

Review Article

Hepatitis-B Vaccine: Its Implication to the Field of Medicine

Shivani Ravi, Nadeem Jeddy, Radhika Thangavelu

Abstract

Hepatitis B infection is a highly communicable viral infection which affects liver. The virus is usually present in the body fluids of infected individuals and can be transmitted through sexual contact, perinatal exposure, blood transfusion, contaminated needles and syringes. Vaccination is mandatory for individuals at high risk as the virus can be transmitted even through insignificant amount of body fluids and result in life-threatening consequences. The existing vaccine developed for this viral infection is highly disputable for its duration of immunity. Studies on immune memory and duration of immunity provided by the vaccine have shown varying results. This review provides an overview on hepatitis B vaccine with emphasis on the duration of immunity provided by the vaccine and its implications in the medical field.

Key Words: Human Hepatitis; Immune process; Immunization; Liver; Vaccination; Viral infection.

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Introduction

The spread of infectious diseases worldwide created the need for the introduction of vaccines which provides active acquired immunity to a particular disease. Vaccination is considered to be the most effective method of preventing infectious diseases. Widespread immunity due to vaccination is responsible for the worldwide eradication of infectious diseases such as smallpox and restriction of certain diseases like polio, measles and tetanus. Among these diseases, Hepatitis B is one of the serious and easily communicable one. The developed vaccine to this viral infection is highly disputable for its duration of immunity. The knowledge and awareness about the duration of immunity provided by this vaccine is highly needed for the dental professionals as hepatitis B viral infection remains as an occupational hazard for them and they get vaccinated against it. This review provides an insight on the hepatitis B vaccine, its duration of immunity and its implications in the field of medicine.

Hepatitis B Infection: Hepatitis B infection, a disease affecting the liver is caused by the hepatitis B virus, a member of the Hepadna viridae family. The virus is present in the body fluids such as saliva, blood, gingival crevicular fluid, etc. It is usually transmitted through contaminated needles and syringes, sexual contact, perinatal exposure, blood transfusion, micro lesions (contact with the blood or body fluids through micro cracks on skin surface).¹ Hepatitis B can cause mild

illness lasting a few weeks, or it can lead to a serious, lifelong illness. The incubation period of the virus ranges from 45–160 days. As this virus can cause serious life-threatening conditions like hepatocellular carcinoma, and even a very little amount (1×10^{-7} ml) of contaminated body fluid can transmit the virus, vaccination is highly recommended, particularly for people who have household contact with infected persons, health care workers, dental surgeons, individuals in rehabilitation facilities and travellers to endemic regions.²

Hepatitis B Infection in Dental Practice:

Hepatitis B infection is a major occupational hazard for dentists as they are frequently in contact with blood and oral fluids. The highest concentration of hepatitis B infection intra orally is in the gingival sulcus. Periodontal diseases, spontaneous bleeding tendencies and poor oral hygiene are associated with the risk of hepatitis B infection. Lichen planus, Sjogren's syndrome and sialadenitis are some of the oral manifestations of the disease.¹ Liver disease results in impaired hemostasis that can be manifested as petechiae in the oral cavity. Minor trauma may cause excessive bleeding in the oral mucosa, particularly in absence of inflammation. Excessive haemorrhage can occur during any type of surgery due to paucity of clotting factors.³ Vaccination is mandatory for the dental professionals as they are more prone to hepatitis B infection and due to the lethal consequences of this viral infection.

Vaccination Against Hepatitis B: An important milestone in the history of preventive medicine is the development of an inactivated hepatitis B vaccine derived from blood serum by Maurice Hilleman and his colleagues. It was proved effective and licensed for general use in the United States of America, November 1981.⁴ In 1986, a safer version of the vaccine derived from yeast came to market which was developed by William Rutter and his colleagues. Immunization is the most effective means of preventing hepatitis B infection and its consequences. The first dose is recommended within 24 hours of birth with either two or three more doses given after that. The vaccination regime for adults is 0, 1 and 6 months.⁵ The vaccine is administered through an intramuscular injection. It is safe for use during pregnancy or while breastfeeding.⁶ These vaccines are mostly based on recombinant major S protein produced and purified from yeast, *Saccharomyces cerevisiae*. Administration of hepatitis B vaccine initiates infection in the body which stimulates the immune system to produce T lymphocytes and antibodies. After the initial infection, 'memory' T lymphocytes as well as B lymphocytes will be left which fight against the disease in future.⁷ The hepatitis B vaccine is available in trade names such as Recombivax HB, Engerix B. Several combination vaccines have been developed to decrease the number of vaccinations given to the infants. These include hepatitis B combined with diphtheria, tetanus, acellular pertussis, and inactivated poliovirus vaccine (DTaP-IPV-HB vaccine) available in the trade name of Pediarix; combined Hepatitis A and Hepatitis B vaccine available as Twinrix; and combined Hepatitis B-Hemophilus influenza type b conjugated vaccine available as Comvax.⁷ The knowledge regarding hepatitis B viral infection, importance of vaccination, precautionary measures is essential to minimize the acquired infections among the health personnel who are at first level of contact between patients and medical care. Therefore, hepatitis B vaccination is a major prerequisite for the students being a part of health care delivery system before they enter their clinical postings.

Hepatitis B vaccine was the first vaccine developed against a chronic disease, the first vaccine against a sexually transmitted infection and the first vaccine against cancer.⁸ The duration of immunity of this vaccine is highly debatable. It is now

believed that the hepatitis B vaccine provides indefinite protection. However, it was previously believed and suggested that the vaccination would only provide effective cover between five and seven years.⁴ Long-term protection is most commonly measured through four methods which involves the anamnestic response after booster dose administration, evaluating the infection rate in vaccinated populations, 'in vitro' testing of B and T cell activity and sero-epidemiological studies.⁹

Immune Response to Hepatitis B

Vaccine: Many studies have been conducted to prove the long-term effectiveness of the vaccine. Interestingly, they showed varying results regarding immune memory and duration of immunity provided by the vaccine. This created a vacuum in the field of preventive medicine and it is believed that the on-going researches on the vaccine will fill it. Numerous studies from different regions of the world demonstrated long term immune response to hepatitis B vaccine and also highlighted the needlessness of a booster dose. The duration of hepatitis B vaccine induced immunity was studied by Krugman and Davidson (1987) in New York using individuals who received plasma-derived hepatitis B vaccine in 1978 and 1979. After five to seven years, their antibody to hepatitis B surface antigen (anti-HBs) present in the serum and anamnestic response after a boosted dose were tested. Their results suggested that the persons who respond favourably to primary immunization may be protected for at least seven years.⁴ In accordance with this study, a study by Li H, et al., in China (1998) identified the persistence of immunity by plasma-derived hepatitis B vaccine seven years after infancy immunization by evaluating the serological effect and the antibody anamnestic response. This study used radioimmunoassay as a viral marker. Their results highlighted the fact that revaccination against hepatitis B is not needed for at least 7 years after the initial immunization.¹⁰

In 2009, McMahon BJ, et al., of Alaska did a 22 year follow-up study using levels of anti-HBs in serum of the individuals who received primary vaccination. The study resulted in a favourable immune retention even after 22 years and also suggested that booster doses are not needed. The authors of the study planned to do an additional

follow-up of 30 years after the primary vaccination.¹¹ The persistence of immunity 20 years after infant vaccination with recombinant hepatitis B vaccine was assessed using qualitative ELISA in a Malaysian study done by Hudu SA, et al., in 2013. They found retention of immunity after 20 years with significant association with the number of vaccinations and also stressed the needlessness of boosters after complete infant vaccination.¹²

A German study in 2016 by Meeren OVD, et al., used chemiluminescence immunoassay to evaluate antibody persistence in children aged 15–16 years who received complete infant vaccination. The results of the study concluded that the immunity to hepatitis B persists for at least 15–16 years old after primary vaccination.¹³ The study by Bruce MG, et al., done on a huge sample size of 1578 Alaskans was a jewel in the crown as estimated that $\geq 90\%$ of participants had evidence of protection 30 years later. The study also suggested that the booster doses are not needed.¹⁴

Need for Booster Vaccine: In contrast to the above studies, certain studies suggested that the booster dose is needed after primary immunization with hepatitis B vaccine. Horowitz MM, et al, in 1988 determined the prevalence of immunity using anti-HBs 3 years after primary vaccination. The results of their study showed low antibody levels (<10 mIU/ml) and thus emphasised the need of periodic boosters to maintain production of anti-HBs.¹⁵ A study by Lu CY, et al., (2008) in Taiwan investigated the persistence of immunity 15-18 years after the primary vaccination using a huge sample size of 6156. They found that a very low percentage of individuals had protective anti-HBs and with that it was concluded that this loss of immune memory 15–18 years later may raise concerns about the need for a booster dose.¹⁶

A study by Boxall EH, et al., in 2004 investigated long-term persistence of immunity to hepatitis B after vaccination during infancy using a mixture of people belonging to different ethnic origins where endemicity is low. The results showed unfavourable immune response in most of the individuals. And so it was suggested that a booster dose may be required between 13 and 15 years of age.¹⁷ Jan CF, et al., in 2009 did a study at Taiwan to determine the

immune memory to Hepatitis B vaccination. The results showed loss of immune memory in most of the individuals and so the authors recommended at least 2 doses of booster vaccines for at-risk youths who received primary vaccinations but are sero-negative for Hepatitis B surface antigen, anti-HBs and Hepatitis B core protein in adolescence.¹⁸

Interestingly, a Brazilian study done by Livramento A, et al., in 2008 produced confusing results which aimed to determine the anti-HBs antibody levels among children and adolescents aged 10-15 who were completely vaccinated for hepatitis B. The study showed almost equal number of participants who have and don't have immune memory. Thus they recommended that further studies with a larger sample size are required to arrive at a better conclusion.¹⁹

Conclusion

Since Hepatitis B is an easily communicable disease and a very little amount of contaminated body fluid is enough to cause the infection, it gains utmost focus for worldwide eradication. On the other hand it is presumed that several decades of effort will be required to accomplish it. As the results of the studies done so far oscillates in two different extremes, we recommend regular testing for anti-HBs and administration of booster vaccine to the immunocompromised individuals or those who lost immune memory. Documentation of the vaccination details while administration may be done for future use. The presence of memory cells may be used as a marker to determine the duration of immunity. Long-term follow-up studies are needed as individuals who received primary vaccination become sexually active and potentially exposed to hepatitis B infection. To study the clinical significance of decline in immune memory, routine surveillance of the infection in adolescents and young adults will be needed. As the duration of immunity provided by the vaccine still remains controversial, we recommend that implication of immunization schemes during adolescence would be more effective to safeguard the population against a disease that is predominantly acquired in adulthood.

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