PATH

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Study Summary

Evaluation of out-of-the-cold-chain approaches for improving on-time delivery of the hepatitis B birth dose in rural areas of China

Background

Hepatitis B virus (HBV) infection is endemic in China and perinatal HBV transmission is significant, causing one-third to one-half of infections. The World Health Organization (WHO) recommends vaccination of all infants against HBV infection. In countries where a high proportion of HBV infections are acquired perinatally, the first dose of hepatitis B (HB) vaccine should be given as soon as possible (within 24 hours) after birth.[1]

In developed parts of China most children are born in hospitals, and the HB birth dose is routinely given; but in rural areas home deliveries are common, and it is much more difficult to meet the 24-hour target for the HB vaccine birth dose. Awareness of the need for an immediate birth dose is low among village providers and rural parents. Where understanding of the need exists, compliance is poor: parents of children born at home are typically asked to take their infant to the hospital for immunization. In many locations the parents are sent to the hospital to pick up a dose of HB vaccine that the midwife or village doctor can then use to vaccinate the newborn.

Village doctors live in most villages, however they typically do not have refrigerators and usually provide vaccinations only during monthly, or less frequent, immunization days.

Chinese HB vaccine is packaged in single-dose ampoules and delivered with AD syringes.

Out-of-cold-chain study design

To improve the on-time delivery of the HB birth dose to children born at home, PATH, the Chinese National Vaccine and Serum Institute, and other partners designed a study to evaluate the safety and effectiveness of using the village doctors to provide the HB vaccine to children born at home. HB vaccine was stored out of the cold chain in the doctors' homes. The use of two different delivery systems, single-dose ampoules, and the Uniject™[*] device, were compared.

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[1] World Health Organization. Hepatitis B vaccine. *Weekly epidemiological record.* 2004; 79(28): 255–263.

[*] Uniject is a trademark of BD.

The study took place in 81 townships in three counties of Hunan Province. A total of 8,000 children were vaccinated with the birth dose of HB during the ten-month study. Townships were randomized into three groups:

1. HB vaccine in ampoules stored in the cold chain.
2. HB vaccine in ampoules stored outside the cold chain.
3. HB vaccine in the Uniject device (HB-Uniject) stored outside the cold chain.

Vaccine Vial Monitors (VVMs) were placed on all HB vaccines. Village doctors were instructed on how to safely store the vaccines out of the cold chain by avoiding direct sunlight and extreme temperatures. Participants from all groups were told of the importance of delivering the birth dose within 24 hours and were trained in safe injection and how to use their respective injection devices.

Baseline and final coverage surveys of 400 children per group were conducted to compare improvements in the delivery rates of the HB birth dose within 24 hours of birth. Interviews were conducted in order to determine the acceptability of the immunization strategies to vaccine providers. Analysis of seroconversion analysis was conducted on a randomly selected, fully immunized subset of each group (200 per group) to compare protective levels of antibody.

Results

Home births

Approximately 40% of the children in the study areas were born at home. Delivery of the HB vaccine birth dose within 24 hours of birth improved in the home birth subset of all three groups, with more substantial improvements occurring in the two out-of-cold-chain groups:

HB vaccine delivered within 24 hours of birth among children born at home

Group	Birth dose delivery within 24 hours of birth Baseline coverage survey	Birth dose delivery within 24 hours of birth Final coverage survey
1. Ampoule in cold chain	2%	25%
2. Ampoule out of cold chain	3%	52%
3. HB-Uniject out of cold chain	1%	67%

Hospital births

For the 60% of the children born in hospitals, on-time HB vaccine coverage was already high (88%–95%) and the study interventions resulted in no significant changes.

Complete HB vaccine coverage

Overall coverage of all three doses of HB vaccine was not impacted by the study interventions: baseline coverage was 71%–72%; final coverage was 70%–80%.

S*eroconversion*

Blood analysis showed comparable seroconversion among all three groups. Geometric mean titer (GMT) levels and protective levels of antibody to HB surface antigen showed no statistically significant difference between vaccine stored in ampoules in the cold chain or out of the cold chain, or vaccine stored in the Uniject device out of the cold chain.

Acceptability

Village doctors (Groups Two and Three) had no problems storing the vaccines out of the cold chain in their home offices. Most felt it was a practical and time-saving approach. Providers found the Uniject device easier to use than the auto-disable (AD) syringe, and most preferred the Uniject device. Over 90% felt the Uniject device was safe, accurate, and could save immunization time.

Temperature exposure

None of the vaccines stored out of the cold chain were exposed to excessive heat as indicated by VVM. Temperature monitoring showed one refrigerator in the cold chain group to be under 0°C for four months. Data loggers in the out-of-cold-chain group showed temperatures of 2°C to 30°C.

Conclusions

In rural areas, out-of-cold chain storage and delivery of HB vaccines is a safe and effective way to improve delivery of the birth dose within 24 hours of birth. Since many children are born at home and hospital-based immunization requires long-distance travel, better use of village-based vaccinators appears to be an effective strategy for improving on-time birth dose coverage. Out-of-cold-chain storage of the vaccines and delivery using the Uniject device or AD syringe mitigate many of the logistic and safety concerns of this approach.

Storing HB vaccine out of the cold chain does not reduce vaccine potency, especially when used with VVMs so that any heat-damaged vaccine can easily be recognized and discarded. In areas where cold chain freezing may occur, out-of-cold-chain storage of HB vaccine with VVMs could improve vaccine potency.

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