinct categories of these drugs. The primary function of these drugs is to improve the quality of life of these patients and provide them with mental security to have an everyday life among other people. There are some adverse effects of antiretroviral therapy in both short-term and long-term usage, but they are nothing compared to the issues AIDS causes. Gastrointestinal tract toxicities, rash, anemia and renal dysfunction are some common side effects of antiretroviral therapy but they are relatively easy to manage. Pre-exposure prophylaxis and post-exposure prophylaxis are two types of treatments used for patients, health workers and any individuals at risk of getting exposed to HIV, like family members of patients. Poor adherence to the drugs is the most common cause of contact and spread of HIV among patients, health workers and exposed individuals. Management of patients affected by AIDS is much easier now than it used to be, and it's getting even better with time.

Keywords: AIDS, HIV, Antiretroviral therapy, Non-nucleoside reverse transcriptase inhibitors, Nucleoside reverse transcriptase inhibitors

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1. INTRODUCTION

In 1981, the initial cases of AIDS were identified among male homosexuals, IV drug abusers, and hemophiliacs in the United States, as well as sexually active heterosexuals in several nations in equatorial Africa. The human immunodeficiency virus (HIV) was initially identified in 1983, and by 1984, it had been clearly linked to AIDS patients and high-risk populations. Prospective epidemiological studies documenting the absolute necessity for HIV infection for the development of AIDS provide the strongest evidence that HIV causes AIDS. Multiple studies have demonstrated that AIDS does not exist in nations where no residents test positive for the virus, but flourishes in nations where many residents test positive. Not only that, but the arrival of AIDS in a nation follows closely on the heels of the introduction of HIV to that country (Fauci and Lane 2020).

Over 25 years ago, HIV was a completely new virus. Early patients usually had a baffling array of neurological signs and symptoms suggesting central nervous system involvement in addition to systemic opportunistic infections. These severe illnesses are now understood to be the last manifestation of an initially hidden and symptomless infection. Before the advent of highly active antiretroviral treatment (HAART), anyone infected with HIV would almost certainly advance from an asymptomatic years-long pre-symptomatic stage to the symptomatic and ultimately lethal end stages (AIDS) (Anthony and Bell, 2008).

HIV responsible for Acquired Immune Deficiency Syndrome (AIDS), and the virus has spread to over 65 million people all over the world. About 14,000 people are infected with HIV every day, and more than 95% of them live in underdeveloped nations. About 12,000 people between the ages of 15 and 49 (mostly women) get infected each year, and 80% of these cases are the result of heterosexual transmission. Twenty-five million of them have already perished (Sudharshan and Biswas 2008).

2. CAUSATIVE AGENT

HIV-1 and HIV-2 are two strains of the HIV, both of which are human retroviruses with RNA genomes and the distinctive 'Reverse transcriptase enzyme. HIV-1 is the primary pathogen in human illness. The virion, measuring 100-120 nm in diameter, is composed of several components. These include an outer envelope, a protein shell forming the core, and an inner core that takes on a cone-shaped structure. Within this inner core, one can find the RNA genome, the enzyme known as "reverse transcriptase", and various core polypeptides. In contrast, HIV-2 is recognized for its comparatively less severe and gradual impact on the immune system. Individuals who exhibit symptoms resembling those of AIDS but yield negative results for HIV-1 should undergo testing for HIV-2 (Sudharshan and Biswas 2008).

There are two distinct categories of helper T cells, known as CD4 T cells, which exhibit varying profiles of cytokine production. The cells primarily impacted in HIV infections are CD4 and CD8 cells. The typical range for CD4 counts is 300 to 1000 cells per cubic millimeter but decreases during the infection (Mosmann and Coffman 1987).

3. MODE OF ACTION OF HIV

Upon cellular infection by HIV, the viral RNA undergoes a process of conversion into viral DNA, facilitated by the enzyme reverse transcriptase. Subsequently, this viral DNA is replicated and integrated into the DNA of the host cell. Subsequently, the viral DNA provides instructions to the host cell, prompting it to engage in replication of the genetic material of the HIV. The protease enzyme facilitates the assembly of replicated viral genetic material into progeny viruses, subsequently enabling their egress from the host cell for the purpose of infecting neighboring cells. The initial category of ARV reverse-transcriptase inhibitors functions during the early stages of HIV life cycle, effectively halting the replication of the virus subsequent to HIV infection (Oguntibeju 2012).

4. TREATMENT STRATEGIES

There are different strategies used for the treatment of HIV patients, they are discussed below.

5. ANTIRETROVIRAL THERAPY

Recent studies have provided evidence that during the initial stages of infection, HIV exhibits a preference for infecting CCR5, CD4 and memory T lymphocytes located in the gastrointestinal tract. This phenomenon leads to a swift, extensive, and potentially irreversible depletion of CD4 cells leading to disruption of the intestinal mucosa and infiltration of microbial translocation products into the systemic circulation (Brenchley et al. 2004). Currently, there are 23 antiretroviral agents available, each with distinct mechanisms of action. These agents can be combined in various ways to optimize treatment outcomes (Palmisano and Vella 2011). Long-term antiretroviral therapy has demonstrated efficacy in reducing the burden of inflammation associated with HIV infection. However, it is essential to note that complete elimination of inflammation is not achievable through this treatment. The presence of inflammation remains causatively linked to various complications, including cardiovascular diseases, which have emerged as a significant concern within the HIV-infected population (Grinspoon and Carr 2005).

Antiretroviral drugs are categorized based on the specific stage of the viral life cycle that they impede. One possible basis for subclassification is the chemical structure of the organisms in question. One significant development in the chronology of HIV disease has been the emergence of novel drug categories during the years 1995-96. This advancement facilitated the implementation of combination HAART and subsequently led to the progressive transformation of HIV infection into a chronic state, typically without fatality (Palella et al. 1998). Until 2010, over 20 antiretroviral agents have been granted licenses, often through an expedited approval process. These licenses were granted based on not only the clinical effectiveness of the agents, but also their impact on plasma HIV RNA concentration. This concentration serves as a validated surrogate marker for measuring HIV activity (Palmisano and Vella 2011). The conventional approach to ART involves the administration of a minimum of three antiretroviral medications in order to effectively suppress the human immunodeficiency virus and halt the advancement of HIV-related illness (Oguntibeju 2012).

The utilization of a strong combination of ART, predominantly comprising a minimum of three antiretroviral medications, has exhibited significant enhancements in the well-being and longevity of individuals afflicted with HIV in regions where ARVs are readily available. Furthermore, there are several preparations available in fixed-dose combinations. These components can be integrated to formulate various efficacious treatment plans for both initial and subsequent therapy. Despite its limitations, ART plays a crucial role in preserving lives and enhancing the functionality of the immune system. Additionally, it mitigates the likelihood of various HIV-related complications, as well as those unrelated to AIDS (Shen et al. 2008).

Furthermore, ART effectively reduces the risk of HIV transmission. There is a growing body of evidence that suggests the potential advantages of ART for individuals with elevated CD4 counts. The utilization of HAART has proven effective in managing the replication of HIV-1. However, when treatment is not administered optimally, it can lead to the emergence of resistance and subsequent resurgence of viral activity (Yang et al. 2020).

6. MODE OF ACTION OF ART DRUGS

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) and Nucleoside Reverse Transcriptase Inhibitors (NRTIs) are the two distinct categories of these pharmaceutical compounds. Typically, NNRTIs interact with the reverse transcriptase enzyme to hinder the conversion of HIV RNA into DNA. Consequently, this

impedes the replication of the virus within the cell's DNA. On the other hand, NRTIs become part of the viral DNA, obstructing its ability to generate viral copies. NRTIs disrupt the replication cycle of HIV by competitively inhibiting the activity of HIV reverse transcriptase enzyme and causing premature termination of the DNA chain (Cox et al. 1994).

7. QUALITY OF LIFE OF PATIENTS USING ART

Given the widely acknowledged significance of health as a primary determinant of overall quality of life (QOL), there has been a proposition positing that QOL might be distinctly influenced by particular diseases, such as HIV/AIDS (Oguntibeju 2012).

Research findings indicate that individuals diagnosed with HIV/AIDS encounter a range of psychological challenges, including but not limited to stigma, poverty, depression, substance abuse, and cultural beliefs. These factors have the potential to impact not only their physical well-being but also their mental and social well-being, thereby compromising their overall quality of life. Consequently, these issues can significantly disrupt the individuals' ability to engage in essential activities and pursue their personal interests (Aranda-Naranjo 2004).

The assessment of clinical progress in individuals with HIV infection who are receiving antiretroviral therapy frequently involves evaluating the decrease in mortality rates, rates of opportunistic infections, or the severity of symptoms associated with advanced AIDS. However, there has been an increasing interest in evaluating the quality of life among individuals who are living with HIV/AIDS, particularly with the availability of more effective and easier treatment regimens. Scientific and clinical research has consistently demonstrated the high efficacy of ART in producing significant benefits for individuals living with HIV and AIDS. Despite the presence of some negative effects, the overall impact of ART on the quality of life and general health of these individuals is positive on a global scale (Burgoyne 2008).

Significant enhancements in the average quality of life were observed among HIV patients who participated in two multicenter clinical trials for antiretroviral therapy. These improvements were evident after 1 and 4 months of receiving new ART regimens, and they remained consistent for a duration of 12 months (Mannheimer 2005). The researchers conducted an assessment of patients' quality of life for a duration of 4 months following the initiation of ART, taking into account the subjective perceptions, values, and preferences of the individuals. The findings revealed that a considerable percentage of patients (66.4%) reported a positive or highly positive QOL after approximately 4 months of ART. Moreover, a significant disparity was observed when comparing these results to the baseline values prior to the commencement of ART treatment (Campos 2009).

8. ADVERSE EFFECTS OF ART

ART exhibits both short-term and long-term adverse effects on the patients that also need avoiding or managing.

9. SHORT TERM EFFECTS

9.1. GASTROINTESTINAL TOXICITIES

The primary causes for discontinuation during the acute phase of treatment, as observed in a retrospective analysis of the HOPS database, were gastrointestinal (GI) toxicities, specifically vomiting, nausea, and diarrhoea (O'Brien et al. 2003).

10. RASH

A skin rash occurs when skin becomes red, inflamed and bumpy. Rash is a frequently observed transient adverse event that can be attributed to a wide range of pharmaceutical agents. However, NNRTIs are primarily implicated as the principal culprits in HAART. The rash commonly observed in individuals taking NNRTIs typically presents as erythematous, maculopapular and exhibits a widespread distribution. Rash has been documented in a range of 10-17% of patients who have been administered NNRTIs (Carr and Cooper 2000).

11. HYPERSENSITIVITY REACTION

Hypersensitivity reactions (HSR) may manifest in response to certain antiretroviral drugs, particularly Abacavir (ABC) and Nevirapine (NVP). HSR is distinguished by a constellation of symptoms including fever, rash, myalgia, abdominal pain, elevated liver transaminases, fatigue, breathing problems, muscle and joint pain, paresthesia and edema. In severe cases, HSR may lead to renal or hepatic failure. A notable characteristic of drug HSR is the potential occurrence of a severe and potentially life-threatening anaphylactic reaction upon re-administration of the causative drug to the patient (Mallal et al. 2008).

12. CNS TOXICITY

The occurrence of Central Nervous System (CNS) toxicity is frequently observed in relation to the NNRTI Efavirenz (EFV). This phenomenon has been evidenced in various research studies, most notably in a specific sub analysis of the AIDS Clinical Trials Group (ACTG) 5095 trial, specifically referred to as ACTG 5097 (Hawkins 2010).

13. ANEMIA

Anemia is a detrimental occurrence primarily linked to ZDV and its myelosuppressive impact. According to the findings of the GS 934 study, it was observed that a proportion of 6% of patients belonging to the Zidovudine (ZDV) group had terminated their participation in the study after 48 weeks due to the presence of anemia (Pozniak et al. 2006).

14. LONG TERM ADVERSE EFFECTS

14.1. CARDIOVASCULAR DISEASE

Cardiovascular disease (CVD) continues to be the primary cause of mortality on a global scale. A substantial multinational cohort consisting of 33,000 patients was established with the primary objective of investigating the correlation between HAART and adverse effects (AEs). There is an increased probability of experiencing myocardial infarction (MI) by 16% for every year of combination HAART, primarily attributed to the utilization of protease inhibitors (PIs). (DAD Study Group 2007).

15. HEPATOTOXICITY

Several antiretroviral agents have the potential to induce hepatotoxicity. NVP is linked to the development of acute liver disease through a HSR. The examination of the ATHENA cohort, focusing on pre-therapy and

current CD4+ cell counts, revealed a 6.2% incidence rate of NVP associated HSR. This risk was found to be comparable between patients who were treatment-naive and those who had prior treatment experience (Hawkins 2010).

15. RENAL DYSFUNCTION

The primary association of renal dysfunction has been observed with TDF, as the parent NRTI tenofovir is actively accumulated in the proximal renal tubule through the activity of renal-specific organic anion transporters 1. The utilization of TDF has been linked to modest yet statistically significant alterations in creatinine clearance, typically ranging from 6 to 10 ml/min. Typically, these alterations do not hold significant clinical relevance when normal renal function is present initially. However, they may acquire significance if renal disease is present (Gallant 2006).

16. LIPODYSTROPHY

Lipodystrophy encompasses various conditions, such as lipoatrophy and/or lipohypertrophy, which are frequently linked to dyslipidemia and insulin resistance. These symptoms have the potential to manifest either in conjunction or independently. Lipoatrophy refers to the condition characterized by the reduction of adipose tissue in specific regions of the body, including the facial region (cheeks), extremities, buttocks, and subcutaneous abdominal fat. Many patients frequently express dissatisfaction with the visibility of their veins, which can be attributed to a decrease in adipose tissue in the surrounding area. Lipohypertrophy refers to the pathological condition characterized by the accumulation of adipose tissue in various regions of the body, including the visceral abdominal area, dorsal cervical region, parotid area, and the development of lipomata or breast enlargement in females (Grinspoon and Carr 2005).

17. DISTAL SENSORY PERIPHERAL NEUROPATHY

Distal sensory peripheral neuropathy is characterized by subjective sensations of numbness and/or pain primarily affecting the extremities, particularly the feet. Clinical manifestations encompass the absence of ankle reflexes, as well as diminished sensory perception of vibration and pinprick stimuli. In recent times, a number of cohort studies have provided confirmation regarding the existence of DSPN, wherein a minimum of one sign or symptom is observed in approximately 30-57% of patients. Among these individuals, symptoms are reported in the range of 5-40% (Ellis et al. 2009).

18. PROPHYLAXIS TREATMENTS

18.1. PRE-EXPOSURE PROPHYLAXIS

Given the significant worldwide spread of HIV, the World Health Organization has emphasized the critical need for innovative, efficacious, and safe interventions in the realm of HIV infection prevention. This phenomenon is particularly prevalent among individuals who are deemed to be at a heightened risk, as a result of the inconsistent implementation of these precautionary measures (Weinhardt et al. 1999).

Pre-exposure prophylaxis (PrEP) represents a formidable instrument in the containment of HIV transmission, whereby the individual undertakes the daily ingestion of an ARV tablet, in conjunction with the implementation of supplementary preventive behavioral strategies, with the ultimate aim of averting

HIV infection. This particular protective mechanism is employed by individuals who have not received a diagnosis of HIV, yet find themselves at a significant risk of contracting the virus due to their lifestyle choices or as a partner in a sero-discordant relationship (Castilla et al. 2005).
The findings derived from clinical trials provide evidence supporting the effectiveness of PrEP, whether utilized as a standalone intervention or in conjunction with other behavioral preventive strategies. These trials have demonstrated that PrEP has the capacity to significantly decrease the occurrence of HIV by as much as 86% or potentially higher, contingent upon strict adherence to the prescribed regimen (Molina et al. 2015).

19. DRUGS COMMONLY USED FOR PREP

On July 16, 2012, the US Food and Drug Administration (FDA) granted approval for [tenofovir (TDF) 300 mg/emtricitabine (FTC) 200 mg] based on the outcomes and evidence obtained from PrEP trials. This medication was deemed effective in preventing sexually acquired HIV as well as other potential modes of HIV transmission, including the use of injectable drugs (Holmes 2012).
The ARV medications currently recommended for oral PrEP consist of either tenofovir (TDF) alone or a combination of TDF and emtricitabine (FTC) (Louissaint et al. 2013). These medications have demonstrated high potency, a favorable resistance profile, and are alleged to have minimal adverse effects, thereby establishing their efficacy and safety for pre-exposure prophylaxis (Baeten et al. 2012).
Several studies have also evaluated the effectiveness of a 1% vaginal gel formulation of Tenofovir Disoproxil Fumarate (TDF) and have reported a reduction in HIV transmission by 39% (Sokal et al. 2013).
Subsequently, the US Centers for Disease Control (CDC) issued guidelines pertaining to the implementation of PrEP in clinical settings. The WHO has recently released guidelines that align with the aforementioned recommendations, advocating for the use of PrEP as a viable preventive measure for individuals who face a significant risk of contracting the Human Immunodeficiency Virus (Tetteh et al. 2017).

20. SUCCESSFUL TRIALS OF PREP

The FEM-PrEP study, which involved a total of 2120 participants, observed 56 new cases of HIV infection after 14 months of study initiation. Notably, these infections were evenly distributed between the Truvada® and placebo groups, with 28 cases occurring in each arm. This finding strongly suggests that the use of Truvada does not provide effective protection against HIV transmission. The overall level of adherence, as reported by participants, was found to be 95%, with no discernible disparity in adherence observed between the two experimental groups (Van Damme 2012).
The study on PrEP conducted in the United States involved a total of 373 participants, with 186 individuals assigned to the TDF group and 187 individuals assigned to the placebo group. The study yielded positive results, as only four individuals from the placebo group and three individuals from the delayed-arm participants experienced seroconversion. The estimated adherence rate based on pill load was found to be 92%, while the adherence rate determined through the use of a medication event monitoring system was 77%. The oral administration of TDF was found to be well-tolerated, with no notable renal issues observed. Furthermore, there were no statistically significant differences in the occurrence of adverse drug events between the TDF and placebo groups (Grohskopf et al. 2019).

21. ADVERSE EFFECTS OF PREP

The combination of TDF/FTC or TDF monotherapy commonly exhibits a favorable tolerability profile when utilized for PrEP. In the majority of studies, there was no significant difference observed in the

incidence of experienced side effects between participants receiving active treatment and those receiving a placebo. The adverse events or side effects primarily stem from the gastrointestinal tract and tend to be more common during the initial period of usage, although they typically diminish within one month of use. The gastrointestinal disturbances typically manifest as abdominal discomfort, accompanied by symptoms such as nausea, vomiting, or diarrhea. Additional adverse events that have been reported, which are not related to GIT origin, include symptoms such as dizziness, headache, loss of weight, fatigue, shortness of breath, cough, anxiety, fever, and joint and muscle pain. In the majority of studies, the incidence of side effects or adverse events did not exhibit a statistically significant difference when compared to the rates observed among participants who were administered a placebo (Tetteh et al. 2017).

Several risk factors have been identified in relation to long-term use of the medication. These factors include the patient's age, the duration of treatment with TDF, elevated levels of baseline creatinine, and the use of protease inhibitor combinations that are boosted with ritonavir. Additionally, individuals of African descent have been found to be at higher risk compared to Caucasians (Mugwanya et al. 2016).

The incidence of nausea and vomiting was found to be greater among individuals receiving TDF compared to those receiving a placebo during the initial two-month period in the Bangkok Tenofovir Study (Choopanya et al. 2013).

The safety trial conducted in the United States on homosexual men did not reveal any significant disparity in the overall occurrence of adverse events between the groups administered TDF and those given a placebo. However, a specific group of men at a site in San Francisco exhibited a slight yet statistically significant reduction in bone mineral density (BMD) at the femoral neck (1.1%) and total hip (0.8% decrease) when using TDF. It is important to note that no instances of bone fractures were observed in this subset (Grohskopf et al. 2013).

22. RESISTANCE TO PREP TREATMENT

In the context of HIV infection, the occurrence of resistance to PrEP among individuals who contract the virus subsequent to randomization is infrequently observed. Participants who exhibit resistance are more likely to be attributed to the presence of pre-existing resistance in the population rather than being solely caused by the use of PrEP. In the PROUD trial, there were no instances of participants developing resistance to Tenofovir Disoproxil Fumarate (McCormack et al. 2016).

23. POST EXPOSURE PROPHYLAXIS

PEP refers to the implementation of short-term ART with the aim of mitigating the likelihood of contracting HIV infection subsequent to exposure. The accessibility of HIV testing has expanded significantly in both occupational and nonoccupational settings. The detection of HIV in regional lymph nodes may require a time frame of up to 72 hours, while detection in blood may take up to 5 days. Detection in the cerebrospinal fluid, on the other hand, may require approximately 8 days. The early initiation of ART presents a valuable opportunity to mitigate the acquisition of HIV infection by impeding viral replication or hindering the spread of infection. (Sultan et al. 2014).

The swift beginning of ART immediately following the diagnosis of HIV infection is of significant importance in the global management of HIV for two primary reasons. In the context of managing the HIV epidemic in the absence of a vaccine or cure, it is important to note that the concept of an undetectable virus corresponds to an untransmissible virus. Furthermore, in order to enhance the well-being of individuals afflicted with HIV (Boyd et al. 2019).

24. ROLE IN VERTICAL TRANSMISSION

Research studies have demonstrated a decrease in the transmission of HIV from mother to child through vertical transmission when pregnant women receive antiretroviral treatment. These findings further validate the effectiveness of PEP. The AIDS Clinical Trials Group (ACTG) 076 study demonstrated a decrease in the occurrence of HIV infection among newborns who were administered a six-week course of zidovudine within 48 hours of birth. This intervention was specifically targeted at women who had not undergone any ART prior to giving birth (Sperling et al. 1996).
Recent empirical findings indicate that neonates born to pregnant women who did not undergo ART exhibit a higher efficacy in preventing mother-to-child transmission when subjected to dual or triple ART, as opposed to monotherapy (Nielsen-Saines et al. 2012).

25. POOR ADHERENCE

Historically, the efficacy of four weeks of post-exposure prophylaxis (PEP) among health-care workers and individuals exposed non-occupationally has been hindered by low adherence and completion rates. The influence of factors beyond pill burden and side-effects, such as psychological distress or the re-evaluation of risk over time, on adherence and completion rates remains uncertain. The completion rates of a study conducted on 401 individuals who were administered dual nucleoside therapy for PEP following non-occupational exposure were found to be 78% (Benn et al. 2011). Participants were provided with a total of three adherence sessions and five risk reduction sessions, which potentially contributed to the observed enhancement in completion rates. The virological outcome in individuals with chronic HIV infection is closely linked to the level of adherence to combination ART. Theoretical consequences of inadequate adherence to PEP regimens include the potential acquisition of a drug-resistant strain of the virus in the event of HIV infection (Benn et al. 2011).

26. OCCUPATIONAL EXPOSURE TO HIV

Prospective randomized controlled trials assessing the efficacy of PEP are lacking, primarily due to ethical considerations surrounding the withholding of a potentially effective treatment and the challenges associated with recruiting a sufficiently large number of participants for such a study.
The justification for the utilization of PEP in human subjects largely stems from an investigation involving health care workers who were occupationally exposed to the HIV. This study revealed that a 28-day regimen of zidovudine exhibited a protective effect (Sultan et al. 2014).
There have been documented instances of PEP failure in occupational settings, with a minimum of 24 reported cases. These failures have predominantly occurred following the administration of zidovudine monotherapy (Tomkins and Ncube 2005).

27. PREVENTION AND TREATMENT OF OPPORTUNISTIC INFECTIONS IN HIV

A considerable body of research has extensively documented the notable decrease in the occurrence of HIV-associated opportunistic infections (OIs) within populations of patients who possess consistent and dependable availability to efficacious ART. Antiretroviral therapy effectively mitigates the risk of developing OIs and malignancies by effectively suppressing plasma HIV RNA levels and simultaneously increasing CD4 cell counts (Masur et al. 2014).
Common OIs that develop under these conditions include disseminated Mycobacterium avium complex illness, TB, CMV retinitis, Pneumocystis pneumonia, and Kaposi sarcoma. Furthermore, it has been

observed that certain individuals who commence ART with low CD4 cell counts may experience a counterintuitive exacerbation of an OI subsequent to the initiation of ART. (Novak et al. 2012).
Furthermore, despite the significant decrease in the occurrence of OIs and AIDS-defining malignancies among patients who have successfully suppressed HIV replication for extended periods of time, enhanced immune function does not completely eliminate the risk of new OIs, even when CD4 cell counts are above 200 cells/µL (Buchacz et al. 2010). There exist extensively documented reports that indicate the persistence of infection risks, particularly for TB, herpes zoster, pneumococcal disease, and Kaposi sarcoma, even at elevated CD4 counts (Van Rie et al. 2011).
Therefore, while the sustained and successful suppression of viral activity over an extended period of time diminishes the likelihood of HIV-associated infectious complications in these individuals, it does not eradicate the risk entirely. Healthcare providers must possess a comprehensive understanding of identifying and effectively addressing OIs. Additionally, they should approach the diagnosis of OIs as a potential indication of late-stage HIV infection, immune reconstitution inflammatory syndrome (IRIS), and illnesses in individuals with elevated CD4 cell counts (Masur et al. 2014).

28. CONCLUSION

Antiretroviral therapy can prove to be a great weapon against a disease like AIDS. It may have some side effects but these are not meant for everyone, in most cases, managing them is more straightforward and has less impact on the quality of life of the patients. Overall, ARV improves patients' quality of life and makes them confident in their daily routines. People at risk may need to adhere correctly to the preventive treatment, but it can be fixed by proper counselling and awareness. Appropriate measures should be taken to limit the spread of this disease and save other people from it before it is too late, as this virus is a matter to be taken seriously.

REFERENCES

Anthony IC and Bell PJ, 2008. The neuropathology of HIV/AIDS. International review of psychiatry 20: 15-24.
Aranda-Naranjo B, 2004. Quality of life in the HIV-positive patient: implications and consequences. Journal of the Association of Nurses in AIDS Care 15: 20-27.
Baeten JM et al., 2012. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. New England journal of medicine 367: 399-410.
Benn P et al., 2011. UK guideline for the use of post-exposure prophylaxis for HIV following sexual exposure (2011). International journal of STD & AIDS 22: 695-708.
Boyd MA et al., 2019. Rapid initiation of antiretroviral therapy at HIV diagnosis: definition, process, knowledge gaps. HIV medicine 20: 3-11.
Brenchley JM et al., 2004. CD4+ T cell depletion during all stages of HIV disease occurs predominantly in the gastrointestinal tract. The Journal of experimental medicine 200: 749-759.
Buchacz K et al., 2010. AIDS-defining opportunistic illnesses in US patients, 1994–2007: a cohort study. AIDS 24: 1549-1559.
Burgoyne RW and Tan DH, 2008. Prolongation and quality of life for HIV-infected adults treated with highly active antiretroviral therapy (HAART): a balancing act. Journal of antimicrobial chemotherapy 61: 469-473.
Campos LN et al., 2009. Quality of life among HIV-infected patients in Brazil after initiation of treatment. Clinics 64: 867-875.
Carr A and Cooper DA, 2000. Adverse effects of antiretroviral therapy. The Lancet 356: 1423-1430.
Castilla J et al., 2005. Effectiveness of highly active antiretroviral therapy in reducing heterosexual transmission of HIV. Journal of Acquired Immune Deficiency Syndromes 40: 96-101.

Choopanya K et al., 2013. Antiretroviral prophylaxis for HIV infection in injecting drug users in Bangkok, Thailand (the Bangkok Tenofovir Study): a randomised, double-blind, placebo-controlled phase 3 trial. The Lancet 381: 2083-2090.

Cox SW et al., 1994. Comparison of the sensitivities of primary isolates of HIV type 2 and HIV type 1 to antiviral drugs and drug combinations. AIDS research and human retroviruses 10: 1725-1729.

DAD Study Group, 2007. Class of antiretroviral drugs and the risk of myocardial infarction. New England Journal of Medicine 356: 1723-1735.

Ellis R et al., 2009, February. Persisting high prevalence of HIV distal sensory peripheral neuropathy in the era of combination ART: correlates in the CHARTER study. In 16th Conference on Retroviruses and Opportunistic Infections 2009: 8-11

Fauci AS and Lane HC, 2020. Four decades of HIV/AIDS—much accomplished, much to do. New England Journal of Medicine 383: 1-4.

Gallant JE et al., 2006. Tenofovir DF, emtricitabine, and efavirenz vs. zidovudine, lamivudine, and efavirenz for HIV. New England Journal of Medicine 354: 251-260.

Grinspoon S and Carr A, 2005. Cardiovascular risk and body-fat abnormalities in HIV-infected adults. New England Journal of Medicine 352: 48-62.

Grohskopf LA et al., 2013. Randomized trial of clinical safety of daily oral tenofovir disoproxil fumarate among HIV-uninfected men who have sex with men in the United States. JAIDS Journal of Acquired Immune Deficiency Syndromes 64: 79-86.

Hawkins T, 2010. Understanding and managing the adverse effects of antiretroviral therapy. Antiviral research 85: 201-209.

Holmes D, 2012. FDA paves the way for pre-exposure HIV prophylaxis. The Lancet 380: 325.

Louissaint NA et al., 2013. Single dose pharmacokinetics of oral tenofovir in plasma, peripheral blood mononuclear cells, colonic tissue, and vaginal tissue. AIDS research and human retroviruses 29:1443-1450.

Mallal S et al., 2008. HLA-B* 5701 screening for hypersensitivity to abacavir. New England Journal of Medicine 358: 568-579.

Mannheimer SB et al., 2005. Beirn Community Programs for Clinical Research on AIDS. Quality of life in HIV-infected individuals receiving antiretroviral therapy is related to adherence. AIDS care 17: 10-22.

Masur H et al., 2014. Prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: Updated Guidelines from the Centers for Disease Control and Prevention, National Institutes of Health, and HIV Medicine Association of the Infectious Diseases Society of America. Clinical infectious diseases 58: 1308-1311.

McCormack S et al., 2016. Pre-exposure prophylaxis to prevent the acquisition of HIV-1 infection (PROUD): effectiveness results from the pilot phase of a pragmatic open-label randomised trial. The Lancet 387: 53-60.

Molina JM et al., 2015. On-demand preexposure prophylaxis in men at high risk for HIV-1 infection. New England Journal of Medicine 373: 2237-2246.

Mosmann TR and Coffman RL, 1987. Two types of mouse helper T-cell clone: implications for immune regulation. Immunology Today 8: 223-227.

Mugwanya KK and Baeten JM, 2016. Safety of oral tenofovir disoproxil fumarate-based pre-exposure prophylaxis for HIV prevention. Expert opinion on drug safety 15: 265-273.

Nielsen-Saines K et al., 2012. Three postpartum antiretroviral regimens to prevent intrapartum HIV infection. New England Journal of Medicine 366: 2368-2379.

Novak RM et al., 2012. Immune reconstitution inflammatory syndrome: incidence and implications for mortality. AIDS (London, England) 26: 721.

O'Brien et al., 2003. Patterns and correlates of discontinuation of the initial HAART regimen in an urban outpatient cohort. Journal of Acquired Immune Deficiency Syndromes 34: 407-414.

Oguntibeju OO, 2012. Quality of life of people living with HIV and AIDS and antiretroviral therapy. HIV/AIDS-Research and Palliative Care 2012: 117-124.

Palella Jr et al., 1998. Declining morbidity and mortality among patients with advanced human immunodeficiency virus infection. New England Journal of Medicine 338: 853-860.

Palmisano L and Vella S, 2011. A brief history of antiretroviral therapy of HIV infection: success and challenges. Annali dell'Istituto superiore di sanitÃ 47: 44-48.

Pozniak AL et al., 2006. Tenofovir disoproxil fumarate, emtricitabine, and efavirenz versus fixed-dose zidovudine/lamivudine and efavirenz in antiretroviral-naive patients: virologic, immunologic, and morphologic changes-a 96-week analysis. JAIDS Journal of Acquired Immune Deficiency Syndromes 43: 535-540.

Shen L et al., 2008. Dose-response curve slope sets class-specific limits on inhibitory potential of anti-HIV drugs. Nature medicine 14: 762-766.

Sokal DC et al., 2013. Safety of tenofovir gel, a vaginal microbicide, in South African women: results of the CAPRISA 004 Trial. Antiviral therapy 18: 301-310.

Sperling RS et al., 1996. Maternal viral load, zidovudine treatment, and the risk of transmission of human immunodeficiency virus type 1 from mother to infant. New England Journal of Medicine 335: 1621-1629.

Sudharshan S and Biswas J, 2008. Introduction and immunopathogenesis of acquired immune deficiency syndrome. Indian journal of ophthalmology 56: 357.

Sultan B et al., 2014. Current perspectives in HIV post-exposure prophylaxis. HIV/AIDS-Research and Palliative Care 2014: 147-158.

Tetteh RA et al., 2017. Pre-exposure prophylaxis for HIV prevention: safety concerns. Drug safety 40: 273-283.

Tomkins S and Ncube F 2005. Occupationally acquired HIV: international reports to December 2002. Weekly releases (1997–2007) 10: 2660.

Van Damme L et al., 2012. Preexposure prophylaxis for HIV infection among African women. New England Journal of Medicine 367: 411-422.

Van Rie A et al., 2011. Tuberculosis in patients receiving antiretroviral treatment: incidence, risk factors and prevention strategies. Journal of acquired immune deficiency syndromes (1999) 56: 349.

Weinhardt LS et al., 1999. Effects of HIV counseling and testing on sexual risk behavior: a meta-analytic review of published research, 1985-1997. American journal of public health 89: 1397-1405.

Yang X et al., 2020. Incomplete immune reconstitution in HIV/AIDS patients on antiretroviral therapy: Challenges of immunological non-responders. Journal of leukocyte biology 107: 597-612.