PREVENTION & CONTROL

HEPATITIS C AND PREGNANCY

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Background: Hepatitis C is caused by a single stranded RNA virus of the family Flaviviridae (1). Six major genotypes of Hepatitis C are distinguished. Hepatitis C is usually transmitted by inoculation of infected blood or blood product or less frequently by sexual intercourse. HCV is more common in males than in females, in blacks than in whites and in middle-aged adults (30-50y) than in other groups. Up to 40% of people infected with Hepatitis C deny any iv drug abuse or high risk sexual behavior (2).

HCV is a major cause of parenterally transmitted hepatitis (90%) with unscreened blood donors. Screening of blood donors has markedly decreased the increased incidence of post-transfusion hepatitis. The incidence of transfusion hepatitis has fallen to 0.03% per unit transfused since the introduction of screening with anti-HCV assays.

The Center for Disease Control and Prevention (1998) cites a seroprevelance of 1.8 percent or 4 million infected Americans (1). In USA, the estimated number of new HCV infections annually exceeds 150.000 (1994, Alter & Mast) (3). Acute hepatitis C typically is mild and unnoticed. Up to 75% of infected individuals become chronic carriers and progress to cirrhosis and primary liver cancer. Chronic hepatitis C and related cirrhosis compete with alcoholic liver disease as the most common conditions seen in hospital hepatology practice in the United States. Together they are the most common cause of primary liver cancer there and in other regions of the world with low endemicity for hepatitis B . Hepatitis C related cirrhosis is the most common indication for liver transplantation in the United States (4).

Diagnosis: First line diagnosis detects antibodies to complementary DNA(cDNA). Second generation antibody tests, ELISA and supplementary RIBA-4 correlate well with results using reverse- transcriptase polymerase chain reaction PT-PCR. A positive antibody test denotes HCV infection but does not distinguish acute from chronic infection and gives no indication of the extent of viremia (HCV RNA level), virus burden in the liver; and the severity and prognosis of underlying liver disease. Further, acute hepatitis C can be overlooked; as seroconversion may be delayed many weeks and discrimination between acute and chronic infection is difficult (2). The incubation period is usually 7-8 weeks but varies from 3-21 weeks. Anti-HCV antibody is not protective in transmission. Hepatitis C antibody is present in approximately 90% of these patients. However the antibody may not be detectable for weeks

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after infection. PCR for HCV-RNA, then becomes useful (5).

Antepartum Management: Antepartum hepatitis C infection is not different compared to non-pregnant women. 75% of anti-HCV (+) individuals have chronic disease. Bahman and colleagues reported that 2.3 % of asymptomatic pregnant women were seropositive for anti-C antibody at Parkland Hospital. The risk factors included iv drug use, STD, increased age and parity, history of transfusion, multiple sex partners. Perinatal outcome was not adversely affected in seropositive women compared with seronegative controls. In similiar populations from San Juan, Puerto Rico, Desedo and associates found 1.9% prevelance. Silverman and colleagues found a seroprevelance of 4.3 % in pregnant women from a university hospital in Philedelphia Clinic. women had an incidence of 5.2% whereas only 1.5% of private patients were anti-HCV positive.

Hepatitis C infection is transmitted vertically to the fetus. 6% of exposed fetuses become infected. Using hepatitis C viral RNA, a marker for viremia, investigators found that 10% of mothers with (+) RNA assays had infected infants. Conversely, no infants born to anti-HCV(+)/HCV RNA(-) mothers developed infection . Floreani and co-workers found that 65% of anti-HCV(+) mothers had HCV-RNA.

Intrapartum Management: Currently, there are no methods to prevent transmission at birth. Also, the Center for Disease Control and Prevention do not recommend screening but neonates of HCV(+) mothers should be tested. No specific recommendations against pregnancy for anti-HCV seropositive individuals and no precautions specific to hepatitis C have been given for infected pregnant women and their babies (1). In HCV (+) women who are co-infected with HIV, elective cesarean section delivery is associated with a reduced risk of vertical transmission of the HIV and HCV. However, elective cesarean section is not recommended for women with chronic HCV infection alone (6).

Postpartum Management: Breast feeding is not contraindicated. HCV RNA and HCV antibodies have been detected in colostrum and breast milk but show no correlation with levels in maternal serum (Hunt et al, 1997). Long term prospective studies are required with large numbers of mother-infant pairs. These should stratify for levels of HCV RNA; with and without HIV RNA, mode of delivery, length of breast feeding and possible confounding factors for horizontal transmission postpartum.

According to the Center for Disease Control , studies to evaluate immunserumglobulin for prophylaxis against hepatitis C have been equivocal. Therefore, it seems reasonable to administer immunglobulin to the newborn of a mother who has anti-C antibody. The results of post exposure immunoprophylaxis, using pooled immunoglobulin preparation containing antibodies to E1/E2 , the "neutralizing" epitopes of HCV are disappointing according to some studies. As with other RNA viruses that have high rates of mutation; the ensuing diversity of genotypes and quasi-species favors emergence of "escape" variants under selective immunpressure.Vaccines are under development (2).

Antiviral Therapies: Women who have HCV-RNA detectable in serum should be considered for therapy after recovery from childbirth. Trials of interferon alpha with ribavirin show clearance of HCV RNA in 10-20% of patients with chronic hepatitis C (2). Women exposed to interferon inadvertently during pregnancy may be encouraged to continue pregnancy. In patients with acute hepatitis C during pregnancy, the use of interferon therapy should be considered with close monitoring (7). Eradication of the virus is most likely with low levels of viremia, elevated liver enzymes, low iron stores in the liver and cirrhosis. Young women with low levels of viremia are especially likely to become sustained responders (2).

Screening and Follow-up of Infants: Infants of women with hepatitis C, should be tested for HCV RNA on two occasions, between the ages of 2 and 6 months and again at 18 to 24 months along with serum anti-HCV (6).

According to another study, in children born to anti-hepatitis C virus antibody positive, hepatitis C virus should be investigated at 18-24 months of life. If alanin aminotransferase values are

normal and anti- hepatitis C virus is undetectable, follow-up should be interrupted. In children born to hepatitis C virus-RNA positive mothers , alanine aminotransferase and hepatitis C virus RNA should be investigated at 3 months of age.

1) Hepatitis C virus- RNA positive children should be considered infected if viremia is confirmed by a second assay performed within the 12 th month,

2) Hepatitis C virus-RNA negative children with abnormal alanine aminotransferase should be tested again for viremia at 6-12 months, and for anti-hepatitis C virus at 18 months

3) Hepatitis C virus-RNA negative children with normal alanine aminotransferase should be tested for anti-hepatitis C virus and alanine aminotransferase at 18-24 months, and should be considered non-infected if alanine-aminotransferase is normal and anti hepatitis C virus undetectable.

4) Anti-hepatitis C virus seropositivity beyond the 18^{th} month in a never-viremic child with normal alanine aminotransferase is likely consistent with past hepatitis C virus. (8)

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