HEPATITIS B CARRIER -

Chronic Hepatitis B Virus (HBV) infection is a significant cause of global morbidity and mortality. There are estimated 350-400 million HBV carriers worldwide with 75% live in the Asia-Pacific region. In Singapore, 6% of our population are HBV carriers. The spectrum of the disease and the natural history of chronic HBV infection are diverse and variable, ranging from a low viremic inactive carrier state to progressive chronic hepatitis, which may eventually evolve to cirrhosis and hepatocellular carcinoma (HCC).

TWO TYPES OF DISEASE

Chronic HBV infection may present as hepatitis B e antigen (HBeAg)-positive or HBeAg-negative chronic infection. HBeAg positive infections are commonly termed "wild type". It typically represents the early phase of chronic infection. These patients are anti-HBe negative and their HBV DNA levels are very high at > 20,000 IU/mL (or > 100,000 copies/mL). HBeAg negative disease, also called "precore mutant", represents a later phase of chronic infection. It is due to replication of naturally occurring HBV variants with nucleotide substitutions in the precore and/or basic core promoter regions of the genome. It is characterized by the presence of anti-HBe and lower HBV DNA level of > 2000 IU/mL (or > 10,000 copies/mL). The prevalence of the HBeAg-negative infection has been increasing over the last decade as a result of aging HBV-infected population and represents the majority of cases in many areas, especially in Asia and Southern Europe.

DISEASE MONITORING IS IMPORTANT

Morbidity and mortality of chronic HBV infection are the results of persistent viral replication and evolution to cirrhosis or HCC. It is estimated 25% of HBV carriers will develop liver cirrhosis and the annual incidence of developing HBV-related HCC ranges from 2% to 5%. HBV-related end stage liver disease or HCC are responsible for over 1 million deaths per year globally. A few landmark studies have showed that high baseline HBV DNA is associated with higher risk of development of liver cirrhosis, HCC and mortality. Suppression of HBV replication with drug therapy can improve the quality of life and survival by preventing these complications from happening. Follow up of HBV carriers at regular interval is therefore essential to identify patients who require treatment and to detect complication earlier when it occurs. Most guidelines recommend 6-monthly HCC surveillance with ultrasound scan of the liver and alphafetoprotein (AFP). Liver function test is done on the same visit.

WHEN TO START TREATMENT?

The goal of therapy for chronic HBV infection is to achieve prolonged and sustained viral suppression and to prevent progression to cirrhosis, decompensated cirrhosis, HCC and death. However anti viral therapy may not be warranted for all chronic HBV patients. Few factors must be taken into consideration before initiating therapy. The physician must weigh the potential benefit of achieving long lasting response versus the likelihood of adverse effects associated with the treatment, the possibility of drug resistance and the potential adverse clinical outcomes in the absence of treatment. The physician must also consider the patient's age, preference and the cost of the medications. The indications for treatment are based mainly on the combination of four criteria: Serum HBV DNA level, serum ALT Level, histological grade/disease stage as well as the age of the patient.

For HBeAg-positive chronic HBV infection, treatment is recommended when HBV DNA level is above 20,000 IU/ml and serum ALT level is persistently elevated. For those aged above 35-40 years with HBV DNA > 20,000 IU/ml but normal ALT, liver biopsy or non invasive fibroscan should be considered and treatment is recommended if the disease shows moderate to severe active necroinflammation or fibrosis. For those with HBV DNA < 20,000 IU/ml and normal ALT, treatment is not required but to continue with 6-monthly ALT monitoring.

With regard to HBeAg-negative chronic HBV infection, treatment is recommended when HBV DNA level is above 2,000 IU/ml and serum ALT level is persistently elevated. For those with HBV DNA > 2,000 IU/ml but normal ALT, liver biopsy or

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HOW TO MANAGE AND WHO TO TREAT?

fibroscan should be considered and treatment is recommended if the disease shows moderate to severe active necroinflammation or fibrosis. For those with HBV DNA < 2,000 IU/ml and normal ALT, treatment is not required but regular ALT monitoring is warranted.

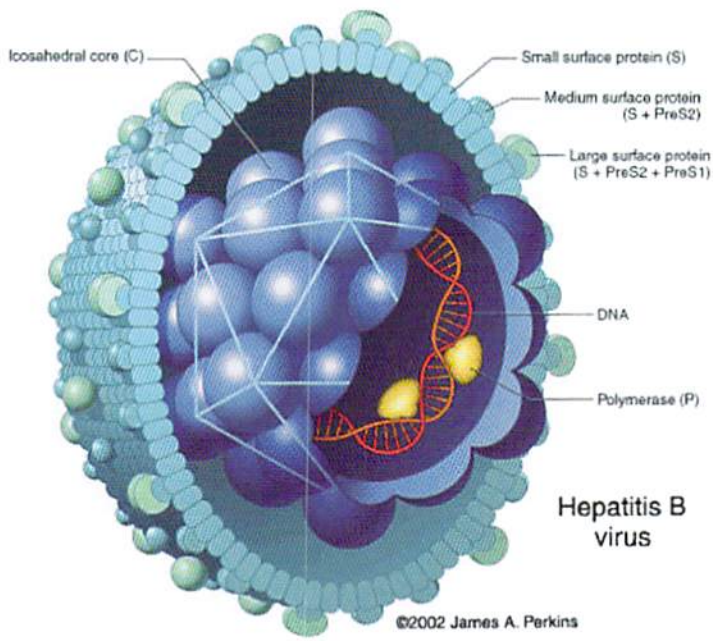
MEDICATIONS USED FOR TREATMENT OF CHRONIC HBV INFECTION

Two different types of medications can be used for the treatment of chronic HBV infection: interferon alfa and nucleoside/nucleotide analogues (NUCs). Currently there are 7 medications licensed for use in Singapore, namely conventional interferon, pegylated interferon alfa-2a, and 5 NUCs - lamivudine, adefovir, entecavir, telbivudine and tenofovir.

NUC is preferred by most of the patients in view of the easy oral administration and minimal adverse effects. The major disadvantages of NUCs are indefinite treatment duration and associated drug resistance. On the contrary, interferon alfa treatment represents a finite course of therapy, and it is not associated with emergence of any resistant virus variants. However, the subcutaneous route of administration and certain adverse effects make it less appealing as compared with NUCs. Interferon alfa can be considered in young patients who may tolerate the adverse effects better, and young women desiring future pregnancy because of its defined period of therapy.

SUMMARY

Chronic HBV infection is a significant cause of global morbidity and mortality. It may present as HBeAg-positive or HBeAg-negative diseases. Follow up and monitoring of chronic HBV patients at regular interval is essential to initiate anti viral therapy if treatment is indicated and to detect complication earlier when it occurs. There are two types of medications used for the treatment of chronic HBV infection namely subcutaneous interferon alfa injection and oral NUCs.



Hepatitis B virus

SPOTLIGHT

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