Viral hepatitis treatment for people with HIV in African settings

Dr Mark Sonderup
Division of Hepatology and Department of Medicine
University of Cape Town & Groote Schuur Hospital
Cape Town, South Africa

Brief outline

1. Focus on sub Saharan Africa
2. Hepatitis B
3. Hepatitis C

HIV/AIDS prevalence in Africa
Hepatitis B

HBsAg prevalence rates in sub-Saharan African HIV-infected individuals per country

HIV/Hepatitis B co-infection prevalence: South Africa

- no community based data available

Available data:
1. Urban HIV clinic in Johannesburg:
   5% HBsAg-positive (47% exposure)
2. ARV program in mining industry in Johannesburg:
   17% HBsAg-positive
Transmission of HBV

Vertical Transmission

Infant

Perinatal

Infants: 90% become chronically infected

Horizontal Transmission

Host

Recipient

Child to Child: dominant mode of transmission in Sub-Saharan Africa

Contaminated Needles

Sexual

Health Care Worker

Btw 6/12 and 5 years: 30 – 50% become chronically infected

> 5 years: 5 - 10% become chronically infected

Chronic Hepatitis B virus infection

Sub-Saharan Africa:

• HBV endemic

• Mostly genotypes A, D, E

• Prevalence ranges:
  * HBsAg 0.3% - 25%
  * HB core IgG 5% - 80% exposure rate

HIV/Hepatitis B co-infection

Patterns of Co-Infection in Africa

• Majority - infected or exposed to HBV in childhood prior to HIV acquisition as adults

• Less commonly
  Perinatal transmission of HIV (and HBV)
  Reactivation of infection in immunocompromised
  De novo adult acquisition of both HBV and HIV

Developed world → HIV and HBV share a similar mode of transmission
**Alterations in the Natural History of HBV Infection in Persons With HBV/HIV Coinfection**

- More likely to become chronic HBV carrier (HBsAg positive)\(^a\)
- More likely to be HBeAg positive\(^b\)
- Less likely to be anti-HBe positive\(^b\)
- Less likely to convert HBeAg to anti-HBe\(^b\)
- More likely to go from HBeAg negative back to HBeAg positive\(^b\)
- Can revert from anti-HBs to HBsAg positive\(^c\)
- Higher levels of HBV DNA\(^c, e\)

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**HIV Co-infection Increases the Risk of ESLD due to HBV**

- MACS, 4,967 men
  - HIV, 47% (n=326)
  - HBV, 6% (n=326)
  - HIV/HBV, 4.3% (n=213)
- HIV/HBV: 17-fold higher risk of liver death compared to HBV alone

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**Liver Mortality by HIV and HBV Status**


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**Effects of HIV on HBV - Liver related mortality**

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Time trend of all-cause liver related mortality for HBV and HCV co-infected

Serological and virological characteristics

* At time of liver biopsy

Management of HIV-HBV Co-infection

* HBV/HIV co-infected patients who require HBV therapy should be treated

<table>
<thead>
<tr>
<th>Not on or Anticipating Antiretroviral Therapy*</th>
<th>Planning Antiretroviral Therapy</th>
<th>Already Receiving Antiretroviral Therapy</th>
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</thead>
<tbody>
<tr>
<td>Treat with antiretroviral regimen that is active vs HIV</td>
<td>Treat with therapies that are effective against both viruses: TDF + (FTC or LAM) preferred (plus ≥ 1 other anti-HIV agent)</td>
<td>If regimen does not include drug active against HBV, may add pegIFN or ADV</td>
</tr>
<tr>
<td>If not on ART, it should not be used in this circumstance</td>
<td>If regimen does not include drug active against HBV, may add pegIFN or ADV</td>
<td>If LAM resistance, add TDF</td>
</tr>
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Guidelines recommend that any HBV/HIV co-infected patient in whom HBV treatment is indicated should initiate a fully suppressive antiretroviral regimen containing 2 drugs with anti-HBV activity.

Incidence of LAM Resistance in HBV and HBV/HIV Patients

Benhamou et al., Hepatology, 1999)

HBV co-infected patients: summary

- Progressive move towards TDF based cART therapy – funded through Global Fund etc.
- Given changes in ART guidelines limited need for Rx in people not requiring ART (e.g. IFN, entecavir)
- Downside:
  - Often no screening for HBsAg: missed surveillance opportunity
  - Missed opportunity to vaccinate or offer HBIG for PMTCT
  - HBV mono-infected are mostly excluded

Hepatitis C
Hepatitis C prevalence in Africa

Hepatitis C genotypes in Africa
HIV HCV co-infection in Africa

- Data on co-infection rates very limited
- Thought to be low
- Dominant mode of transmission unclear – vertical rates low
- IDU and other modes of transmission uncommon in Africa
- ? Sub-populations more at risk

Access to HCV therapy

- Almost non-existent
- To date need for ART been major focus
- Peg-RBV combination
  - costly
  - difficult to manage
  - poor response rates
- Simple DAA combos eagerly awaited
  - cost will remain an issue!!