

HIGH PREVALENCE OF HEPATITIS C INFECTION AMONG BRAZILIAN HEMODIALYSIS PATIENTS IN RIO DE JANEIRO: A ONE-YEAR FOLLOW-UP STUDY

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SUMMARY

Nearly 400 hemodialysis patients treated at 5 different hemodialysis units in Rio de Janeiro were tested for one year for the presence of hepatitis C and B markers. During the same period, samples were also obtained from 35 continuous ambulatory peritoneal dialysis (CAPD) patients and from 242 health care workers. Depending on the hemodialysis unit studied, anti-HCV prevalence rates ranging from 47% to 82% (mean 65%) were detected. CAPD patients showed a lower prevalence of 17%. The prevalence of antibodies against hepatitis C virus (anti-HCV) among health care workers was 2.9%. We observed a hepatitis C attack rate of 11.5% per year in the anti-HCV-negative hemodialysis patient population. An average of 9.4% of the hemodialysis patients were chronic carriers of hepatitis B virus (HBV) (range 1.8% - 20.4%), while 48.9% showed markers of previous HBV infection. The HBV attack rate was 4.5% per year (range 0% - 6%). These results indicate an alarming high prevalence of anti-HCV among hemodialysis patients of this studied region.

KEYWORDS: Hemodialysis; CAPD, Health care workers; Hepatitis C virus; Hepatitis B virus; Hepatitis C transmission; Brazil.

INTRODUCTION

As the transmission of hepatitis C virus (HCV) occurs parenterally via blood and blood products, hemodialysis patients are necessarily at high risk for acquiring this disease. Indeed, studies have shown that while the prevalence of antibodies against hepatitis C virus (anti-HCV) among hemodialysis patients may vary widely depending the hemodialysis unit, rates as high as 12% in the U.S.A.^{1, 8}, 20-35% in Japan^{6, 7}, 30% in Germany¹², and 47% in Taiwan¹³ have been documented.

Here we present our findings on the prevalences of anti-HCV and serological markers for hepatitis B virus

(HBV) among hemodialysis patients, continuous ambulatory peritoneal dialysis (CAPD) patients, and house staff members at hemodialysis units in Rio de Janeiro who were followed up for a period of 1 year. We found a alarmingly high degree of anti-HCV positivity among the hemodialysis patients.

MATERIAL AND METHODS

Subjects

Our study was performed during 1991 at 5 hemodialysis units located in different parts of Rio de Janeiro. During a one-year period, serum samples were collected monthly from 270 hemodialysis patients frequenting five of the hemodialysis units, and every three

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months from 35 patients undergoing CAPD at the fifth unit. Control samples from 242 staff members were collected at least twice during this study. All serum samples were aliquoted and stored at -20°C.

Serological tests

All collected material was tested for the presence of the hepatitis B markers HBsAg and anti-HBs (Biomanguinhos, Fiocruz, Brazil), and anti-HBc (Laboratory of Hepatitis, Fiocruz, Brazil) by enzyme immunoassay (EIA).

Anti-HCV antibodies were detected using an in-house EIA based on synthetic peptides originating from the NS4, NS5, and core proteins of HCV. All samples were also tested using the HCV line immunoassay (LIA) (InnoLIA HCV Ab II, Innogenetics NV, Ghent, Belgium). This assay is based on immunodominant epitopes of NS4, NS5, and core of HCV, which are separately coated as parallel lines on a nylon membrane strip with plastic backing. Positive or negative results are determined by visual reading or by means of the 'LIA-Scan Infectious Diseases software' (Innogenetics NV, Ghent, Belgium). A sample was considered positive if at least one antigen line gave a clear positive reaction.

Classification of patients

The status of each patient after one year of follow-up was defined after analyzing the consecutive serological results obtained for anti-HCV reaction and HBV markers during this period. A patient was considered positive for anti-HCV, or one of the HBV markers, if a positive reaction against one of these antigens was observed from the beginning until the end of the study. Cases with constant borderline reactivity were classified as indeterminate. Seroconverting patients were defined as negative at the beginning of the study, but becoming positive during the follow-up.

Statistical evaluation

Statistical evaluations were performed using the Epiinfo 5.01b program developed by Andrew G.

Dean and others (Centers for Disease Control, Atlanta, GA, USA).

RESULTS

Hemodialysis patients

As summarized in Table 1, 253 (64.7%) of the 391 hemodialysis patients were positive for anti-HCV. Seven patients whose sera remained indeterminate throughout the study were withdrawn from further evaluations. Prevalence rates for anti-HCV ranging from 46.9 to 77.2 percent were found depending on the hemodialysis unit. Of the 156 anti-HCV negative patients at the beginning of the study, 18 seroconverted in the course of the year. This resulted in an anti-HCV attack rate of 11.6% per year. The highest attack rate was found in Unit A (30.4%), while no seroconversions occurred in Unit C (Table 2). No correlation between attack rate and prevalence was observed. Although no exact figures on the number of blood transfusions were available, approximately 5% of the anti-HCV positive patients never received a previous blood transfusion.

Serological testing indicated that 194 (48.9%) patients had suffered a prior HBV infection (Table 3) and 25 (6.3%) seroconverted to anti-HBc during the study (data not shown). In this latter group, 7 patients also became positive for HBsAg, indicating a recent infection. Forty-four (11.1%) of the patients had temporary or permanently circulating HBsAg during the follow-up period. Nine new cases of HBsAg antigenemia were observed.

The attack rate per year for HBV was 2.6% (range 0 - 8.3%); all cases of HBsAg seroconversion were observed in Unit B and C only. An HBV outbreak may well have occurred in Unit B: 6 patients were infected, and one patient probably had either a reactivation of an infection or suffered a second HBV infection (HBc positive, and conversion for HBsAg). HBV and HCV co-infections were found in 7.3% of the HCV positive cases.

TABLE 1
Prevalence of anti-HCV positivity in five hemodialysis units in Rio de Janeiro

Serological Marker	A	B	C	D	E	Total
HCV+	40 (71.4)*	38 (46.9)	32 (64.0)	61 (77.2)	82 (65.6)	253 (64.7)
HCV-	16 (28.6)	43 (53.1)	18 (36.0)	18 (22.8)	43 (34.4)	138 (35.3)

* percent

TABLE 2

Attack rates for anti-HCV among patients at different hemodialysis units

Hemodialysis Unit	N° Patients	Sero-Conversions	Attack Rate (%)
A	56	7	30.4
B	81	4	8.5
C	50	0	0
D	79	4	18.2
E	125	3	6.5

A very high turnover of patients was observed. Morbidity during the one-year period was 13.1% among the 398 patients who entered the study. Fifty patients, of whom 48% were anti-HCV positive, were transferred to other hemodialysis units, while 28 (7%) patients underwent kidney transplantation. Nineteen (68%) of the patients who received a kidney transplant were positive for anti-HCV before they underwent surgery.

CAPD patients

Of the 35 CAPD patients studied, 6 (17%) were reactive against HCV, and one seroconversion occurred. No co-infection with HBV was observed in the anti-HCV positive patients. In contrast to the hemodialysis patients, only 9.4% of the CAPD patients were anti-HBc positive.

Health care personnel

Only 2.9% of the health care staff were anti-HCV positive, and no seroconversions were observed during the study. HBsAg positivity was 2.1%, whereas 19.5% of the staff were found to be positive for HBc antibody, indicating prior HBV infection.

DISCUSSION

At the time we started our study, anti-HCV screen-

ing had never been carried out on Brazilian hemodialysis patients. Our results demonstrate a very high anti-HCV prevalence (65%) among such patients in Rio de Janeiro. Indeed, the values found in this population are much higher than those observed in hemodialysis patients in other countries where anti-HCV values range from 0.6% in the U.S. ⁸ to 47% in Taiwan ¹³.

In a previous study, a high prevalence of anti-HCV (2.7%) in blood donors from Rio de Janeiro ¹⁶ was observed. It should be noted that Rio de Janeiro has already suffered various Dengue epidemics ¹⁰. Bearing this in mind, we ascertained that the antigens used in the Innostest HCV Ab, which are the same used as in this study, did not cross-react with other Flaviviruses ¹³.

The high prevalence of anti-HCV among blood donors may well contribute to the high attack rates and prevalence of anti-HCV in our hemodialysis patient population. The prevalence of anti-HCV in our sampled patient population is 24 times higher than in the normal blood donor population. However, comparable ratios are also found in other countries such as Japan (20 times) ^{6,7}, Korea (29.7 times) ¹¹, The Netherlands (20 times) ¹⁷, and Italy (21.5 times) ³.

Five percent (5%) of the tested patients presented anti-HCV antibodies without a previous history of blood transfusion. This supports the findings of other groups in which alternative HCV transmission routes, other than direct parenteral transmission between hemodialysis patients, were observed ¹⁵⁻²⁰. This alternative transmission pathway is more likely between hemodialysis patients, and does not appear to have a significant impact on staff members, in whom we found a similar percentage of anti-HCV prevalence as that in the blood donor population.

TABLE 3

Prevalence of Hepatitis B markers among hemodialysis patients in Rio de Janeiro

Marker	A	B	C	D	E	Total (%)
anti-HBc +	23	45	41	43	42	194 (48.9)
anti-HBc -	30	32	26	5	79	172 (43.2)
HBsAg + (carrier)	2	8	11	15	8	44 (11.1)
HBsAg conversion (recent infection)	0	7	2	0	0	9 (2.3)
anti-Hbs + / anti-Hbc + (natural acquired immunity)	11	13	16	9	17	66 (16.6)
anti-HBs + / anti-HBc - (vaccinated)	2	1	0	2	7	12 (3.0)

If we analyze the hemodialysis units individually, we could not find any correlation between anti-HCV prevalence and attack rate within the different units (Table 2). This may indicate that some other factors such as hygienic conditions, or membrane and machine treatment between different hemodialysis sessions might be involved in sporadic HCV transmission. On the other hand, certain HCV genotype populations may be more efficient in non-parenteral HCV transmission¹⁴ than others.

Attack rates for HBV infection (HBsAg conversion) were 4.5 times less than those for HCV, indicating an adequate infrastructure in most units to localize and isolate HBV-infected patients, and to prevent transmission via infirmary and dialysis material. Nevertheless, it should be observed that 48.9% of the hemodialysis patients had already suffered a HBV infection. Most of these infections probably originated before improved methods for prophylaxis and prevention of HBV transmission were established.

Our data reveal that anti-HCV prevalence among hemodialysis patients in Rio de Janeiro is very high in comparison with other parts of the world. High prevalence rates in Rio de Janeiro blood donors, which are the direct suppliers for blood derivatives to the units studied, and the lack of an efficient infrastructure and understanding of HCV transmission within the units, may well be causing the spread of HCV among hemodialysis patients. In order to improve the control of HCV spread in the hemodialysis patient population, the regular screening of all patients, combined with the use of different hemodialysis machines in physically separated areas for HCV-positive and confirmed negative patients (tested by serological and PCR methods) could be an initial step to control HCV transmission.

RESUMO

Alta prevalência de infecção pelo vírus da hepatite C em pacientes de hemodiálise do Rio de Janeiro: estudo de acompanhamento durante 1 ano

Aproximadamente 400 pacientes de hemodiálise tratados em 5 diferentes unidades no Rio de Janeiro foram acompanhados durante 1 ano para presença de marcadores virais de hepatite B e C. Durante o mesmo período, amostras foram também de 35 pacientes ambulatoriais de diálise peritonial contínua (CAPD) e de 242 funcionários das unidades. Dependendo da unidade

em estudo foram detectadas prevalências de anti-HCV variando de 47% a 82% (média 65%). Pacientes de CAPD demonstraram uma baixa prevalência de 17%. A prevalência de anti-HCV em funcionários foi de 2.9%. Observamos uma taxa de ataque de hepatite C de 11.5% por ano na população paciente de hemodiálise anti-HCV-negativo. Uma média de 9.4% de pacientes de hemodiálise eram portadores crônicos do vírus da hepatite B (VHB) (taxa de 1.8% a 20.4%), enquanto 48.9% apresentaram marcadores de infecção passada de HBV. A taxa de ataque de HBV foi de 4.5% por ano (taxa de 0% a 6%). Esses resultados indicam uma alarmante prevalência alta de anti-HCV em pacientes de hemodiálise dessa região estudada.

ACKNOWLEDGEMENTS

The authors thank Lucy Dalva de Almeida and Felipe Loponte Saback for their excellent technical assistance, and Fred Shapiro for manuscript editing.

REFERENCES

1. ALTER, M. J.; HADLER, S. C.; JUDSON, F. N. et al. - Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. *J. Amer. med. Ass.*, 264: 2231-2235, 1990.
2. ARIMA, T.; TAKAMIZAWA, A.; MORI, C. et al. - A lambda gt11-cDNA clone specific for chronic hepatitis V generated from pooled serum presumably infected by hepatitis C virus. *Gastroent. jap.*, 24: 545-548, 1989.
3. CHIARAMONTE, M.; STROFFOLINI, T.; CAPORASO, N. et al. - Hepatitis-C virus infection in Italy: a multicentric seroepidemiological study (a report from the HCV study group of the Italian Association for the Study of the Liver). *Ital. J. Gastroent.*, 23: 555-558, 1991.
4. CHOOM, Q. L.; KUO, G.; WEINER, A. J. et al. - Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. *Science*, 244: 359-362, 1989.
5. DA PORTO, A.; ADAMI, A.; SUSANNA, F. et al. - Hepatitis C virus in dialysis units: a multicenter study. *Nephron*, 61: 309-310, 1992.
6. FUJIYAMA, S.; KAWANO, S.; SATO, S. et al. - The prevalence of anti-HCV antibodies in hemodialysis patients. *Gastroent. jap.*, 26 (suppl. 3): 206-208, 1991.
7. HAYASHI, J.; NAKASHIMA, K.; KAJIYAMA, W. et al. - Prevalence of antibody to hepatitis C virus in hemodialysis patients. *Amer. J. Epidem.*, 134: 651-657, 1991.
8. JEFFERS, L. J.; PEREZ, G. O.; de MEDINA, M. D. et al. - Hepatitis C infection in two urban hemodialysis units. *Kidney Int.*, 38: 320-322, 1990.
9. KIYOSIMA, K.; TANAKA, E.; SODEYAMA, T. et al. - Transition of antibody to hepatitis C virus from chronic hepatitis to

- hepatocellular carcinoma. **Jap. J. Cancer. Res.**, 81: 1089-1091, 1990.
10. NOGUEIRA, R. M. R.; MIAGOSTOVICH, M. P.; LAMPE, E. & SCHATZMAYR, H. G. - Isolation of dengue virus type 2 in Rio de Janeiro. **Mem. Inst. Oswaldo Cruz**, 85: 253, 1990.
11. PARK, Y. M.; KIM, I. S.; LEE, C. D. & KIM, B. S. - Seroprevalence of antibody against hepatitis C virus (anti-HCV) in various groups of individuals in Korea. **Gastroent. jap.**, 26 (suppl. 3): 159-163, 1991.
12. SCHLIPKOTER, U.; GLADZIWA, U.; CHOLMAKOV, K. et al. - Prevalence of hepatitis C virus infections in dialysis patients and their contacts using a second generation enzyme-linked immunosorbent assay. **Med. Microbiol. Immunol.**, 181: 173-180, 1992.
13. SHEU, J. C.; LEE, S. H.; WANG, J. T. et al. - Prevalence of anti-HCV and HCV viremia in hemodialysis patients in Taiwan. **J. med. Virol.**, 37: 108-112, 1992.
14. STUYVER, L.; ROSSAU, R.; WYSEUR, A. et al. - Typing of hepatitis C virus (HCV) isolates and characterization of new (sub)types using a line Probe Assay. **J. gen. Virol.**, 74: 1093-1102, 1993.
15. VANDELLI, L.; MEDICI, G.; SAVAZZI, A. M. et al. - Behaviour of antibody profile against hepatitis C virus in patients on maintenance hemodialysis. **Nephron**, 61: 260-262, 1992.
16. VANDERBORGHT, B. O. M.; REIS, A. M. M.; ROUZERE, C. et al. - Prevalence of anti-hepatitis C virus in the blood donor population of Rio de Janeiro. **Vox Sang.** (Basel), 65: 122-125, 1993.
17. VAN DER POEL, C. L.; REESINK, H. W.; MAUSER BUNSCHOTEN, E. P. et al. - Prevalence of anti-HCV antibodies confirmed by recombinant immunoblot in different population subsets in The Netherlands. **Vox Sang.** (Basel), 61: 30-36, 1991.
18. YOSHIDA, C. F. T.; ROUZERE, C. D.; NOGUEIRA, R. M. R. et al. - Human antibodies to dengue and yellow fever do not react in diagnostic assay for hepatitis C virus. **Braz. J. med. biol. Res.**, 25: 1131-1135, 1992.
19. YOSHIDA, C. F. T.; SOARES, O. A.; SCHATZMAYR, H. G.; UY, A. & GERLICH, W. H. - Early appearance and biphasic kinetics of IgG antibody against hepatitis C virus protein C100-3. **Med. Microbiol. Immunol.**, 180: 279-287, 1992.
20. YOSHIDA, C. F. T.; TAKAHASHI, Y.; VANDERBORGHT, B. O. M. et al. - Antibodies against non-structural c100/3 and structural core antigen of hepatitis C virus (HCV) in hemodialysis patients. **Rev. Inst. Med. trop. S. Paulo**, 35: 315-321, 1993.

Recebido para publicação em 06/05/1994.

Aceito para publicação em 25/08/1994.