PRINCIPLES OF PREVENTION IN HEPATITIS B INFECTION

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Abstract

The main objectives of hepatitis B prevention programs are reduction of chronic hepatitis B virus (HBV) infection and HBV-related chronic liver disease. General measures have to be taken. Routine screening of transfused blood and blood products (for hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B core antigen (anti-HBc) has greatly reduced the risk of post-transfusion hepatitis B virus infection. Although risk-reduction counselling and services, and effective infection control practices can reduce or eliminate the potential risk for HBV transmission, immunization is by far the single most effective prevention measure.

Worldwide, the integration of hepatitis B vaccine into existing childhood vaccination schedules has the greatest likelihood of long-term success. In addition, efforts must be strengthened to vaccinate older adolescents and adults with high-risk behaviours or occupations in countries where most HBV transmission and the morbidity associated with acute hepatitis B occur among persons in these age groups. Other general measures like practising universal precautions (using disposable needles and syringes and barrier contraception) have an important role.

Key words: HBV, public health, chronicity, vaccination, HB immunoglobulin, lamivudine

INTRODUCTION

Hepatitis B virus (HBV) infection is a global public health problem, with approximately 400 million people chronically infected. Outcome of acute hepatitis B virus infection ranges from asymptomatic subclinical infection (70%) and symptomatic acute hepatitis (30%) to fulminant hepatic failure (0.1-0.5%). A proportion of people infected with hepatitis B virus (5%-10% among adults) progress to chronicity, defined as persistence of infection for more than six months. The rate of chronicity is much higher among neonates and children.

The spectrum of chronic hepatitis B virus infection ranges from the asymptomatic carrier state to chronic hepatitis B, liver cirrhosis, and hepatocellular carcinoma. The clinical course of hepatitis B virus infection is complex and is influenced by several factors.

Overall, chronic hepatitis progresses to end stage liver disease in 15-40% of patients. The magnitude and clinical consequences of chronic hepatitis B make a strong case for its prevention and treatment.

Several strategies have been demonstrated to prevent hepatitis B virus infection. Vaccination is the main method of prevention. Specific hepatitis B immunoglobulin (HBIg) and lamivudine are useful in specific settings.

Factors influencing the progress of chronic hepatitis B virus infection

Viral factors:

- Level of hepatitis B virus replication
- Hepatitis B virus genotype
- Mutations in viral genome

Host factors:

- Age at acquisition of infection
- Immune status and associated chronic pathology
- Concurrent infection with other hepatotropic viruses
- Alcohol intake or other drug dependences
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Preventive strategies for hepatitis B

Hepatitis B vaccination is more important in high risk groups and in newborn infants. Screening of blood and blood products is influencing the incidence of HBV infection. Another important preventive measure is the use of universal precautions in healthcare settings. Avoiding needles sharing among injecting drug users and promoting safe sex practices are also imperative requests.

There are other methods of prevention in special settings:

- Preventing vertical transmission (giving hepatitis B vaccine and hepatitis B immunoglobulin to newborns of HBsAg and HBeAg positive mothers)
- Post-exposure prophylaxis (hepatitis B immunoglobulin, lamivudine)
- Preventing transmission in patients with liver transplants (lamivudine, adefovir, hepatitis B immunoglobulin)
- Prevention of infection HBV in HIV infected patients

MATERIALS AND METHODS

General measures of prevention

General measures like practising universal precautions (using disposable needles and syringes and barrier contraception) have an important role. Routine screening of transfused blood and blood products (for hepatitis B surface antigen (HBsAg) and antibodies to hepatitis B core antigen (anti-HBc) has greatly reduced the risk of post-transfusion hepatitis B virus infection.

Hepatitis B vaccine

For active protection, or vaccination, a harmless HBV antigen is given to stimulate the body's immune system to produce protective antibodies against HBV. The vaccine thereby prevents HBV infection. Vaccination programs are also proving to reduce the risk for liver cancer. Vaccination against hepatitis B stimulates the body's immune defences and protects most people. However, people undergoing dialysis, people with cirrhosis, and people with an impaired immune system may derive less protection from vaccination. Vaccination is especially important for people at risk of contracting hepatitis B. The following people should be vaccinated:

- All newborns and children 19 years of age or younger
- Health care and public safety workers with exposure to blood in the workplace
- Patients receiving chronic kidney dialysis (haemodialysis)
- Persons with clotting factor disorders, such as haemophiliacs
- Patients in institutions for the developmentally disabled
- Persons with chronic liver disease, including hepatitis C
- Household contacts and sexual partners of persons with hepatitis B
- Anyone with more than one sex partner in a 6 month period, gay and bisexual men
- Illicit drug users (injection and non-injection)

- International travellers to areas where hepatitis B is common (includes all areas of the world except Canada, Western Europe, Scandinavia, New Zealand, Australia.)
- Persons born in countries with high rates of hepatitis B and their family members
- Anyone else who wants protection against hepatitis B

Hepatitis B vaccines are of two types, plasma derived and recombinant. Recombinant vaccines are produced by cloning the gene encoding HBsAg into yeast cells and are increasingly replacing plasma derived vaccines. Several inactivated virus vaccines, including Recombivax HB, GenHevac B, Hepagene, and Engerix-B, can prevent HBV infection and are safe, even for infants and children. A triple-antigen hepatitis B vaccine (Hepacare) is proving to be effective for people who do not respond to the standard vaccines. A combination vaccine (Twinrix) that contains Engerix-B and Havrix, a hepatitis A vaccine, is now approved for people with risk factors for both hepatitis A and B.

Vaccines are given in three doses (at 0, 1, and 6 months) of 10-30 µg (usually 20 µg for adults and 10 µg for children). The vaccines are extremely safe and induce antibodies that will neutralise HBsAg (anti-HBs) in most (> 95%) recipients; antibody levels in excess of 10 mIU/ml are considered protective. Certain groups, as people aged over 40 years, obese people, those with chronic renal failure, haemodialysis recipients, immunosuppressed individuals, organ transplant recipients, have poorer response rates. The protection lasts for at least 15 years and because of strong immunological memory it continues after anti-HBs have become undetectable. Immunity is thus believed to be lifelong, and boosters are not recommended routinely; however, these may have a role in immunosuppressed individuals and those at a particularly high risk of exposure. Non-responders to three doses may benefit from additional doses of the vaccine.

The availability of effective and safe vaccines makes primary prevention of hepatitis B an attractive strategy. Universal neonatal vaccination is effective and has been shown to favourably alter the clinical course of hepatitis B virus infection in regions where the disease is endemic. This strategy is cost effective even in low income countries with intermediate hepatitis B virus endemicity rates. Even in low endemicity regions like Europe, neonatal vaccination is preferable, although immunisation in late childhood or adulthood may be a reasonable alternative.

Romania is one of the European countries that have implemented universal neonatal hepatitis B immunisation since 1995. Viral mutants that are not neutralised by antibodies induced by the available vaccines have been detected. Though currently a minor problem, these have led to a renewed interest in developing vaccines targeted at multiple viral antigens.

RESULTS

Prevention of hepatitis B virus transmission in special settings

Maternal-foetal transmission.

All pregnant women should be screened for HBsAg. Among infants born to HBsAg positive mothers, the risk of vertical transmission is particularly high if the mother is positive for hepatitis B e antigen (HBeAg), has a high viral load, or is infected with HIV. Such infants should receive both vaccine and HBIg (0.5 ml) within 12 hours of birth. They should be tested for HBsAg, anti-HBs, and anti-HBc at 12 months of age; presence of anti-HBs indicates vaccine induced immunity and detection of both anti-HBs and anti-HBc indicates infection modified by immunoprophylaxis, whereas presence of HBsAg indicates failure of prophylaxis.

Accidental exposure to hepatitis B virus.

People who have not been immunised and are exposed to hepatitis B (through needle stick injury, splashing, or sexual exposure to partners infected with hepatitis B virus) should receive HBIg (0.04-0.07 ml/kg) as soon after exposure as possible. Vaccination should be started simultaneously, with the first dose given at a site different from that for HBIg; an accelerated four dose immunisation schedule (0, 1, 2, and 12 months) is preferred in this setting.

Liver transplantation.

Among patients who receive transplants because of hepatitis B virus related liver disease, infection of grafted liver is nearly universal. Lifelong HBIg after transplantation reduces the graft infection rate; however, this approach is costly and is associated with 20% infection by two years and emergence of HBIg-resistant hepatitis B surface protein mutants. Lamivudine, alone or in combination with HBIg, prevents recurrence of hepatitis B virus after transplantation. In preliminary studies, adefovir has shown promise.

Prevention of infection HBV in HIV infected patients.

There are remarkable similarities between the modes of transmission of HBV and HIV (Human Immunodeficiency Virus) which is thought to cause Acquired Immune Deficiency Syndrome (AIDS). Methods similar to those used for preventing blood borne transmission of HBV can be used for preventing blood borne transmission of HIV. A serological test of donors for HIV (and antibodies against it) can be performed on the same serum specimen required for testing for HBV. Much of the same equipment can be used for the two tests. The techniques described above to prevent transmission of HBV by needles and other equipment will also be effective for preventing transmission of HIV.

CONCLUSIONS

- The implementation of effective vaccination programs in many

countries has resulted in a significant decrease in the incidence of acute hepatitis B. Nevertheless, hepatitis B remains an important cause of morbidity and mortality.

- Worldwide, the integration of hepatitis B vaccine into existing

childhood vaccination schedules has the greatest likelihood of long-term success. In addition, efforts must be strengthened to vaccinate older adolescents and adults with high-risk behaviours or occupations in countries where most HBV transmission and the morbidity associated with acute hepatitis B occur among persons in these age groups. Other general measures like practising universal precautions (using disposable needles and syringes and barrier contraception) have an important role.

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