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In Vitro Susceptibility of HIV Isolates with High Growth Capability to Antiretroviral Drugs

Narayana Seth*

Department of Clinical Virology, University of Delhi, Delhi, India

Introduction

Recent statistics indicate that 37.7 million people live with HIV/AIDS, which continues to be the primary cause of death for approximately 1 million people annually. This is the case despite the overall decline in HIV-related mortality. In light of this difficulty, ongoing global efforts to expand antiretroviral therapy have significantly increased the number of HIV-positive individuals receiving treatment in recent years, particularly in nations with limited resources. 73% of all HIV-infected people will have received treatment by 2020, and 66% will have their virus suppressed. Antiretroviral therapy's primary objective is to reduce viral load to an undetectable level and stop it from spreading to others who are not infected.

Description

The World Health Organization (WHO) offers treatment options that provide guidelines for when and what antiretroviral regimens should be given to patients. The following three antiretroviral agents are included in the initial antiretroviral regimens utilized by the majority of national treatment programs in resource-constrained settings, as per the most recent WHO guidelines: one important antiretroviral medication, either a non-nucleotide integrase, protease, or reverse transcriptase inhibitor; among the nucleoside/nucleotide reverse transcriptase inhibitors, as well as two backbone antiretroviral medications. Lifelong viral suppression is possible thanks to these combined antiretroviral regimens' excellent potency, safety, and tolerability.

However, the decreased susceptibility to antiretroviral drugs has frequently hampered the aforementioned treatment options. Limited treatment monitoring, poor drug adherence and tolerance, and the emergence of resistance-related mutations during antiretroviral therapy are typically associated with this condition. Although the precise mechanism by which HIV viral factors interfere with virological control is still unknown, it is likely to involve the virus's inherent capacity for replication. HIV replication capability appears to affect antiretroviral therapy response and clinical outcomes, according to recent research. Selhorst and others demonstrated that even during antiretroviral drug therapy, a virus with a high growth capability during early infection significantly contributed to disease progression. Using 13 synthetic antiretroviral compounds, representative HIV isolates with relatively high growth capabilities were subjected to drug screening. At the highest concentration used in the assay, none of the tested antiretroviral compounds showed cytotoxicity of more than 50%. Efavirenz is a non-nucleoside/nucleotide reverse transcriptase inhibitor that is utilized by the majority of national treatment programs. It has also been determined that HIV isolates containing drug resistance-related mutations in tenofovir disoproxil fumarate respond to tenofovir alafenamide.

Antiretroviral drugs were tested on HIV isolates with higher growth capabilities but no known drug resistance-related mutation. Because of its inherent capacity for viral growth, HIV acquires a replicative advantage and increases the number of viral copies produced by drugs like nucleoside/nucleotide reverse transcriptase inhibitors and non-nucleotide reverse transcriptase inhibitors. Because these regimens are the most widely used first-line HIV treatments worldwide, the reduced antiretroviral susceptibility of HIV isolates with a high growth capability is crucial. Consider the high growth capability of epidemic strains because high growth capability isolates are less susceptible to antiretroviral medications [1-5].

Conclusion

Even in the absence of specific drug resistance-related mutations, tenofovir, lamivudine, emtricitabine, and efavirenz reduced antiretroviral drug susceptibility in HIV isolates with high growth capability. Since only a small number of high growth capability isolates were tested against antiretroviral therapy, this evidence, if not all of it, suggests that surveillance is necessary to support the idea that the intrinsic viral growth capability of viral isolates influences their susceptibility to antiretroviral medications. In addition, the behavior of antiretroviral drugs and their response to HIV's inherent high viral growth capability could be better understood through binding thermodynamic analysis. That, on the other hand, needs to be investigated further. In addition, efficient and time-saving assays should be developed using high-throughput assay development. Lastly, this research may aid in the development of diagnostic tools that can identify this viral factor as an additional factor that contributes to treatment failure and enable the appropriate tailoring of antiretroviral therapy.

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***Address for Correspondence:** Narayana Seth, Department of Clinical Virology, University of Delhi, Delhi, India, E-mail: sethnarayana@gmail.com*

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