



Immune response to hepatitis B vaccine in patients who lost hepatitis B surface antigen during follow up

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Dear Editor,

We read with interest the article by Taheri *et al.* regarding the efficacy of Hepatitis B vaccine in those who lost Hepatitis B surface antigen (HbsAg) during follow up (1). As the authors mentioned, a protective anti-HBs level developed in 24% of chronic HBsAg-positive subjects who had already lost their HBsAg after hepatitis B vaccination, and the remaining cases need to be monitored for occult HBV infection. Subjects with no response after hepatitis B vaccination may have low levels of HBsAg or have immunologic tolerance to hepatitis B vaccination and no ability to produce anti-HBs antibody as reported previously (2). Detection of HBV DNA in the absence of a detectable HBsAg level and occasionally other HBV serologic markers is termed occult hepatitis B (OHB) (3). These patients can not only transmit HBV to others but also may progress to chronic hepatitis, cirrhosis, and hepatocellular carcinoma. The prevalence and outcomes of OHB in chronic HBV-infected individuals have not yet been re-

ported. On the other hand, patients who lost HbsAg and have not seroconverted to anti-HBs with no detectable HBV DNA are frequently seen in clinical practice, and the outcomes for this group of patients are not clear. A study by our research group on the long-term outcomes of chronic hepatitis B surface antigen (HbsAg) carriers in the general population in northeastern Greece showed that HbsAg to anti-HBs seroconversion was observed in 10 out of 195 (5.1%) patients at the inactive carrier state, with an estimated annual prevalence rate of 1%. Additionally, six patients lost HbsAg (3.1%) without developing anti-HBs immunity. All patients who lost HbsAg during the follow up period were HBeAg negative and anti-HBe positive and had undetectable serum HBV-DNA and normal ALT levels (4). In another study, we determined that the frequency chronic HBV patients with isolated anti-HBc was 6% in the general population of northeastern Greece, where HbsAg endemicity is about 3% (5). Serum HBV-DNA levels were less than 2,000 IU/ml and were detected in 9 out of 93 (9.7%) anti-HBc positive, anti-HBe positive individuals, of whom 3 developed anti-HBs during the follow up period despite the persistence of serum HBV-DNA (6). In patients with detectable levels of HBV-DNA, no mutation was detected in the S gene. These subjects either have chronic HBV infection but lost HbsAg over time or

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resolved HBV infection with a decrease in anti-HBs antibody levels below 10 IU/L (6). For patients with isolated anti-HBc antibody who receive the hepatitis B vaccination, several studies have reported significant anti-HBs levels of 91%–96% of the subjects (2,7-9). Lok *et al.* reported no response rate after three doses of hepatitis B vaccine in 28% of 32 subjects with isolated anti-HBc antibody (2). Lai *et al.* reported no anti-HBs response in 22.9% of 48 cases with isolated anti-HBc after three doses of the hepatitis B vaccination (9). Our data are in agreement with the results of the above studies and suggest a relatively low percentage (26%) of no anti-HBs response in patients who are anti-HBc positive only (unpublished data). Although Taheri *et al.* found that 24% of chronic HBsAg-positive subjects who lost HBsAg developed anti-HBs after receiving the hepatitis B vaccination, we have to take into account spontaneous HBsAg seroconversion. Indeed, according to our results, 47.8% (163/341) of individuals with detectable anti-HBc levels at presentation developed anti-HBs immunity (annual rate of 9.5%) and had undetectable serum HBV-DNA during the observation period of up to 17 years (10). Our data are in agreement with the results of Taheri *et al.* (1) that chronic HBsAg-positive cases who lost their HBsAg and are negative for HBV DNA mostly responded to hepatitis B vaccination. Additionally, these patients differed from the remaining patients who lost HBsAg during follow up and were positive for HBV DNA, who still might have OHB and must be followed up with.

References

1. Taheri H, Hasanjani Roushan MR, Soleimani Amiri MJ, Pouralijan M, Bijani A. Efficacy of hepatitis B vaccine in those who lost hepatitis B surface antigen during follow-up. *Hepat Mon*. 2011;11(2):119-22.
2. Lok AS, Lai CL, Wu PC. Prevalence of isolated antibody to hepatitis B core antigen in an area endemic for hepatitis B virus infection: implications in hepatitis B vaccination programs. *Hepatology*. 1988;8(4):766-70.
3. Brechot C, Degos F, Lugassy C, Thiers V, Zafrani S, Franco D, et al. Hepatitis B virus DNA in patients with chronic liver disease and negative tests for hepatitis B surface antigen. *N Engl J Med*. 1985;312(5):270-6.
4. Zacharakis GH, Koskinas J, Kotsiou S, Papoutselis M, Tzara F, Vafeiadis N, et al. Natural history of chronic HBV infection: a cohort study with up to 12 years follow-up in North Greece (part of the Interreg I-II/EC-project). *J Med Virol*. 2005;77(2):173-9.
5. Zacharakis G, Kotsiou S, Papoutselis M, Vafeiadis N, Tzara F, Pouliou E, et al. Changes in the epidemiology of hepatitis B virus infection following the implementation of immunisation programmes in northeastern Greece. *Euro Surveill*. 2009;14(32).
6. Zacharakis GH, Koskinas J, Papoutselis M, Tzara E, Vafeiadis N, Maltezos E, et al. 521 Clinical significance of anti-HBc as the only marker of hbv infection in general population. A cohort study with an observational period of up to 12 years. *hepatol*. 2006;44(Suppl 2):S194.
7. Chan CY, Lee SD, Tsai YT, Lo KJ. Hepatitis B vaccination alone is not adequate for the categorizing of adult subjects with isolated anti-HBc. *J Gastroenterol Hepatol*. 1995;10(2):192-7.
8. Tseng KC, Lei HY, Cheng PN, Young KC, Jen CM, Wu CH, et al. Immune response to hepatitis B vaccine of subjects with isolated antibody to hepatitis B core antigen. *Hepatogastroenterology*. 2003;50(53):1474-7.
9. Lai CL, Lau JY, Yeoh EK, Chang WK, Lin HJ. Significance of isolated anti-HBc seropositivity by ELISA: implications and the role of radioimmunoassay. *J Med Virol*. 1992;36(3):180-3.
10. Kotsiou S, Zacharakis G, Koskinas J, Tzara F, Vafeiadis N, Papoutselis M, et al. Factors associated with HBsAg seroclearance in symptomatic carriers of endemic areas during a long follow-up period of up to 17 years. *Hepatology*. 2007;46(suppl 1).