Vaccine 37 (2019) 223–225

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

WHO Report

Hepatitis B vaccines: WHO position paper, July 2017 – Recommendations

World Health Organization

World Health Organization, Immunization, Vaccines and Biologicals, 20 Ave Appia, CH-1211 Geneva 27, Switzerland

ARTICLE INFO

Article history:
Received 7 July 2017
Accepted 13 July 2017
Available online 22 July 2017

Keywords:
Hepatitis B vaccines
Hepatitis B virus
HBV
Birth dose
Position paper
WHO
Immunization programmes
Health policy
OPV
BCG

ABSTRACT

This article presents the World Health Organization's (WHO) recommendations on the use of hepatitis B vaccines excerpted from the *Hepatitis B vaccines: WHO position paper, July 2017*, published in the Weekly Epidemiological Record (Hepatitis B vaccines, 2017) [1]. This position paper replaces the May 2009 WHO position paper on hepatitis B vaccines (Hepatitis B vaccines, 2009) [2].

The position paper gives updated information on hepatitis B vaccines and their storage, transport and deployment. The recommendations concern the target groups for vaccination and the appropriate schedules. In particular, the recommendations stress the importance of vaccination of all infants at birth as the most effective intervention for the prevention of hepatitis B virus-associated disease worldwide.

Footnotes to this paper provide a number of core references including references to grading tables that assess the quality of the scientific evidence, and to the evidence-to-recommendation table. In accordance with its mandate to provide guidance to Member States on health policy matters, WHO issues a series of regularly updated position papers on vaccines and combinations of vaccines against diseases that have an international public health impact. These papers are concerned primarily with the use of vaccines in large-scale immunization programmes; they summarize essential background information on diseases and vaccines, and conclude with WHO's current position on the use of vaccines in the global context. Recommendations on the use of hepatitis B vaccines were discussed by SAGE in October 2016; evidence presented at these meetings can be accessed at: http://www.who.int/immunization/sage/meetings/2016/October/presentations_background_docs/en/.

1. WHO position

WHO recognizes the importance of hepatocellular carcinoma and other hepatitis B virus (HBV)-related diseases as global public health problems and reiterates its recommendation that hepatitis B vaccines should be included in national immunization programmes. A comprehensive approach to eliminating HBV transmission must address prevention of infections acquired perinatally and during childhood, as well as prevention of infections acquired by adolescents and adults.

Hepatitis B vaccination is recommended for all children worldwide. Reaching all children with at least 3 doses of hepatitis B vaccine should be the standard for all national immunization programmes. Importantly, all national programmes should include a monovalent hepatitis B vaccine birth dose.

National strategies to prevent perinatal transmission should ensure high and timely coverage of the birth dose through a combination of strengthened maternal and infant care at birth with skilled health workers present to administer the vaccine, and innovative outreach strategies to provide vaccine for infants born at home.

WHO recommends hepatitis B vaccination of persons at high risk of HBV infection in older age groups and catch-up vaccination of unvaccinated cohorts if the necessary resources are available.

1.1. Hepatitis B vaccine birth dose

Since perinatal or early postnatal transmission is the most important source of chronic HBV infection globally, all infants (including low birth weight and premature infants) should receive their first dose of hepatitis B vaccine as soon as possible after birth, ideally within 24 h. If administration within 24 h is not feasible, a late birth dose has some effectiveness. Although effectiveness declines progressively in the days after birth, after 7 days, a late birth dose can still be effective in preventing horizontal transmission and therefore remains beneficial. WHO recommends that all infants receive the late birth dose during the first contact with

E-mail address: sageexecsec@who.int

http://dx.doi.org/10.1016/j.vaccine.2017.07.046
0264-410X/

health-care providers at any time up to the time of the next dose of the primary schedule [3,4].

In settings where administration of a birth dose is restricted by access to cold storage, out of cold chain (OCC) storage of monovalent hepatitis B vaccine and exposure to ambient temperatures for limited time periods at the point of delivery could improve birth-dose coverage. If an OCC policy for a monovalent hepatitis B vaccine product is adopted, which is an off-label use of the vaccine, it is strongly recommended that the WHO recommendations [5] for OCC and controlled temperature chain (CTC) use of vaccines be followed [3].

Temporary immunity may be obtained by administering hepatitis B immune globulin (HBIG) for post-exposure prophylaxis. HBIG prophylaxis in conjunction with hepatitis B vaccination may be of additional benefit for newborn infants whose mothers are HBeAg-positive.

1.2. Vaccination schedule

The birth dose should be followed by 2 or 3 additional doses to complete the primary series. Both of the following options are considered appropriate: (i) a 3-dose schedule of hepatitis B vaccine, with the first dose (monovalent) being given at birth and the second and third (monovalent or as part of a combined vaccine) given at the same time as the first and third doses of DTP-containing vaccine; or (ii) 4 doses, where a monovalent birth dose is followed by 3 (monovalent or combined vaccine) doses, usually given with other routine infant vaccines; the additional dose does not cause any harm. The interval between doses should be at least 4 weeks.

There is no evidence to support the need for a booster dose of hepatitis B vaccine after completion of the primary vaccination series in routine immunization programmes. However, additional longer-term studies should be conducted to explore life-long protection conferred by hepatitis B vaccine and the need for booster doses in different subgroups of the population [6].

For delayed or interrupted scheduling of vaccination for children, adolescent and adults, 3 doses are recommended, with the second dose administered at least 1 month after the first, and the third dose 6 months after the first dose. If the vaccination schedule is interrupted it is not necessary to restart the vaccine series.

1.3. Catch-up vaccination

In countries with intermediate or low endemicity, substantial disease burden may result from acute and chronic HBV infection acquired by unvaccinated individuals, many of whom may have been born prior to the adoption of universal childhood hepatitis B vaccination. In these countries, implementation of routine infant immunization will produce broad population-based immunity to HBV infection and eventually prevent HBV transmission in all age groups. For catch-up vaccination priority should be given to younger age groups since the risk of chronic infection is the highest in these cohorts. Catch-up vaccination is a time-limited opportunity for prevention and should be considered based on the available resources and priority. Unvaccinated individuals should be vaccinated with a 0, 1, 6 month schedule.

1.4. Interchangeability and co-administration with other vaccines

The available hepatitis B vaccines may be used interchangeably within immunization programmes. Hepatitis B and other vaccines may be co-administered at different anatomical sites. In particular, monovalent hepatitis B vaccine can be co-administered with oral polio vaccine (OPV) and Bacillus Calmette–Guérin (BCG) at birth.

1.5. Vaccination of special groups

Vaccination of groups at highest risk of acquiring HBV infection is recommended. These include patients who frequently require blood or blood products, dialysis patients, diabetes patients, recipients of solid organ transplantation, persons with chronic liver disease including those with hepatitis C, persons with human immunodeficiency virus (HIV) infection, persons interned in prisons, injecting drug users, household and sexual contacts of persons with chronic HBV infection, men who have sex with men, persons with multiple sexual partners, as well as health-care workers and others who may be exposed to blood, blood products or other potentially infectious body fluids during their work.

Infants with birth weight less than 2000 g: A birth dose of hepatitis B vaccine can be given to low birth weight and premature infants. For these infants, the birth dose should not count as part of the primary 3-dose series; the 3 doses of the standard primary series should be given according to the national vaccination schedule.

HIV-positive and immunocompromised persons: To obtain optimal immune responses to vaccination, it is essential that HIV-positive individuals are vaccinated as early as possible in the course of the HIV infection. In immunocompromised individuals, including patients with chronic renal failure, chronic liver disease, coeliac disease, and diabetes, the immune response following vaccination is often reduced. For adult immunocompromised patients, hepatitis B vaccine adjuvanted with aluminium phosphate and monophosphoryl lipid A is available.

Pregnant and lactating women: Hepatitis B vaccine can be administered safely to pregnant and lactating women.

Health-care workers and others with occupational exposure: Hepatitis B vaccination is recommended for all health-care workers who have not received a complete primary series.

Travellers: For non-immune travellers, hepatitis B vaccine should be administered according to the national schedule.

1.6. Contraindication

Allergy to yeast is considered a contraindication to immunization with yeast-produced hepatitis B vaccine.

1.7. Pre-vaccination and post-vaccination testing

Routine pre-vaccination or post-vaccination testing is not recommended. Where laboratory facilities are available and pre-vaccination testing is considered cost-effective, serological testing may reduce the number of unnecessary vaccinations of people who are already immune to HBV. The following groups should be considered for post-vaccination testing: (i) persons at risk of occupational exposure to HBV infection, e.g. health-care workers; (ii) infants born to hepatitis B surface antigen (HBsAg)-positive mothers; (iii) chronic haemodialysis patients; (iv) HIV-positive and other immunocompromised persons; and (v) sex partners or needle-sharing partners of persons who are HBsAg-positive. Testing should be carried out 1–2 months after administration of the last dose of the vaccine series using a method that allows for a quantitative determination of the anti-HBs antibody level with a detection limit <10 mIU/mL.

1.8. Monitoring

The timely delivery (within 24 h of birth) of the hepatitis B vaccine birth dose should be a performance measure for all immunization programmes, and reporting and monitoring systems should be strengthened to improve the quality of data on the birth dose. To monitor accurately the delivery of doses given within 24 h of birth,

these doses should be recorded as "timely birth dose" of hepatitis B vaccine to differentiate them from birth doses given later ("late birth dose").

The use of outcome measures is essential to monitor progress towards global control goals. Serological surveys of HBsAg prevalence, representative of the target population, will serve as the primary tool to measure the impact of vaccination and verify achievement of the hepatitis B control goals.

References

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