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Hepatitis B seroprevalence and anamnestic response amongst Taiwanese young adults with full vaccination in infancy, 20 years subsequent to national hepatitis B vaccination

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Abstract

The long-term protective effect of hepatitis B virus (HB) vaccination against HB infection and the necessity for routine booster vaccination in young-adult age subsequent to full HB immunization at birth remain issues of some debate currently. This study is aimed at evaluating the seroprevalence of HB infection and the response to HB booster vaccination amongst young-adult university students who had previously undergone full vaccination during their infancy. Eight hundred and forty-three subjects (mean age 18.7 ± 0.4 years), 492 males and 351 females, with a complete HB vaccination during infancy were enrolled into this study. The prevalence of natural HB infection, chronic HB-carrier status, and HB-naïve group was, respectively, 4.1%, 1.4%, and 62.3%. Amongst 316 study subjects who were naïve to HB infection and had received one HB booster at time of university entrance health examination, 49.6%, 91.4%, and 97.5% of the participants with a serum anti-HBs level <0.1, 0.1 to <1.0 and 1.0 to <10.0 mIU/mL prior to the booster vaccination, respectively, developed an anamnestic response (i.e., ≥10 mIU/mL) to a booster dose of HB vaccine. Full implementation of national-wide HB vaccination program in 1986 has significantly reduced the incidence of HB infection and associated carrier rate in Taiwan. Approximately three-quarter of the subjects who were naïve to HB infection and had received one HB booster demonstrated an anamnestic response to a booster HB vaccine. The higher the anti-HBs titers remained for an individual subsequent to primary vaccination, the greater the anamnestic response observed. Additional long-term follow-up studies are needed for young adults initially vaccinated for HB in their infancy.

Keywords: Hepatitis B vaccination; Hepatitis B antibodies; Booster dose; Taiwan

1. Introduction

Infection by the hepatitis B virus (HB) is a worldwide health issue, this being particularly so for the residents of many Asia-Pacific countries [1]. It has been estimated that, globally, around 350 million people are believed to be chronic

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HB carriers and one million people die annually from HB-related diseases including hepatocellular carcinoma (HCC), liver cirrhosis, chronic hepatitis and acute hepatitis [2].

In Taiwan, HB infection is an important cause of chronic hepatitis, liver cirrhosis and HCC [3–5]. Prior to the introduction of the HB-vaccination program in Taiwan in 1984, the hepatitis B surface antigen (HBsAg) carrier rate amongst the general Taiwanese population was in the range of 15–20% [6–8]. At time of writing, death due to hepatitis and cirrhosis ranked seventh amongst all causes of death in Taiwan, and HCC had become the second leading cause of cancer death in Taiwan [9]. Thus, chronic HB infection constitutes an extremely important health problem in Taiwan.

In order to tackle this health problem, a nationwide HB publicity campaign, including public education and the overall improvement in hygiene and general health practices was launched in 1983 [10,11]. In addition, in 1984, Taiwan's government launched an universal HB vaccination program for newborns, it being one of the first countries in the world to commence such a program [12,13]. At the commencement of the program, the HB carrier rate amongst children less than 12 years of age was 9.8% [14]. As time has passed following program inception, a number of post-program-commencement studies (namely the 5-, 10-, 15-, 16-, 18- and 20-year follow-up studies post-implementation of this mass HB vaccination program) have indicated that both the HB-infection and HB-carrier rates have declined progressively and continuously subsequent to program implementation in 1984 [12,13,15–19]. The long-term success and efficacy of a mass-vaccination program such as this, is extremely important in terms of the potential for the funding of future related health policies.

In this report, we examined the long-term seroprevalence of serum antibody to hepatitis B surface antigen (anti-HBs) in a group of year-2006 university freshmen who had originally received a course of completed four-dose plasma-derived HB vaccine during their infancy. We also assessed the status of immunological "memory" for HB by evaluating the response to a booster dose of a HB recombinant vaccine for those university new entrants whose serum anti-HBs level had fallen to a level below 10 mIU/mL.

2. Materials and methods

2.1. National vaccination program

The nation-wide HB-vaccination program in Taiwan was first launched in July 1984. During the initial 2-year period of the program, only infants born to HBsAg carrier mothers were immunized, whereas from July 1986 onwards, all infants were scheduled to be immunized. In principle, all infants were to be vaccinated with four doses of plasma-derived vaccine (Havac B; Pasteur-Merieux, Lyon, France, or its equivalent derivative, Lifeguard hepatitis B vaccine; Hsin-Chu, Taiwan), one dose at birth, and the remaining three doses at, respectively, 1, 2 and 12 months of age. Newborns from highly infectious carrier mothers were also given 0.5 mL of hepatitis B immunoglobulin at birth. HB screening of pregnant women and the provision of HB vaccine and hepatitis B immunoglobulin for infants has been entirely government subsidized. From October 1990 onwards, the free-of-charge service program was expanded to include all children under the age of 7 years, all medical personnel involved with patient care, and also certain selected population groups, e.g., elementary-school children in aboriginal areas and offshore islands. Since July 1991, the vaccination records for elementary-school entrants have been checked for evidence of previous HB vaccination, and non- or incompletely vaccinated elementary-school students were provided the opportunity to undergo "catch-up" vaccinations.

2.2. Study participants and methods

The data collected for this study pertained to a group of new undergraduate entrants (1459 students) to Yuan Ze University, located in northern Taiwan, who had been born on or after 1 July 1986 and underwent a compulsory health-screening examination including a survey of serum HBsAg, anti-HBs and antibody to hepatitis B core antigen (anti-HBc) status and a record of HB vaccination history prior to their university entrance in September 2006. Amongst these new entrants, 843 students who (492 males, 351 females, mean age: 18.7 ± 0.4 years) featured records of completed four-dose HB vaccination, using plasma-derived vaccine, during their infancy were enrolled. Those students who were not able to provide a vaccination record or who had received a previous HB-booster inoculation in their childhood and/or adolescence were excluded from this study. Five hundred and twenty-five students with status of HBsAg negativity, anti-HBc negativity and anti-HBs negativity (HB-naïve group) were offered one booster dose of a recombinant DNA HB vaccine. Three hundred and sixteen HB-naïve students actually voluntarily received this single booster dose subsequent to offer and, 4 weeks subsequent to booster vaccination, a blood sample was taken from them for serum anti-HBs-level assessment.

The serum HBsAg, anti-HBs and anti-HBc levels were determined using a commercially available enzyme immunoassay kit (AxSYM, Abbott Laboratories, North Chicago, IL, USA). The detection limit of the anti-HBs enzyme immunoassay kit was 0.1 mIU/mL. Samples featuring an anti-HBs titer of <0.1 mIU/mL and 0.1 to <10.0 mIU/mL were interpreted as being undetectable and nonprotective, respectively. Those patient samples for which the serum anti-HBs titer was equal to or greater than 10 mIU/mL but less than 100 mIU/mL were grouped as borderline protective. The blood samples which revealed a serum anti-HBs titer of greater than 100 mIU/mL were deemed to be demonstrated a protective anti-HBs status. An anamnestic response to a hepatitis B vaccine booster dose was defined as a rise in ant-HBs titer from prior to, to subsequent to booster