Effective Management of Human Immunodeficiency Virus (HIV)

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Abstract:

Human Immunodeficiency virus (HIV) destroys body's defense mechanism by attacking CD4 cells of our immune system and making host vulnerable to other infections and influencing their quality of life. Therefore, this is mandatory to look for effective management plan for patients suffering from HIV. The purpose of this study is to analyze the recent findings and to present evidences for effective management of HIV using different approaches and providing adequate holistic care to prevent or treat opportunistic infection (OI) and co morbidities. The main aspect of this article is to unveil new Avenues to change course of disease management with curable possibilities. The method used for data analysis to get pertinent evidences. The result shows that HIV management has helped a lot but due to poor compliance to treatment and other new challenges like drug resistance and limitation of antiretroviral therapy (ART) are emerging therefore, other future avenues are expected to yield curable interventions for HIV.

Keywords:

Effective management plan, holistic care, new Avenues, drug resistance, curable interventions

Introduction:

There were 36.9 million in the world living with human immunodeficiency virus (HIV) infection/acquired immunodeficiency syndrome (AIDS) as of 2017, and new infections have seen a reduction by 18% since 2010. But this rate of decline is not sufficient for the goal of eradication of AIDS by 2030. Only 21.7 million people infected with HIV have accesses to antiretroviral therapy, with the rest at risk of the potential complications of HIV infection. [(1)]

Therefore, since decades the health care workers are emphasizing on giving the patients who are suffering from HIV the holistic care to restore their immune status. Moreover, the primary management of HIV incorporate three important aspects.

The pharmacological approach to treat HIV employs the use of antiretroviral therapy (ART) which is the most effective way to treat HIV by suppressing the viral replication. Other non-pharmacological way to treat HIV is through broadly neutralizing antibodies (bNAbs) which kill

the viral genome. Another aspect is prevention and treatment of opportunistic infections and complications (co-morbidities) to provide longer and healthier lives to patients. These interventions are also limited as the challenges such as drug resistance and poor compliance to treatment are appearing. Therefore, the clinical trials are going on to bring innovation to cure HIV in future.

Method:

For this literature review, various online databases were used which includes Google scholar, PubMed, JAMA and Science Direct. The search string used was 'New Avenues in the Management of Human Immunodeficiency virus' which showed many review articles from 2015 onwards with publication date from last 5 years. The references of few articles were also scanned. The following key words were used: New Avenues/prevention of HIV/preventing and treating HIV complications/neutralizing antibodies/ opportunistic infections.

The search showed more than 200 articles after limiting it to five years. The titles of all the Articles were viewed to select the relevant content related to our topic
and after sorting those articles more than 60 articles were scanned by going through their Abstract first and from 50 articles 15 most pertinent articles were included in
this literature review which were read to get comprehensive overview and further analyzed and appraised properly. The articles included had been published in the following journals: Periodontol 2000, Infect Dis Clin North Am, Home Healthc Now, Curr Opin HIV AIDS, Retrovirology, Nat Rev Neurol, Curr HIV/AIDS Rep, JAMA, Blood, Nursing Research.

TYPE OF REVIEW:

This article is a simple review which was done by data searching, collection and analysis which is then included in this article in an organized manner. The evidences from the searched articles are included.

Discussion:

Antiretroviral Therapy (ART):

Antiretroviral pharmacology has progressed significantly since the Food and Drug Administration's (FDA) approval of the first antiretroviral, the nucleoside reverse transcriptase inhibitor zidovudine, in 1987. Because multiple medications are required to prevent the development of resistance, clinicians need to understand the off-target effects of antiretroviral, their metabolic pathways, and the important range of potential drug interactions. Before initiating or changing ART, or when starting any new medications in a patient currently on ART, providers should consult authoritative resources for potential drug interactions. [(2)]

Medicines for HIV are grouped into six drug classes according to where they act in the HIV life cycle:

• Nonnucleoside reverse transcriptase inhibitors (NNRTIs) • Nucleoside reverse transcriptase inhibitors (NRTIs) • Protease inhibitors (PIs) • Fusion inhibitors • CCR5 antagonists (CCR5s) (also called entry inhibitors) • Integrase strand transfer inhibitors (INSTIs)

Fusion inhibitors act by blocking HIV from entering the host cell. Chemokine co receptor 5 (CCR5) antagonists are also entry inhibitors that block HIV from latching on to the CCR5 receptor and gaining entry into the host cell. Both NRTIs and NNRTIs act by blocking the HIV enzyme reverse transcriptase that prevents HIV from changing its RNA into DNA. Therefore, these drugs block HIV from replicating. INSTIs block HIV from inserting its viral DNA into the host cell DNA. This in turn blocks HIV from replicating itself inside the host cell. PIs block HIV from synthesizing the pieces that are needed to synthesize more HIV particles in the host cell.[(3)]

In addition to this, compliance to ART treatment is essential and should not be compromised. Therefore, adherence to ART is prime responsibility of both patient and health care workers.

We recommend routine clinical assessment and anticipatory guidance for HIV disclosure and stigma concerns, as these contextual factors are likely to influence patterns of adherence behavior. Developmentally tailored, multicomponent interventions targeting contextual factors known to influence adherence self-management behaviors are desperately needed for HIV-infected racial and ethnic minority emerging adults.[(6)]

Moreover, providing a welcoming clinic environment, addressing social determinants of health, and ensuring continuous access to ART, and providing holistic treatment are important factors in caring for all PWH and particularly for those with advanced HIV.[(4)]

Effective control of HIV infection usually requires a combination of antiretroviral medications in order to prevent virological failure and the development of drug resistance. Therefore, the development of the injectable formulation of RPV-LA is a promising strategy to overcome adherence issues and to reduce pill burden in both HIV infected patients and in HIV PrEP users [(5)]

Broadly Neutralizing Antibodies (bNAbs):

bNAbs are expected to have favorable safety and pharmacokinetic profiles compared with traditional ART. The expected increased dosing intervals and improved safety profile may improve adherence rates for both prevention and treatment. In addition to their potential role in HIV-1 prevention and treatment, bNAbs are also being explored in cure strategies. Unlike traditional ART, bNAbs can engage the host immune system by virtue of their Fc effector

domains to clear cell-free virus, induce antibody dependent cytotoxicity (ADCC), and produce immune complexes that enhance antigen presentation.

In humans, a mathematical model of HIV-1 dynamics was used to examine the rate of viral clearance after a single infusion of 3BNC117. The kinetics of viral suppression suggested that 3BNC117 cleared cell-free virus and blocked new infection, and also accelerated the clearance of infected cells. Antibody–antigen immune complexes can activate dendritic cells to enhance antigen presentation and adaptive immunity, a phenomenon known as vaccinal effect [(7)]

First results suggest that bNAb-mediated therapy is particularly effective in individuals with low or suppressed starting viral loads. Therefore, an initial phase of ART followed by bNAb-mediated therapy is a promising strategy for long-term control of the virus. Broadly neutralizing antibodies differ from classical antiretroviral drugs in that they directly target the circulating virus, recognize HIV-1-infected cells expressing HIV-1 Env and can engage with the host immune system. Indeed, Fc-mediated interactions have been demonstrated to be important for effective bNAb-mediated (S) HIV control and prevention in animal models. [(8)]

Management of Opportunistic Infection (OI) and HIV related complications:

OI of the CNS, such as cryptococcal meningitis, cerebral toxoplasmosis, and tuberculous meningitis, are a major cause of morbidity and mortality in HIV-positive individuals. In patients with HIV or AIDS, treatment with antiretroviral drugs in the setting of OI can lead to a paradoxical worsening of symptoms, caused by immune reconstitution inflammatory syndrome. [(9)]

HIV increases the risk of co-morbidities including lipid abnormalities, Cardiovascular disease, osteoporosis and renal disease. The ART has greater benefits for patients to improve their immunity and live a longer and healthier lives but it also causes metabolic syndromes.

A cross-sectional analysis of 99 HIV infected children and young adults aged 12–20 years conducted in Spain noted an overall high prevalence of dyslipidemia (40 % with hypertriglyceridemia, 27 % with elevated total cholesterol, 26 % with elevated LDL cholesterol, and 14 % with low HDL cholesterol) The authors did not find an association between HDL cholesterol and ART treatment, but they did find an association between higher levels of TG and protease inhibitor (PI) use. [(10)]

Primary OI Prophylaxis with ART universally recommended, the incidence of Pneumocystis pneumonia and major AIDS-associated OIs has declined to less than 1.45 and 0.4 per 100 person-years, respectively, in the United States.16 for individuals with viral suppression while taking ART, the incidence and overall mortality of Mycobacterium avium complex disease is sufficiently low.[(11)]

Future directions:

NANOTECHNOLOGY:

Nanotechnologies have been proposed to solve this problem. Among the three nanotechnology applications in HIV treatment, peptides have been mostly studied for cell targeting and cell penetration in delivery of small molecules and/or biologics for treatment and prevention of HIV. The synthetic and chemical approach to HIV treatment has left much to be desired in the ways a technology can overcome current drug resistances, reduce toxic effects, and improve ease of administration for wider acceptance, compliance, and application in global settings, especially in resource-limited areas.[(12)]

Future Directions New treatments continue to be developed. Injectable rilpivirine combined with cabotegravir was successful in phase 2 studies148 and is being evaluated in phase 3 clinical trials (NCT03299049). Injectable and other long-acting preparations for PrEP, such as injectable cabotegravir149 and the dapivirine vaginal ring, are in clinical trials (NCT01617096). Open-label trials of the dapivirine vaginal ring demonstrated higher uptake and adherence than in the blinded trials, as well asHIV-1 incidence that was half the expected rate. These interventions are moving forward in clinical trials. [(11)]

GENE THERAPY:

Patients already undergoing autologous stem cell transplant for relapsed and refractory lymphoma have been studied in an early trial of gene therapy to engineer reinfused stem cells resistant to HIV. Four patients received a lentivirus vector with 3 RNA-based anti-HIV moieties (tat/rev short hairpin RNA, TAR decoy, and CCR5 ribozyme). Low levels of transcripts were detectable at 24 months. This pilot study was not designed to eradicate HIV, only to explore the feasibility of gene therapy. Gene therapy is an active area of research with newer vectors and anticipated higher rates of transduction (AMC-097 ClinicalTrials.gov Identifier: NCT02797470). If AMC-097 is successful, future trials could explore similarly transduced autologous hematopoietic stem cells in HIV patients without malignancy in an effort to cure HIV infection.[(13)]

THERAPEUTIC VACCINATION:

From studies in HIV controllers, we have observed that potent, poly functional T-cell responses can effectively suppress viral load in the absence of ART. However, eliciting poly functional T-cell responses in all HIV infected individuals independent of HLA background, disease state etc. remains a challenge. Here we have laid out the potential cornerstones for a successful therapeutic vaccine: a vaccine that induces broad, high-quality, and follicle-penetrating HIV-specific T-cell responses that are durable and rapidly responsive to clear reactivating reservoir cells. Together with the help of ICB, LRA and/or other immunomodulatory support, to recover immune exhaustion and reverse viral latency, future studies will show if the concept of therapeutic vaccination will ultimately be successful.[(14)]

Study Title	Author	Year	Findings
Common oral opportunistic infections in Human Immunodeficiency Virus infection/Acquired Immunodeficiency Syndrome**:** Changing epidemiology; diagnostic criteria and methods; management protocols	Ranganathan, K. Umadevi, K. M. R.	2019	Since HIV deteriorates body's immunity so OI gain control which needs timely interventions.
Key Principles of Antiretroviral Pharmacology	Dionne, B.	2019	It highlights the pharmacology of ART including its effects on viral entity and alternative ways such as intramuscular injections as future possibility.
HIV/AIDS: An Update for Home Healthcare Clinicians	Capriotti, T.	2018	Significant role of clinicians is to provide holistic care to patient and to prevent complications through proper regimen and management.
Management of Advanced HIV Disease	Summers, N. A. Armstrong, W. S.	2019	It signifies the precautions that need to be taken prior to initiating and monitoring medications for the patients with low CD4 counts.
Rilpivirine long-acting for the prevention and treatment of HIV infection	Ferretti, F. Boffito, M.	2018	The development of injectable formulation of RPV LA (rilpivirine Nano suspension Drug Class) and its convenient use for patients suffering from HIV.
Adherence Self-Management and the Influence of Contextual Factors Among Emerging Adults With Human Immunodeficiency Virus	Dunn Navarra, Ann-Margaret Whittemore, Robin Bakken, Suzanne Rosenberg, Michael J. Gormley, Maurade Bethea, John Gwadz, Marya Cleland, Charles Liang, Eva D'Eramo Melkus, Gail	2020	The self-management and adherence to regimen to assess patient's behavioral approach towards their disease management.
Broadly neutralizing antibodies for treatment and prevention of HIV-1 infection	Cohen, Y. Z. Caskey, M.	2018	The features of bNAb in preventing and treating HIV by killing the viral epitope is under clinical trials.
Antibody-mediated prevention and treatment of HIV-1 infection	Gruell, H. Klein, F.	2018	The features of bNAbs in HIV management and preclinical and clinical studies and their implications for future use are included.
HIV-associated opportunistic CNS infections:	Bowen, L. N. Smith, B. Reich, D.	2016	The complications which can caused by poor compliance to drugs of HIV leads to OI

pathophysiology, diagnosis and treatment	Quezado, M. Nath, A.		
Complications of Treatment in Youth with HIV	Eckard, A. R. Fowler, S. L. Haston, J. C. Dixon, T. C.	2016	The effects of ART regimen on patient's overall health includes comorbidities like cardiovascular disease, osteoporosis and other metabolic syndromes in youth.
Antiretroviral Drugs for Treatment and Prevention of HIV Infection in Adults	Saag, Michael S. Benson, Constance A. Gandhi, Rajesh T. Hoy, Jennifer F. Landovitz, Raphael J. Mugavero, Michael J. Sax, Paul E. Smith, Davey M. Thompson, Melanie A. Buchbinder, Susan P. del Rio, Carlos Eron, Joseph J., Jr. Fätkenheuer, Gerd Günthard, Huldrych F. Molina, Jean-Michel Jacobsen, Donna M. Volberding, Paul A.	2018	The most crucial thing is relevant drug regimen to be selected for the patient and being cautious while administrating the therapy.
Development of peptide inhibitors of HIV transmission	Shi, S. Nguyen, P. K. Cabral, H. J. Diez-Barroso, R. Derry, P. J. Kanahara, S. M. Kumar, V. A.	2016	Peptide inhibitors are seemed to be more effective in viral inhibition and therefore it shows new avenue in HIV management which is under trial.
Optimizing treatment of HIV-associated lymphoma	Noy, A.	2019	Gene therapy by autologous stem cells is another field of interest to cure HIV which is under trial.
Therapeutic Vaccines for the Treatment of HIV	Chen, Zhilin Julg, Boris	2020	Therapeutic vaccination is another new Avenue for HIV management.
Management of Human Immunodeficiency Virus in the Emergency Department	Torres, M. Moayedi, S.	2018	This study clearly reflects the benefits of drug regimen being more tolerable and less toxic. Moreover, the emergency providers managed to look after the cases of Acute HIV very well.

Conclusion:

The article reflects that HIV management is essential for which ART is most effective. It is evident that due to weak immunity the patients are at high risk to acquire OI and co-morbidities therefore holistic care and mainly adherence to ART are needed as poor compliance to treatment can cause drug resistance or other infections. The crucial aspect is to predict the future possibilities and trends by looking forward to find ways to cure HIV and eradicate it.

Research focusing on management of HIV as a chronic inflammatory state shows promise for new types of therapies and interventions to control the virus. Optimized therapy provides hope for a functional cure in the future. Given the expansion of HIV transmission prevention efforts and successes in treatment worldwide. These changes represent great progress in HIV care.[(15)]

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