Antiretroviral Therapy is Highly Effective Against Incident Hepatitis B Disease Acquisition Among HIV-Infected Adults in Rakai, Uganda

Abstract 30

Background and objective: Co-infection with Hepatitis B (HBV) and HIV is common in sub-Saharan Africa (SSA) and accelerates progression of liver disease to cirrhosis, hepatocellular carcinoma (HCC) and other complications. About 60% of HCC in Africa is attributed to HBV. In Uganda, 80% of HCC patients have HBV and 20% have HIV/HBV coinfection. HCC is the 4th commonest cancer among Ugandan males and the 6th commonest in females. It is almost always a fatal malignancy in SSA. Prevention of HBV is best achieved through vaccination. Vaccination of HIV-infected adults for HBV is standard of care in developed countries but not in SSA where HBV is believed to be acquired in childhood and where there is lack of HBV incidence data. We investigated the incidence and risk factors associated with HBV among HIV-infected adults in Rakai, Uganda.

Methods: We screened stored sera from 944 HIV infected adults enrolled in the Rakai Community Cohort Study between September 2003 and March 2015 for evidence of HBV exposure using the anti-HBc marker. Serum from participants who tested anti-HBc negative (497) at the baseline round was tested over 3-7 consecutive survey rounds for either anti-HBc or HBsAg sero-conversion. The time of HBV incidence was defined as the median date between the last anti-Hbc or HBsAg negative sample and the first positive anti-HBc or HBsAg serum sample. Almost all ART treatment regimens contained at least one HBV active medication. Exact poisson incidence methods were used to estimate the incidence of HBV with 95% confidence intervals while the Cox proportional regression methods were used to estimate adjusted hazard ratios of ART use and other confounders.

Results: Thirty nine infections occurred (8 positive for both HBsAg and anti-HBc, 3 for HBsAg only, and 28 for anti-HBc only) over 3,342 person-years (pys), incidence 1.17/100 person-years. HBV incidence was significantly lower with ART use: 0.48 /100 person-years with ART use and 2.34/100 person-years without ART ($p<0.001$) and with HIVRNA suppression: 0.6/100pys with HIVRNA $\leqslant$400 copies/mL 6.0/100pys with >400copies/mL ($p<0.001$). It also decreased significantly with age: 2.60/100 pys if aged 15-29 years, 1.32/100 pys if aged 30-39 years and 0.48/100 pys if aged 40-50 years ($p<0.001$). The adjusted hazard ratios of HBV incidence significantly differed by ART use: non ART use versus ART use, aHR=0.24 (95% CI, 0.1-0.5), lamivudine (3TC) use: no ART versus 3TC-based ART, aHR= 0.24(0.1-0.5), p=<0.001), HIVRNA suppression $\leqslant$400 versus >400copies/mL, aHR= 6.4(2.2-19.0) and by age: 40-50 years versus 15-29 years, aHR= 3.66 (1.3-10.2); 40-50 years versus 30-39 years, aHR=2.18(0.9-5.4). No new HBV infections occurred among participants on a tenofovir-based regimen and there was no statistical significant differences by gender, occupation, marital status or number of sex partners, duration on ART or baseline CD4 count.

Conclusion: The protective effects of HBV-active ART medications underscores additional benefits of earlier initiation of ART. Ongoing HBV transmission demonstrated by this study represents an opportunity for vaccine preventive strategies which could ultimately significantly reduce the burden of HCC in SSA.

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