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LETTER

Requirement for further validation on the seroconversion of hepatitis B surface antigen in successful vaccinees

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ABSTRACT

Hepatitis B vaccination can provide long-term protection against transmission of hepatitis B virus (HBV). An article recently published in Human Vaccine & Immunotherapeutics reported that 3.5% (5/143) of the individuals who had been successfully vaccinated against hepatitis B at infancy became positive for hepatitis B surface antigen (HBsAg) at their young adulthood during a period of four years, indicating that hepatitis B vaccination appears to have no long-term protection. We concern on the exceptional results in that article since the critical data are lacking, questionable, or very implausible. We consider that any exceptional data should be validated as far as possible before the data are used to obtain a conclusion.

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We read with interest the article by Zheng and colleagues on the seroconversion of hepatitis B surface antigen (HBsAg) among successful vaccinees in Southern China.[1] They reported the HBsAg prevalence in two cross-sectional seroepidemiological surveys (in 2015 and 2019) in individuals born between 1987 and 1993, who were assumed to have been successfully vaccinated against hepatitis B at infancy. The HBsAg prevalence was 3.5% (53/1527) in 2015 and 5.3% (27/511) in 2019, and 5 (3.5%) of 143 participants who were HBsAg negative in 2015 became HBsAg positive in 2019.[1] However, we worried about the exceptionally high incidence (3.5%) of chronic hepatitis B virus (HBV) infection in the successful vaccinees during a period of four years because of the following reasons.

First, the authors assumed that the participants were successfully vaccinated against hepatitis B, but the authors did not provide any data on the response of hepatitis B surface antibody (anti-HBs) after the completion of hepatitis B vaccination. The authors considered that all infants born after the implementation of the universal immunization program were vaccinated against hepatitis B. However, the vaccination coverage at the beginning of the program was usually suboptimal.[2] The relatively high HBsAg prevalence (3.5–5.3%) in vaccinated persons in Zheng and colleagues' report[1] also implies that a considerable proportion of participants did not receive hepatitis B vaccination, since HBsAg prevalence is around 1% in the population with high vaccination coverage.[3,4]

Second, of the five individuals who showed HBsAg negative in 2015 but positive in 2019, three had very low HBsAg titers (1.3–2.8 IU/ml, Table 3 of the article),[1] which is very unusual. These individuals had at most only four years of infection history. If they were chronically infected, it was less likely to have so low concentrations of HBsAg because excessive large amount of HBsAg is overexpressed in hepatocytes and the concentration of circulation HBsAg is as high as 200 μg/ml.[5] If they were in the early convalescent phase of acute infection, IgM hepatitis B core antibody should be tested. The remaining two individuals were less likely to be infected with HBV, with the exception of infection with mutant HBV, because they had sufficient amounts of anti-HBs (81 and 112 mIU/ml) in 2015. Successful vaccinees in whom anti-HBs levels decline to lower than 10 mIU/ml are still immune to HBV.[6] However, the authors did not provide HBV DNA sequencing data. DNA sequencing is now routinely performed in China[7,8] and the authors should have serum DNA samples for sequencing as the quantification of HBV DNA was performed.[1]

Third, the authors reported that the occurrence of HBsAg in individuals with positive anti-HBs was similar to that in those with negative anti-HBs (4.2% [2/48] vs 3.2% [3/95]). If the data really reflect the fact, these results indicate that hepatitis B vaccination had no long-term protection. However, hepatitis B vaccination is highly effective against HBV infection and the duration of protection can provide long-term protection, even more than 30 years.[2,9,10]

Fourth, the authors reported that the prevalence of hepatitis B core antibody (anti-HBc) in 143 individuals in 2015 and 2019 was 23.1% and 7.7%, respectively (Table 2 of the article).[1] This age-decline of anti-HBc prevalence is obviously implausible. Because hepatitis B core antigen is the most immunogenic antigen of HBV, anti-HBc prevalence is usually constant or increased by age.[4,10] If the aforementioned five individuals were really infected with

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HBV at the interval of four years, much more individuals would have anti-HBc positive in 2019, since >90% of acute HBV infection in adults is self-resolving.

Thus, based on the data in the article,[1] the statement "the finding is unique" is not convincing. The hepatitis B vaccination and anti-HBs response in all the study participants and negativity of HBsAg in these individuals with novel HBV infection occurred between 2015 and 2019 require further validation based on the evidence of good practice. At least, another follow-up of these five individuals with HBV infection between 2015 and 2019 is required to clarify whether true HBV infection occurred.

Disclosure of potential conflicts of interest

No potential conflicts of interest were disclosed.

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