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Review Articles

HEPATITIS B INFECTION: WHAT THE PRIMARY CARE DOCTORS SHOULD KNOW

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EPIDEMIOLOGY

Hepatitis B infection is a global public health problem and causes significant morbidity and mortality. The worldwide prevalence of chronic hepatitis B infection is about 400 million people, and it causes 500 thousand deaths each year.[1,2] The prevalence of chronic HBV infection is high (>8%) in certain part of Asia and Southeast Asia, including China, Korea, Indonesia, and the Philippines.[1-3] In Malaysia about 1.1 million people are thought to be chronically infected with hepatitis B virus. The estimated prevalence of HBsAg among the population is approximately 4.7%. These data are obtained from Malaysian Liver Foundation in 1998.[8]

Hepatitis B infection is caused by the hepatitis B virus (HBV). The clinical manifestations of HBV infection (Figure 1) range in severity from asymptomatic subclinical infection (70%), symptomatic hepatitis (30%) to fulminant severe hepatitis with liver failure (0.10-0.5%).[1,2] Following the exposure to HBV, up to about 10% of the patient will progress to chronic hepatitis B, which is defined as persistence of the infection for more than 6 months duration.[5,6] The chronic hepatitis B then progress to liver cirrhosis and hepatocellular carcinoma in about 15-40% of the patients.[1] The laboratory markers for hepatitis B infection and its interpretation are summarised in Table 1.

Table 1. Laboratory markers for HBV infection and its interpretation

Marker*	Interpretation
HBsAg	Exposure to Hepatitis B virus. Present in acute or chronic infection
Anti-HBs antibody	Immunity acquired via natural infection or immunisation
HBeAg	Marker of infectivity. It correlates with high level of viral replication
Anti-HBe antibody	It correlates with low level of viral replication
Anti-HBc IgM antibody	Infection in previous 6 months
Anti-HBc IgG antibody	Distant HBV infection or chronic HBV infection
Hep B DNA >10^5 copies /mL	Rapid viral replication

*HBsAg Hepatitis B surface antigen, HBeAg Hepatitis B e antigen, Anti-HBc Anti-Hepatitis B core

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PREVENTION OF HEPATITIS B

In view of the magnitude and chronic complications, prevention of hepatitis B infection is paramount for the population in endemic regions and for those who are visiting endemic areas.

Health care workers, medical laboratory workers and blood bank staff who handle blood, blood products and body fluid must strictly adhere to standard precautions regulations so as to minimise unwanted accidental needle prick injury and direct contact with blood products. Screening of all blood products for blood transfusion has also been shown to reduce the risk of transfusion associated hepatitis B infection.[1]

HEPATITIS B VACCINATION

Among all the recommended strategies for preventing hepatitis B infection, vaccination is the most important one. Hepatitis B recombinant vaccine is available in most primary care clinics in Malaysia. The usual schedule of primary vaccination consists of three intramuscular doses of the vaccine. Universal neonatal vaccination against hepatitis B is effective and has been shown to favourably change the clinical course of hepatitis B infection especially in regions where this disease is endemic.[7,8] According to the Ministry of Health Malaysia childhood immunisation programme, all babies are given first dose of hepatitis B vaccine at birth; followed by 2nd dose at first month and 3rd dose at fifth month. This vaccine is very safe and has very few adverse effects. Common mild side effects are pain at the injection site (3%-29%) and elevated temperature >37.7°C (1%-6%).[8] All adults who are at high risk of infection such as health care workers, blood bank staffs, public health workers, patients who require multiple transfusion or blood products, haemodialysis patients, homosexual men and intravenous drug users must be vaccinated. Testing for hepatitis B surface antibody titre should be done 6-8 weeks after the last dose.[8] The protection following vaccination lasts 10-15 years. After 15 years from the last vaccination, it is advisable to get a booster dose. Those with chronic renal failure, immunosuppressed patient, haemodialysis patients and elderly may have a lower response rates.[6,7]

After vaccination, an antibody level of 10 mIU/mL is considered not responsive. A protective antibody level

should be 100mIU/mL or more. Those who have antibody level 10-100mIU/mL are considered poor responders and should receive a booster dose.[8]

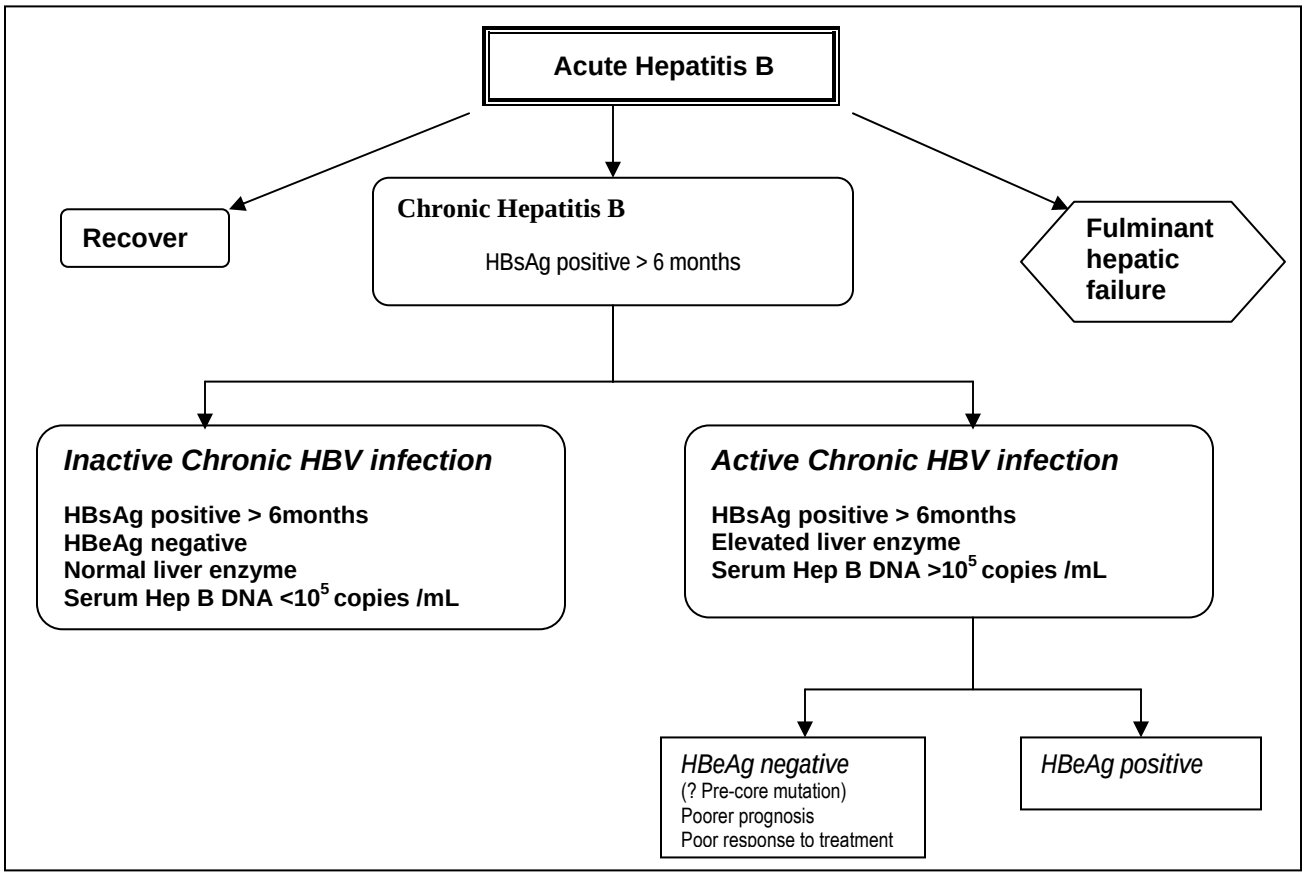
PREVENTION OF MATERNAL-FOETAL TRANSMISSION

Ideally all pregnant mothers should be screened for HBsAg (not a mandatory test for antenatal screening in Malaysia). The risk of vertical transmission of hepatitis B from mother to baby is very high when the mother is HBeAg positive, has a high viral load or co-infection with HIV.[1,5] It was reported when the mother is HBsAg positive, the perinatal transmission risk is 10%. The risk goes up to 90% when the mother is HBeAg positive.[5] All babies of mothers who are tested HBsAg positive must be given HBV immunoglobulin and Hepatitis B vaccine within 12 hours at birth , these preventive measures have been proven to reduce the risk of transmission of Hepatitis B to less than 3%.[5]

CHRONIC HEPATITIS B

Chronic hepatitis B (CHB) is defined as persistent presence of HBsAg for more than six months. Diagnosis of CHB is suspected when the patient presents with features listed in Figure 1. CHB carries the highest risk of progression to liver cirrhosis and hepatocellular carcinoma. It was estimated that about 12% of patients with chronic HBV infection develop cirrhosis annually. The development of cirrhosis and hepatocellular carcinoma is the result of immune-mediated inflammatory response. This condition is also found to be associated though uncommonly with systemic vasculitis, membranoproliferative glomerulo-nephritis and polyarteritis nodosa.[2] Laboratory investigations for CHB patients include liver function tests, HBV markers, serum HBV DNA load, alpha-feto protein and ultrasonography of the liver. Laboratory tests may be normal in CHB, however many patients have mild to moderate elevation of aminotransferases.[6] These Persistent raised liver enzymes two to three times the normal range, elevated alpha fetoprotein and abnormal findings on liver ultrasonography are indications for referral to hepatologist for further detailed evaluation and treatment. In Malaysia, screening for hepatocellular carcinoma is recommended for hepatitis B carriers more than 40 years of age and hepatitis B carriers less than 40 years of age with at least two risk factors. Risk factors include a family history of hepatocellular carcinoma, hepatitis C infection, liver cirrhosis, hemochromatosis, and chronic alcohol consumption.[15]

Figure 1. Clinical course of hepatitis B infection



The decision to treat CHB is based on a combination of clinical, laboratory and histological factors. The primary goal of treatment for CHB is to eliminate or permanent suppress HBV. This will decrease pathogenicity and infectivity.[7] Currently interferon-alpha (IFN-α), lamivudine and adefovir have been licensed globally for the treatment of CHB. IFN-α, an immunomodulator, works by affecting viral replication. Studies had shown that the response rate to IFN- α is approximately 33% after 4-6 month course of treatment.[9,10] Treatment for longer than 12 months may improve the rate of HBeAg seroconversion. Re-treatment of relapsed CHB patients with this drug has a response rate which varies from 20-40%.[9] In one randomised trial it was shown that In chronic hepatitis B, treatment with interferon- α2b (5 million units per day for 16 weeks) was effective in inducing a sustained loss of viral replication and achieving remission, assessed both biochemically and histologically, in over a third of patients.[10] Lamivudine is a nucleoside analogue which inhibits the viral reverse transcriptase.[11] The advantages of Lamivudine include high degree of tolerability and also safe even in patients with decompensated cirrhosis. It can also be used as first line therapy or following IFN-α failure.[12] Adefovir is a synthetic acyclic adenine nucleotide analogue and it is also a potent inhibitor of hepatitis B reverse transcriptase. Studies had shown that there were significant improvements in histological, virologic and biochemical markers after 48 weeks of treatment.[13,14] The main advantage is the low incidence of drug resistance and its ability to suppress lamivudine-resistant mutants.[13,14]

CONCLUSION

Hepatitis B virus infection is a global public health problem. The prevalence of hepatitis B infection is higher in Asia. The rate of HBsAg carriage in the general population ranges from 2-20%. The WHO has recommended that by the end of 21st century hepatitis B vaccination should be incorporated into routine childhood immunisation programmes for all nations. Vaccination against hepatitis B remains the most important aspect of preventive care. Most importantly hepatitis B vaccination can protect individual from fulminant hepatitis, liver cirrhosis and hepatocellular carcinoma. Primary care physicians must be familiar with the pathology, epidemiological and clinical presentations of this disease and be able to refer patients for appropriate treatment at the tertiary centre.

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