

Nucleos(t)ide Analogue-based Therapy for CHB

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Oral nucleos(t)ide analogues (NUCs) are currently the most commonly prescribed treatment for chronic hepatitis B. Compared with interferon-based therapy, NUCs can conveniently be dosed orally as a daily regime. They carry few side effects and can reliably suppress the hepatitis B virus (HBV) in the majority of cases. After long-term treatment, most patients have no to minimal hepatic necroinflammation and regression of fibrosis. Up to 70% of patients with compensated cirrhosis can even achieve reversal of cirrhosis in 5 years. This is translated to reduced risk of cirrhotic complications and hepatocellular carcinoma and improved survival.

Although patients receiving NUCs have higher rate of hepatitis B e antigen seroconversion than untreated patients, the effect is likely to be indirect via viral suppression. In other words, NUCs do not have direct immunomodulatory effect. As a result, hepatitis B surface antigen (HBsAg) seroclearance is rare in NUC-treated patients, and virologic relapse is common after cessation of NUCs.

Until new treatments are available, this means most patients would require long-term NUC therapy. In the past, drug resistance was a major problem of long-term NUC therapy. However, the currently available tenofovir and entecavir are NUCs with minimal risk of resistance and should be the first-line treatment. Data from clinical trials and cohort studies also suggest that NUCs have excellent long-term safety profiles. The remaining concern is bone toxicity from nucleotide analogues which may take longer to manifest.

NUCs have clearly transformed the management of chronic hepatitis B. The next step, however, would be to find ways to clear HBsAg and achieve sustained off-treatment response. Recent data already suggest the possibility to use peginterferon to treat patients well controlled with NUCs. Numerous studies are also under way to tackle HBV via different targets.