دکتر دهقان نیری

مهر ۹۶

HBV/HCV Coinfection

HBV/HCV coinfection is not uncommon and is frequently found in HBV-endemic areas such as Asia, sub-Saharan Africa and South America

The exact number of HBV/HCV co-infected patients is unknown

Estimated 7 – 20 million individuals affected worldwide.

Patients with HBV/HCV coinfection

have an increased risk for cirrhosis, hepatocellular carcinoma (HCC)and even death.

The rates of HCV coinfection in HBsAg positive patients vary from 9 to 30% depending on geographic region.

8.4% of patients with chronic HCV infection were co-infected with HBV .

HBV/HCV coinfection are more often present in patients with comorbidities, intravenous drug abuse, HIV-infected patients or in patients who require hemodialysis or regular blood Transfusion...

- the rate of HBV/HCV coinfection is probably higher than usually estimated as the diagnosis of occult HBV infection (detectable HBV-DNA without HBsAg) is underestimated.
- Occult HBV infection has frequently been identified in patients with chronic HCV infection and has the highest prevalence in Asian countries.

The overall prevalence of occult HBV in different studies has been reported to be up to 52% among patients with chronic HCV infection.

The most important reason for the diversity in prevalence of occult HBVmight be the heterogenicity of the study populations including groups with different risk-factor profiles.

Risk factors of HBV co-infection in HCV infected patients

age less than 50 years, male sex, HIV infection, history of hemophilia and thalassemia, history of blood transfusion,

and cocaine use ,Asian ethnicity, intravenous drug use, and a greater number of sexual partners

- In patients with chronic HBV infection, HCV co-infection accelerates liver disease progression and increases the risk of HCC.
- Therefore, all chronic HBV patients should be screened for HCV as well as for other blood bourne viruses.

HBV and HCV may occur simultaneously or as superinfection. However, frequently the order of infection cannot be defined, and in this setting the term ‘concurrent’ infection is frequently used.

Superinfection of chronic HBV carriers with HCV occurs more frequently, especially in HBV endemic areas.

WhileHBVsuperinfection of chronic HCV is a rare event

- HBVsuperinfection may suppress HCV replication, resulting in clearance of HCV-RNA soon after the clinical onset of acute
- Hepatitis B envelope antigen positive (HBeAg-positive)
- HCV and HBV seem to inhibit each other’s replication.

Viral dominance

Viral dominance can be defined as one virus showing significant viral replication (HCV RNA > 50,000 IU/ml; HBV DNA > 2000 IU/ml) with the other virus being suppressed (HCVRNA negative or HBV DNA negative or < 2000 IU/ml).

- HBV/HCV coinfected patients also have lower levels of HBV-DNA, as decreased activity of HBV-DNA polymerase, HBsAg and HBcAg in the liver
- In this regard, HCV superinfection can result not only in suppression of HBV-DNA, but also in HBe seroconversion or even in clearance of HBsAg

A longitudinal follow-up study revealed that HBs seroconversion occured more frequently in HBV/HCV coinfected patients than in HBV monoinfection (2.08 and 0.43%, respectively)

By contrast, some findings indicate a reciprocal inhibition or even a dominant role of HBV.

Another Italian study reported significant higher rates of HCV clearance compared with HCV monoinfection. (71 vs 14%, respectively)

However, and in line with previous studies, the overall dominant effect seems to be that HCV suppresses HBV (in approximately 50% of patients)

patients may in addition be coinfected with hepatitis delta virus (HDV).

Thus, all HBsAg + patients should be tested for anti-HDV requiring additional, specific diagnostic steps

Treatment

of HBV/HCV coinfection

Treatment must be individualized based on patient variables such as:

1-hepatitis virology

2- patient's previous exposure to antiviral

treatment,3- the presence of other similarly transmitted viruses such as HDV, HIV

4-stage and grade of liver disease and comorbidities.

Several studies suggest a reciprocal inhibition of replication by HBV and HCV which may fluctuate over time.

Therefore, the antiviral regimen of HBV/HCV coinfected patients should be based on virological patterns determined during a screening phase of at least 3 – 6 months.

Detailed serological and virological testing is required to establish the ‘dominant’ virus infection before initiation of therapy.

In some HBV/HCV coinfected patients a longer follow-up of more than 6 months after the initiation of antiviral treatment is essential, as HBV relapse can occur even after years.

When HCV is replicating and causes liver disease, it should be treated with PegIFN/RBV following the same rules as applied to mono-infected patients.

The SVR rates in this group are broadly comparable to those in HCV mono-infected patients, or even higher.

There is a potential risk of HBVreactivation during or after HCV clearance.

In that case,or if HBV replication is detectable at a significant level, concurrent.

HBV nucleoside/nucleotide analogue therapy may be indicated,

Interferon-based therapy may suppress replication of both HCV and HBV viruses that the risk of HBV reactivation during and after combined (IFN + RBV) treatment was low.

DDAs Therapy

- There is a potential risk of HBV reactivation during DAAs therapy or after clearance of HCV.
- risk of HBV reactivation may be greater with newer HCV treatment regimens(DAA) compared to PegIFN + RBV because of their higher potency against HCV and lack of anti-HBV activity.

- HBsAg-negative, anti-HBc positive patients undergoing DAA should be monitored and tested for HBV reactivation in case of ALT elevation.
- Reactivation of hepatitis B is defined as an abrupt reappearance or rise of HBV DNA serum level in patients with previously resolved or inactive HBV infection.

The authors concluded that close monitoring of HBV DNA during anti-HCV DAA therapy and anti-HBV therapy after increased HBV DNA should be considered in patients with HBV/HCV co-infection.

- The authors proposed simultaneous anti-HBV treatment as a more reasonable option for patients with HBV/HCV co-infection treated with DAAs.

- HBV reactivation may occur irrespective of theHCVgenotype or the class of usedDAAs.
- No HBV virological reactivation was observed in patients with pastHBVinfection.
- Most patients treated for HBV experienced decreased HBV DNA and improved liver function and clinical symptoms.

Risk Factors for HBV Reactivation

- The strong risk factor for developing hepatitis during treatment was the presence of HBsAg before DAA treatment,
- HBVreactivation is independent of HCVgenotype,DAAuse, and baselineHBVdisease parameters

- Uptonow, the mechanism bywhich HCV – therapy might cause HBVreactivation is not known and there are no genetic markers for prediction of HBV reactivation.

- guidelines from the AASLD/IDSA now recommend that all patients starting HCV DAA therapy should be assessed for HBV co-infection with HBsAg, anti-HBs, and anti-HBc testing.

- For HBsAg positive patients, the test for HBV DNA should be obtained and patients meeting criteria for HBV treatment should start therapy at the same time or before HCV DAA therapy initiation.

- patients with low or undetectable HBVDNAlevels should be monitored at regular intervals for HBV reactivation. For patients with the presence of anti-HBc alone or for anti-HBs and anti-HBc,the possibility of HBV reactivation should be considered in case of an increase in LFTs during or after DAAs treatment

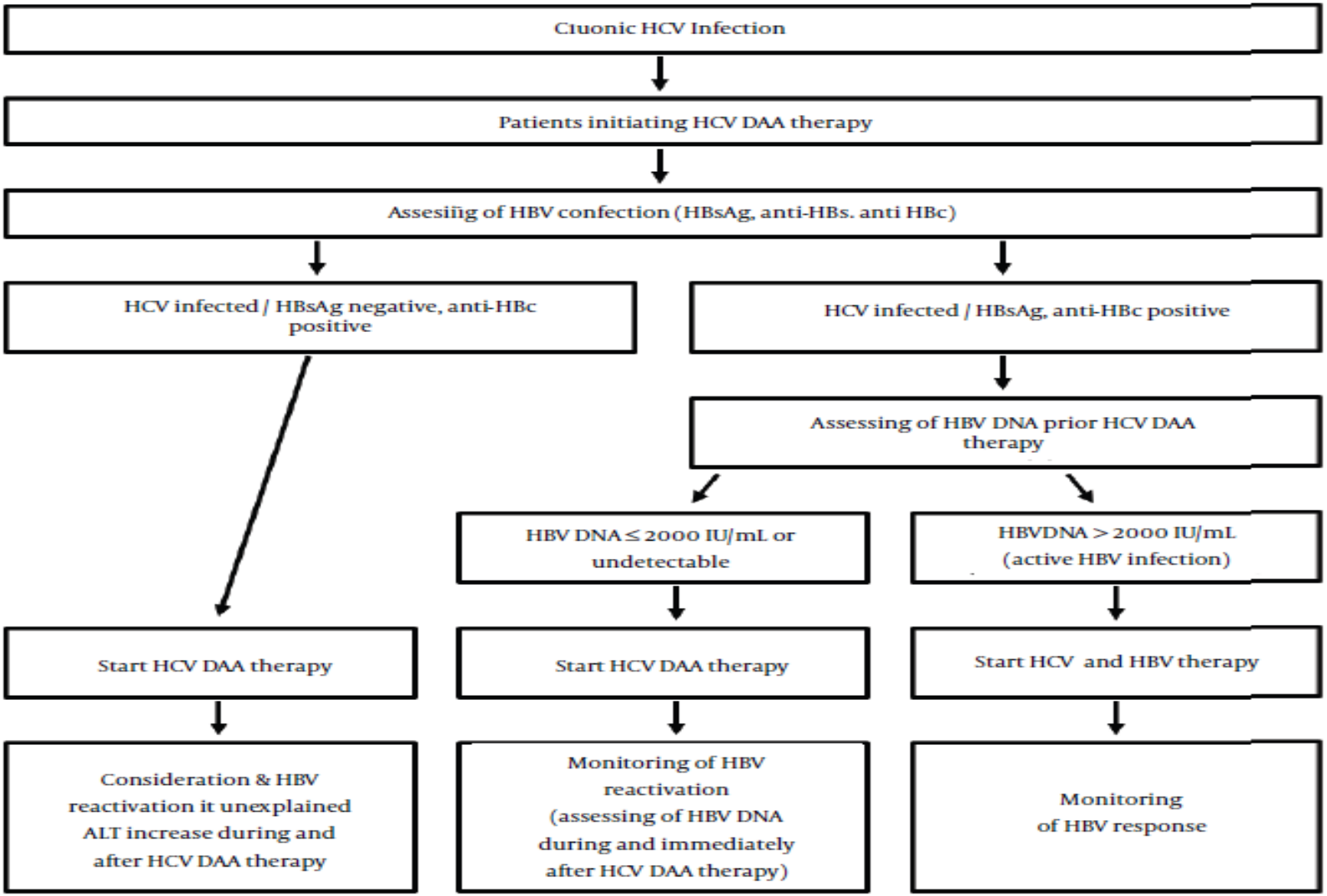

Figure 1. Algorithm for the Management of HBV/HCV Co-Infected Patients Prior to HCV DAA Therapy

- present data on PEG-IFN-a plus ribavirin
- strongly indicate that this regimen should be the treatment of choice in patients with dominant HCV replication.
- In patients with dominant HBV disease other options, especially nucleoside analog alone or in combination with interferons, should be tested.
- After treatment and eradication of the dominant virus, the other one may then become active.

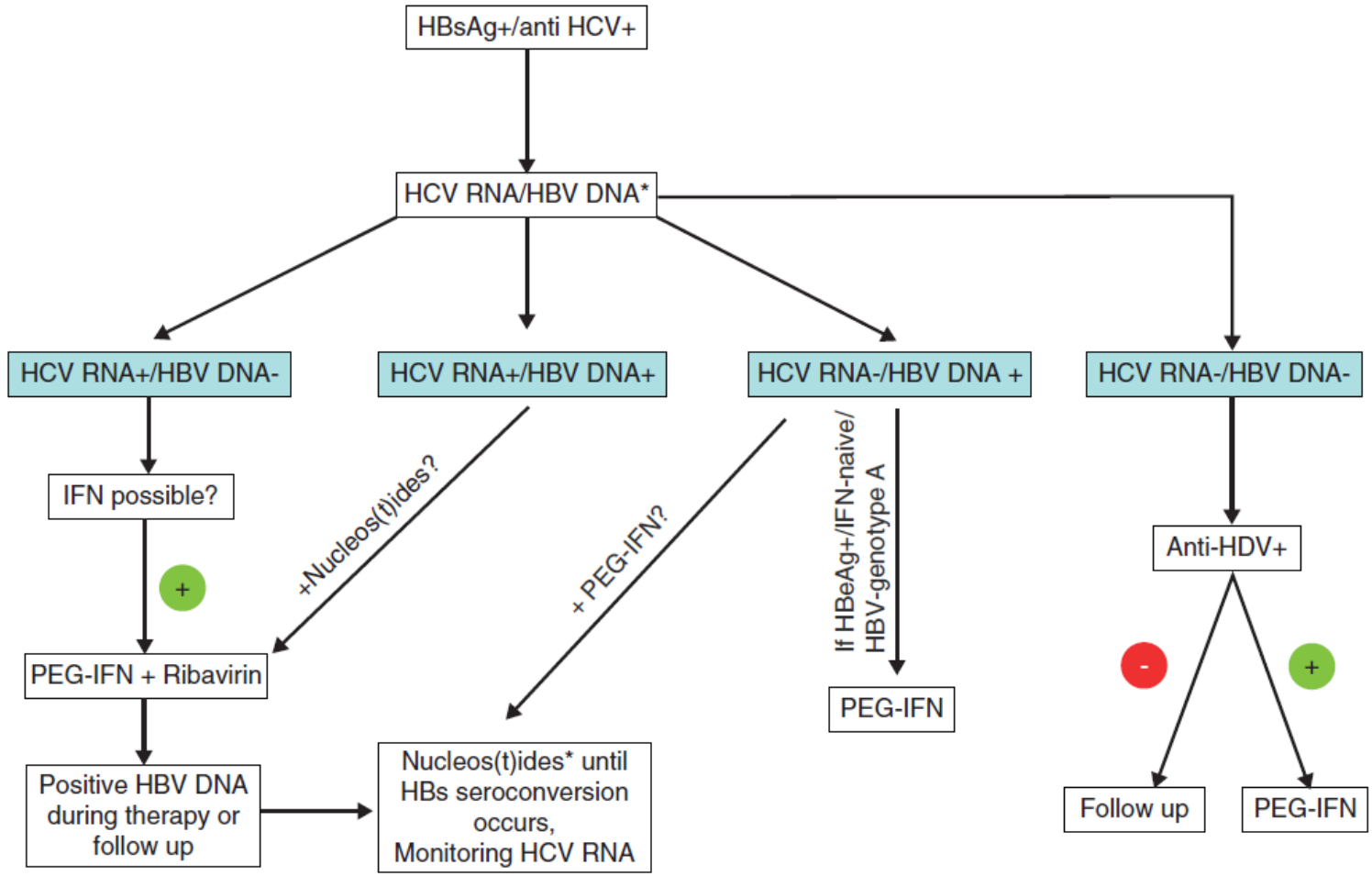

Figure 1. Therapeutic algorithm in HBV/HCV co-infection.

*Assessment of HCV RNA and HBV DNA at least at two different time-points.