Infezione da HBV in PLWH in terapia con tenofovir e inibitori delle integrasi nella coorte SCOLTA: prevalenza e durabilità della terapia antiretrovirale.

Prevalence of HBV in PLWH receiving tenofovir together with integrase inhibitors: data from the SCOLTA project.

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Riassunto

Il rischio atteso di infezione da HBV in persone che vivono con infezione da HIV (PLWH) è più alto rispetto alla popolazione generale. In questo studio abbiamo valutato la prevalenza di Antigene HBs in PLWH in terapia con tenofovir (disoproxil o alafenamide) e inibitori delle integrasi (INI), come parte della terapia antiretrovirale (ART), arruolati nelle coorti prospettiche dello studio SCOLTA. Abbiamo inoltre valutato la durabilità della ART in PLWH con co-infezione da HBV e le cause di interruzione.

In totale, 1338 PLWH sono stati valutati per gli obbiettivi di

Abstract

HBV prevalence is expected to be high in people living with HIV (PLWH).

We report on HBs Antigen (HBsAg) seroprevalence in PLWH receiving tenofovir (either disoproxil or alafenamide) together with HIV integrate inhibitors as part of their antiretroviral regimens (ART).

HBsAntigen (HBsAg) positive PLWH enrolled in the integrase inhibitors cohorts of the SCOLTA Project were included. Durability of the antiretroviral regimen was evaluated at 6-months and at the last available follow up.

questo studio. Di questi, 92 ((6.9%, 95%CI 5.6%-8.3%) presentavano coinfezione HBV. Di questi, il 25% era precedentemente naive a ART. Per 88 PLWH risultava registrata una visita di follow up successiva all'inizio della terapia con INI; di questi il follow up mediano è stato di 33 (IQR 20-40) mesi.
In 4 casi sono stati registrati eventi avversi che hanno portato alla modificazione della ART in corso. Non sono stati riportati fallimenti virologici. La prevalenza dell'infezione da HBV in PLWH nella nostra coorte è risultata simile a quanto precedentemente riportato in Europa Occidentale. Il regime contenente INI e tenofovir è risultato sicuro ed efficace. Il rischio di aderenza alle visite di controllo rimane un motivo di preoccupazione in questo setting.

Of 1338 PLWH, 92 (6.9%, 95%CI 5.6%-8.3%) were HBV co-infected. Of them, 25% were previously naïve to ART. A subsequent visit has not been registered so far for 4 cases. Of the remaining 88, 67 were still on treatment after a median observation time of 33 (IQR 20-40) months. Adverse events accounted for 4 cases of treatment discontinuation; no HIV virological failure was reported. HBV prevalence was as high as previously reported in similar settings in Western Europe. Integrase inhibitor-based regimen was safe and effective. The risk for low adherence to follow-up visits is still a reason of concern in PLWH with HBV coinfection.

Introduction

The worldwide prevalence of hepatitis B virus (HBV) active infection in people living with HIV (PLWH) is estimated to be 7.4% (interquartile range, IQR, 1.4%-15.7%) (1). In this setting, prevalence estimates are higher than in the general population given the sharing of transmission routes, the impaired immune response and the high rates of vaccine hesitancy (2).
Tenofovir (either disoproxil, TDF, or alafenamide, TAF) is currently recommended as part of the antiretroviral regimen (ART) in people who tested positive for HBV S Antigen (HBsAg) (3). The availability of tenofovir-based ART is a major opportunity for achieving global targets towards HBV elimination in PLWH, either by simultaneous treatment of both HBV and HIV infection or by reducing the risk of mother-to-child transmission of HBV alongside HIV (1). Integrase inhibitors (INI) are currently among the preferred drugs for HIV treatment. However, a few real-word data explored how frequently INI-based ART is administered in HBV co-infected PLWH.
This study aimed to describe the prevalence of HBV infection and assess the ART durability in PLWH receiving TDF or TAF-including regimens.

Methods

A multicentric cohort study was conducted within the SCOLTA (Surveillance Cohort Long-Term Toxicity Antiretrovirals/Antivirals) Project, an active pharmacovigilance system supported by the CISAI (Coordinamento Italiano per lo Studio delle Allergie e dell'Infezione da HIV) study group. The SCOLTA study protocol was approved in 2002 and subsequently modified in 2013, 2019, 2020 and 2023. All study participants gave written consent for study participation.
For the aims of this study, data prospectively collected for PLWH with HBV co-infection receiving TDF or TAF were evaluated if an INI was started as part of the antiretroviral regimen.
HBV infection was defined by HBsAg positive serostatus. Demographic and clinical features were reported. The baseline was set off when the integrase inhibitor (INI) was started. The durability of the ART regimen was evaluated at a 6-months and the last available follow-up.
Prevalence was expressed as a percentage (95% confidence interval, CI). Patients were described using frequency (%) for categorical variables and median (IQR) or mean (standard deviation, SD) for continuous variables.

Results

Overall, 1338 PLWH registered in the integrase inhibitors SCOLTA cohorts received tenofovir as part of their antiretroviral regimen. Of them, 92 (6,9%, IC 95% 5,6%-8,3%) had HBsAg positive serostatus and were thus evaluated for the present study. Study cohort features are reported in **Table 1**. The majority of PLWH included in the present study were males (91.3%), of Caucasian origin (95.7%) and with CDC stage of HIV infection A1 (40.2%). Five patients harbored chronic HCV infection (i.e. had detectable HCV viral load at blood tests) and 26.1% had metabolic syndrome. Of the 92 individuals included, 63 (55.4%) were on treatment with bictegravir/emtricitabine/TAF; 23 (25%) were previously naive to antiretrovirals. Of 69 ART experienced PLWH, 14 (20.3%) had HIV-RNA > 50 cp/mL at the start of INI.

	N (%)
Gender, male	84 (91.3)
Age (median, IQR)	50 (45-56)
BMI (median, IQR)	24.3 (22-26.8)
Ethnicity, Caucasian	88 (95.7)
Hepatitis C virus co-infection (n=90)	
HCV-Ab negative	71 (77.2)
HCV-Ab+/HCV-RNA-	16 (17.4)
HCV-Ab+/HCV-RNA+	5 (5.4)
Previously ART Naïve, yes	23 (25)
CDC, stage A (n, %)	37 (40.2)
CD4 T cell count (n=90)	
<250/mm3	24 (26.7)
250-499/mm3	25 (27.8)
≥500-749/mm3	41 (45.6)
HIV- RNA < 50 copies/mL *	55/69 (79.7)
eGFR ≤60	8 (8.7)
Antiretroviral regimen:	
FTC/TAF/BIC	51 (55.4)
FTC/TDF + DTG	12 (13.1)
FTC/TDF/EVG/COBI	29 (31.5)
Total cholesterol mg/dL, mean (SD)	185 (44.4)
HDL cholesterol mg/dL, mean (SD)	43.6 (12.8)
Triglycerides mg/dL, median (IQR)	128.5 (103-171)
Blood glucose mg/dL, mean (SD)	98.6 (29.7)
Metabolic syndrome, yes	24 (26.1)

Footnotes: IQR: *among ART experienced PLWH; interquartile range, HCV, hepatitis C virus; **ART:** antiretroviral treatment; **FTC:** emtricitabine; **TAF:** tenofovir alafenamide; **BIC:** bictegravir; **TDF:** tenofovir disoproxil; **DTG:** dolutegravir; **EVG:** elvitegravir; **COBI:** cobicistat; **SD:** standard deviations.

Table 1. Characteristics of 92 people living with HIV and HBV.

Durability of the antiretroviral regimen was evaluated for 88 of 92 cases, as a follow up visit was not yet available for the remaining four.

The median observation time was 33 (IQR 20-40) months. At a 6 month follow up, 79/88 (89.8%) PLWH were still on the same antiretroviral regimen. At the last available follow-up 67/88 (76.1%) individuals were still on the same regimen. Reasons for treatment interruption were: adverse events (n=4: 2 renal insufficiency, 1 body weight increase, 1 depression), simplification to single-tablet regimens (n=7), low adherence (n=3), death (n=3: 2 for liver tumors, 1 cerebrovascular accident), loss to follow up (n=4).

Discussion

Sustainable development goals for the end of the epidemics of AIDS and other communicable diseases include combating viral hepatitis.

In particular, targets for 2030 are a 90% reduction in new hepatitis infections and a 65% reduction in hepatitis-related deaths (4). In PLWH, HBV infection has been associated with a higher risk of liver disease complications than in the general population (5).

Thus, improving knowledge on HBV prevalence and treatment discontinuation in this setting may be helpful to target interventions needed to achieve hepatitis elimination goals.

In this study, a large Italian cohort of PLWH receiving tenofovir together with INI as part of the ART regimen, HBsAg prevalence was as high as 6.9%, similar to previous reports in PLWH in Western Europe (1).

Data from the ICONA cohort evidence a 5.8% HBsAg positive prevalence among tested individuals (6). The risk we found was slightly higher, probably because of the inclusion criteria of our study that selected only people receiving tenofovir including ART.

TDF- or TAF-including INI-based ART was well tolerated in this setting, with a 4.5% risk of discontinuation due to adverse events. No liver-related adverse events were reported.

Our study has several limitations. First, our study population was limited to PLWH receiving anti-HBV active antiretroviral regimen, thus HBV prevalence is not generalizable.

Second, we did not track antiretroviral regimen changes, thus we could not argue if patients who changed antiretroviral regimen is still receiving anti-HBV active antiretrovirals or not.

Finally, we did not report on the outcome of HBV infection and hepatitis delta co-infection, although we recorded two deaths related to liver cancer, as it was beyond the aims of our study.

With these limits, our data suggest that HBV infection is still highly prevalent in PLWH.

The low rate of treatment interruption for virological failure or side effects demonstrates that TDF or TAF plus INI including ART is safe and effective for the treatment of HIV infection in people with HBV co-infection. ■

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