Antiretroviral Therapy for Prevention of Human Immunodeficiency Virus Infection

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KEYWORDS

- Human immunodeficiency virus (HIV) infection • Antiretroviral therapy (ART)
- HIV prevention • HIV treatment as prevention • Pre-exposure prophylaxis (PrEP)
- Postexposure prophylaxis (PEP)
- Non-occupational postexposure prophylaxis (nPEP)
- Prevention of mother-to-child transmission (PMTCT)

KEY POINTS

- Human immunodeficiency virus (HIV) is now a chronic medical illness.
- All patients with HIV should be considered for treatment initiation with combination antiretroviral therapy (cART).
- cART serves a critical public health role in the prevention of HIV transmission in high-risk individuals.
- A comprehensive understanding of the pharmacotherapy of HIV drugs will be beneficial to primary care physicians to optimize chance of HIV treatment success and for HIV prevention.

INTRODUCTION

The evolution of combination antiretroviral therapy (cART) as human immunodeficiency virus (HIV) treatment is one of the great biomedical advancements of the twenty-first century. Since the discovery of zidovudine (AZT) in the 1980s, the armamentarium of drugs active against HIV has grown rapidly and the concept of a combination drug treatment of HIV has turned the tide of the epidemic. What was once a uniformly fatal disease has now become a chronic medical illness because cART has led to a remarkable reduction in overall morbidity and mortality.[1,2] As a result, life expectancy of the

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HIV-infected population has caught up with that of the general public, requiring that primary care physicians become well grounded in the care of these individuals. This becomes especially important in the context of treating the widely acknowledged, non-infectious complications of HIV, including cardiovascular disease, malignancies not defined by acquired immunodeficiency syndrome (AIDS), bone disease, and metabolic syndrome. Furthermore, the use of antiretroviral therapy (ART) as chemoprophylaxis against HIV acquisition (pre-exposure prophylaxis [PrEP]) is now supported by data from large multicenter randomized trials. Consequently, primary care physicians also have a unique opportunity to advocate for and implement risk-reduction strategies, including PrEP, in patients at high risk for acquiring the infection. This article provides an overview of the most commonly used HIV therapeutic agents as they are prescribed for HIV infection in treatment-naïve individuals and for prevention of HIV transmission.

ANTIRETROVIRAL THERAPY FOR PREVENTION

The last decade has seen a marked paradigm shift in the public health discourse around HIV with the emergence of the concept of using ART for HIV prevention. This field can be divided into 4 main categories: treatment as prevention; prevention of mother-to-child transmission (PMTCT); postexposure prophylaxis (PEP), including non-occupational exposures (nPEP), and most recently, PrEP.

TREATMENT AS PREVENTION

The hypothesis of HIV treatment as prevention as a public health approach is rooted in the principle that treating HIV-infected individuals with cART decreases their viral load, making them less infectious to their sexual partners.[3] Several persuasive observational studies in HIV serodiscordant couples and ecological studies in community populations have supported this theory, culminating with the landmark HPTN052 study, a randomized multicenter clinical trial that followed 1763 HIV-serodiscordant couples, 98% of whom were heterosexual.[3–11] Half the subjects were randomized to receive cART early, whereas the rest started cART when the HIV-infected partner had a CD4 count lower than or equal to 350 cells/mm^3 or an AIDS-defining illness. The primary endpoint was genetically linked HIV transmission to the uninfected partner. Four years after enrollment began in 2007, 39 HIV transmission events had been recorded, only 4 in the early therapy cohort. Of these 4, only 1 was genetically linked to the infected partner, representing a 96% reduction in risk of transmission. Furthermore, the single linked transmission in the early therapy group likely occurred in the first 3 months of treatment initiation, when the viral load was probably not suppressed. In 2011, the data safety monitoring board (DSMB) discontinued the study early when it became apparent that the individuals on cART were 20 times less likely to infect their partners than those left untreated.[5] The European PARTNER study in both heterosexual and men who have sex with men (MSM) serodiscordant couples has also reported similarly low rates of HIV transmission when the HIV-infected partner is taking cART and has an HIV viral load less than 200 copies per milliliter. As of 2014, no linked transmission events had been reported.[12] These studies lend credence to the scientific validity of HIV treatment as prevention while endorsing its applicability to heterosexual, MSM, and injection drug use groups at risk.

WHEN TO START HUMAN IMMUNODEFICIENCY VIRUS TREATMENT

The timing for cART initiation has evolved considerably as observational studies established marked benefits in AIDS and non-AIDS related morbidity and mortality