Hepatitis B Vaccines; Efficacy and Necessity of Booster Immunizations

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General Understanding

Most hepatitis B (HB) vaccines are based on recombinant major S protein produced and purified from yeast. To decrease the number of vaccinations, several combination vaccines have been developed, and are commonly used for infant [1-3]. These include HB combined with diphtheria, tetanus, acellular pertussis, and inactivated poliovirus vaccine (DTaP–IPV–HB vaccine); combined hepatitis A and HB vaccine; and combined HB-Hemophilus influenza type b (HiB)-conjugated vaccine. HB vaccine is recommended for all infants, all children aged < 19 years who were not previously vaccinated, hemodialysis patients, susceptible sexual partners of HB surface antigen (HBsAg)-positive individuals, healthcare professionals, patients with HIV, men who have sex with men, and intravenous drug users. In 2013, HB vaccination was recommended for all healthcare professionals [4].

Response and efficacy of HB vaccines

The World Health Organization (WHO) recommends that all infants receive the HB vaccine as soon as possible after birth, preferably within 24 h. Universal vaccination was started in 31 countries in 1992 based on the WHO recommendations, and subsequently increased to 183 countries in 2013 [5]. Routine vaccination reduced the prevalence of HBs antigen to < 1% in the United States [6]. Taiwan, an HBV-endemic region, successfully implemented a universal vaccination program and the prevalence of HBsAg decreased from 9.8% in 1984 to 0.7% in 1999 [7,8]. In general, vaccine responders are defined as individuals whose anti-HBs remains stable at > 10 mIU/ml after active immunization [3]. Complete vaccination induces protective antibodies in > 95% of vaccinated individuals. However, the response of vaccination is sometimes decreased in adult over 40 years of age and some individuals do not retain anti-HBs antibodies after complete vaccination. Recent study revealed that the level of anti-HBs antibody after vaccination in diabetic children and adolescents was not sufficient to protect from HBV infection [9]. A meta-analysis showed that HLA class II DRB1 and DQB1 alleles were associated with the vaccine response in China [10]. Another HB recombinant vaccine containing the small S and Pre-S regions was reported to increase the efficacy of vaccination in non-responders to conventional HB vaccines [11].

Protection against α-epitope escape mutations

The widely distributed recombinant HB vaccine promotes the formation of antibodies to the neutralizing epitope known as the “α determinant”. Amino acid changes, especially the G145R mutation, within this region could render HBV resistant to the neutralizing effect of anti-HBs, and threaten the effectiveness of HB vaccines [12]. However, it was reported that the mutant HBV strain did not lead to HB infection in vaccinated individuals [13]. Instead, it seems that the vaccine escape mutants appear after vaccination in individuals previously exposed to wild-type HBV, and do not represent new infection in previously vaccinated individuals who retain anti-HBs antibodies.

Is a boost necessary?

It is still not clear how long the protective effect persist after neonatal vaccination. According to the United States Centers for Disease Control and Prevention guidelines, a booster is not necessary in prior responders with a normal immune system because memorized immunity will be activated following HBV exposure [3]. Studies from Gambia and Alaska revealed that long-term protection persist in adolescents vaccinated in infancy and booster dose was not necessary [13-15]. However, some vaccinated individuals express anti-HBc antibodies, which is suspected to be due to HBV infection after the disappearance of anti-HBs antibodies. Studies from Taiwan reported that most of memorized immunity was disappeared after 20 years post vaccination and booster vaccination was necessary to maintain anti-HBs seropositive [16,17]. In European countries, a booster immunization is recommended if the individual's anti-HBs antibodies falls below 10 mIU/ml [18]. Especially, the regular testing for anti-HBs antibody and booster infection is recommended for immunocompromised patients [19]. So far, there is no randomized trial and it is still difficult to conclude this issue.
References


