POLICY ON THE USE OF PASSIVE IMMUNISATION WITH HEPATITIS B IMMUNOGLOBULIN (HBIG) FOR INFANTS BORN TO HEPATITIS B INFECTED MOTHERS

Introduction

Infants born to hepatitis B virus (HBV) infected mothers are at high risk of acquiring HBV infection themselves, particularly if the mother has a high level of HBV DNA and hepatitis B e antigen (HBeAg) in her plasma. Without intervention the risk of transmission from an HBeAg seropositive mother is 70%-90% compared with the risk of about 10% from an HBeAg negative mother.[1,2,3]

Role of post exposure prophylaxis (PEP)

A combination of various doses of hepatitis B vaccine and human anti-HBs immunoglobulin (HBIG) has been shown in many studies in Europe[4,5,6] and elsewhere,[7] to be highly effective in reducing vertical transmission from chronically infected women. Studies with groups given recombinant vaccine starting at birth at a dose of 5 micrograms or more, have suggested protective efficacy levels above 90% even without the use additional HBIG.[8,9,10] A review in 1994 concluded that the factors which influence protection are vaccine dose, starting immunisation at birth and completing the course of immunisation. Studies in HBeAg seropositive women have suggested that the development of chronic infection in the infant – that is vaccine failure – is associated with high maternal viral load; the role of specific viral mutations is less certain.[11,12,13]

The vast majority of these studies were limited to term infants born to HBeAg seropositive women and so provide little evidence for the effectiveness of PEP in babies of anti-HBe positive women. Studies of infants born to anti-HBe positive women suggest that the development of chronic infection is uncommon, even in those given vaccine alone.[4,5,14] The UK recommendation is therefore that such infants should only receive vaccine, without additional HBIG. The lack of evidence for the additional benefit of immunoglobulin in such infants was recently restated in a systematic review.[15] Studies in pre-term infants are limited to those that document the immune response to vaccine and no data on the effectiveness of PEP in premature infants exists. The early response to hepatitis B vaccination, however, is known to be lower in pre-term than term infants,[16] although final response rates are comparable. Since 2006, as a precautionary measure, HBIG has been recommended, in addition to vaccination, in very premature infants born to any HBV infected woman.[17]

Current policy and procedures

Since April 2000 it has been recommended that all pregnant women in England and Wales should be offered testing for hepatitis B through screening for HBsAg, and that all babies of HBsAg seropositive women should be immunised (HSC 1998/127).[18] A dose of paediatric hepatitis B vaccine is recommended for all infants born to an HBV infected mother as soon as possible after birth, then at 1 and 2, and 12 months of age. For the “high-risk” infants (Box 1) of HBsAg seropositive mothers, 200iu HBIG is recommended by deep intramuscular injection as soon as possible after birth, not later than 48 hours.[17]

BOX 1

The following infants are considered "high-risk" and should receive both vaccine and HBIG (2006)

Mother is HBsAg seropositive and HBeAg positive

Mother is HBsAg seropositive and HBeAg/anti-HBe negative

Mother is HBsAg seropositive and e markers are not available,

Mother has acute hepatitis B in pregnancy

Mother is HBsAg seropositive and infant is born weighing 1500g or less

Infants of "low-risk" HBsAg seropositive mothers with a birth weight above 1500g should receive vaccine alone as soon as possible after birth, then at 1 and 2, and 12 months of age.

The Health Protection Agency holds supplies of HBIG and issues each dose in readiness for the birth of a named baby to a "high-risk" woman. The infant is then followed via the GP or paediatrician and the immunisation dates and results of testing collected. For "low-risk" women, follow up is usually by paediatric specialist or general practitioner and local coordination and audit is recommended.[18]

Evaluation of the current policy

An HPA audit of infants eligible for HBIG in the UK confirmed chronic infection in around 26/543 (4.9%) of their infants rate despite receiving HBIG and vaccination.[19] The chance of a baby becoming infected with hepatitis B depended on year of birth, maternal HBeAg status and ethnic group. There was a higher risk of infection in the babies born to mothers who were HBeAg seropositive and anti-HBe seronegative compared with other groups eligible for HBIG (see above). The role of gestational age or birthweight was not examined.

A more recent audit of HBsAg seropositive women in Bradford documented chronic infection in 4/57 (7%) infants born to HBeAg positive women compared to 0/219 (0%) infants born to anti-HBe positive women who were given vaccine alone (personal communication, Leema Inamdar). In addition to infants who developed chronic infection, only a small proportion of babies had convincing evidence of resolved infection (an anti-HBc inhibition of 90% or above). In total the transmission rate in was 11/57 (19%) and 1/211 (0.5%) in babies born to HBeAg seropositive and anti-HBe positive women respectively. The single infection detected in the child of an anti-HBe positive woman was vaccinated on the date of birth but the second dose was delayed to 7 weeks of age. This suggests that vaccination alone is sufficient to largely prevent transmission and therefore to prevent cases of both chronic and acute infection in infants born to anti-HBe positive women. These data support the effectiveness of the current UK policy when correctly implemented.

Other UK audits of the programme show a wide range of vaccine coverage and timeliness of vaccine administration.[20,21,22,23] Two evaluations in inner city districts with high population mobility and relatively high HBV prevalence managed to achieve 90%

coverage for three doses of vaccine, but routine data submitted from 121 English PCTs to the HPA suggests that only 70% of eligible children have received three doses of vaccine by the age of one year.[24] Nearly all published evaluations have failed to document follow up blood testing of a representative sample of the at-risk population. Improving the coverage of immunisation and follow up testing is therefore clearly a priority for local resource allocation.

The role of viral load testing

Over recent years, viral load testing has become a common investigation in the management of chronically infected individuals. Many antenatal women may have been assessed prior to pregnancy or, if identified during pregnancy, are now being assessed before delivery. This has raised the question of whether infants born to anti-HBe seropositive HBV infected women with high viral loads should be considered for HBIG.

Based on the evidence outlined above there is no compelling case to offer HBIG to the infants of anti-HBe positive women, and therefore no case for recommending routine viral load testing in pregnancy. However, it is recognised that for women who have viral loads measured for their own management, a small number will be found to have levels approaching those in HBeAg positive women. It is therefore proposed to permit the use of HBIG in infants of women who are found to have viral load equal to or above 1×10^6 ius/ml. This level correlates well with HBeAg status in one London study,[25] and equates to a level of around 5×10^6 copies/ml which correlated with HBeAg status in the review for the Department of Health policy on infected health care workers.[26] From 1st September 2008, HBIG will therefore be issued by the HPA for the following babies (Box 2).

BOX 2

The following infants are considered "high-risk" and should receive both vaccine and HBIG (2008)

Mother is HBsAg seropositive and HBeAg positive

Mother is HBsAg seropositive and HBeAg/anti-HBe negative

Mother is HBsAg seropositive and e markers are not available,

Mother has acute hepatitis B in pregnancy

Mother is HBsAg seropositive and infant is born weighing 1500g or less

A woman who is HBsAg seropositive and known to have an HBV DNA level equal to or above 1×10^6 ius/ml in an antenatal sample*

* Please note the HPA is not advising routine viral load testing to inform the management of the infant.

Requests for immunoglobulin should be sent by post using the attached form (appendix 1) to:

Hepatitis B Infant Study Co-ordinator, Immunisation Dept
Health Protection Agency, Centre for Infections
61 Colindale Avenue, London, NW9 5EQ.
or faxed to 020 8327 7404.

To avoid delay, information on markers of infection, including viral load where performed should be clearly written on the form. HBIG will be issued to the named individual on the form approximately six weeks before EDD. Out of hours requests should go through the Colindale duty doctor on 0208-200-6868.

Mary Ramsay
On behalf of the Hepatitis Programme Board
12/08/2008

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ISSUE OF HEPATITIS B IMMUNOGLOBULIN FOR INFANTS AT RISK OF HEPATITIS B INFECTION

ANTENATAL PATIENT DETAILS

Mother's surname: _____ **First Name:**_____ **DOB:** _____

Hospital number: _____ **NHS Number:** _____

Home Address: _____

Ethnic Group: ☐ **Chinese** ☐ **Other Asian (Indian sub continent)** ☐ **Black** ☐ **White**

☐ **Other** **If other, please give details:** _____

Country of birth: _____ **PCT name:** _____

GP name & address: _____

_____

INDICATION FOR HBIG

Immunoglobulin is indicated for infants of mother with acute hepatitis or those who are HBsAg positive and anti-HBe negative or unknown

Acute Hepatitis **Yes** ☐ **Please give details of other risk factor for HBV infection:**_____

	Positive	Negative	Not tested
HBsAg	☐	☐	☐
HBeAg	☐	☐	☐
Anti-HBe	☐	☐	☐

Viral Load testing

For labs where Viral Load is taken, please note that HBIg will only be issued to women with viral loads which are greater than **1 x 10^6 iu/ml**

Viral load: ..... iu/ml

CURRENT STATUS

200iu HBIG will be posted to the designated person approximately six weeks prior to EDD

Delivered ☐ **In Labour** ☐ **Expected** ☐ **If expected, please give expected delivery date: __/__/____**

NOTE: IF BABY HAS ALREADY BEEN DELIVERED PLEASE ALSO COMPLETE THE BACK OF THE FORM

HBIG ISSUE

Please name the person authorised to receive/store HBIG at your location

Sister in Charge ☐ **Midwife in charge** ☐ **Pharmacist** ☐ **Other** ☐ **Please specify:**_____

Authorised person: _____

Deliver to:

Ward/Dept/Unit: _____ **Hospital Name:** _____

_____ **Tel no:** _____

Completed by: _____ **Contact no:** _____ **Date:** _____

During working hours: In an **emergency, HBIG** will be issued in response to a telephone call on **020 8327 6439 followed** by a faxed request to **020 8327 7404. Out of hours:** please telephone 020 8200 6868 and speak to a duty doctor. **Please send completed request form to: Hepatitis B Infant Study Co-ordinator, Health Protection Agency, Immunisation Dept, Centre for Infections, 61 Colindale Avenue, London, NW9 5EQ**

Customer Verified ☐

PLEASE COMPLETE AFTER BIRTH (CONTINUED FROM OVERLEAF)

DETAILS OF DELIVERY

Infant's surname: _____ **First name:** _____

Hospital number: _____ **NHS Number:** _____

Sex: Male ☐ **Female** ☐ **Date of Birth:** _____ **Time:** _____

Type of delivery: _____ **Birthweight:** _____

If multiple birth please specify: _____ **(Please complete a separate form for each sibling)**

DETAILS OF ADMINISTRATION

*The infant should receive **200iu** of **HBIG intra-muscular injection** and **0.5ml** of **Hepatitis B vaccine** shortly after birth*

HBIG
Date given: _____ **Time given:** _____ **Dose given:** _____ **Batch No:** _____

VACCINE
Date given: _____ **Dose given:** _____ **Make of vaccine:** _____**Batch No:** _____

DOCTOR RESPONSIBLE FOR FUTURE CARE OF THE INFANT

Who will be responsible for future vaccination of the infant?:

Paediatrician ☐ **GP** ☐

Consultant paediatrician: _____

Trust name: _____

Trust address: _____

_____

(only complete this section if GP details are not stated on page 1)

Name of GP: _____

GP address: _____

_____

Completed by:_____ **Contact no**: _____ **Date**: _____

Please arrange for an appointment for the infant to be given the **second dose of vaccine ONE-month** after the first.

Please send completed form to: **Hepatitis B Infant Study Co-ordinator, Immunisation Dept**
Health Protection Agency Centre for Infections
61 Colindale Avenue, London, NW9 5EQ