Infectious Diseases in Obstetrics and Gynecology 7:283–286 (1999)

Risk of Hepatitis B Transmission After Amniocentesis in Chronic Hepatitis B Carriers

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ABSTRACT

Objective: To measure the risk of perinatal transmission of HBV in chronic carriers who undergo amniocentesis.

Methods: This was a prospective, longitudinal study from 1990 to 1995 of women who were HBV carriers and underwent amniocentesis. The infants of these women were followed from birth to one year of age. Maternal data examined included HBV antigen and antibody status, liver function tests (LFTs) and the amniocentesis report.

Results: Twenty-eight women were identified. Two of 28 neonates were stillborn unrelated to hepatitis. Five infants were lost to follow-up leaving 21 mother-child pairs to evaluate. All 21 women were chronic HBV carriers at the time of amniocentesis for delivery. No mother had abnormal LFTs, and only one of 21 women was positive for hepatitis B e antigen (HBeAg). Thirteen amniocenteses were for advanced maternal age, and four were for abnormal maternal serum alphafetoprotein (MSAFP) screening. None of the amniocenteses were recorded as bloody, and the placenta was anterior in 6 of 21 procedures. None of the 21 infants (95% CI: 0–16.8%) were positive for HbsAg during the first month of life or at 12 months of age. All infants received HBV vaccine and HBIG immunoprophylaxis.

Conclusion: The risk of transmission of HBV to the fetus after amniocentesis in women who are HBV carriers is low. Immunoprophylaxis in these infants was successful. Infect. Dis. Obstet. Gynecol. 7:283–286; 1999. © 1999 Wiley-Liss, Inc.

KEY WORDS

hepatitis B; amniocentesis; perinatal transmission

Hepatitis B virus (HBV) is readily transmitted from mother to infant. The majority of this transmission occurs to asymptomatic HBV carriers during labor and delivery. Although the mechanism of infection is uncertain, it is presumed to result from exposure to maternal blood, maternal secretions or maternal-fetal transfusion[1–5] and is more common in women with the hepatitis B e antigen.[2,5–7] Some authors have found indirect evidence of transplacental passage based on the presence of hepatitis B surface antigen (HBsAg) in amniotic fluid, the very early development of neonatal disease (< 1 month) and the development of hepatitis in a neonate whose mother's HBsAg disappeared in the third trimester.[4,7] These authors have suggested that transplacental passage may occur up to 10% of the time; however the mechanism for this transmission is not well understood.

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Clinical Study

Received 5 May 1999
Accepted 8 August 1999

Today, infants of mothers with active HBV infection receive hepatitis B immunoglobulin at birth and the hepatitis B vaccine series substantially reducing the risk of neonatal transmission.[8–12] Failures of immunoprophylaxis programs (as low as 1%) are usually due to noncompliance with vaccination protocols; however, a few failures (estimated to be less than 10%) may be due to antepartum transmission. [1,2,4–7,11]

Although the mechanism of antepartum fetal hepatitis B transmission is not well understood, there is concern that invasive procedures such as amniocentesis may increase the risk. Amniocentesis can result in disruption of the placenta with fetal and maternal blood exchange. Additionally, maternal blood from the uterus can be introduced into the amniotic fluid. It is unknown if fetal swallowing of infected amniotic fluid could lead to infection. Whether amniocentesis actually increases the fetal risk of hepatitis B acquisition through these mechanisms is unknown, and clinical reports are limited [13,14]. In this report, we review our experience with amniocentesis in a United States population of HBV carriers to measure if this procedure is associated with an increased risk of perinatal transmission.

SUBJECTS AND METHODS

In 1988 the Dallas County Health Department and Parkland Hospital began a comprehensive program to prevent perinatal transmission of HBV.[15–17] This program includes identification of mothers with HBV through HBsAG screening in pregnancy. The serologic diagnosis was confirmed by the presence of hepatitis B core IgG antibody and the absence of hepatitis B core IgM antibody. No quantitative testing for HBV by polymerase chain reaction was performed.

Infants born to mothers who are HBV carriers are given hepatitis B immunoglobulin (HBIG) at birth and started on the hepatitis B vaccine series. The vaccine series starts within 24 hours of birth, and continues at one and 6 months of age. Infants are followed from age 9 to 15 months and tested for hepatitis B surface antibody (HBsAb) response to the vaccine. If they are found to have an inadequate response and lack HbsAb, a repeat series of vaccinations is given. The presence of HBsAG indicates a prophylaxis failure.

Since 1990, an ongoing surveillance of maternal HBV carriers and their infants has been done jointly by the Health Department and Parkland Hospital. Women who were HBV chronic carriers and underwent amniocentesis during a pregnancy were identified. During this period, there were 101,002 deliveries at Parkland Hospital, and the HBV carrier rate was 0.6% (data not shown).

Statistical analysis was performed with EpiInfo 6.04a (Centers for Disease Control and Prevention, Atlanta, GA). Means and exact binomial 95% confidence intervals were calculated.

RESULTS

Six hundred and six women who were HBV chronic carriers were identified and underwent amniocentesis during their pregnancies. Five of the mothers and their infants were lost to follow-up. The remaining 23 mothers were chronic HBV carriers at the time of amniocentesis and at delivery. No women had evidence of liver transaminase dysfunction, and only one (5%) was positive for the hepatitis B e antigen (HBeAg). This incidence of HBeAg positivity is consistent with our obstetric population of HBV chronic carriers. One of the 23 infants presented at 32 weeks with hydrops and hydramnios. As part of the diagnostic work-up, an amniocentesis was performed. Two days after the amniocentesis, premature rupture of membranes with preterm labor occurred and a stillborn, severely hydropic fetus was delivered. The etiology of the hydrops was never determined, and no autopsy was performed. Another of the 23 infants was born with trisomy 18. The infant left the hospital with hospice care and died at 42 days of life prior to obtaining hepatitis B serology.

There were 21 remaining patients with liveborn infants and complete follow-up. The mean maternal age was 34 years, and 17 patients were over age 35. Fifteen women were black, four were Asian, and two were Caucasian. The mean gestational age at amniocentesis was 19.5 weeks. The primary indications for amniocentesis are listed in Table 1. Thirteen amniocenteses were performed for maternal age 35 years or greater, one amniocentesis was for abnormal MSAFP and four procedures were performed in women who were both greater than 35 years of age and had an abnormal MSAFP. One patient had multiple amniocenteses for Rh disease and two women had amniocenteses for lecithin-sphingomyelin (L/S) determinations. No proce-

TABLE 1. Indication and gestational age at the time of amniocentesis

Indication	Gestational age	# Patients
Abnormal MSAFP screen	16–20 weeks	1
Maternal age >35	16–20 weeks	13
Maternal age >35 and abnormal MSAFP screen	16–20 weeks	4
Rh disease	16,26,29,33 weeks	1
L/S determination	37 weeks	2

dures were recorded as bloody although 6 of the 21 procedures were performed in women with anterior placentas.

The mean gestational age at delivery was 38.4 weeks. All infants received HBIG at birth and completed the full course of the hepatitis B vaccine series. No infants were positive for HBsAg after completing the vaccine series when tested at 9 to 15 months of age (95% CI; 0–16.1%).

DISCUSSION

The majority of neonatal transmission of HBV occurs during labor and delivery.[1–2,11,4–5] Current immunoprophylaxis regimens which include maternal HbsAg screening, HBIG at birth and neonatal HBV vaccination, are effective in preventing most peripartum transmission.[3,8,9–10] With the success of neonatal prevention programs, attention should now be given to antepartum transmission, as neonatal immunoprophylaxis would likely be ineffective in fetuses infected prior to labor, in particular, those fetuses infected remote from delivery. Invasive antepartum procedures such as amniocentesis may increase the risk of antepartum transmission due to the possible introduction of maternal infected blood into the fetal circulation or the amniotic fluid. Because of the potential risk of transmission, many have recommended avoiding invasive antenatal procedures.[18–19]

Recent reports from Taiwan[13] and from the Netherlands[14] have reported the risk of HBV transmission in women who underwent amniocentesis. The Taiwan study reports on a group of HBV carriers with a high incidence of HBeAg (28%). This is a more infectious group of patients than is typically seen in the United States and in our population of patients where the incidence of the HBeAg is < 5%. In their study, two cohorts of patients were examined. In the first cohort, cord blood was compared in 35 HBV carriers who underwent amniocentesis with 65 HBV carriers who did not undergo amniocentesis. There was no difference in the occurrence of HBsAg in cord blood (2.9 vs 3.1% respectively). The researchers then compared 32 infants of chronic HBV carriers who underwent amniocentesis and completed immunoprophylaxis at birth with 3454 infants who did not have amniocentesis from the Taiwan National HBV Prevention Program. When tested at 9 months to 5 years of age, no difference was seen in HBV infection (9.4 vs 11%). Based on these results, the authors concluded that the risk of HBV infection after amniocentesis is low.

The report from the Netherlands described 15 HBV carriers. The group had a lower risk of infectivity than the Taiwan paper with only two (13%) women having HBeAg at the time of amniocentesis. None of the 15 infants were infected with HBV at birth. All infants received HBIG followed by vaccination, and all infants had protective levels of HBsAb at 12 months of age. The authors concluded that the risk of transmission of hepatitis B from amniocentesis was low in their study population. Their conclusions were limited by sample size and few highly infectious HBeAg positive women.

We reported our experience with 21 women in the United States who underwent amniocentesis and had complete follow-up of their infants. In our cohort, amniocentesis during the second and third trimester did not result in an increased risk of HBV transmission, even though 6 of the 21 procedures were in women with anterior placentas and one woman underwent multiple procedures. No neonate was born with congenital HBV infection, and immunoprophylaxis was successful when tested at 9 to 15 months of age.

Our sample size is small, which resulted in a 95% confidence interval of 0 to 16%. Because of this wide confidence interval, we cannot say amniocentesis does not increase the risk of HBV transmission. However, to decrease the confidence interval to < 5% would take 72 patients and 16 years at our hospital. Our findings, when considered with other reports, suggest that the risk of HBV transmission is low after amniocentesis. Our study population had a low incidence of HBeAg positivity, and we cannot make conclusions about the effect of HBeAg on the risk of transmission.

In summary, amniocentesis in a United States population of HBV carriers with a low prevalence

of HBeAg does not appear to increase the risk of antenatal HBV transmission. Hepatitis B virus chronic carriers who are contemplating amniocentesis may be counseled about the observed low risk of HBV transmission. Women with HBeAg and high infectivity should be counseled that the risk for HBV transmission may be higher and is currently uncertain.

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