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B aware

Chronic hepatitis B treatment: Where are we now?

By TAN SRI DATUK SERI DR HJ MOHD ISMAIL MERICAN

CHRONIC hepatitis B is a worldwide phenomenon, and two billion people (approximately one-third of the world's population) have been infected.

It is estimated that there are more than 350 million hepatitis B virus (HBV) carriers in the world, with 75% of them living in the Asia Pacific region, where the majority of infections are acquired perinatally (period immediately before and after birth) or in early childhood.

Approximately one million people die from HBV-related liver disease every year. The implementation of effective vaccination programmes in many countries has resulted in a significant decrease in the incidence of acute hepatitis B.

Compulsory HBV vaccination has been instituted in Malaysia since 1989. Nevertheless, hepatitis B remains an important cause of morbidity and mortality, and many individuals who carry the virus (HBsAg-positive) remain undetected and unaware of the infection, and therefore, pose a danger to themselves and others close to them.

Patients with chronic hepatitis B seldom exhibit symptoms apart from fatigue, unless they have complications such as decompensated liver cirrhosis.

Physical examination may be completely normal. Those with end-stage liver disease may have jaundice, big spleen, ascites, leg swelling and encephalopathy.

Routine laboratory tests may be normal. There may be mild to moderate increase in liver enzymes (serum AST and ALT), which can increase dramatically and substantially in patients who develop exacerbations.

Doctors following up patients with apparent "silent" chronic hepatitis B will look for signs of progression to cirrhosis evidenced by hypersplenism (big spleen with decreased white blood cell and platelet counts) or impaired liver synthetic function, such as low serum albumin, prolonged prothrombin time and high serum bilirubin levels.

The natural course of chronic hepatitis B infection is determined by the interplay between virus replication and the host immune response.

Other factors that can influence the progression of HBV-related liver disease include gender, alcohol consumption and concomitant infection with other hepatitis viruses.

The outcome of chronic hepatitis B infection depends on how severe the liver disease is at the time HBV replication is suppressed.

Patients with this infection may be in an inactive carrier state, but can progress to cirrhosis, hepatic decompensation and liver cancer, which may prove fatal.

The prognosis is worse in HBV-infected patients from endemic areas like South-East Asia.

Twelve to 20% of patients with chronic hepatitis B may progress to cirrhosis; 20 to 23% of those with compensated cirrhosis can progress to hepatic decompensation; while 6 to 15% will progress to liver cancer within five years.

Patients with compensated cirrhosis have an 85% survival rate at five years, while those with decompensated cirrhosis have survival rates of 55 to 70% at one year and 14 to 35% at five years.

Presently, doctors may wish to know the viral genotype of their chronic hepatitis B patients. Traditionally, eight genotypes (A to H) have been identified, with genotypes B and C being more prevalent in East Asia and South-East Asia, where perinatal or vertical transmission plays an important role.

Genotype B patients are also associated with spontaneous seroconversion (HBeAg to antiHBe) at a younger age, have less active liver disease, and show slower progression to cirrhosis and less frequent liver cancer than genotype C.

It is not the intention of this article to provide information on how patients with chronic hepatitis B should be treated. We leave that to doctors who have been trained to treat such patients.

Suffice it to say that treatment for chronic hepatitis B is no longer straightforward. Many factors need to be taken into consideration.

Clinical decisions regarding individual patients should be based upon patient-specific clinical information and test results.

The initial evaluation of patients with chronic hepatitis B infection should include, as always, a thorough history and physical examination to look for risk factors for co-infection with hepatitis C and/or HIV, use of alcohol and family history of hepatitis B infection, liver disease and liver cancer.

Laboratory tests include a complete

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blood count, liver enzymes (AST, ALT), total bilirubin, alkaline phosphatase, albumin, prothrombin time and tests for HBV replication (HBeAg, anti-HBe, HBV DNA).

Other causes of liver disease, including hepatitis C, have to be excluded.

Liver biopsy is not always done but may be considered for patients who do not meet current criteria for treatment, but are suspected to have active or advanced liver disease, and may therefore, benefit from treatment.

Age or duration of infection is important in predicting the severity of liver disease in patients with high HBV DNA levels.

As for treatment, the rationale is to reduce the risk of progressive chronic liver disease and long-term complications, such as cirrhosis, liver cancer and transmission to others. Your doctor will be able to decide whether you're eligible for treatment.

At present, drugs normally used for treating chronic hepatitis B include injectable pegylated interferon or oral drugs such as lamivudine, adefovir, telbivudine, entecavir and tenofovir.

The advantages of interferon (IFN) are its finite duration of treatment (six to 12 months), the absence of resistant mutants and a more durable response.

These benefits are, however, at the risk of side effects, which can be severe.

IFN is best for young patients with well compensated liver disease, those who prefer short-term treatment, or female patients who wish to start a family within the next two to three years.

Although entecavir and tenofovir are the preferred drugs currently, the optimal duration of treatment for these oral drugs is not well-established.

Most patients will require at least four to five years of treatment, and some may require much longer treatment.

HBV carriers should be counselled regarding the risk of transmission to others, and patients should be advised regarding prevention of sexual transmission, perinatal transmission and risk of exposure from blood.

Spouses of patients and household members should be vaccinated if they test negative for HBV serologic markers.

HBsAg-positive pregnant women should alert their doctors, so that their infants can receive hepatitis B immunoglobulin and vaccine immediately after delivery.

Healthcare workers found to be HBeAg-positive should not perform invasive procedures without prior counselling and advice from an expert review panel.

I would also advise all patients who are HBsAg-positive to go for regular three-monthly (if already cirrhotic) or six-monthly check-ups for early detection of signs of chronic liver disease and liver cancer, even if they feel well and have no symptoms.

Early detection is better than cure, and please be reminded that 80% of our patients with liver cancer come too late for definitive treatment.

Finally, liver cancer associated with hepatitis B can be prevented through vaccination.

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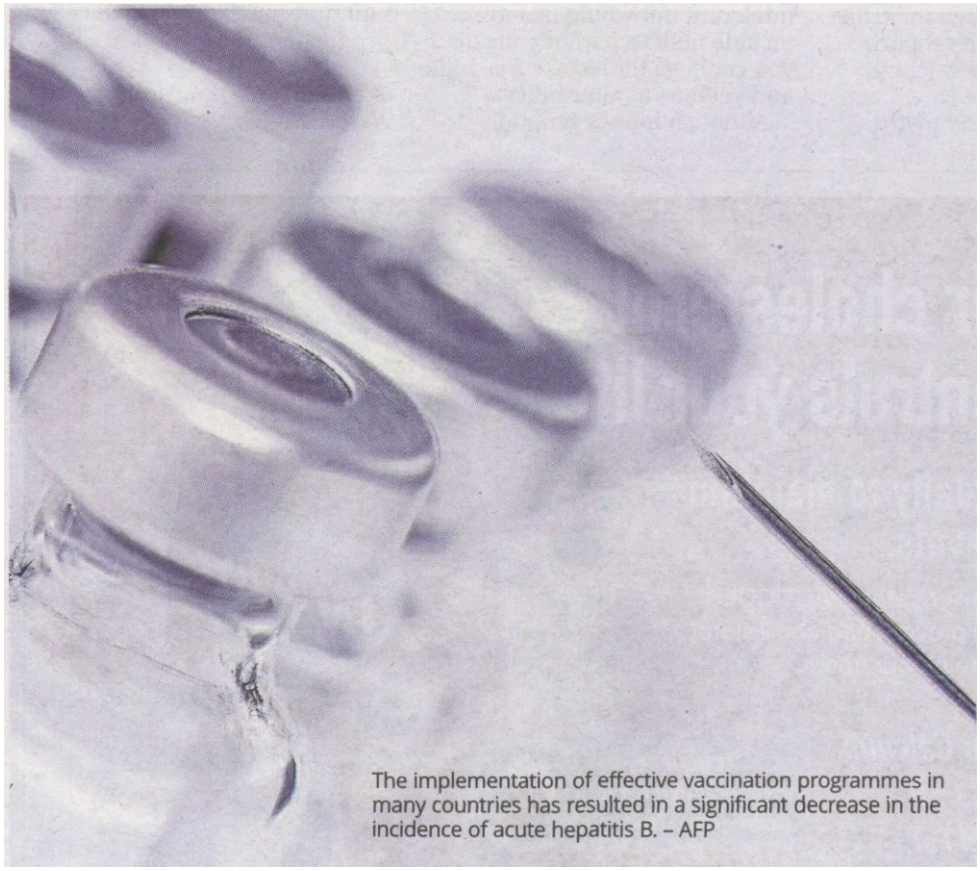

The implementation of effective vaccination programmes in many countries has resulted in a significant decrease in the incidence of acute hepatitis B. – AFP

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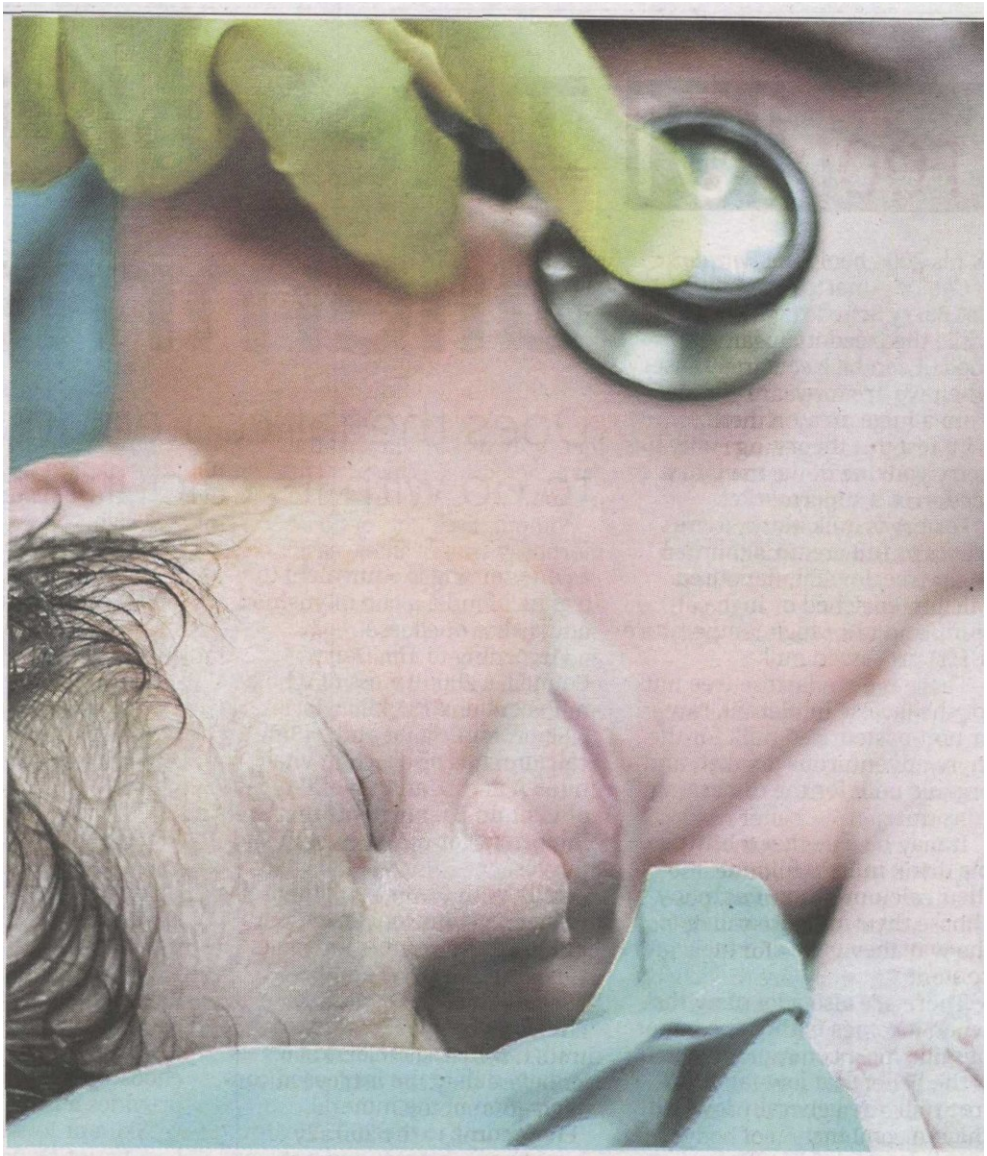

In the Asia Pacific region, the majority of hepatitis B infections are acquired perinatally (period immediately before and after birth) or in early childhood. – AFP