Acute Hepatitis B infections after reducing ART among vaccinated patients living with HIV: HBV “PrEP-effect” of TDF/FTC?

Eve Todesco[1], Marc-Antoine Valantin[2], Sepideh Akhavan[1], Marc Wirden[1], Priscila Passe-Coutrin[2], Cathia Soulié[1], Basma Abdi[1], Théophile Cocherie[1], Vincent Calvez[1], Roland Tubiana[2], Romain Palich[2], Valérie Pourcher[2], Anne-Geneviève Marcelin[1], Sophie Seang[2]

[1] Sorbonne Université, INSERM, Institut Pierre Louis d’Épidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Pitié-Salpêtrière, Service de Virologie, Paris, France; [2] Sorbonne Université, INSERM, Institut Pierre Louis d’Épidémiologie et de Santé Publique (iPLESP), Assistance Publique-Hôpitaux de Paris (AP-HP), Hôpital Pitié-Salpêtrière, Service des Maladies Infectieuses et Tropicales, Paris, France.

Background

In order to improve quality of life and lessen ART burden and toxicity, reduced ART approaches have become a significant part of HIV therapeutic guidelines. In such strategies, one of the options is to remove one drug that may have a dual anti-HBV/HIV activity such as Tenofovir disoproxil (TDF) and Emtricitabine (FTC). We report here some clinical cases of acute hepatitis B (HBV) infections after withdrawal of TDF/ FTC among HBV-vaccinated patients living with HIV.

Materiel and Methods

This descriptive case-report study included patients living with HIV and followed in Infectious Diseases Department of Pitié-Salpètrière hospital (Paris, France). Clinical and socio-demographic data were obtained from patient’s medical records. HBV serologies were performed by Alinity® (Abbott, Chicago, IL, USA) and viral loads by Cobas 6800® devices (Roche Diagnostics, Bâle, Switzerland).

Results

Three male patients living with HIV, HBV-vaccinated and virologically suppressed were switched from a TDF/FTC-based regimen (+Rilpivirine or Elvitegravir) to a TDF-free dual therapy (Rilpivirine+Dolutegravir or Cabotegravir). After 3, 3.5 and 8 months respectively, they suffered an acute HBV infection (positive HBs antigen, anti-HBc IgM and HBV viral loads above 6 $\log_{10}$IU/ml) that required hospitalization for one of them (Prothrombin time: 62%). FTC/TDF 200/245mg/d or Entecavir 1mg/d were introduced in order to treat the HBV infection, with a dramatic decrease of HBV viral loads for the three patients and a positive clinical evolution.

At the time of HBV diagnosis, HIV stages of infection were A1 (n=2) or A2, CD4 cell counts were 754, 739 and 557/mm^3 and ALT titers were 917, 3086 and 409 UI/L, respectively. Nadir of CD4 cell counts were 527, 632 and 356/mm^3 and CD4 cell counts were 697, 854 and 456 /mm^3 at the time of the first vaccine injection.

HBs antigen and anti-HBc antibodies were in all 3 cases negative before the ART switch. All of them had received HBV vaccine before the ART switch (Engerix B 20ug, at least 3 injections, single dose). One patient displayed an anti-HBs antibodies (HBsAb) titer of 41UI/L a few months before acute infection but HBV sequencing did not reveal any immune escape substitution. For the two other patients, no protective HBsAb were observed before and up to 7 and 9 months after the HBV infection (<10UI/L).

Risk factors for HBV infection were condomless sex, and use of IV drugs for two of the patients.

Patients Age	1 60 years	2 37 years	3 45 years
HIV Diagnostic (stage)	2018 (A2)	2012 (A1)	2018 (A1)
Initial ART	TDF/FTC/EVG	TDF/FTC/RPV	TDF/FTC/RPV
Switching ART (date)	DTG/RPV (October 2022)	CAB/RPV (November 2022)	RPV/DTG (March 2022)
HIV-1 undetectability	≥ 5 years (3 blips <50 cp/ml)	≥ 5 years	≥ 3 years
CD4+ cell counts (cells/mm³)	➢ Nadir : 356 ➢ First vaccine injection : 456 ➢ HBV infection : 557	➢ Nadir : 527 ➢ First vaccine injection : 697 ➢ HBV infection : 754	➢ Nadir : 632 ➢ First vaccine injection : 854 ➢ HBV infection : 739
Hepatite B vaccine by Engerix® (single dose)	3 injections (2019)	3 injections (2013) + 1 injection (2022) + 1 injection (January 2023)	3 injections (2021/2022)
HBs antibodies before HBV infection	Negative	Negative	**41 UI/L (April 2022)**
HBsAg positivity date (time from the switch, months)	June 2023 (8)	March 2023 (3,5)	June 2022 (3)
ALT peak (UI/L)	409	976	3086 (PT: 62%)

Table 1. Characteristics and clinical evolution of the 3 patients

Conclusions

Humoral response to HBV vaccine is known to be impaired among patients living with HIV and should be checked after the schedule of vaccination, even for patients with high CD4 cell counts. Moreover, cellular immune responses need to be further investigated in people living with HIV. Indeed, these three cases of acute HBV infection addressed several questions about the protective correlate for HBV among people living with HIV. The HBV “PrEP-effect” of TDF/FTC, already reported by several authors [1,2,3], is suggested once again by these case reports.

➡ In conclusion, withdrawal of an active anti-HBV drug should be considered with caution in case of risky behavior towards sexually transmitted infections and absence or low immune response to HBV vaccine.

References

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