Hepatic safety profile of antiretroviral drugs in HIV-1 and Hepatitis C (HCV) co-infected individuals

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Introduction

Globally, 150 million individuals are chronically infected with HCV and approximately 4-5 million HIV-infected individuals have chronic HCV co-infection. HIV therapy in HCV co-infected individuals is complicated by hepatotoxicity of antiretroviral agents. Abnormal levels of serum liver enzymes are used to categorize hepatotoxicity of HAART in HIV-infected individuals

Newer antiretroviral agents exhibiting less frequent liver enzyme elevations may be less toxic HIV therapy for the co-infected. The integrase inhibitor RAL has increasingly been favoured in this context. In chronic HCV/HIV co-infected individuals, Macias J et al [1] reported that Raltegravir (RAL)-containing HAART regimens were safe. We evaluated the hepatic safety profile of different classes of ARVs in HIV and Chronic HCV coinfected individuals who were ARV and HCV treatment naïve.

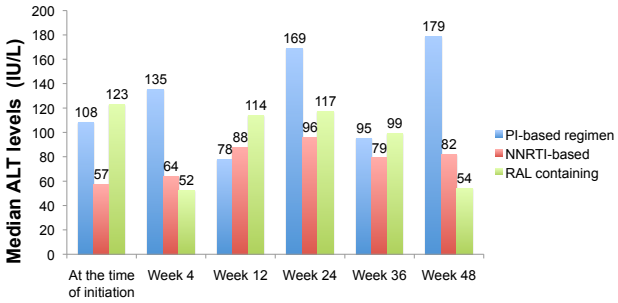
Methods

All individuals attending our unit have data regarding their background, disease and antiretroviral therapy entered on a departmental database. All ART-naïve HIV-infected individuals with chronic HCV who did not receive HCV treatment in the past were identified from this database. Patients who started ART were evaluated retrospectively at baseline, weeks 4, 12, 36 and week 48 after the initiation of antiretroviral treatment. Ninety three individuals were identified, but 60 were excluded from analysis due to: loss to follow up (n=17), initiation of HCV treatment (n=20), high ETOH intake (40 units/week)(n=15) and HBV infection (n=8).

Results

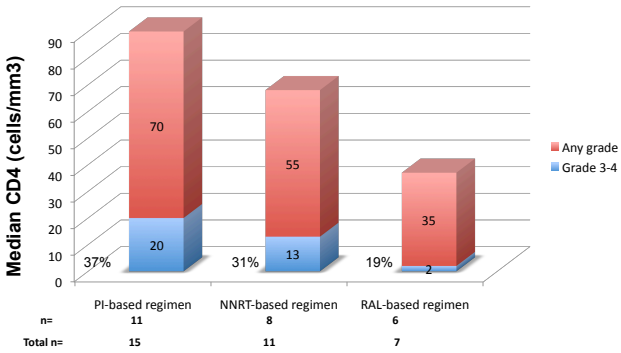
Thirty-three individuals (2 female) were identified with a median age of 38 years (Range 26-69). Fifteen individuals commenced an NNRTI-based regimen (all on Efavirenz), 11 individuals commenced a PI-based regimen and seven individuals commenced a RAL-containing regimen. The most common PIs used were Atazanavir (64%), Darunavir (27%) and Lopinavir (9%). All individuals had HIV VL of <40 copies/mL at week 48.

Figure 1: Median ALT levels up to 48 weeks



Median CD4 count at baseline was 202 cells/mm3 in NNRTI arm, 295cells/mm3 in PI arm and 263cells/mm3 in RAL arm, which increased significantly to 514 cells/mm3, 437 cells/mm3 and 515 cells/mm3 respectively at Week 48. Median ALT levels increased significantly from baseline through to Week 48 in both NNRTI and PI-based arms as its shown in Figure 1. Whereas in the RAL arm median ALT level was 123 IU/L which remained stable at 117 IU/L at Week 24 and decreased significantly to 54 IU/L at Week 48 ($p<0.05$).

Figure 2: Liver enzyme elevations over 48 weeks period



In those individuals with Grade 2 or less liver enzyme abnormalities (LEA) at baseline Grade 3 or 4 LEA after the initiation of treatment were significantly higher on the PI-based regimen (37%) ($p<0.05$) and NNRTI-based regimen (31%) ($p<0.05$) compared to RAL-containing regimen (19%) Figure 2.

Discussion

In individuals with Chronic HCV/HIV coinfection initiation of antiretroviral treatment led to a high degree of antiviral success in individuals treated with either NNRTI, PI or Raltegravir based regimens, but liver enzyme elevations were less common in those treated with Raltegravir.

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