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Review

Viral hepatitis: Global goals for vaccination

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ABSTRACT

In countries where hepatitis A is highly endemic, exposure to hepatitis A virus (HAV) is almost universal before the age of 10 years, and large-scale immunization efforts are not required. In contrast, in areas of intermediate endemicity or in transition from high to intermediate endemicity, where transmission occurs primarily from person to person in the general community (often with periodic outbreaks), control of hepatitis A may be achieved through widespread vaccination programmes.

Hepatitis B virus (HBV) is one of the world's most widespread infectious agents and the cause of millions of infections each year. Between 500,000 and 700,000 people die each year from chronic infection-related cirrhosis, hepatocellular carcinoma (HCC) or from acute hepatitis B. Hepatitis B vaccine provides protection against infection and its complications including liver cirrhosis and HCC. It is therefore, the first vaccine against a cancer, the first vaccine protecting from a sexually transmitted infection, and the first vaccine against a chronic disease ever licensed. Control and significant reduction in incidence of new HBV infections as well as hepatocellular carcinoma has repeatedly been reported in countries in East Asia (i.e. Taiwan) and Africa (i.e. The Gambia).

Two experimental vaccines against hepatitis E have been developed; one of them has been recently licensed but is not yet widely available. Attempts to develop a hepatitis C vaccine were so far unsuccessful.

Contents

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1. Summary

This article focuses on vaccines available or not for the prevention and control of infections associated with the hepatitis A–E viruses. Control and even elimination of hepatitis A, B and D are feasible goals with the currently available vaccines, provided that appropriate public health policies for immunization are put in place in all countries. Unfortunately this is not the case for hepatitis C where a vaccine is still awaited and necessary. For hepatitis E, two vaccines with promising protection data have been developed, one has been recently licensed in China, the other one is not licensed due to insufficient public health commitment.

2. Viral hepatitis A

2.1. Introduction

Hepatitis A occurs worldwide, and geographical areas can be characterized by high, intermediate, or low levels of endemicity, related to hygienic and sanitary conditions. Almost all HAV infections are spread by the fecal–oral route.[1,2] Although hepatitis A is self-limiting and rarely fatal, widespread clinical disease may be associated with a substantial economic burden, particularly in countries with low and intermediate incidence rates.[3,4] Countries in transition from developing to developed economies will gradually move from high to intermediate endemicity, and hepatitis A is likely to become a more serious problem.[5–7]

2.2. Preventive measures

Educating the public about good sanitation and personal hygiene, with special emphasis on careful hand-washing and sanitary disposal of feces will lower the occurrence of sporadic cases and of epidemics. From a public health perspective, it is essential to provide quality standard water treatment and distribution systems and proper sewage and sanitary disposal throughout the country.[8,9]

2.3. Vaccines

As of today, millions of persons have received a hepatitis A vaccine, and currently licensed vaccines are all highly immunogenic, safe, and efficacious.[2,8,10,11] The protective efficacy of HAV vaccines against clinical disease for adults, children and adolescents was determined to be 94–100% following two doses of vaccine given one month apart.[12–14] Protection against clinical hepatitis A may begin as soon as 14–21 days after a single dose of vaccine, and nearly all subject develop protective levels of antibody 30 days after receiving the first dose of vaccine. Two doses are currently recommended to ensure long-term protection.[2] Kinetic models of antibody decay indicate that the duration of protection is likely to be at least 15–30 years, and possibly lifelong, but long-term post-marketing surveillance studies are needed to determine the need for a booster.[11,15,16] Hepatitis A vaccine can be administered with all other vaccines included in the Expanded Programme on Immunization and with vaccines commonly given for travel.[17]

2.4. Immunization

WHO has issued recommendations for the use of hepatitis A vaccine.[1,2] Two types of monovalent HAV vaccines are currently used worldwide. Inactivated hepatitis A virus vaccines are used in most countries (usually given in two intramuscular injections at 6–36 months interval); live attenuated vaccines are manufactured and mainly used in China and sporadically in India (one injection only).[2] In addition to monovalent vaccines, combination vaccines for hepatitis A and hepatitis B or for hepatitis A and typhoid fever have been licensed.[2] A comprehensive list of products can be found in the WHO Immunological Basis for Immunization Series, module 18.[2] Hepatitis A vaccine should be considered for all populations with increased risk of hepatitis A infection. In countries with high rates of disease in specific high-risk populations, general vaccination of these populations may be recommended.[8,10,18,19]

All susceptible travelers to intermediate or highly endemic areas, including Africa, the Middle East, Asia, Eastern Europe and Central and South America should be given two doses of hepatitis A vaccine prior to departure.[7,20] A rapid vaccination scheme for short term protection before departure has been recommended.[21] If immediate protection is warranted, the hepatitis A vaccine may be given together with a single dose of IG (0.02 ml/kg, or 2 ml for adults).[22] If vaccine administration is contraindicated, 0.06 ml/kg or 5 ml should be given and repeated for every 4–6 months, if exposure continues.

Close personal contacts (e.g. household, sexual) of hepatitis A patients should be given postexposure prophylaxis with hepatitis A vaccine within 2 weeks after exposure.[1,22,23] Since the clinical presentation of hepatitis A frequently does not enable a reliable diagnosis, serological confirmation by IgM anti-HAV antibody testing in index patients should be obtained before postexposure prophylaxis of contacts is undertaken. In day care centers, if one or more hepatitis A cases occur, or if cases are identified in two or more households of attendants, hepatitis A vaccine should be administered to the staff and attendants, possibly in combination with IG. Hepatitis A vaccine is not indicated for contacts in the usual office, school or industrial settings.[22,24,25]

If a common source outbreak is linked to a food handler diagnosed with hepatitis A, vaccine and IG should be administered to other food handlers in the same establishment. Hepatitis A vaccine is usually not offered to clients, but this may be considered if the food handlers were involved in the preparation of foods that were not cooked, if deficiencies in personal hygiene practices were identified, if the food handler has had diarrhea, and if the hepatitis A vaccine can be given within 2 weeks after the last exposure.[22,26]

The use of hepatitis A vaccine to control community-wide outbreaks has been most successful, but recommendations in outbreak situations depend on the epidemiology of hepatitis A in the community and the feasibility of rapidly implementing a widespread vaccination program.[24–30] In countries where clinical hepatitis A is an important health problem, universal immunization would successfully control hepatitis A, although at present, high costs and limited availability of vaccines may preclude such a policy.[1,31–35] However, before deciding on national policies, and considering planning and implementing large-scale immunization programmes against hepatitis A, it is necessary to consider it in the context of other immunization interventions already implemented or available (e.g. hepatitis B, *Haemophilus influenzae* type b (Hib), rubella and yellow fever), all of which may have a more profound public health impact.[1,36]

3. Hepatitis B

3.1. Introduction

Hepatitis B virus (HBV) is one of the world's most widespread infectious agents and the cause of millions of infections each year.[37] Between 500,000 and 700,000 people die each year from chronic infection-related cirrhosis, hepatocellular carcinoma (HCC) or from acute hepatitis B.[37–39] Transmission occurs due to percutaneous and mucosal exposure to infective body fluids. The most common routes of transmission are therefore, transfusions of HBV-infected blood and blood products, contaminated injections during medical procedures, sharing of needles, syringes and paraphernalia among