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ORIGINAL ARTICLE

A model program for hepatitis B vaccination and education of schoolchildren in rural China

Jonathan J. Chen · Ellen T. Chang · Yi-Ren Chen · Meredith B. Bailey · Samuel K. S. So

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Abstract
Objectives Incomplete hepatitis B virus (HBV) vaccine coverage and poor HBV-related knowledge in China leave millions of children unprotected from this life-threatening infection. To address these gaps, a pilot program for HBV education and vaccination was launched in rural China.
Methods In 2006, public and private organizations in the US and China collaborated to provide HBV education and vaccination to 55,000 school-age children in the remote, highly HBV-endemic area of Qinghai Province. The impact of the educational program on HBV-related knowledge was evaluated among more than 2,800 elementary school students.
Results Between September 2006 and March 2007, the three-shot hepatitis B vaccine series was administered to 54,680 students, with a completion rate of 99.4%. From low pre-existing knowledge levels, classroom educational sessions statistically significantly increased knowledge about HBV risks, symptoms, transmission, and prevention.
Conclusions This program offers an effective and sustainable model for HBV catch-up vaccination and education that can be replicated throughout China, as well as in other underserved HBV-endemic regions, as a strategy to reduce chronic HBV infection, liver failure, and liver cancer.

Keywords Hepatitis B · Vaccine · Education · China

J. J. Chen · E. T. Chang · Y.-R. Chen · M. B. Bailey · S. K. S. So (✉)
Asian Liver Center at Stanford University, 490 S. California Avenue, Suite 300, Palo Alto, CA 94306, USA
e-mail: samso@stanford.edu

E. T. Chang
Cancer Prevention Institute of California, Fremont, CA, USA

E. T. Chang · Y.-R. Chen · S. K. S. So
Stanford University School of Medicine, Campus Drive, Stanford, CA, USA

Introduction

In China, hepatitis B virus (HBV) is the primary cause of liver cancer, the second leading cause of cancer death among men and the fifth among women (Curado et al. 2007). Roughly 100 million people in China, comprising 7–10% of the nation's population, are chronically infected with HBV (Liu and Fan 2007; Custer et al. 2004), and the infection kills more people in China each year than tuberculosis, HIV, and malaria combined (Goldstein et al. 2005; World Health Organization (WHO) 2009; World Health Organization (WHO) et al. 2006; World Health Organization (WHO) 2008b).

Without adequate protection, as many as 90% of newborns who acquire HBV from their chronically infected mothers at birth will themselves go on to develop chronic (i.e., lifelong) HBV infection (World Health Organization (WHO) 2007), putting them at a 1-in-4 risk of eventually dying from liver cancer or liver failure (World Health Organization (WHO) 2008a). In China, up to 40% of chronic HBV infections are acquired through this route, and another 50% are acquired horizontally during childhood, most likely through close contact with infected family members (Gust 1996; Yao 1996; World Health Organization (WHO) 2007). The remaining small minority of chronic infections in China are acquired later in life through sexual, health-care-related, parenteral (especially through injection-drug use), and other routes of

transmission (Shepard et al. 2006). Because nearly all chronic HBV infections in China are acquired in early life, the prevalence of chronic infection reaches its peak in 5- to 9-year-olds and is higher in rural areas, where rigorous preventive health care measures are less common and families are larger, than in urban areas (Yao 1996). Thus, early life is a critical window of opportunity for preventing HBV transmission through population-wide use of the hepatitis B vaccine.

In partnership with the Global Alliance for Vaccines and Immunization (GAVI), the Chinese government took the first major step toward eliminating HBV by providing universal free immunization of newborns starting in 2002 (Kane 2003). However, population coverage is incomplete, with timely administration of the hepatitis B vaccine birth dose estimated at 75.8% in 2003 (Centers for Disease Control and Prevention (CDC) 2007), and millions of children born both before and after the initiation of the newborn immunization program remain unprotected. Therefore, catch-up vaccination is needed for this vulnerable population that remains at high risk of chronic HBV infection.

Barriers to the elimination of HBV in China include not only incomplete vaccine coverage, but also a pervasive lack of knowledge about the disease. Even among healthcare and public health professionals in China, as many as one-third are unaware of the long-term health risks of chronic HBV infection, its asymptomatic nature, its routes of transmission, and how best to prevent transmission (Chao et al. 2010). Knowledge about HBV transmission and prevention is considerably lower in the general population (Cui et al. 2009; Li et al. 2009) and contributes to poor preventive practices (Xu et al. 2009), as well as widespread discrimination against those who are chronically infected (The Economist 2006; Xinhua Economic News Service 2009). Education about HBV is thus an important component of any program aiming to prevent HBV transmission in China.

Therefore, to take the first step toward creating a nationwide catch-up vaccination and education program, we developed a collaborative pilot program to provide free HBV education and catch-up vaccination to elementary schoolchildren of rural Hainan Prefecture in Qinghai Province, China. The prevalence of chronic HBV infection in Qinghai Province is as high as 18% (Xia et al. 1996), and pastoral populations in the region report liver problems as the most common disease and hepatitis as the most common infection (Foggin et al. 2006). Further, challenging socioeconomic, environmental, and geographic factors represent significant barriers to healthcare delivery in rural Qinghai Province. In the poor western provinces (including Qinghai) targeted by the China-GAVI project, timely hepatitis B vaccine birth-dose coverage in 2001–2003 was 68.0% and complete three-dose vaccine coverage was 49.5% (Centers for Disease Control and Prevention (CDC) 2007). By comparison, coverage rates were 94.1 and 81.9%, respectively, in the wealthier eastern provinces, where higher incomes and easier routes of transportation facilitate access to hospital care for childbirth, with related immunization services (Centers for Disease Control and Prevention (CDC) 2007; Cui et al. 2010). Therefore, this catch-up vaccination and education program was developed in a particularly challenging setting to ensure that it would be replicable and sustainable in other regions throughout China.

Methods

Study setting

The project took place from September 2006 to March 2007 and targeted ~55,000 boys and girls, aged 5–12 years, attending all 331 elementary schools in Hainan Prefecture, one of the six Tibetan autonomous prefectures in Qinghai Province, China. Qinghai is the largest yet least populated province in China (excluding autonomous regions), and Hainan Prefecture is among the nation's poorest prefectures, with 50% of rural households below the poverty line (International Fund for Agricultural Development, IFAD 2011). There are no major cities in Hainan Prefecture, and the mountainous terrain and limited routes of transportation make it difficult to administer healthcare. The population is mostly Tibetan and also includes Han, Hui, Mongolian, Tu, Salar, and other ethnicities (Qinghai Provincial Investment Promotion Bureau 2010), further complicating education and healthcare delivery.

Study partners

This program was developed through a partnership among the Asian Liver Center at Stanford University (ALC), the ZeShan Foundation, the China Foundation for Hepatitis Prevention and Control, the China and Qinghai Centers for Disease Control and Prevention (CDC), the Qinghai government, local hospitals, health and education departments, and elementary schools. The ALC developed and provided the educational materials and curriculum and performed educational training; the ZeShen Foundation donated funding support for the program; the China Foundation and CDCs coordinated the national and regional vaccination efforts, including the procurement of vaccines; and the Qinghai government and local health care providers administered the vaccines and coordinated the educational efforts with local elementary schools.

Vaccine administration

Doses of the hepatitis B vaccine were administered on-site at schools by local doctors, nurses, and CDC staff, under the supervision of the Qinghai CDC. Consent forms and information about the immunization program were developed by the Qinghai Health and Education departments, and distributed by each school to parents for their signatures. Vaccinations were scheduled around the school's academic calendar; the first shot was given during the first week of school in September, the second shot a month later, and the last was given 5 months later, during the week after spring break. Children who missed any shots were invited to receive free shots at local hospitals or clinics. Those who completed the three-shot vaccine course were given a keepsake, jade-colored "LiveRight" bracelet to promote hepatitis B awareness (Fig. 1). The health department took responsibility for any vaccine-related liabilities and reporting. Total vaccine and administrative costs were ~$2.50 USD per dose.

To prevent discrimination against chronically infected individuals (Economist 2006), we did not test for existing HBV infection status prior to vaccination. Therefore, all children in the program received the vaccine regardless of their infection status. No adverse vaccine-related events were reported.

Educational program

The initial phase of the educational program was implemented at 26 target schools with a total of 1,925 students. An instructor from the ALC led 45-minute classes on HBV risks, prevention, transmission, symptoms, and management, using newly developed teaching guides such as an educational song for younger students, cartoon posters for school hallways and classrooms (Fig. 2), informational calendars for students to bring home to their families, and Chinese-language reference handbooks for teachers and China CDC personnel. Because all students were vaccinated without prior serological testing for HBV, the educational program aimed to dispel any false sense of security by emphasizing that chronic HBV infection usually occurs early in life, that vaccination after infection is not protective, and that serological testing is needed to detect chronic HBV infection. Six-question multiple-choice knowledge surveys, which covered the topics of HBV prevalence in China, modes of transmission, symptoms, prevention, and vaccination, were completed anonymously by the students before and shortly after the educational session.

Fig. 1 Jade-colored "LiveRight" bracelets awarded to elementary school students who completed the three-shot hepatitis B vaccine series, Hainan Prefecture, Qinghai Province, China, 2006–2007

Fig. 2 Elementary school students viewing educational cartoon posters to increase hepatitis B awareness in Hainan Prefecture, Qinghai Province, China, 2006–2007

After initial results showed a significant improvement in HBV-related knowledge, the educational program was modified such that the ALC-developed educational materials were provided to China CDC staff members, who then distributed the materials and provided HBV-related training to local schoolteachers. These teachers then educated their students directly at all 305 remaining elementary schools in Hainan Prefecture (Fig. 3). This approach was adopted to integrate the educational program into existing school structure and to overcome language barriers resulting from the ethnic heterogeneity of the population, as teachers were able to use appropriate languages and regional dialects for their classes. Fourteen schools with a total of 908 students were randomly selected for measurement of HBV-related knowledge after the class using the anonymous six-question, multiple-choice knowledge survey.

Further documentation of the Qinghai hepatitis B vaccination and education program is viewable online at http://liver.stanford.edu/Media/documentaries.html#embed ("Across Qinghai").

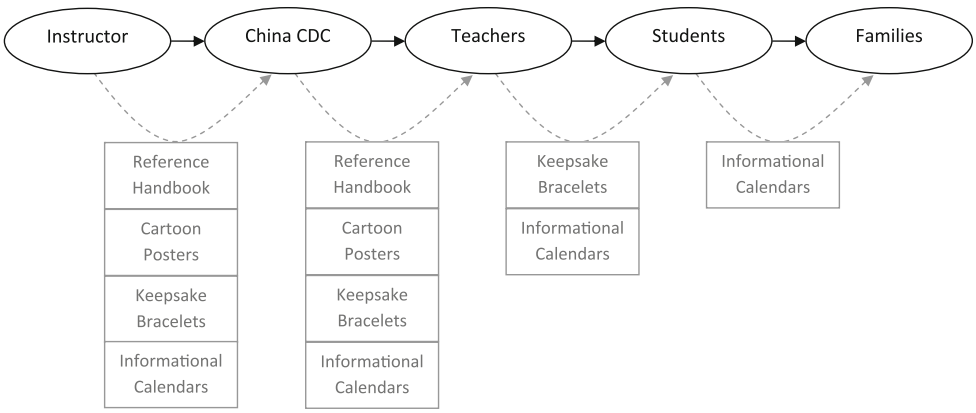

Fig. 3 Distribution chain of hepatitis B-related educational materials provided to elementary school students in Hainan Prefecture, Qinghai Province, China, 2006–2007

Statistical analysis

Chi-square tests were used to compare HBV-related knowledge survey results before and after the teaching sessions. Pre-existing knowledge about HBV and liver cancer was consistently poor across elementary schools in Hainan Prefecture, and post-education knowledge levels were similar between the 26 schools in the initial educational phase and the 14 randomly selected schools in the subsequent phase (data not shown). Therefore, we assumed that the pre-education data from the initial 26 schools were applicable to the remaining 14 schools, and we analyzed data from all 40 schools (2,833 students) together. All analyses were performed using SAS version 9.1, and all reported P values are two-sided.

Results

Of 55,010 Hainan Prefecture students at 331 elementary schools who received the HBV vaccine through this program, 54,680 students (99.4%) completed the full three-shot vaccine series at their school. Some of those who did not receive the second and/or third shots at their school may have completed the vaccine series at a local hospital or clinic, but these shots were not tracked.

Among the 1,925 students at 26 elementary schools who completed the initial phase of the educational program, HBV-related knowledge improved statistically significantly after the teaching sessions ($P < 0.0001$ for each survey question; raw data not shown). When survey data from all 2,833 students were combined, post-education knowledge was likewise significantly improved, as described below and shown in Table 1.

Prior to the educational sessions, only 21% of the students correctly answered that 1 in 10 Chinese are chronically infected with HBV, whereas the remaining 79% believed that chronic HBV infection was less common (from 1 in 100 to 1 in 10,000). After the sessions, 90% were aware of the true prevalence of chronic HBV infection in China, showing a statistically significant increase in knowledge ($P < 0.0001$).

On the pre-education survey, fewer than half of the students (49%) knew that HBV cannot be transmitted by sharing food with or casually contacting (e.g., shaking hands with or hugging) a chronically infected person. Of the remaining students, 22% thought that perinatal transmission—one of the major routes of HBV transmission in China—could not occur, while 29% were not aware that HBV can be transmitted via blood. After the educational sessions, 68% correctly identified shared food and casual contact as routes by which HBV is not transmitted ($P < 0.0001$)—a significant yet still incomplete gain in knowledge.

Before the teaching sessions, 61% of the students were aware that chronic HBV infection is usually asymptomatic, and that chronic carriers generally do not feel sick. After learning more about HBV through the educational program, this percentage increased to 82% ($P < 0.0001$).

Prior to the educational sessions, only about half (54%) of the students reported that getting vaccinated and developing immunity was the best method of preventing HBV infection. Instead, 16% reported that proper cleaning of food was the ideal preventive measure, and 12% believed that HBV transmission could best be prevented by avoiding dirty drinking water. Although disposing of used needles and syringes can indeed help to prevent HBV transmission, it is not the best preventive measure, as believed by 18% of students. On the post-education survey, 73% of students were knowledgeable about the most effective method of prevention ($P < 0.0001$).

Before completing the educational program, only a minority of students (46%) were aware that HBV cannot be transmitted through contaminated food and water, consistent with the minority of students aware that sharing food and casual contact are not routes of HBV transmission.

Table 1 Distribution of responses to hepatitis B knowledge survey among elementary school students in Hainan Prefecture, Qinghai Province, China, 2006–2007

Question and response	Pre-education survey*		Post-education survey†		*P* value
	N	%	*N*	%	
In China, 1 in __ people have chronic hepatitis B					
10,000	427	23	80	3	
1,000	416	22	62	2	
100	649	34	133	5	
10	394	21	2,515	90	<0.0001
Of the following routes, which will not transmit hepatitis B?					
Mother to child at birth	409	22	328	12	
Blood on knives	168	9	160	6	
Blood transfusion	376	20	383	14	
Sharing food, shaking hands, or hugging	916	49	1,847	68	<0.0001
Most people with chronic hepatitis B …					
… Feel sick	729	39	487	18	
… Do not usually feel sick	1,144	61	2,285	82	<0.0001
Of these methods, which is the best way to prevent hepatitis B?					
Making sure food is clean	305	16	205	7	
Getting vaccinated and developing immunity	1,003	54	2,021	73	
Not reusing needles and syringes	343	18	425	15	
Avoiding dirty drinking water	223	12	126	5	<0.0001
Hepatitis B is transmitted through food and water: true or false?					
True	1,006	54	537	19	
False	847	46	2,231	81	<0.0001
You need __ to be fully protected from hepatitis B					
1 shot	201	11	27	1	
2 shots	196	10	35	1	
3 shots	1,474	79	2,718	98	<0.0001

Missing and invalid responses are excluded

* Based on data from 26 schools with 1,925 students

† Based on data from 40 schools with 2,833 students

Subsequently, the percentage of students who correctly answered this question increased statistically significantly to 81% ($P < 0.0001$).

Finally, 79% of the students were already aware that 3 shots of the hepatitis B vaccine are required to confer protection against infection. Nevertheless, at the end of the teaching sessions, 98% of the students correctly answered this question, demonstrating a statistically significant improvement ($P < 0.0001$).

Discussion

In this pilot catch-up vaccination program in Hainan Prefecture, Qinghai Province, China, we successfully immunized 54,680 school-age children against HBV and increased their understanding of HBV risks, transmission, and prevention. We also educated local schoolteachers about HBV, thereby enabling them to continue educating future classes of students about the disease. In addition, by giving students informational materials to bring home to their families, we offered a means of disseminating HBV-related knowledge across multiple generations, with the goal of increasing community-wide preventive activity, eliminating misconceptions, and reducing discrimination against chronically infected individuals.

Of the children included in the immunization program, 99.4% completed the full three-shot hepatitis B vaccine series—a rate substantially higher than the 89.9% completion rate reported for newborns in China (Centers for Disease Control and Prevention (CDC) 2007), as well as high-risk populations in the United States (Louther et al. 1998; Doebbeling et al. 1996; Altice et al. 2005; Campbell et al. 2007; Sansom et al. 2003; Chang et al. 2009). The high completion rate in our vaccination program is likely attributable in part to the diverse coalition of partners in

this project, including academics, private foundations, local and national CDC divisions, health and education departments, hospitals, schools, and the provincial government, which maximized the knowledge base, reach, and public recognition and trust of the program. In addition, the immunization program was designed for maximum convenience to students by scheduling vaccination dates at the start of the school year and the return from spring holidays, when students are most likely to attend classes, and avoiding times of the year when students skip school to assist their families with farming. Finally, the vaccine completion rate may have been boosted by linking the immunization program with an educational program to increase students' and their family members' knowledge about the critical importance of HBV vaccination.

We could not evaluate whether educating students and local schoolteachers about hepatitis B had an effect on the vaccine completion rate. A randomized controlled trial of an education-only strategy to increase school-based hepatitis B vaccination in Australia showed no beneficial effect on vaccination rates (Skinner et al. 2000), but a U.S. program achieved higher hepatitis B vaccination rates in schools that provided educational interventions than those that did not (Wilson and Harman 2000). Whether or not it impacted the vaccine completion rate, the educational component of our program was appropriate given the low pre-existing knowledge about HBV that we observed among students. Before the teaching sessions, nearly half of the students did not realize that getting vaccinated was the best way to prevent HBV infection. In addition, the majority of students believed that HBV can be transmitted by sharing food, shaking hands, hugging, and consuming contaminated food and water. Based on such findings, it is not surprising that discrimination against chronically infected individuals is customary in China. Until recently, it was legal and commonplace for HBV testing to be required among students enrolling in schools and employees joining new companies, and for anyone who tested positive to be barred from entry (China Digital Times 2009). These discriminatory practices motivated our decision not to test students for HBV infection prior to vaccination, even though it is virtually certain that some of them were already chronically infected and therefore did not benefit from being vaccinated. Although the practice of mandatory HBV testing was prohibited by the Chinese Ministry of Health at the end of 2009 (Juan 2009), plans for enforcing the new policy are unclear. Regardless of the improvements in education and employment policy, social discrimination against chronically infected individuals remains prevalent in the general population, largely due to the misconceptions about how HBV is transmitted and how to prevent it. Thus, to abolish such discrimination, there is a clear need for education and catch-up vaccination to both inform and protect the vulnerable population. Such programs are not only beneficial to public health and society, but also cost-effective. Specifically, implementation of catch-up vaccinations in China—when compared with the thousands of dollars required for treating active chronic HBV infection, cirrhosis, or liver cancer (Zhiqiang et al. 2004)—could yield a net savings of 840 million in 2008 US dollars (5.7 million Chinese RMB) (Hutton et al. 2010). Other components of a comprehensive strategy to prevent HBV transmission include routine testing of all pregnant women for the hepatitis B surface antigen [implemented by the Chinese government in 2011 (Juan and Yao 2011)]; universal hepatitis B vaccination of newborns (with administration of birth doses of the vaccine and hepatitis B immune globulin, followed by post-vaccination serological testing, for all newborns of chronically infected mothers) (Centers for Disease Control and Prevention, CDC 2005); testing of high-risk individuals, including persons born in geographic regions with intermediate or high HBV endemicity, men who have sex with men, past or current injection-drug users, and persons receiving cytotoxic or immunosuppressive therapy (Weinbaum et al. 2008); and vaccination of individuals at risk for infection by sexual exposure, by percutaneous or mucosal exposure to blood (e.g., through injection-drug use or occupational work in health care or public safety), or during international travel to HBV-endemic regions (Centers for Disease Control and Prevention, CDC 2006).

Our results should be interpreted in light of some limitations. HBV-related knowledge was assessed shortly after the educational sessions, and we did not perform long-term follow-up to evaluate students' retention of HBV-related knowledge over time. Likewise, there was no practical way to follow students to determine whether they engaged in HBV-related preventive activity, such as getting tested for HBV infection, advising friends and family members to get tested and vaccinated, or teaching others about HBV prevalence, risks, transmission, and prevention. Finally, because we did not record students' demographic or other personal characteristics, we could not examine whether HBV-related knowledge or the likelihood of completing the vaccine series varied among important participant subgroups.

Despite these limitations, this project achieved an unprecedented 99.4% HBV vaccine completion rate in a geographically remote, ethnically and culturally heterogeneous, and materially disadvantaged population at high risk of chronic HBV infection. In addition, we significantly increased HBV-related knowledge among elementary schoolchildren and equipped existing schoolteachers with the tools and knowledge to educate future classes about HBV and liver cancer, thereby lending long-term sustainability to the project. Our accomplishments in such a

challenging environment suggest that our approach could be readily adapted for replication in other HBV-endemic regions. Based on our success, in 2008 we launched an expanded catch-up immunization effort to encompass the entire province of Qinghai. Widespread publicity and media coverage of this program, along with pre-publication notification of results from a cost-effectiveness analysis showing the benefits of a nationwide hepatitis B catch-up vaccination program in China (Hutton et al. 2010), helped to motivate the Chinese Ministry of Health in 2009 to introduce a 3-year nationwide program to provide free catch-up vaccination to all children under age 15 years. As a result of this nationwide effort, the Ministry of Health estimates that by the end of 2011, 83 million children under 15 years will have been vaccinated against hepatitis B. Such far-reaching efforts are essential to protect China's 340 million children (United States Census Bureau 2010) from falling victim to this lethal yet preventable disease.

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