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Does Nigeria need the birth dose of the hepatitis B vaccine?

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Abstract: The control of hepatitis B infection involves several strategies of which the most effective is vaccination. Schedules which include a birth dose (which can prevent vertical transmission when administered within 24 hours of birth) are recommended for use in countries with a high rate of vertical transmission. Nigeria is highly endemic for hepatitis B infection. Nigeria had hitherto utilized the monovalent HBV vaccine in the three dose schedule that includes a birth dose, the recent introduction of an HBV containing pentavalent vaccine (which cannot be administered at birth) calls to question whether there should be continued use of the birth dose of HBV (using the monovalent vaccine) in addition to three doses of the pentavalent vaccine given subsequently. This is given the fact that most infections in Nigeria are reportedly acquired in childhood through horizontal rather than vertical transmission. There is also the question of cost- effectiveness of the four dose schedule compared to the three dose schedule in the setting of Nigeria's hepatitis B epidemiologic profile.

A review of the available evidence indicates that a significant proportion of Nigerian women of child bearing age and pregnant women are seropositive for HBsAg and HBeAg. Maternal to child transmission rates of HBsAg of 47-53.3% have been documented while a significant proportion of newborns were noted to have serological markers for HBV infection before receiving their first immunization. These data indicate that there is a significant potential for vertical transmission of HBV in Nigerian infants providing a compelling reason for the continued use of the birth dose of the HBV vaccine. Cost-effectiveness was not examined in this review.

There are, however, challenges to the universal delivery of the birth dose in a timely fashion. Encouraging institutional delivery, routine screening of pregnant women (with the administration of HBV within 24 hours of birth to infants of seropositive mothers), retraining of health care workers on ensuring the timely receipt of the birth dose of HBV vaccine and health education of mothers and the community on the need for immunization within 24 hours of birth are suggested strategies to improve the timely uptake of the birth dose of HBV

Keywords: Birth dose, Hepatitis B vaccine, Nigeria, Infants

Introduction

Hepatitis B virus (HBV) infection is a worldwide public health problem.[1] About a third of the world population has been infected while about 350 million persons are chronically infected.[1] Approximately 15-40% of infected persons will develop cirrhosis, liver failure or hepatocellular cancer.[2] HBV related deaths are about 600,000 annually making HBV the tenth leading cause of death worldwide.[2,3] Nigeria is highly endemic for the hepatitis B virus and most infections are reportedly acquired in childhood through horizontal transmission.[4] In Nigerian studies, lower prevalence of hepatitis B has been found in infants with prevalence increasing as age increases.[5,6] These studies did not however determine the contribution of vertical transmission. In Asia- Pacific region half of the chronic hepatitis B burden results from vertical transmission.[7]

The main strategy for prevention of HBV is vaccination.[8] For vaccination to be effective in preventing vertical transmission a birth dose of the HBV vaccine is required.[1] Nigeria had since 2004 utilised monovalent HBV vaccine in providing three doses of HBV immunization starting at birth.[9] In providing immunization against Haemophilus influenza type B a pentavalent vaccine comprising DPT, HBV and HiB was introduced to replace the trivalent DPT and monovalent HBV in

2012.[10] The pentavalent vaccine is administered as three doses commencing at the age of six weeks. Since the pentavalent vaccine cannot be given at birth Nigeria has continued to use the monovalent HBV vaccine to provide the birth dose of HBV vaccine. But does Nigeria need the birth dose of the HBV vaccine if infections are acquired horizontally? The World Health Organization recommends that in countries where a lower proportion of chronic HBV infection is acquired perinatally (e.g. in Africa) the administration of a birth dose may be considered after evaluating the relative contribution of perinatal HBV to the overall disease burden and the feasibility and cost effectiveness of providing a birth dose.[1] This article reviews the available evidence.

Epidemiology of Hepatitis B

The HBV is a small DNA virus. Humans are the only known natural host.[8] It is a 42nm virus made up of the surface antigen-HBsAg (which are 22nm spherical and tubular particles) and the core antigen HBcAg. The complete virion (Dane particle) comprises both the surface and the core antigens. The virus also has the HBeAg which is a soluble protein.

The prevalence of HBV varies from region to region as well as in different population groups.[2] The level of endemicity of HBV is based on the level of seroprevalence for HBsAg. Areas with HBsAg seroprevalence of greater than 8% are regarded as highly endemic while those with seroprevalence of 2-7% are considered to be of intermediate endemicity.[1] Areas with seroprevalence of less than 2% have low endemicity.[1] About 45% of the world population live in areas that are highly endemic for hepatitis B virus.[1] These include south East Asia, Sub Saharan Africa, the Pacific Islands and the Amazon basin. Areas of intermediate endemicity include Eastern Europe and China while areas of low endemicity include North America, Western Europe and Australia. Nigeria is considered to be highly endemic for HBV as various studies report seroprevalence rates of 9.1-12% in the general population[11,12] and 4.5-44.7% in children.[5,13,14]HBV is reported to contribute to 58% of chronic liver disease in a Nigerian study[15] while another study reported the presence of HBsAg in 59.3% of hepatocellular cancer cases in Nigeria.[16]

Transmission of hepatitis B and risk factors

The HBV is transmitted through percutaneous and mucous membrane contact with infected blood and other body fluids or contaminated sharp objects.[1,2] The major routes of transmission are vertically from an infected mother to her baby, horizontally from child to child, transfusion of unscreened blood and blood products, sexually, use of contaminated sharp objects during procedures such as administering injections, surgery, dental procedures, circumcision, tattooing, scarifications, traditional uvulectomy and ear piercing.[1,2,4,8] Other potential routes of transmission include sharing of tooth brushes etc.[4] Certain groups are considered to be at increased risk of HBV infection. These include household contacts of infected individuals, intravenous drug users, health care workers, homosexuals and individuals with multiple sexual partners.[8]

Vertical transmission is dependent on the presence of HBeAg in mothers.[1] Mothers who are HBeAg seropositive are 70-90% likely to transmit the infection to their babies compared to 5-20% of mothers who are HBeAg negative.[1] Vertical transmission is the major route of transmission in south East Asia where HBeAg seropositivity is high. In sub-Saharan Africa horizontal transmission is thought to be the commonest route of transmission with children becoming infected early in childhood and during the school years.[17] Newborn infection is uncommon in West Africa.[17]

The age at acquisition of HBV has important implications for outcome as infections acquired in infancy or early childhood are more likely to become chronic. About 80-90 % of infections acquired in the first year of life become chronic while 30-50% of infections acquired between 1-4 years of age become chronic.[1] Infections acquired in adulthood lead to chronicity in only2-5 % of cases.[1] Over time 25% of persons who acquire HBV as children will develop primary liver cancer or cirrhosis as adults.[2]

In Nigeria, children are believed to acquire most of their infections horizontally.[4] Eke et al[18] in a recent publication however suggests that vertical transmission may be the major route of transmission in Nigeria. Blood transfusion is also considered a significant route of transmission but several studies have shown a lack of association between blood transfusion and being seropositive for hepatitis B.[18,19] It has been suggested that this may be due to improved blood transfusion practices.

Prevention of Hepatitis B Virus Infection

Hepatitis B virus infection is preventable. There are various strategies for the prevention of hepatitis B. These include vaccination, strict observance of universal precautions and screening of blood and blood products for Hepatitis B infection. Vaccination is the most effective tool in preventing the transmission of HBV infection.[2] The HBV vaccine has been available and licensed for use since 1982.[1] There are various vaccination strategies. These include universal infant immunization, screening of all pregnant women so that babies born to those who are seropositive are offered the vaccine and HBIG within 24 hours of birth, adolescent immunization programme and targeted immunization of at risk groups such as health care workers and intravenous drug users. Improved blood transfusion practices have made the risk of transfusion –transmitted HBV extremely rare in the United States of America.[20] The United States of America uses a combination of strategies.[8]

The World Health Organization recommended the inclusion of the vaccine in all immunization programmes in 1997.[1] As at 2007 171 of the 193 WHO member states had included the vaccine in their national childhood vac-

cination programmes.[21] HBV vaccine alone given within 24 hours of birth has been shown to be 70-95% effective in preventing vertical transmission. The concomitant use of HBIG also given within 24 hours of birth is 85-95% effective in preventing both HBV infection and the chronic carrier state.[22] The use of universal infant immunization has reduced the prevalence of HBV related disease in countries where it has been introduced. Taiwan reduced the prevalence of HBsAg from 9.8% to 0.6% 20 years after the introduction of the HBV vaccine.[23] There was also a reduction in the incidence of hepatocellular cancer in children.[23] In Italy, after over 20 years of universal infant immunization HBsAg rates reduced from 13.4% to 0.91%.[24] A common factor among all these success stories is the fact that there was high coverage for the vaccine.

Hepatitis B Vaccine Schedules

There are at least three different schedules recommended by the World Health Organization for use in the introduction of the HBV vaccine into childhood immunization programmes (Table1).

Table 1: Hepatitis B vaccination schedules[1]

Age	Visit	Hepatitis B vaccine I	II	Dosing schedules III
Birth	1	HepB-birth[1]	HepB-birth[1]	
6weeks	2	HepB1[2]	HepB2[1]	DTP-HepB1[3]
10 weeks	3	HepB2[2]		DTP-HepB2[3]
14 weeks	4	HepB3[2]	HepB3[1]	DTP-HepB3[3]

1 Monovalent vaccine
2 Monovalent or combination vaccine
3 Combination vaccine

Countries where vertical transmission is a major mode of transmission are advised to use schedules that have a birth dose.[1] Nigeria adopted the three dose schedule starting at birth, then at 6weeks and 14 weeks into its immunization programme in 1995 and the vaccine became widely available in 2004. In this schedule the monovalent HBV vaccine was utilized. More recently in 2012 Nigeria introduced the pentavalent vaccine which comprises DPT,HBV and HIB. The pentavalent vaccine replaced the trivalent DPT and monovalent HBV. The pentavalent vaccine can only be commenced at 6 weeks thus Nigeria has retained the birth dose of monovalent HBV which is recommended to be given within the first two weeks of life. The question is does Nigeria need the birth dose of HBV if the major route of transmission is horizontal?

Hepatitis B in Women of Child Bearing Age and Pregnant Women

Many studies in Nigeria have reported HBsAg seroprevalence in pregnant women. Luka et al[25] reported a prevalence of 8.3% among pregnant women in Kaduna; a similar prevalence was also reported by Eke et al[19] in pregnant women in Nnewi. In Benin City a prevalence of 12.8% was reported also in pregnant women while a prevalence of 8.9% was reported among women of child bearing age in Lagos.[26,27]

The presence of HBsAg in a significant proportion of pregnant Nigerian women suggests that Nigerian infants are indeed at risk of vertically acquiring the infection. There have also been studies on HBeAg in the Nigerian population. In a study of 572 HBsAg positive persons 110(19.2%) were found to be positive for HBeAg.[28] Of those positive for the HBeAg the majority (81.8%) were however males. In another study that compared pregnant and non-pregnant women of child bearing age HBsAg was found in 7.9% of pregnant women and 7.6% of the non-pregnant women.[29] However, significantly more of the seropositive pregnant women (62.5%) were also positive for HBeAg compared to the non-pregnant women. The authors did not have an explanation for the significant difference. Another study on pregnant women reported that 7.9% of those seropositive for HBsAg were also positive for HBeAg.[30] Although the prevalence of HBeAg, a marker of viral replication and infectivity, which is also associated with higher vertical transmission rates is not as high as reported in south East Asia it nevertheless indicates the potential for significant vertical transmission of hepatitis B in Nigerian mothers.

In a study on mother infant pairs Onakewhor et al[31] reported a transmission rate of 42.86%. In a similar study in south west Nigeria a transmission rate of 53.3% was documented.[32] In a study of Nigerian mothers and their children (under-fives) 4 of the 7 seropositive children had mothers who were also seropositive while the mothers of the other 3 were seronegative.[6] This study could not however determine whether the transmission was vertical or post natal. In another study that examined mother-child pairs 13.2% of the mothers were seropositive while 6.9% of the children were seropositive.[33] Of the seropositive mothers 27.9% were also seropositive for HBeAg. 85% of the seropositive children were born to HBsAg positive mothers while 77.7% of HBeAg positive mothers had seropositive children. Although the findings of this study suggest that the children acquired the infections from their mothers it could not determine whether the infections were acquired vertically or horizontally.

A recent study on infants presenting for their first immunization noted that serological markers for HBV was present in29.4 % of the studied infants.[34] Most of these infants did not also receive the HBV vaccine within 24 hours of birth suggesting that even though they eventually did receive the vaccine they may have already been infected thereby constituting a waste of the vaccine. It is however pertinent to note that the presence of these markers do not necessarily mean infection as the markers may be a reflection of maternally transferred antibodies and the infants may clear the markers eventually.[35-37] That study as well as those on perinatal transmission is limited by their cross-sectional design as they could not determine if the infants with serological markers were eventually infected.

Justification for the Birth Dose of Hepatitis B Vaccine in Nigeria

The high HBsAg seroprevalence in pregnant Nigerian mothers, the presence of HBeAg in a significant proportion of HBsAg positive mothers and the study indicating the presence of serological markers in infants before receipt of their first immunization are compelling reasons for Nigeria to continue to offer the birth dose of the HBV to Nigerian infants. Also commencing immunization at birth is a better option since it can prevent both vertical and horizontal transmission.[34] It should however, be administered within the recommended time frame especially in infants of mothers who are positive or whose status is unknown.

Challenges of administering the birth dose of HBV in Nigeria

For the birth dose of HBV to be effective in preventing vertical transmission it is recommended that it be given within 24 hours of birth. There are several challenges to achieving the timeliness of delivery of the birth dose in Nigeria. Firstly many Nigerian women do not receive antenatal care. Antenatal care rate is 58% for at least one visit.[38] In addition many health care providers do not screen mothers for HBV antenatally. In one study only 5.9% of the mothers had been screened for hepatitis B infection even though over 80% had received antenatal care.[34] Such screening can identify babies at risk of vertical transmission who can then be offered the HBV vaccine within 24hours of birth in addition to HBIG given at a different site also within 24 hours of birth.

Another challenge is that most Nigerian women deliver outside health facilities. Institutional delivery rate is only 35%.[38] Babies born outside health facilities may not be able to access health care facilities for immunization within 24 hours. Many Nigerian infants initiate immunization late. Sadoh et al[39] reported that only 2 of 512 children presented for their first immunization in the first day of life, In another recent study only 1.3% of the studied infants presented within 24 hours of birth for immunization.[34] Olusanya et al[40] also reported that 31.8% of infants in Lagos were delayed beyond 3 months for the receipt of BCG, a vaccine that should be received at birth. In Sadoh et al's[39] study they also noted that despite the fact that many babies were born in health facilities they did not receive the birth dose of recommended immunizations before leaving the health facility.

For the Nigerian hepatitis B immunization programme to achieve a substantial decrease in HBV infections attempts should be made to ensure that birth doses of the vaccine are administered within 24 hours of birth. Nevertheless, a late birth dose may be better than no birth dose.

Strategies to improve uptake of the birth dose of hepatitis B vaccine

Several strategies are suggested to improve the uptake of the birth dose of the HBV vaccine. These include encouraging institutional delivery. If mothers deliver in health facilities then health care workers will be able to administer the birth doses of the vaccine to babies delivered in their facilities. Health workers will need to be retrained on the need for and strategies for timely administration of birth doses of vaccines to babies born in their facilities.

Innovative strategies such as the provision of single dose hepatitis B vaccine vials such as Uniject can be used to reach babies born outside of health care settings.[1] This would be within the framework of community care for newborns and their mothers. Community health extension workers attached to Primary health care facilities can be taught to use these single dose vaccines during home visits to parturients.

Health education of mothers and their communities on the need for timely administration of birth doses will ensure that babies are brought for birth doses of vaccines within 24 hours of delivery.
Prenatal screening of mothers will ensure that mothers know their status before delivery. For mothers who test positive health workers will emphasize the need for timely receipt of birth dose of the HBV vaccine. This strategy will be akin to that of the prevention of maternal to child transmission of HIV which has been found to be successful in reducing new cases of childhood HIV.

Further research

Most studies on the effectiveness of the HBV vaccine in prevention of perinatal transmission have had the birth dose of the vaccine given within 24 to 48 hours of birth.[41,42] The Paediatric Association of Nigeria (PAN) recommends that the birth dose be given from birth up to 2 weeks after birth.[43] Studies are needed to determine if such delayed birth doses are effective since if they are not they may constitute a waste of resources.

Cost effectiveness studies are also needed to determine if the 4 dose regimen is cost effective in Nigeria. This would also require the quantification of the contribution of vertical transmission to chronic HBV carriage in Nigeria. This is in tandem with PAN recommendation that there should be periodic review of the routine immunization schedule to enable its adaptation to changing disease and vaccine trends.

Conclusion

There is a significant potential for vertical and horizontal transmission of the hepatitis B virus in Nigeria. Therefore, administering the birth dose of the hepatitis B

vaccine is a good option for control of the hepatitis B infection in Nigeria as it protects the baby as early as possible from hepatitis B virus infection preventing both, vertical and horizontal transmission. The major challenge is in ensuring the timely administration of the birth dose to every child regardless of whether they are born in a health facility or not.

Author's contribution
Sadoh AE, Sadoh WE: : Conceptualized work, literature search and final draft.

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