Follow Up of Infants Born to Women with Hepatitis B in the National Maternity Hospital

Abstract:

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Abstract

Infants born to women with hepatitis B virus (HBV) are at risk of vertical transmission. This risk is significantly reduced with correct post-natal treatment. After initial perinatal management and neonatal treatment, these infants receive subsequent follow up HBV immunisations at two, four and six months. These infants then require post vaccination serological testing. This review was conducted to determine the number of infants born to mothers with HBV in the National Maternity Hospital who had appropriate post vaccination serological testing. There were seventyâ eight HBV infections identified antenatally in the years 2010 and 2011 resulting in seventy live born infants at our institution. Thirteen (18.6%) infants had evidence of post vaccination serological testing. This is below international rates of follow up. There is an urgent need for a centralised national programme to ensure adequate follow up and management of all infants born to women with HBV in Ireland.

Introduction

Infants born to women with acute hepatitis B infection or chronic carriers of hepatitis B virus are at risk of acquiring hepatitis B infection by vertical transmission. Without treatment, the risk of acquiring HBV perinatally is 70-90% in infants of women who are both hepatitis B surface antigen (HBsAg) positive and hepatitis B e antigen (HBeAg) positive. The risk of acquiring HBV infection is 5-20% in infants of women who are HBsAg positive but HBeAg negative[1]. Infants infected with HBV have a 90% risk of developing chronic infection with a 15-25% risk for premature death from cirrhosis or cancer of the liver[2]. It is estimated that between two and three hundred HBsAg positive women give birth in Ireland per year. There is currently no nationally agreed policy with regard to the management of these women and their infants. In the National Maternity Hospital (NMH) pregnant women are screened for hepatitis B infection as part of routine antenatal care. The risk of vertical transmission of HBV is decreased through antenatal serological screening and subsequent treatment of infants postnatally[3]. Perinatal transmission of HBV infection can be prevented in approximately 95% of infants with appropriate treatment. During delivery of the infant exposure to maternal blood is avoided as far as possible e.g. by avoiding use of fetal scalp electrodes and fetal blood sampling. The newborn infant is then routinely bathed in the delivery room. Following careful disinfection of the skin with alcohol, babies born to mothers who are HBsAg positive receive Hepatitis B Immunoglobulin (HBIG) via intravenous injection and HBV vaccination via intramuscular injection to provide both passive and active immunisation respectively. This treatment should be provided within 12 hours of delivery[2]. The practice in NMH is to provide treatment as soon as possible after delivery. All children then receive additional HBV vaccines at two, four and six months as part of the national immunisation schedule. Infants of mothers with hepatitis B require HBV serology at least 2 months after completion of this vaccination course to monitor response to treatment.

In the National Maternity Hospital, upon infant discharge, a letter is sent out to the registered GP requesting HBV serological testing at 8-10 months of age. Serum should be tested for HBsAg to exclude infection and anti-HBs to check for immunity[4]. If HBsAg is positive it is recommended to refer the infant to a Paediatric Infectious Diseases Physician. The Immunization Guidelines for Ireland state that an anti-HBs level > 10 mIU/ml is accepted as protecting against HBV. A booster of hepatitis B vaccine is recommended for low responders (levels between 10 and 99 mIU/ml) as infants born to mothers with active HBV infection are at increased risk of infection. It is recognized by the authors that international bodies including the Centers for Disease Control and Prevention (CDC) do not recommend a booster for all low responders. This may reflect a more conservative approach to the management of infants with hepatitis B in Ireland. It is expected that these infants are at increased risk of exposure to hepatitis B in the future from household contacts with known hepatitis B. An anti-HBs level greater than 99 mIU/ml indicates a good response to vaccination and these infants require no further action. This aim of this audit was to determine the number of infants born to mothers with HBV that had appropriate serological follow up.

Methods

The National Maternity Hospital microbiology database was used to determine the number of HBV notifications in the years 2010 and 2011. The hospital patient administration system (PAS) was then used to identify infants born to these women. At the National Virus Reference Laboratory (NVRL) each sample from a patient is given a unique bar-coded label on receipt of the specimen. All patient demographics are linked to this unique number and entered onto the laboratory information system (LIS). The LIS can be interrogated using specific patient search parameters to identify all laboratory records linked to that patient. In relation to the current study, this enabled the LIS to be searched for evidence of follow up samples from this patient cohort and the investigations performed. All following tests, using the Abbott Architect platform, the Architect HBsAg Qualitative II, the Architect anti-HBs and Architect anti-HBc were utilized. When necessary, additional assays for anti-HBs and anti-HBc were used to confirm the presence of low levels of anti-HBs or anti-HBc. This study was approved by the National Maternity Hospital Ethics Committee.

Results

There were seventy-eight HBV notifications in NMH over the two year period. The seventy-eight HBsAg positive women delivered seventy live-born infants at our institution. These included two sets of twins. One woman had a miscarriage and there was one infant stillborn. Fifteen of these infants would be considered high risk (HBeAg positive). There was no record of delivery for eight of the women with HBV notifications. Of the seventy live-born infants, there was evidence of post vaccination serological testing in thirteen (18.6%) infants. Three of these infants were in the high risk category. One of the thirteen tested infants was not tested for HBsAg. None of the twelve infants tested for HBsAg were positive. One other of the thirteen tested infants was not tested for anti-HBs. Of the twelve infants tested for anti-HBs,one infant had evidence of low response, although this infant was considered immune. Nine infants were tested for anti-HBc and seven of these infants were anti-HBc positive. The age at which infants were tested ranged from seven months to twenty-five months. The mean age at which infants were tested was ten and a half months.

Discussion

There was no evidence of post vaccination serological follow up in the majority of infants delivered to mothers with HBV in NMH during this time period. If we include only those women who had confirmed delivery of infants in NMH this shows that 13/70 (18.6%) had evidence of follow up. This is below international rates of follow up. The figure for post vaccination serological testing in the United States is over sixty three percent[2]. In the Netherlands this figure is higher again at eighty percent of children followed up with testing[5]. Post vaccination serological testing is important for guiding further management of infants born to mothers infected with Hepatitis B by allowing identification of infected or at risk infants[2]. In total four out of the thirteen (30.8%) infants tested had the correct tests performed at the correct time. The recommended tests of HBsAg and Anti-HBs were carried out in eleven out of thirteen infants tested. One infant was tested for HBsAg while not being tested for

Anti-HBs. Another infant was tested for Anti-HBs but not for HBsAg.

Among those tested, one infant out of thirteen had evidence of low response, although this infant was considered immune. The median seroprotection following a completed vaccination schedule in infants born to mothers with hepatitis B is as high as 98%[6]. Eight infants were tested for anti-HBc but this test is not considered a necessary part of follow up. This test usually reflects passive transplacental transfer of maternal IgG anti-HBc.

The age at which infants were tested although often exceeding the recommended time period on the standard letter sent to GPs of between eight and ten months, was still mostly within the time frame for testing according to the CDC of between 9 and 18 months[2]. Eleven of the thirteen infants were tested between eight months and twelve and a half months. One infant was tested just before seven months of age. The CDC does not recommend testing within one month of the completion of the standard HBV vaccine series. Detection of anti-HBs at this age may occur on account of the HBIG administered in the neonatal period. Testing at the recommended time improves the likelihood of detecting late HBV infection[7]. One infant was tested just before twenty-five months of age which is older than the recommended age and puts the infant at risk of either a delay in diagnosis of HBV infection or a delay in recognition of non-response to vaccination. It was noted that eight of the seventy eight women identified through antenatal screening did not deliver in NMH. It is unknown whether these women delivered infants in another hospital inside or outside of Ireland. This may be an indication that the group of women involved may reflect a highly mobile population. This possibility would create challenges for follow up of infants. GPs may not be informed of changes in address of infants in this group should they move elsewhere. Many of the women identified through antenatal screening are from countries where HBV is endemic[8]. As clinicians it is important to ensure that these patients understand the instructions that are provided with regard to follow up of their infants. This may include both written and verbal instruction in their first language and the use of patient held vaccine records. Such strategies may improve adherence to recommended follow up[9,10].

In Ireland, in spite of recommendations[11], there is no national program for screening of pregnant women for HBV infection or the follow up of infants born to mothers with HBV. It is estimated that between two to three hundred women with HBV deliver at risk infants in Ireland each year. About 50 of these infants would be considered highest risk for vertical transmission (maternal HBeAg positive). It is known that even with optimal treatment there remains a risk of transmission of HBV[12]. Although it is not possible to quantify harm in this audit, there is a potential that some children may develop hepatitis B infection or have non-response to vaccination and be at risk of acquiring hepatitis B infection in the future. Follow up of these infants has evolved on an ad hoc basis. The low level of serological testing identified in this study indicates that the current system for follow up of these infants relying on primary care is not working. It must be noted that this is a single centre study with limited generalisability. As there is currently no unified approach to follow up of infants born to women with hepatitis B in Ireland, it is probable that the method of follow up of infants in NMH is different from other units in the country who may have their own local policies.

There is a need for a centralised national programme to ensure adequate management and follow up of all infants born to mothers with HBV[13]. Resource implications would include the employment of a full-time nurse to ensure follow up occurs as per the Immunisation Guidelines for Ireland. Quality improvement programs could include family reminders, education, provider reminders and community coordination[14]. Accuracy and completeness of perinatal Hepatitis B infection reporting can help progress to eliminate HBV transmission[12]. Intensified follow up programs of at risk children have been shown to improve the completion of post vaccination serological testing[15]. The recent step towards the creation of a National Strategy and Protocol for Management of Infants Born to Mothers with Hepatitis B Infection is a welcome development. However, without supervision of such recommendations at a national level it is likely that many infants will remain at risk of hepatitis B infection.

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