Hepatitis C in Pregnancy

GEBELİKTE HEPATIT C

Murat SÖNMEZER*, Cem ATABEKOĞLU*, Cem DEMİREL*,Gülay KURTAY

***Dept. of Obstetrics and Gynecology Medical School of Ankara University, Ankara, TURKEY**

Summary

Objective: To research the recent literature about HCVand it's effects on pregnancy.

Result: Hepatit B virus has been long known the leading causative agent of the chronic hepatocellular disease. With demonstrating of HCV using molecular cloning techniques more attention has been taken to hepatit C virus since HCV is the most encountered agent of the patients with chronic hepatocellular disease recently.

Key Words: Hepatit C virus, Pregnancy

T Klin J Gynecol Obst 1999, 9:221-223

Özet

Amaç: Hepatit C virüsü ve gebelik üzerindeki etkilerini içeren en son literatür bilgilerini gözden geçirmek.

Sonuç: Uzun yıllar hepatit B virüsü kronik hepatosellüler karaciğer hastalığına en sık yol açan etken olarak bilinmekteydi. 1980 'li yılların başında moleküler klonlama tekniği kullanılarak HCV genomunun ortaya çıkarılması ve kronik hepatosellüler karaciğer hastalığı olanlarda en sık olarak HCV saptanması nedeniyle son yıllarda HCV'ye artan bir önem olmuştur.

Anahtar Kelimeler: Hepatit C virüsü, Gebelik

T Klin Jinekol Obst 1999, 9:221-223

HCV genome , differently from other agents of viral hepatitis, was demonstrated in the late 1980's using molecular cloning techniques (1). HCV is a RNA virus included in the flaviviridae group and causative agent of the disease known as "parenterally transmitted non-A , non -B hepatitis" for long time. It is among the most encountered agents of chronic hepatocellular disease and generally reported as to be the primary cause in developed countries such as USA, Japan and Western Europe.

Hepatitis C is responsible for the majority of post transfusion hepatitis (%90). A great proportion of acute infection results in asymptomatic carriage status, even though there is no clinically evident symptom in this stage, in liver biopsy chronic active hepatitis leading to cirrhosis can be observed (2).

Geliş Tarihi: 13.07.1998

Yazışma Adresi: Dr.Murat SÖNMEZER
1. Cadde 106/2
Bahçelievler, ANKARA

Diagnosis and Prevalence

Acute hepatitis C manifests itself as a mild, often subclinical infection within 6-9 months of viral exposure. Presenting prodromal symptoms are more frequently systemic and nonspecific such as nausea, vomiting, low grade fever ,coryzia , right upper quadrant pain, arthralgia, loss of appetite, fatigue and mild weight loss in some patients. Jaundice may not always accompany other symptoms. The episodically elevated transaminases is diagnostic for HCV infection and can not be observed in other forms of viral hepatitis. Protrombin time is generally not changed and if found to be prolonged then could be accepted as predictive of serious hepatocellular necrosis. With resolving acute infection aminotransferase levels usually return to normal values. It should be taken into account that the bilirubin levels remaining unchanged over 20 mg/dl is also accepted as predictive of severe disease.

Before the availability of reliable specific serologic tests for HCV, the diagnosis could be made

Table 1. Risk factors and prevalence of HCV (12)

risk factors		prevalence	
parenteral substance abuse	21-42%	parenteral substance abuse	70.8%
blood transfusion	6-17%	HIV (+) patients	11.6%
multiple sexual partners	6%	prostitutes	8.8%
no identifiable risk factor	40-50%	health care providers	1.2%

after exclusion of hepatitis A and B in patients with compatible history of hepatitis infection. Anti HCV specific antibodies appear within 3-5 months of the viral exposure. Even after the presence of specific serologic tests since serum levels of anti HCV antibodies can fluctuate, the diagnosis of hepatitis C could not always be made. In addition the detection rate of antibodies in acute infection is only 50 % (3) and does not differentiate between past and current infection . Considering these, the clinical significance of detecting anti HCV antibodies in acute phase is of limited value.

Though first generation ELISA lacks specificity and sensitivity, most of the authors recommend for repeating the results taken by first generation ELISA , using "recombinant immunoblot assay (RIBA)" and second generation ELISA. Furthermore also with second generation ELISA, when results is repeated it will have a false positivity rate of 50 % (4). The prevalence of HCV was reported to be 0.4-0.8% in volunteer blood donors. Because high risk groups are prevented from donating, this probably reflects an underestimated rate. This result is also confirmed in the study of Liddle and colleagues reporting the rate in Australia to be 0.3% (5). Nevertheless in a prospective study conducted by Marcellin and associates in an unselected population (pregnant women) the prevalence is reported as 3.9% with second generation ELISA (this rate dropped 2% with RIBA) (6). In another study by Reinus et all from New York it's reported as 4.5% in HIV (-) pregnant women (2. generation ELISA) (7).

In patients with positive anti HCV antibody results, using PCR technology the HCV RNA is detected by 26-92% (8-9).

Vertical Transmission of Hepatitis C Infection

Transmission routes of HCV is mostly similar to that of hepatitis B. Predominant risk factors include parenteral drug use , exposure to blood and / or it's products, tattoo, having multiple sexual partners, being health care provider. Recently it has taken attention that the prevalence of HCV is rather high in iv drug users. It has been also reported that it can be as high as 90% in individuals with regular parenteral substance abusing (5). Sexual transmission rate of HCV is reported as approximately 5% (5). HCV nucleotide sequences have been demonstrated in viral isolates from sexual partners of HCV positive patients (10). According to the size of injury , transmission could occur about 5-15 % in one needle stick (11). Even there couldn't be found any risk factor in as high as 50% of patients known to be infected by HCV, and in 25-50% of pregnant women , the most encountered risk factor is iv drug use in pregnant women.

Even if HCV transmits vertically, unlike hepatitis B and HIV infections it's transmission rate is not as high as reported earlier (45-67%) (5,13), and is not observed frequently in uncomplicated otherwise normal pregnancies (14). Studies from Europe reports a 50% rate , but it is much more in Japan. In a study conducted by Chang and colleagues vertical transmission rate of HCV is reported to be 0-15% (average 4.7%) (13). The most important factors influencing HCV transmission are circulating maternal viral titers and coinfection status with HIV. Currently it is known that low maternal circulating viral titers is linked to the low perinatal transmission rate. In addition it is observed that, in patients with concomitant HIV infection HCV transmission is higher. It is assumed that HIV does it by facilitating HCV replication.

While in patients having low HCV RNA titers no transmission is observed , the highest transmis-

sion rate is reported in patients having >1 million copies / ml (15). Furthermore as the transmission rate is reported to be 0-18% in HIV (-) patients, HIV (+) mothers transmit HCV as a high rate of 6-36%. Chang and associates proved high transmission rates of 39% in patients either having concomitant HIV infection or in those having high maternal circulating viral HCV RNA titers (>1 million HCV RNA copies/ml) (13).

Even if low titers of HCV RNA was detected in colostrum, it could not have been proved that HCV transmission occurs via breast feeding (16,17). In addition it is suggested that the titers of RNA levels in colostrum is not correlated with those in maternal serum (17). Also a study reports that cesarean section could reduce the transmission rate, it hasn't been confirmed by other investigators (18). Today it's not a routinely accepted concept to perform cesarean section in order to lower the transmission rate and currently there is not any effective way to prevent transmission.

Effects on Pregnancy and Treatment

As in non pregnant women the treatment is mainly supportive. Nausea, vomiting, prolonged difficulty of oral intake can induce premature uterine contractions by causing dehydration. It is wise to hospitalize these patients , provide sufficient hydration and monitorize for premature contractions. Patients must be encouraged about that it is not teratogenic, does not cause any kind of anomaly and not increase obstetric complications (19,20).

It's known that interferon a2b treatment is effective in mild and moderate forms of diseases but not in those with cirrhosis (21). Besides, this treatment modality is not recommended in pregnant women. There is no vaccine available for HCV and pre-exposure prophylaxis and post-exposure immune globulin use are not beneficial. Most experts are not optimistic that a vaccine will be developed in the next 10 years because of the subgroup diversity and frequent mutations.

Neonatal immunoprophlaxis doesn't seem to be available for neonates born from HCV (+) mothers currently (22).

REFERENCES

1. Choo Q-L, Kuo G, Weiner AJ. Isolation of a clone DNA clone derived from a bloodborne non-A , non-B viral hepatitis genome. Science 1989; 244:359-62.

2. Dienstag JL, Wands JR, Isselbacher KJ. Acute hepatitis Chapter 252 in Wilson JD, Braunwald E, Isselbacher KJ. Harrison's Principles of Internal Medicine, 12th ed. New York: McGrawHill, 1992: 1191.

3. Mara J, Dismoor. Hepatitis in the obstetric patient. Infectios Disease Clinics of North America 1997; 11(1): 77-91.

4. Lam JPH, McOmish F, Bums SM. Infrequent vertical transmission of hepatitis C virus. J Infect Dis 1993; 167 :572.

5. Marcellin P, Bernuau J. Prevalence of hepatitis C virus infection in asymptomatic anti- HIV1 negative pregnant women and their children. Dig Dis Sci 1993; 38:2151.

6. Reinus JF, Leikin EL, Alter HJ. Failure to detect vertical transmission of hepatitis C virus. Ann Intrn Med 1992; 117:881.

7. Liddle C. Hepatitis C. Anaest Intensive Care 1996; (24) 2:180-3.

8. Francois M, Dubois F, Brand D. Prevalence and significance of hepatitis C virus viremia in HCV antibody - positive subjects from various populations. J Clin Microbiol 1993; 31:1189.

9. Martinot-Peignous M, Maecellin P, Xu LZ. Reactivity of c33c antigen as a marker of hepatitis virus C multiplication. J Infect Dis 1992; 165:595.

10. Dienstag JL. Sexual and perinatal transmission of hepatitis C. Hepatology 1997; 26 (3 suppl 1): 66-70.

11 .Tibbs CJ. Methods of transmission of hepatitis C. J Viral Hepat 1995; 2(3):113-9.

12. Lynch-Salamon DI, Combs CA. Hepatitis C in obstetrics and gynecology. Obstet Gynecol 1992; 79(4): 621-9.

13. Chang MH. Mother-to-infant transmission of hepatitis C virus. Clin Invest Med 1996; 19 (5): 368-72.

14. Cuthbert JA. Hepatitis C: Progress and problems. Clin Microbiol Rev 1994; 7: 505.

15. Hunt CM, Carson KL, Sharara AI. Hepatitis C in pregnancy. Obstet Gynecol 1997; 89 (5 Pt 2): 883-90.

16. Grayson ML. Braniff KM, Bowden DS. Breastfeeding and risk of vertical transmission of hepatitis C virus. Med J Aust 1995; 163:107.

17. Lin HH, Kao JH, Hsu HY. Absence of infection in breastfed infants born to hepatitis C virus-infected mothers. J Pediatr 1995; 126:589.

18. Paccagnini S, Principi N, Massironi E. Perinatal transmission and manifestation of hepatitis C virus infection in high risk population. Pediatr Infect Dis J 1995; 14:195.

19. Bohman VR, Stetler RW, Little BB. Seroprevalence and risk factors for hepatitis C virus antibody in pregnant women. Obstet Gynecol 1992; 80: 609.

20. Floreani A, Paternoster D, Zappala F. Hepatitis C virus infection in pregnancy. Br J Obstet Gynecol 1996; 103:325.

21 .Davis GL, Balart LA, Schiff ER. Treatment of chronic hepatitis C with interferon alfa: multi - center randomized controlled trial . N Eng J Med 1989; 321:1501 -06.

22.Simms J, Duff P. Viral hepatitis in pregnancy. Semin Perinatol 1993; 17(6): 384-93.