Chapter 54

What is New in Hepatology?

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INTRODUCTION

Many new exciting developments are taking place in the field of hepatology. Health care providers are better able to serve their communities and keep them healthy. I will focus on the management of hepatitis B, hepatitis C and hepatocellular carcinoma (HCC).

HEPATITIS B

Hepatitis B is a global issue. The prevalence of chronic hepatitis B varies according to the regions. For example, in the Indian subcontinent 2–7% of the population is affected, whereas in Southeast Asia almost 8–15% of the population is affected and in the United States of America less than 2% of the population is affected.1

The number of enrolled patients for liver transplantation due to hepatitis B-related HCC increased by 146% between 1990 and 2005, whereas the number of persons waitlisted for hepatitis B-related liver transplantations has declined in recent years. The Risk Evaluation of Viral Load Elevation and Associated Liver Disease/Cancer-Hepatitis B Virus (REVEAL-HBV) study from Taiwan has shown that persistent viral replication and high viral load leads to cirrhosis and HCC.3

The current treatment with oral nucleoside and nucleotide analogs has demonstrated the resolution of fibrosis and in certain cases the complete resolution of cirrhosis. The recent 5-year study of tenofovir treatment has shown that 74% of patients with cirrhosis at baseline were no longer cirrhotic at the end of 5 years. Ninety eight percent of the patients on tenofovir had undetectable HBV DNA level, less than 400 copies per milliliter.4 In 2012, at Asian Pacific association for study of liver disease, Tsai et al. presented that 89% (16 out of 18) of lamivudine-experienced patients when treated with tenofovir who were cirrhotic at the baseline were no longer cirrhotic at the end of 5 years.

Though we are making strides in the management of hepatitis B, there are still unmet needs and unanswered questions. For example, how long do we continue to treat our hepatitis Be antigen (HBeAg) negative patients? In HBeAg positive patients, who do not clear the e antigen after long-term treatment, how long to continue the treatment? What will be the next course? How do we handle the “covalently closed circular” DNA? Would combination of the treatment with pegylated interferon and oral nucleoside/tide analogs answer some of these questions? What about occult B infection (OBI)? Future studies will give us some answers.

CHRONIC HEPATITIS C

Hepatitis C is a global problem. In the United States of America the number one cause for liver transplantation is chronic hepatitis C, but new developments in the management of chronic hepatitis C will change the landscape of this disease. In fact, the current recommendations by the Centers for Disease Control, USA have called for screening of those born between 1945 and 1964 for hepatitis C because of high prevalence among those cohorts.

Treatment for chronic hepatitis C began in 1991 with mono-therapy of interferon. In 2001 treatment regimen included pegylated interferon and ribavirin which yielded the sustained viral response (SVR) rate of 55%. Currently the addition of direct acting antiviral treatments has improved the SVR to 67–75%.5 Once the viral clearance (SVR) occurs, the reversal of fibrosis and improvement in histology has been demonstrated.

The advance study has shown that telaprevir in combination with Pegasis and ribavirin have yielded SVR in 75% of naïve patients.6 Even patients with cirrhosis have demonstrated 62% SVR. Patients with interleukin 28B (IL28B) “CC” alleles, “CT” alleles and “TT” alleles have demonstrated 90%, 71% and 73% SVR respectively.7 SPRINT 2 study demonstrated the use of boceprevir in combination with Peg-Intron and ribavirin have yielded 68% SVR in naïve genotype 1 patients.8 52% of cirrhotic patients achieved SVR.9 With the addition of new protease inhibitors, the treatment duration has been shortened based upon the patient’s response (response-guided therapy). These two protease inhibitors have taken us to the next level in the rate of clearance of virus and thereby diminishing the long-term complications and consequences of chronic hepatitis C.

There are many barriers to this current treatment. The side effects of the combination of pegylated interferon and ribavirin and protease inhibitors have increased the appearance of rash and anemia. Also, those patients who are not sensitive to interferon (null responders) are more prone to develop resistant mutant variants.

In a few more years, we will be able to treat and cure our patients with hepatitis C without interferon but with oral drugs alone, for shorter duration and with less side effects.

Currently, many clinical trials are being done involving newer molecules targeting NSSA replication complex and NS3B polymerase inhibitors which appear to be promising.

HEPATOCELLULAR CARCINOMA

The incidence of hepatocellular carcinoma (HCC) is increasing worldwide. In Eastern Asia almost 40 per 100,000 males and 15 per 100,000 females are inflicted with HCC, and in the United States of America, 8 per 100,000 males and 4 per 100,000 females are affected.10 Heavy alcohol drinkers (more than 600 liters in a lifetime) have a fivefold increase in HCC risk, compared to nondrinkers or moderate drinkers.11 Patients with diabetes mellitus, obesity and overall metabolic syndrome have the odds ratio of 2.9, 1.93 and 2.58 respectively to develop HCC. Obese males with a body mass index (BMI) above 35 have an HCC-related mortality rate of 50 per 100,000.
The survival of patients with HCC depends on early detection and treatment. Screening at risk population for HCC will identify patients at an early stage so effective treatment can be offered. In the United States, persons of 50–59 years of age demonstrate the highest mean annual percentage change in incidence rates of HCC. This is due to the consequences of hepatitis C, improved survival of cirrhotic patients, increasing obesity and diabetes. Due to the evolving better treatment, the survival of the patients with HCC has been increasing over the past years. In 2007, 5-year survival has increased to 14% as compared to 2% in 1986.

Unfortunately, most patients have advanced disease at the time of diagnosis. The current treatment for localized disease has improved 1-year survival by 83% and the distant disease by 30%.

Recent new development have shown the metabolic syndrome and nonalcoholic fatty liver disease as a major risk factor for the development of HCC.

In their randomized controlled trial in China, Zhang et al. demonstrated that screening patients with HBV reduced the cumulative mortality by 37% over a 5-year period. Kuo et al. showed with effective surveillance, the survival over a 5-year period increased by 30%. They also demonstrated that with surveillance, 46% of patient received curative treatment compared to 23% in non-surveillance patients.

The current guidelines published by Bruix recommend screening the following patients:

- Asian males with chronic hepatitis B over the age of 40
- Asian females with chronic hepatitis B over the age of 50
- Chronic hepatitis B with a family history of HCC
- African and North American blacks with chronic hepatitis B at a younger age, above 20 years
- Hepatitis B cirrhosis
- Hepatitis C cirrhosis
- Other cirrhosis

The Asians Pacific Association for Study of Liver Disease and United States Veterans Administration screening guidelines recommend measurement of alpha-fetoprotein (AFP) and ultrasound of the liver every 6 months, but American Association for Study of Liver Disease and European Association for Study of Liver Disease recommend only ultrasound of liver every 6 months.

So, effective screening will be able to improve the treatment of HCC patients.

REFERENCES