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TECHNOTES

HBV Diagnosis

Role of HBV markers in diagnosis & monitoring of hepatitis B infection

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Tulip Block, Dr. Rego Bagh, Alto Santacruz, Bambolim Complex P.O., Bambolim, Goa - 403 202, India.
Tel.: + 91 832 2458546-51. Fax: +91 832 2458544. e-mail: sales@tulipgroup.com

Role of HBV markers in diagnosis & monitoring of hepatitis B infection

Background

Hepatitis B infection is the second most common cause of acute viral hepatitis worldwide. is often transmitted parenterally, typically by contaminated blood or blood products. Transmission of HBV can also occur through Sharing of shaving kit, sharing of toothbrushes, close contact with infected person and infected mother to new born. Risk of HBV transmission is high among patients in renal dialysis in oncology units and for hospital personnel in contact with blood.

Different stages of infection and their different etiologies of HBV typify it as a most thoroughly characterized and complex hepatitis virus. HBV produces a wide spectrum of liver diseases, from a subclinical carrier state to severe or fulminant acute hepatitis, particularly in the elderly, in whom mortality can reach 10 to 15%. 5 to 10% of all patients with HBV develop chronic hepatitis or become inactive carriers.

Chronic HBV carriers provide a worldwide reservoir of infection. These carriers are clinically asymptomatic but can transmit the infection which is considered to be most dangerous side of this infection. Further more hepatocellular carcinoma can ultimately develop in chronic HBV infection, even without being preceded by cirrhosis.

So today early diagnosis, identification of infection stages and proper prognosis of HBV infection is gaining importance.

The serologic patterns of chronic HBV infection are varied and complex. Antigens and antibodies associated with HBV infection include HBsAg and antibody to HBsAg (anti-HBs), hepatitis B core antigen (HBcAg) and antibody to HBcAg (anti-HBc), and hepatitis B e antigen (HBeAg) and antibody to HBeAg (anti-HBe). Testing also can be performed to assess the presence and concentration of circulating HBV DNA. At least one serologic marker is present during each of the different phases of HBV infection. Serologic assays are available commercially for all markers except HBcAg, because no free HBcAg circulates in blood.

The serologic markers typically used to differentiate among acute, resolving, and chronic infection are HBsAg, anti-HBc, and anti-HBs. The presence of HBeAg and HBV DNA generally indicates high levels of viral replication.

Serological Markers of HBV diagnosis and their significance

HBsAg

In newly infected persons, HBsAg is the only serologic marker detected during the first 3–5 weeks after infection. The average time from exposure to detection of HBsAg is 30 days (range: 6–60 days). Highly sensitive single-sample nucleic acid tests can detect HBV DNA in the serum of an infected person 10–20 days before detection of HBsAg. Transient HBsAg positivity has been reported for up to 18 days after hepatitis B vaccination and is clinically insignificant.

Anti HBc

Anti-HBc appears at the onset of symptoms or liver-test abnormalities in acute HBV infection and persists for life in the majority of persons. Acute or recently acquired infection can be distinguished from chronic infection by the presence of the IgM class of anti-HBc, which is detected at the onset of acute hepatitis B and persists for up to 6 months if the infection resolves. In patients with chronic HBV infection, IgM anti-HBc can persist during viral replication at low levels. However, persons with exacerbations of chronic infection can test positive for IgM anti-HBc. Because the positive predictive value of this test is low in asymptomatic persons, IgM anti-HBc testing for diagnosis of acute hepatitis B should be limited to persons with clinical evidence of acute hepatitis or an epidemiologic link to a person with HBV infection.

In certain persons, total anti-HBc is the only detectable HBV serologic marker. Isolated anti-HBc positivity can represent,

- Chronic infection in which circulating HBsAg is not detectable by commercial serology, most commonly in high-prevalence populations and among persons with HIV or HCV infection (HBV DNA has been isolated from the blood in <5% of persons with isolated anti-HBc).
- In low-prevalence populations, isolated anti-HBc may be found in 10%–20% of persons with serologic markers of HBV infection, most of whom will demonstrate a primary response after hepatitis B vaccination. Persons positive only for anti-HBc are unlikely to be infectious except under unusual circumstances in which they are the source for direct percutaneous exposure of susceptible recipients to substantial quantities of virus (e.g.blood transfusion or organ transplant).

HBeAg

HBeAg can be detected in the serum of persons with acute or chronic HBV infection. In the majority of those with chronic infection, HBeAg is cleared over time, and anti-HBe appears. Presence of HBeAg correlates with more active disease: patients with HBeAg typically have high levels of HBV DNA (106–1010 IU/mL), whereas those who are HBeAg-negative and anti-HBe-positive generally have low or only modest HBV DNA levels (0–105 IU/mL).

Anti HBe

Antibodies to HBe are produced by the immune system temporarily during acute HBV infection or consistently during or after a burst in viral replication. Spontaneous conversion from e antigen to e antibody (a change known as seroconversion) is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV.

Anti HBs

In persons who recover from HBV infection, HBsAg and HBV DNA usually are eliminated from the blood, and anti-HBs appear. In persons who become chronically infected, HBsAg and HBV DNA persist. In persons in whom chronic infection resolves, HBsAg becomes undetectable; anti-HBc persists and anti-HBs will occur in the majority of these persons.

Diagnostic significances of HBV markers

Tests	Result Interpretation	Remarks
HBsAg Anti HBc	HBsAg – Positive Anti HBc – Positive	● Confirm active HBV infection or exposure. Go for tests of markers HBeAg & HBeAb along with HBsAg. Positivity of both tests more than six months without clinical symptoms indicates carrier stage.
	HBsAg – Negative Anti HBc - Positive	
	HBsAg – Positive Anti HBc - Negative	● Suspected infection in early stage. Repeat the tests after one month.
	HBsAg – Negative Anti HBc - Negative	● Consider no infection of HBV.
HBeAg Anti HBe	HBeAg – Positive Anti HBe - Negative	● Highly infectious stage. Usually last for 1-2 months in self limiting condition. Repeat the tests until appearance of anti HBe. ● Positivity of HBeAg more than six months indicates chronic stage.
	HBeAg – Negative Anti HBe - Positive	● Indicates resolving condition of the disease. Go for anti HBs test after one month.
	HBeAg – Negative Anti HBe - Negative	● Very rare. Repeat the test after one month.
Anti HBs	Positive	● Confirmed recovery and immunity.
	Negative	● Repeat the test until positivity.

Carrier stage of HBV infection and it's risk

In carrier stage virus persists in body fluid in inactive condition. HBV carriers have neither ongoing liver damage, nor any clinical symptoms; but hepatitis B surface antigen test demonstrates the presence of that viral antigen in their blood stream. Therefore they can pass on the viral infection to others and are considered potentially infectious and are reservoirs of HBV. 350 million HBV carriers including 34 million in India has estimated worldwide. Positivity in HBsAg & Anti HBc tests for more than six months without any relevant clinical symptoms indicates carrier stage.

Conclusion

In conclusion diagnoses through above markers aid in assessing the actual sero status of the patient. Therefore medical practitioners can initiate the correct anti viral therapy, which is very essential in chronic or carrier stage. These tests are now available in rapid ICT format with good sensitivity, specificity and are easy to perform.

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