Treating HCV/HBV co-infection

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How common is this?

- **Worldwide prevalence**
  - HBV – 250 million
  - HCV more than 70 million
  - Co-infection 1-15%

- **United States**
  - HBV -1.9 million
  - HCV – 2.4 million
  - Co-infection 1.4%

Mavilia MG, Wu GY. HBV-HCV Coinfection: Viral Interactions, Management, and Viral Reactivation. J Clin Transl Hepatol. 2018 Sep 28;6(3):296-305. doi: 10.14218/JCTH.2018.00016. Epub 2018 Jul 6. PMID: 30271742; PMCID: PMC6160312.

Difference in co-infection vs mono infection on disease progression

- **Study by Pol S et al.**
  - 850 patients – 95 co-infected with HBV and HCV, 375 mono infected with HBC, 380 mono infected with HCV
  - **Severe fibrosis or cirrhosis:**
    - coinfected patients (58%)
    - HBV-monoinfected patients (32%, $P < .0001$)
    - HCV-monoinfected patients (52%, $P = .3142$)
  - **Decompensated cirrhosis:**
    - coinfected patients (11%)
    - HBV and HCV-monoinfected groups (2% and 4%, respectively, $P = .0275$).

Pol S, Haour G, Fontaine H, Dorival C, Petrov-Sanchez V, Bourliere M, Capeau J, Carrieri P, Larrey D, Larsen C, Marcellin P, Pawlostky JM, Nahon P, Zoulim F, Cacoub P, de Ledinghen V, Mathurin P, Negro F, Pageaux GP, Yazdanpanah Y, Wittkop L, Zarski JP, Carrat F; French Anrs Co22 Hepather Cohort. The negative impact of HBV/HCV coinfection on cirrhosis and its consequences. Aliment Pharmacol Ther. 2017 Dec;46(11-12):1054-1060. doi: 10.1111/apt.14352. Epub 2017 Oct 9. PMID: 28994127.

Co-infection and HCC

- **Some controversy over risk**
- **Benvegnu L et al.**
  - 368 patients at University of Tokyo from 1991 to 1995
  - 36% of coinfected individuals, 6% of HCV monoinfected and 11% of HBV monoinfected

Benvegnù L, Fattovich G, Noventa F, Tremolada F, Chemello L, Cecchetto A. Concurrent hepatitis B and C virus infection and risk of hepatocellular carcinoma in cirrhosis. A prospective study. Cancer 1994;74:2442-2448

Co-infection and HCC

- **Kuper et al.**
  - 333 patients in Greece from January 1995 to December 1998
  - Odds ratios of developing HCC
    - 46.2 for HBV, 53.5 for HCV and 32.3 for co-infection

Kuper, H., Tzonou, A., Kaklamani, E. *et al.* Hepatitis B and C viruses in the etiology of hepatocellular carcinoma; a study in Greece using third-generation assays. *Cancer Causes Control* **11**, 171–175 (2000). https://doi.org/10.1023/A:1008951901148

Does treatment help?

- **Study with PegINF/RBV**
  - All cause mortality decreased in the treated vs non treated group (7.4 vs 19.6%)
  - Liver related mortality decreased (5 vs 11.9%)
  - Risk of developing HCC decreased by 34%

Liu CJ, Chu YT, Shau WY, Kuo RN, Chen PJ, Lai MS. Treatment of patients with dual hepatitis C and B by peginterferon α and ribavirin reduced risk of hepatocellular carcinoma and mortality. Gut 2014;63:506-514

Is treatment as effective?

- **Italian retrospective study**
  - 104 cirrhotic HCV patients
    - 8 HBsAg positive
      - 100% SVR among coinfected

- Calvaruso V, Ferraro D, Licata A, Bavetta MG, Petta S, Bronte F. HBV reactivation in patients with HCV/HBV cirrhosis on treatment with direct-acting antivirals. J Viral Hepat 2018;25:72-79

AASLD Recommendations for treatment

- Those with detectable HCV RNA should be treated
- Those with detectable HBV DNA
  - Treatment should be determined by HBV DNA and ALT levels

Monitoring per AASLD

- **HBsAg positive**
  - At risk of flares with DAA treatment
  - Monitor every 4-8 weeks during treatment and for 3 months post treatment
- **HBsAg negative, anti HBc-positive**
  - Very low risk of reactivation
  - ALT levels should be monitored at baseline and at end of treatment and during follow up
  - HBV DNA and HBsAg testing reserved for those with ALT level increases or those that fail to normalize during or post treatment.

Reactivation

- **Taiwanese study by Ming-Lun Yeh et al.**
- **81 co-infected patients treated with DAA**
  - 38% experienced reactivation (≥ 1 log increase in DNA from baseline in patient with detectable DNA pretreatment or ≥100 IU/mL in patient pretreatment undetectable DNA)
    - 76.7% occurred during treatment
  - 6 patient with clinic reactivation (ALT ≥2-fold from nadir and >100 U/L or ≥2 –fold increase from baseline with concomitant HBV reactivation)
  - **4 were cirrhotic and 2 died**

Yeh ML, Huang CF, Huang CI, Holmes JA, Hsieh MH, Tsai YS, Liang PC, Tsai PC, Hsieh MY, Lin ZY, Chen SC, Huang JF, Dai CY, Chuang WL, Chung RT, Yu ML. Hepatitis B-related outcomes following direct-acting antiviral therapy in Taiwanese patients with chronic HBV/HCV co-infection. J Hepatol. 2020 Jul;73(1):62-71. doi: 10.1016/j.jhep.2020.01.027. Epub 2020 Feb 14. PMID: 32061869.

Takeaways

- **HCV is usually the dominate virus**
- **Co-infection increases risk for advanced fibrosis and HCC**
- **Treatment of HCV is recommended**
  - HBV prophylaxis is not required but monitoring for reactivation is
  - No drug interactions between HBV nucs and DAA's
  - SVR rates are similar to mono infected
- **Reactivation is not uncommon with HBsAg + patients**
  - Clinical reactivation is rare
  - HBsAg -,HBcAb+ reactivation is even more rare and likely occult infection
  - Cirrhotic patients are at increased risk for bad outcomes

Questions?