Prevalence of hepatitis G virus in a haemodialysis unit

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Summary

Background **: Recently, a novel blood-borne virus has been identified and named hepatitis G virus. Transfusion is the main route of transmission. It is known that patients on maintenance dialysis are more susceptible to infections with parenterally-transmitted viruses than the general population. The aim of the present study was to determine the prevalence of hepatitis G infection in a Belgian dialysis unit.**

Methods **: The entire population of our dialysis unit (82 patients) was tested for the presence of hepatitis G virus (HGV) by reverse transcriptase polymerase chain reaction. History of transfusion or renal transplantation, coinfections with hepatitis B and C viruses, and serum aminotransferase levels were also tested.**

Results **: Thirteen patients (16%) were found positive for HGV-RNA. Among these patients, 69.2% were infected by the G virus alone, 15.4% were coinfected with B virus, and 15.4% with C virus. All but one patient had a history of transfusion. Ten of the thirteen infected patients (77%) had normal aminotransferase (< 30 UI/l). Three patients had elevated aminotransferase levels (23%) ; one was coinfected with B virus, one with C virus, and the last one had a diabetes-induced fatty liver infiltration. No liver biopsies were performed.**

Conclusions **: It is concluded that infection with G virus is common among dialyzed patients. This high rate of infection could be related to previous transfusions, but may as well be due to nosocomial transmission. In our series, at least one patient has been contaminated by another road than transplantation or transfusion. Finally, it does not appear clearly that chronic infection with hepatitis G virus induces liver disease, as defined by elevated aminotransferase level.** (Acta gastroenterol. belg., **1999**, 62, **13-15**).

Key words : GB virus C, hepatitis G virus, haemodialysis, viral hepatitis, non-A-E hepatitis.

Introduction

A new virus has recently been identifed, almost simultaneously, by two independent teams from the plasma samples of patients with chronic hepatitis. It has been named GB virus C (GBV-C) by one of these teams (1,2), and hepatitis G virus (HGV) by the other (3). GBV-C and HGV show over 95% homology in their nucleic acid sequences, and can therefore be considered to represent the same virus. It contains a single stranded, linear, positively polarized RNA of 9400 nucleotides (3). In common with the hepatitis C virus, it belongs to the flaviviridae family. It is, however, distinct from this virus, with which it shows only 25% sequence homology. The detection of HGV relies on the polymerase chain reaction (PCR) ; no commercial test capable of detecting viral antigen in serum is yet available.

Numerous studies are under way to better characterize the pathogenic role and modes of transmission of this virus. It now seems apparent that the transmission of HGV is primarily by the parenteral route, especially by transfusion of contaminated blood or blood products. Because patients having chronic haemodialysis are at high risk of infection with parenterally transmitted agents, this study was carried out on such a population, in order to determine the prevalence of the infection.

Patients and methods

All of the patients of the haemodialysis unit of the CHU Sart Tilman (Liège, Belgium) were asked to participate to the study of prevalence of virus G infection in the unit. All of them agreed and gave oral consent for blood analyses. This represented 82 patients (51 men and 31 women). The mean age of the patients was 56.0 ± 16.4 years (range 18-81). The patients had been treated by hemodialysis for chronic renal failure for a mean duration of 5.7 ± 5.6 years (range 0.02-28.07).

Serum from the patients was tested for markers of hepatitis virus infection, and serum levels of aminotransferase were measured.

HGV RNA was detected using a reverse transcription polymerase chain reaction (RT-PCR) using (G8-G11) primers deduced from the non-structural region (NS3) (4). We simultaneously sought markers of hepatitis B and C infections, in order to assess coinfections. Serum samples were tested for HBsAg, anti-HBs, and anti-HBc by enzyme-linked immunosorbent assay (EIA) using commercially available tests (Abbott laboratories North Chicago). Serum samples were also analyzed for anti-HCV antibodies with a third generation EIA (Abbott laboratories North Chicago). Finally, we attempted to determine if there was a relation between the presence of HGV infection, and the duration of dialysis, a history of renal transplantation or transfusions, and/or altered levels of aminotransferases.

For comparison of ratios we used Fisher's exact test and for comparaison of continued parametres we used a Student's t-test.

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Results

Table I summarises characteristics of the 82 patients on maintenance haemodialysis. Thirteen of the 82 patients were found to be positive for HGV-RNA (16%), nine patients were HCV seropositive (11%), three patients were HBsAg carriers (4%), and 16 patients presented profiles typical of resolved HBV infection (19.5%).

Table I. — **Characteristics of dialyzed patients**

Number of patients	82
Sex	
men	51 (62%)
women	31 (38%)
Duration of dialysis (mean (range))	5.7 years (0.02-28)
Age (mean (range))	56 (18-81)
Etiology of renal insufficiency :	
– glomerulonephritis	15 (18%)
– vascular nephritis	16 (19%)
– tubulointerstitial nephritis	4 (5%)
– diabetic nephropathy	8 (10%)
– pyelonephritis	10 (12%)
– polycystic kidney disease	10 (12%)
– miscellaneous	17 (21%)
– unknown origine	2 (2%)
Previous transplantation	19 (23%)
Transfusion	70 (80%)
Abnormal aminotransferases	6 (7%)
Serology HBV :	
– chronic HBV carrier	3 (4%)
– resolved hepatitis B infection	16 (19,5%)
– HB vaccinated patients	44 (53,5%)
– non-responder to HB vaccination	19 (23%)
Serology HCV	9 (11%)
HGV-RNA	13 (16%)

The majority of patients infected with HGV were men (85%). The mean age was the same for the HGV positive versus HGV negative patients (53.11 ± 15.89 years versus 57.01 ± 16.42 years ($t = 0.78$; NS)). Duration of dialysis was slightly longer for HGV positive than for the HGV negative patients (8.55 ± 6.77 years versus 5.16 ± 6.30 years ($t = 1.74$; $p < 0.05$)). Six HGV positive patients had undergone renal transplantation (46%), all of them had been transfused. History of transfusion was reported in 12 of the thirteen HGV positive patients (92%). The thirteenth patients' route of contamination could not be elucidated. Among the 13 patients infected with HGV, 9 were infected by the G virus only (69.2%), 2 were coinfected with the B virus (15.4%) and 2 were coinfected with the C virus (15.4%). Three patients infected with HGV had elevated levels of serum aminotransferases : one had a coinfection with B virus in replicative stage, the second had a coinfection with C virus, and the third had no coinfection but had fatty liver infiltration due to insulin-dependent diabetes.

Discussion

The prevalence of HGV infection in our dialysis population was 16%. This is close to that observed in other European countries, with 25% reported in Denmark (5), 8% in Germany (6), 26% in Spain (7), 12.5% in France (8), 16% in Belgium (9) and the United States (10). It is, on the other hand, higher than that seen in Japan (3.1%) (4). The chronic hepatitis G carrier state in the dialysis population is therefore frequent. Furthermore, it should be noted that the number of patients having had contact with the virus is probably even greater than the number of patients carrying the virus. Indeed, while in most patients infection with HGV is persistent, approximately one third of patients eliminate the virus within three years of the acute infection (11). Demonstration of infection by showing a persistent viremia using PCR therefore underestimates the real incidence of the problem.

The prevalence of infection with HGV in dialyzed patients is greater than that seen in blood donors in Europe (1.4-5.5%) (6,7,12-15), or in Japan (0.5-0.9%) (4,16). This population is therefore at higher risk of this infection, as it is for hepatitis B and C. In the literature, increased prevalences are found in haemophiliacs (from 15.8-32% in Europe) (12,17), and in intravenous drug abusers (38% in Europe, from 9.6-14.6% in the United States, and 43% in Japan) (10,12,18,19). This evidence strongly suggests the parenteral route as the principle means of transmission of the infection. The frequent existence of coinfection with hepatitis B and/or C (15% for each virus in our population), for which parenteral transmission is well established, also argues for the predominance of this modality of infection. Parenteral infection alone does not, however, seem to account for all infections. In our study, one of the 13 infected patients had neither been transfused nor transplanted. The literature documents other routes of transmission, including sexual contacts (20), and transplacental transmission (21). Nosocomial infection occurring in haemodialysis units could also be incriminated.

The majority of our dialysis patients infected with the hepatitis G virus had normal levels of serum aminotransferases. It has to be remember however that many patients treated by haemodialysis have low serum values of transaminases, possibly related to repeated dialysis or pyridoxine depletion (22). Only three of the thirteen patients (23%) infected with hepatitis G virus had abnormal results. One of these three patients was coinfected with hepatitis B, and had a chronic hepatitis in the replicative phase. Another patient was coinfected with hepatitis C, while the third had fatty infiltration of the liver induced by insulin-dependent diabetes mellitus. In all three, therefore, elevated enzyme levels could be attributed to causes other than infection with hepatitis G virus. None of these patients had liver biopsy, given the poor risk/benefit ratio of this test in this population. Other workers also suggest mild

effects on hepatic function by hepatitis G virus infection (11,23-25). In these studies, when liver function was abnormal, the derangements were only mild and transitory. Furthermore, when hepatitis G was present in a patient with hepatitis C, no aggravation was apparent, either in the clinical course (11,23-25), in the results of liver function (11,23-25), or in the histology of the organ itself (26).

It would, however, be dangerous to conclude, given the current state of knowledge on the hepatitis G virus, that infection with this agent is completely benign. The discovery of this agent in a number of cases of otherwise unexplained fulminant hepatitis is worrisome (13, 27-29).

In conclusion, the prevalence of infection with hepatitis G in our population of dialysis patients is high, and greater than that seen for the hepatitis B and C viruses. Transfusion-related transmission was possible in all but one case, which was assumed to represent sporadic contamination. The majority of the infected patients had normal aminotransferase levels. When abnormal levels were seen, other causes were usually present to explain the anomaly.

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