First evaluation of the serum level of anti-hepatitis B surface antigen after vaccination in Libya

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ABSTRACT The hepatitis B virus (HBV) vaccination schedule in Libya follows international recommendations (1st dose at birth, 2nd after 1 month and 3rd after 6 months). This research aimed to evaluate the long-term protection of the HBV immunization programme in Tripoli and to determine the best age to administer booster doses. Serum levels of hepatitis B surface antigen were determined in 277 randomly selected children aged 1–12 years. The response to HBV vaccine in 1–3-year-olds was 93.2%, but this declined with age and at 7–9 years after initial vaccination only 53.1% of children had protective titres (≥ 10 mIU/mL). No significant differences between males and females in antibody persistence or response to vaccine were observed. We recommend continuing the HBV vaccination programme and that a booster dose be given to 6-year-old children to ensure maximum protection during the period of school entry and beyond.

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Introduction

Approximately 2 billion people, about 33% of the world population, are infected by hepatitis B virus (HBV). Over 300 million among them are chronically infected, which represents about 5% of the population, and about a quarter of them suffers from the serious consequences of liver diseases such as chronic hepatitis, primary hepatocellular carcinoma and cirrhosis [1]. HBV kills 1–2 million people every year [2]. The hepatitis B surface antigen (HBsAg) carrier rate varies from less than 1% in Europe to 20% in sub-Saharan Africa.

The prevalence of disease among Libyans was 2.18% and 2.20% in 2004 and 2005 respectively [3]. Libya is considered an area of intermediate endemicity for HBV infection, and the frequency of HBV is lower among immunized people. The number of HBsAg carriers in Libya is estimated between 120,000 and 150,000, and the infections have occurred mostly among high-risk behaviour people: those with a history of scarification (29.0%), contact with hepatitis B patients (22.8%), history of jaundice (19.0%), family history of hepatitis B (10.7%), history of blood transfusion (9.0%) and multiple sexual partners (7.2%) [4]. However, the exact number of infected people is not known, and therefore many people receive no counselling or treatment or even testing [4].

Despite the World Health Organization (WHO) recommendation to all countries to start HBV vaccination by 1997 [5], in Libya the neonatal vaccination programme against HBV started in 1993. Later on, age cohorts born in 1991–92 and 1989–90 were vaccinated by the vaccination campaigns in 2005 and 2006 respectively. The Libyan vaccination schedule follows WHO and Advisory Committee on Immunization Practices (ACIP) suggestions: 1st dose given at birth, the 2nd after 1 month and the 3rd after 6 months. The duration of protection provided by the vaccine in Libya is unknown and this study was carried out in order to evaluate the long-term protection of hepatitis B vaccine and the need for booster doses.

Methods

Sample

The study was performed on 277 randomly selected children (156 boys and 125 girls) aged 1–12 years from different areas of Tripoli. This is the capital city of Libya and different Libyan subgroups are represented in the population. All children received 3 doses of recombinant hepatitis B vaccine at the birth, after 1 month and after 6 months.

Ethical approval was obtained from the Academy of Graduate Studies in Tripoli. All the samples were obtained after informed consent had been given; as patients were under age, approval was obtained from parents.

Data collection

Samples were collected from children in Alkadedia medical centre and Alga hospital in Tripoli between February and July 2009, 3 mL of venous blood was taken by venepuncture into heparinized tubes.

Anti-HBsAg quantification was performed at Al-Mubdeoun laboratory in Tripoli in October 2009. The sera were separated after clotting using centrifugation. Serum samples were stored at −20 °C until analyses were performed. Serological analyses were performed using bioMérieux mini VIDAS autoimmunoassay chemistry system.

Results

The children were analysed in 4 groups according to age: 1–3 years (88 children), 4–6 years (98 children), 7–9 years (49 children) and 10–12 years (42 children). Statistical analyses were performed using the software SPSS, version 17.0.

Analysis

The results collected from the 277 children screened for anti-HBs showed that 89 had anti-HBs antibody < 10 mIU/mL, which is considered non-protective and 188 children showed a titre ≥ 10 mIU/mL, which is considered protective. Of the 88 children aged 1–3 years who received the 3 doses of vaccine 6 (6.8%) did not show a positive response to the vaccination (Table 1) and 93.2% showed a positive response. At age 4–6 years 73.3% responded, at age 7–9 years 60.0% and by age 10–12 years only 25.0% had a positive response (Table 1).

Figure 1 shows that the response to vaccine (i.e. the percentage of children with a titre ≥ 10 mIU/mL) and the anti-HBs titre declined linearly with age across the 4 age groups, from the highest response at ages 1–3 years to lowest at 10–12 years.

No significant differences were observed in the titre values between males and females, either in the response to vaccine or in the decrease of antibody titres across age groups (P = 0.817 and P = 0.386 respectively) (Table 1).

Discussion

This study in Libya showed that only 6.8% of the 1–3-year-old cohort who received the 3 doses of vaccine did not respond positively to the vaccination. This result is slightly higher compared with the findings of other studies performed in Taiwan, Turkey,
The Gambia and Palestine (Gaza) that show percentages of non-responders of 3.3%, 2.3%, 5% and 5.5% respectively [6–8]. Further studies in the future will be needed to identify the reason for lower immune responses (pathology, ethnicity, family history, etc.). The total positive response to hepatitis B vaccine among infants (93.2%) confirmed a good vaccination coverage in Libya. This is in agreement with Egyptian data, which revealed a response rate of 93.3% 1 month after vaccination [9], and with data reported by the Ministry of Health in New Zealand [10] and Desombere et al. in Belgium [11], indicating a positive response in children varying from 90% to 95%.

Different factors can affect the responsiveness to hepatitis B vaccine [12]. In general, variations in immune response among individuals, the age of the vaccine, differences in manufacturing and the timing of the 3rd vaccine dose administration are considered the main factors that can affect the response to vaccination [13]. Hadler et al. found that response to vaccination was improved with increasing age but also that the response was improved by increasing the time between doses to more than 7 months [14]. In contrast to this observation, Inskip et al. reported that the only additional factor which contributed to the response was the logarithm of the length of time between the first and the second dose of vaccine, with a longer interval resulting in a lower antibody level. So when there was a doubling of the interval between the first and second dose from 4 to 8 weeks the reduction in antibody level was approximately 12% [15].

Age-group analysis showed that the response to vaccine and the anti-HBs titre declined across the 4 age group cohorts, indicating a decrease in vaccine efficacy against infection with time. The titre decline observed in this study disagrees with a study from The Gambia, which is considered an HBV endemic country, that concluded that vaccination early in life can provide long-lasting efficacy [15]. In contrast, our findings are in agreement with the results of the vaccination of Iranian children, which is an intermediate prevalence country [1]. Research carried out in Egypt showed a faster rate in the waning of the titre than our finding: 5 years after vaccination the anti-HBs titre was 53.3% [9]. In addition, a study performed in Senegal showed that the titre fell to < 10 mIU/mL in 33% of children during the 5th and 6th years of life and the authors recommended the introduction of a booster 4th dose after 5 years in order to maximize the vaccination effect [16].
Conclusions

This study showed a decreasing immunogenicity associated with increased age. Although 70.4% of the vaccinated children aged 4–6 years old were protected only half of the children (53.1%) who had been vaccinated from birth had anti-HBs levels ≥ 10 mIU/mL 7–9 years after the last dose of vaccine was administered. Hepatitis B vaccine is highly immunogenic and immunization with hepatitis B vaccine in Libya showed a high response in infants aged 1–3 years (93.2%), which is likely to have a beneficial impact on HBV transmission in this age group. This study strongly suggests that continuation of the hepatitis B immunization programme would be beneficial in Libya, in line with findings from the available literature and the WHO recommendations that emphasize the importance of administering the 1st dose of the hepatitis B vaccine immediately after birth in order to avoid transmission of HBV during childhood.

The findings of this research have confirmed that the response to hepatitis B vaccine disappears over time. Therefore a booster dose might be necessary for children at least 6 years after the first vaccination to ensure maximum protection in the period of school entry and adulthood. This observation must be evaluated depending on the country, the endemicity of the disease and the condition and schedule of the immunization programme.

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References


