Vertical transmission of hepatitis C virus (HCV) detected by HCV-RNA analysis

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Abstract

The rate of transmission of hepatitis C virus (HCV) from patients with chronic hepatitis C to their children was studied. Of the 64 children with a parent with chronic hepatitis C, two (3%) had abnormal alanine aminotransferase (ALT) activities, six (9%) had anti-HCV detected by c100 ELISA, seven (11%) had anti-HCV detected by ELISA-II, and 21 (33%) had HCV-RNA by polymerase chain reaction (PCR). Anti-HCV detected by ELISA-II disappeared within six months in all six infants. Of the five children whose mothers were given a blood transfusion after the child's first birthday, none had anti-HCV or HCV-RNA. In the five families whose elder or eldest offspring had HCV-RNA, all of the younger offspring had HCV-RNA. The vertical transmission rate of HCV was low if judged by the presence of anti-HCV or abnormal ALT values, but the rate was high (33%) if judged by the presence of HCV-RNA.

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Parenteral transmission of hepatitis C virus (HCV) is well documented. In about half of the cases of chronic hepatitis C, however, the route of transmission is unknown. Kamitsukasa *et al*¹ and Everhart *et al*² report that the risk of HCV infection through personal contact in the family is not high. Both studies, using anti-HCV detection, estimated the rate of familial transmission of HCV to be less than 10%. HCV-RNA can be detected by the polymerase chain reaction (PCR), results of which have shown that some carriers of HCV do not have anti-HCV. Thus, to evaluate the actual incidence of HCV infection, the presence of HCV-RNA should be determined. We evaluated the rate of vertical transmission and the prevalence of HCV infection among familial contacts of patients with chronic

hepatitis C, assessing the rate of transmission not only by the alanine aminotransferase (ALT) activities or anti-HCV, but also by the presence of HCV-RNA.

Methods

SUBJECTS

Index subjects consisted of 40 patients with chronic hepatitis C aged 21-54 years. All patients gave informed consent to the study. Of the 110 family members without a history of blood transfusion or drug abuse, eight spouses and 14 children refused to give a blood sample. The remaining 88 subjects (24 spouses aged 21-57 years and 64 offspring aged 2 months to 23 years) were tested for ALT, anti-HCV, and HCV-RNA. All 64 children had been breastfed after birth.

ANTI-HCV AND HCV-RNA TESTING

Anti-HCV was assayed with a c100 ELISA (ELISA-I; Ortho Diagnostics, Tokyo) and a second generation ELISA (ELISA-II, Ortho). HCV-RNA was detected by PCR, as previously described.^{3 4}

Results

AGE GROUPS

Of the 64 offspring taking part in the study, two (3%) had abnormal ALT values, six (9%) had anti-HCV by ELISA-I, seven (11%) had anti-HCV by ELISA-II, and 21 (33%) had HCV-RNA by PCR. Of the 14 children aged less than 1 year, one (7%) had an abnormal ALT value, five (36%) had anti-HCV detected by ELISA-I, six (43%) had anti-HCV detected by ELISA-II, and eight (57%) had HCV-RNA. Of the six infants with anti-HCV detected by ELISA-II, all were aged less than 6 months and their antibodies disappeared within six months of the first assay. These infants had detectable HCV-DNA but their anti-HCV seemed to have been transmitted from the mother. None of the children aged 1 to 5 years had an abnormal ALT or anti-HCV, but three (23%) had HCV-RNA. Of the 19 children aged 6 to 17 years, none had an abnormal ALT value or anti-HCV, but five (26%) had HCV-RNA. Of the 18 offspring aged 18 years and over (the oldest was 23), one had an abnormal ALT value and anti-HCV, and six (28%) had HCV-RNA (Table I).

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TABLE I Factors suggestive of hepatitis C virus (HCV) transmission to children, according to age group

Age	<1 year	1-5 years	6-17 years	≥18 years
Raised alanine aminotransferase activity (no (%))	1/14 (7)	0/13 (0)	0/19 (0)	1/18 (6)
Anti-HCV+ve:				
By first generation (ELISA-I) (no (%))	5/14 (36)	0/13 (0)	0/19 (0)	1/18 (6)
By second generation (ELISA-II) (no (%))	6/14 (43)	0/13 (0)	0/19 (0)	1/18 (6)
HCV-RNA+ve (PCR) (no (%))	8/14 (57)	3/13 (23)	5/19 (26)	6/18 (33)

TABLE II Factors suggestive of hepatitis C virus (HCV) transmission to children, according to the order of birth

	First offspring	Second offspring
Raised alanine aminotransferase activity (no (%))	1/23 (4)	0/23 (0)
Anti-HCV+ve:		
By first generation (ELISA-I) (no (%))	1/23 (4)	3/23 (13)
By second generation (ELISA-II) (no (%))	1/23 (4)	3/23 (13)
HCV-RNA+ve (PCR) (no (%))	5/23 (22)	9/23 (39)

TABLE III History of transfusion in mothers and relation to hepatitis C virus (HCV)-RNA in children

	Children with HCV-RNA	Children without HCV-RNA
Mothers without history of transfusion	2	4
Mothers given transfusion before birth of child	5	7
Mothers given transfusion in first year of child's life	3	9
Mothers given transfusion after child's first birthday	0	5

MULTIPLE OFFSPRING

Twenty three of the 40 families studied contained at least two offspring. Of the 23 elder or eldest offspring, five had HCV-RNA; all of the younger offspring and most of the other family members also had HCV-RNA. Four younger offspring had elder siblings without HCV-RNA; in two cases, the mother had received a blood transfusion after the birth of the first child but before the birth of the second (Table II).

The mothers who had received transfusions at some time before the birth of a child had a total of 12 children; of these children, five (42%) had HCV-RNA. The mothers who were given transfusions at some time after delivery of the child but before the child's first birthday had a total of 12 children; of these children, three (25%), in three different families, had HCV-RNA. In one of these families, HCV-RNA was detected in the breast milk. The mothers of five other children were given transfusions at some point after the child's first birthday. None of these children were positive for HCV-RNA (Table III).

Discussion

HCV is known to be transmitted by blood transfusion but the frequency of infection by sexual intercourse or by vertical transmission is apparently low when assessed by the presence of anti-HCV.^{1 2 4} Some reports suggest that HCV carriers may have normal ALT activities and lack anti-HCV antibodies.⁶⁻⁸ These

carriers can be identified by PCR. Thaler *et al*⁹ reported that all the children of eight mothers with HCV infection had HCV-RNA detected by PCR, contradicting the results of previous reports. Our results, as those of earlier reports, show a low rate of vertical transmission detected by the ALT value and the presence of anti-HCV but a much higher rate (33%) when HCV-RNA was detected by PCR. None of the children who were 1 year or older when their mother received a blood transfusion were infected; this suggests that HCV transmission generally occurs at birth or during nursing.

Clustering of HCV infection occurs in some families but not in others;^{10 11} the reason for this is unknown. It is possible that the amount of HCV in the serum affects the risk of transmission, as has been reported for hepatitis B virus.¹² Our 40 index patients were being treated for liver damage, and all had a high titre of anti-HCV and a large amount of HCV-RNA. This may explain the unexpectedly high rate of infection among their spouses and children.

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