Impact of revised antiretroviral treatment on the immunological, virological and clinical parameters among people infected with HIV

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Abstract
Introduction: In resource-limited countries like India, where resistance testing is often not available, an accurate treatment history can guide doctors in quantifying suboptimal drug exposure and thus anticipate drug resistance.
Materials and Methods: In the present longitudinal study, a total of 75 patients failing antiretroviral therapy; the effective drug exposure was calculated after taking into account the adherence, appropriateness of prescriptions, and pharmacokinetic interactions. Treatment was modified and patients were followed up.
Results: Of the total 75 patients included in the study; 69 (92.0%), 63 (84.0%) and 42 (56.0%) patients had virological, immunological and clinical failure respectively. Suspected reasons for antiretroviral drug failure were non-adherence in 48 (64.0%), improper prescriptions in 12(16.0%) and drug interactions in 12 (16.0%). We observed that following treatment change, CD4 count increased by a mean of 127 cells/μl and 33 (44.0%) patients had fully suppressed viral loads.
Conclusion: Our results show that empirical treatment changes based on a comprehensive drug history, followed by good adherence lead to good treatment outcomes in patients showing one or other evidence of drug resistance.

Keywords: HIV, AIDS, Drug-resistance, Antiretroviral.

Introduction

Antiretroviral therapy (ART) has significantly reduced mortality and morbidity in individuals with human immunodeficiency virus infection.[1] At the same time, ART has succeeded in improving the quality of life of people living with HIV/AIDS.[2] However, it is noticed that very often patients switch to alternate drug combinations due to drug toxicity, intolerable adverse effects, inconvenience or costs, but also due to worsening clinical outcomes.[3] Among people living with HIV/AIDS (PLHA) reappearance of HIV RNA in plasma may or may not be always associated with drug resistance mutations (DRM). DRM is frequently due to poor adherence but is also due to a high genetic barrier to resistance for some drugs.[4]

To date, only a few observational studies have been conducted to assess the virological response to ARV and have reported conflicting results on the consequences for disease progression by the various patterns of drug resistance and treatment failure.[5] Also, it is well known that the viral load (VL) levels at treatment initiation play a determinative role in the first-line treatment response and the development of DRM.[6] We, therefore, studied the outcome of empirical treatment change in patients failing the first-line antiretroviral treatment. The present study was conducted with the objective to determine the factors related to suboptimal drug exposure and outcome of renewed empirical treatment.

Materials and Methods
Study Design: This was a longitudinal study.
Source of Study Participants: all the patients registered for receiving ARV treatment at P. D. Hinduja medical centre were enrolled in the present study.
Sample Size: all patients fulfilling the inclusion criteria during the period of study. Following this norm, we enrolled a total of 75 patients failing antiretroviral therapy.
Case Definition: Definition of failure of therapy was based on a combination of clinical, immunological, and virological parameters.[7,8] A comprehensive and detailed history of clinical progression of the disease and the treatments received till date were recorded. Self-reported adherence to the antiretroviral therapy was recorded. Improper prescriptions were noted and interacting drugs were identified from available prescription slips. Patients were counselled regarding the importance of adherence to antiretroviral drugs prior to changing treatment.
Follow-up: The duration of follow-up varied; the period of following ranged from minimum three months to a maximum of one year. We attempted to quantify effects on drug exposure by considering the kinetic interactions. For example, rifampicin is known to reduce nevirapine levels by as much as 58%.[9-11] Therefore; it was considered that the patient had 42% drug exposure to nevirapine while on rifampicin.[9-11] Also, inappropriate prescription involving monotherapy or dual therapy was noted. If only 2 drugs of 3 were prescribed, drug exposure was considered as 67% for

Discussion

Of the 75 study participants 69(92.0%) had virological and 63(84.0%) had immunological failure whereas; clinical failure was evident in 42(56.0%) of them. These figures underscore the fact that laboratory monitoring of CD4 counts and viral loads is of utmost importance in detecting early treatment failure in patients with HIV. Before modifying treatment, there were only 6 patients who had a viral load of <50 but had an immunological failure, clinical progression and were clearly on suboptimal treatment. It is possible that presence of M184V mutation might have prevented the rise in viral load, although resistance must be present in these patients.[13,14] Although, it was found that among about 64% of patients the possible causes of treatment failure were non-adherence to therapy, 32.0% patients had inappropriate prescriptions and drug interactions as a cause of failure. These circumstances may be peculiar to our setting where the physician and patient education programs are suboptimal.[15] Of the total 75 study participants included in the study, only one patient failed despite appropriate treatment and full adherence possibly as an inevitable consequence of long-term HAART.[16] Current guidelines recommend resistance testing to optimize drug selection after treatment failure.[17,18] However, resistance tests require a resistant viral population of more than 10-20% to detect resistance. They may not predict hyper-susceptibility or efficacy of combinations and boosting.[19] Finally, the resistance tests are expensive and are not generally available.[20,21] Thus in our study, the resistance testing could be performed only in 15 (20.0%) patients. It was observed that the results correlated well with the drugs to which the resistance was anticipated.

Conclusion

Our results show that empirical treatment changes based on a comprehensive drug history, followed by good adherence lead to good treatment outcomes in patients showing one or other evidence of drug resistance. Using immunological criteria to predict which patient has not achieved virological suppression results in significant misclassification of therapeutic responses. There is an urgent need for the availability of viral load testing in initiation as well as monitoring of ART. Also, the development of standardized and universally accepted definitions of virological failure is necessary to allow meaningful therapeutic interventions.

Limitations

In our opinion following were the limitations of the present study. Firstly, the adherence as defined in this study was self-reported by the patients. Although the optimal way to assess adherence to antiretroviral therapy is not known, self-reported adherence appears to be the most feasible method.[9-12] In our study, CD4 cell count and viral loads were not always done at the same laboratory. The consequence of poor adherence might be different when the viral load was expected to be high than when it was low. This might have important implications for anticipating resistance in that one might give a different weight to early non-adherence as compared to late non-adherence. This factor could not be taken into consideration in this study. Despite these limitations, our results show that in patients failing antiretroviral therapy empiric treatment change followed by good adherence and drug exposure leads to good clinical, immunologic and virological outcome.

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