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The independent impact of newborn hepatitis B vaccination on reducing HBV prevalence in China, 1992–2006: A mathematical model analysis

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HIGHLIGHTS

- Newborn hepatitis B vaccination of the first 14 years in China from its introduction in 1992 to 2006 could account for more than 50% of the reduction of the total HBV prevalence.
- The higher the full 3-dose and timely birth dose coverage rates, the higher the contribution rate of newborn hepatitis B vaccination on reducing HBV prevalence.
- Newborn vaccination with high full 3-dose and timely birth dose coverage rates is the decisive factor in controlling hepatitis B in China.

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ABSTRACT

Objective: To evaluate the independent impact of newborn hepatitis B vaccination on reducing HBV prevalence in China, from its introduction in 1992–2006.
Methods: An age- and time-dependent discrete dynamic model was developed to simulate HBV transmission in China under the assumptions of no any change in interventions and only with newborn vaccination introduction. The initial conditions of the model were determined according to the national serosurvey in 1992. The simulated results were compared with the observed results of the national serosurvey in 2006, and the contribution rate of newborn vaccination on reducing HBV prevalence was calculated overall and by birth cohort.
Results: The total HBV prevalence would remain stable through the 14-year period if no any change in interventions, but decrease year by year if only with newborn vaccination introduction. Newborn vaccination could account for more than 50% of the reduction of the total HBV prevalence, although the full 3-dose and timely birth dose vaccination coverage rates were low in the early years. The results by birth cohort showed that the higher the two coverage rates, the higher contribution rate on reducing HBV prevalence. For the 2005 birth cohort which had high levels in the two coverage rates, the contribution rate could reach more than 95%.
Conclusion: Newborn hepatitis B vaccination from 1992 to 2006 in China had played the most important role in reducing HBV prevalence. Newborn vaccination with high full 3-dose and timely birth dose coverage rates is the decisive factor in controlling hepatitis B in China.

1. Introduction

Hepatitis B virus (HBV) infection has long been a major health problem in China. The first and second national viral hepatitis serosurveys done in 1979 and 1992 respectively showed that 9.05% and 9.75% of Chinese aged 1–59 years were positive for HBV surface antigen (HBsAg) (Dai and Qi, 1999; Xia et al., 1996). In 1992, the Chinese Ministry of Health recommended routine hepatitis B

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vaccination for newborns. This strategy was fully integrated into the National Children Immunization Program in 2002. Fourteen years after the strategy was carried out, in 2006, the third national serosurvey showed that the HBsAg prevalence of Chinese aged 1–59 years had dropped to 7.18% (Qi and Wang, 2011). The reduction was very obvious in children aged 1–4 years and 5–14 years, from 9.67% and 10.74% in 1992 to 0.96% and 2.42% in 2006 (Qi and Wang, 2011), respectively. Newborn hepatitis B vaccination is considered as the most important measure to control hepatitis B in China and other highly HBV-endemic areas (Liang et al., 2009a, 2009b; Romano et al., 2011; Zanetti et al., 2008). However, up to now, few studies have estimated the independent impact of newborn hepatitis B vaccination on the control of hepatitis B. With the introduction of newborn hepatitis B vaccination, other interventions were also implemented, in China including hepatitis B vaccination in other age populations by the "self-select and self-pay" policy, urge policies for hospitalized delivery, safe injection practice, HBsAg screening of blood for transfusion, blood exposure prevention in medical settings, management and treatment of chronic HBV-infected persons, etc. These interventions should produce their appropriate effects.

This study aimed at evaluating the independent impact of newborn hepatitis B vaccination on reducing HBV prevalence in China, from 1992 to 2006, by the mathematical modeling method. This work will help understand the effectiveness of newborn hepatitis B vaccination and guide the preventive practice of hepatitis B.

2. Methods

2.1. Mathematical model

We developed an age- and time-dependent discrete dynamic model to simulate HBV transmission in a population in which newborn hepatitis B vaccination was introduced. Based on the characteristics of HBV transmission, the population was divided into three chronic health states or compartments: susceptible to HBV $S(a,t)$; immune due to infection or vaccination $I(a,t)$; and chronic infection $C(a,t)$. Here "a" represents the age and "t" represents the time. Acute infection, as a transient process by which a susceptible person would obtain immunity, become chronically infected or die due to fulminant hepatitis (Liaw and Chu, 2009), was not considered as a compartment of the model. We further divided the population into 101 age groups, one per year of age, from 0 to 100 years old and used a year as a running time unit. From year t to year $t+1$, all individuals would grow one year old with transitions occurring by respective transition probabilities, and meanwhile newborns (aged 0 year) would enter the population. All newborns were considered susceptible to HBV at birth due to the very low incidence of intrauterine infection (Hsu et al., 1992; Tang et al., 1998; Zhao et al., 2000), and they would enter the susceptible or immune compartment according to whether to receive the vaccination and obtain the protection. The protection obtained from natural infection or vaccination was considered lifelong (Kretzschmar et al., 2009; Shouval, 2003; Williams et al., 1996; Zanetti et al., 2008; Zhao et al., 2000). Fig. 1 illustrated the model structure and parameters, and the related first order ordinary difference equations were showed below (Eqs. (1) and (2)).

For individuals aged 0 year:

$$\begin{cases} S(0,t) = b(t)N(t)[1-v(t)\omega(t)] \\ C(0,t) = 0 \\ I(0,t) = b(t)N(t)v(t)\omega(t) \end{cases} \quad (1)$$

Where $N(t)$ is the total number of individuals in the population in year t. For individuals aged 1–100 years:

$$\begin{cases} S(a+1,t+1) = S(a,t)\left[1-\lambda(a,t)-\mu(a,t)\right] \\ C(a+1,t+1) = C(a,t)\left[1-\mu C(a)-\mu(a,t)-\gamma\right]+S(a,t)\lambda(a,t)\left[1-\mu A(a)\right]q(a) \\ I(a+1,t+1) = I(a,t)\left[1-\mu(a,t)\right]+S(a,t)\lambda(a,t)\left[1-\mu A(a)\right][1-q(a)]+C(a,t)\gamma \end{cases} \quad (2)$$

The model was run from 1992 to 2006 using the software of Matlab 2010b (the MathWorks, Inc.).

2.2. The force of HBV infection

The force of infection (λ) is defined as the probability per unit of time that a susceptible person becomes infected (Muench, 1959). Theoretically, it can be written as follows (World Health Organization, 2008):

$$\lambda = k\beta\frac{C}{N} \quad (3)$$

Where C is the number of infectious individuals, N the total number of individuals in the population, k the average number of contacts made by an infectious individual, and β the probability of transmission following a contact between infectious and susceptible individuals.

This expression represents the simplified case that the force of infection of an infectious disease depends on both the nature of the disease (β) and population characteristics (k and C/N). We modified Eq. (3) to Eq. (4) to express the age- and time-dependent force of HBV infection in our model.

$$\lambda(a,t) = k(a,t)\beta(a,t)\frac{C(t)}{N(a,t)} = \varphi(a,t)\frac{C(t)}{N(a,t)} \quad (4)$$

Where $C(t)$ denotes the total number of individuals with chronic HBV infection in the population in year t, $N(a,t)$ the total number of individuals in age group a in year t, $k(a,t)$ the average number of contacts in age group a in year t made by an infectious individual with any age, and $\beta(a,t)$ the probability of transmission in age group a in year t following a contact between infectious and susceptible individuals. φ is the product of k and β, which is usually called the "transmission coefficient" in mathematics. $C(t)$ was not divided into different age groups, and that is because available data are insufficient to characterize the transmission relationship between different ages.

We estimated the age-dependent force of HBV infection in the initial year of the model from the national serosurvey data in 1992 (Dai and Qi, 1999), by a modified simple catalytic model (Eq. (5)). Catalytic model (Muench, 1959), a method of estimating the incidence of infection from the prevalence of antigen and/or antibody to the infectious agent, has been widely used in infectious diseases (Yukich et al., 2012; Zhuang et al., 2008).

$$P(a) = 1-\exp\left[-\int^{0a}\lambda(a)da\right] \quad (5)$$

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