Hepatitis-C Virus Antibodies (Anti HCV) in Haemodialyzed vs Non-Dialyzed Patients

Pages with reference to book, From 28 To 30

Haren Kumar (The Kidney Centre, stadium Road, Karachi.)
S. A.J. Naqvi (Department of Nephrourology, Jinnah Postgraduate Medical centre, stadium Road, Karachi.)
Aasim Ahmed (Department of Medicine, Aga Khan University Hospital, stadium Road, Karachi.)
Saeed Hamid (Department of Medicine, Aga Khan University Hospital, Stadium Road, Karachi.)

Abstract

Anti HCV was checked using Enzyme Immuno assay (EIA) (C100-3- Abbott) in 68 patients with chronic renal failure (CRF) who were on maintenance haemodialysis and 48 patients on conservative management. Mean age of the patients was 50 years. The duration of illness ranged from 3 months to 18 years (mean 3 years). All patients were Hepatitis B surface antigen (HBs Ag) negative. In haemodialyzed group 31(46%) and in conservative group only 3(6%) were Anti HCV positive. High Frequency of Anti HCV positivity In haemodialyzed group was related to period on dialysis (1 year) and number of blood transfusions (>4 units). Patients in whom dialyzer was re-used showed 60% positivity as compared to only 17% in those with single use. Anti HCV positivity predominated in females as compared to males, 42.6% vs 20.3%. Nine out of 10 patients with a history of jaundice and six out of 8 patients with raised transaminase levels were Anti HCV positive. Fifteen of 37 Anti HBc (igG) positive cases were Anti HCV +ve (JPMA 44 : 28, 1994).

Introduction

Parenterally transmitted hepatitis virus infection has always been a major health problem in patients with chronic renal failure especially in those on haemodialysis. Epidemics of hepatitis B (HBV) was a major cause of morbidity and mortality in these patients[1]. Lately the incidence of HBV infections in dialysis patients has been controlled to a great extent following universal precautions[2]. Inspite of this sporadic outbreaks of post transfusion hepatitis continued to occur and with continuous search parenterally transmitted Hepatitis C virus (HCV) was identified[3,4]. It appears to be the major cause of hepatitis in haemodialysis units because of repeated transfusions, use of common equipments and the immuno compromised status of these patients[5,6]. Majority of the HCV positive cases are asymptomatic showing moderate rise in transaminases with characteristic, fluctuations throughout the course of the disease and a higher rate of progression to chronicity[7-9]. The HCV antibody assay based on recombinant viral antigen (C100- 3) is now available for detection of HCV. This study reports the frequency of Anti HCV in chronic renal failure managed conservatively and by haemodialysis.

Patients and Methods

One hundred and sixteen, Hepatitis B surface antigen negative chronic renal failure patients seen between 1st March to 30th September, 1992 were studied. Patients were divided - into two groups, 68 patients on maintenance haemodialysis (selected from The Kidney Centre) and 48 non-dialyzed patients on conservative management (from Jinnah Postgraduate Medical Centre and Aga Khan University Hospital). All patients were dialyzed on SPS 450 and SPS 550 Baxter haemodialysis machines using only hollow fibre dialyzer. Twenty three patients were on single use of dialyzer and 45 were on 4 times re-use. Patients were selected on the basis of history, clinical examination and specific

renal investigations. Other tests included standard LET's, hepatitis B surface antigen, hepatitis B surface antibody, hepatitis B core antibody and hepatitis C virus antibody using Auszyme monoclonal 3rd generation EIA, Ausab EJA and Corzyme EJA (Abbott) and 2nd generation EIA (C100-3 Abbott). The dialyzer for re-use was prepared manually after flushing with 4 litres of water and sterilization with 3% formaldehyde at the end of dialysis and cleaned with 4 litres of 0.9% normal saline before the start of each dialysis. Only purffied and treated water obtained from Reserve Osmosis water treatment plant was used for the preparation of acetate dialy sate in the ratio of 1:34. The statistical analysis were carried out with students 't' test.

Results

Of 116 hepatitis B surface antigen negative patients with chronic renal failure, 68 were on maintenance haemodialysis and 48 on conservative management. There were 69 males and 47 females whose ages ranged between 18-77 years (mean 50 years). Chronic glomerulonephritis was the commonest etiology, 39 (33.5%) followed by diabetes mellitus 31 (26.7%), hypertension 12(10.3%), calculus disease 10(8.6%), polycystic kidneys 8 (6.8%) and others 16(13.7%). Of 68 patients in haemodialysis group, 31 (46%) and in non- dialyzed group of 48, only 3 (6%) were anti HCV positive (P= <0.001). Anti HCV positivity predominated in females 20 (42.6%) as compared to males 14 (20.3%) (P= <0.005). In haemodialyzed group the frequency of blood transfusion, duration on dialysis and the type of dialyzer used showed strong association to Anti HCV positivity (Table I).

Table I. Haemodialyzed group.

Parameter	Patients N	Anti HCV Positive	Anti HCV Negative	P Value
(A) Blood Transfusions				
(i) 0-3 Units	33	07 (21%)	26 (79%)	
(ii) 4-9 Units	13	06 (46%)	07 (54%)	P = <0.05
(iii) > 10 Units	22	18 (82%)	04 (18%)	
(B) Duration on Dialysis				
(i) < 1 year	31	08 (26%)	23 (74%)	
(ii) 1-3 years	32	18 (56%)	14 (44%)	P = <0.01
(iii) < 3 years	05	05 (100%)	00 (00%)	
(C) Dialyzer				
(i) Single use	23	04 (17%)	19 (83%)	
(ii) 4 Times Re-use	45	27 (60%)	18 (40%)	P = <0.002

Table II. Relationship of Anti HCV to various parameters in all CRF patients.

Parameter	Patients N	Anti HCV Positive	Anti HCV Negative	P Value
History of Jaundice				
Yes	10	09 (90%)	01 (10%)	P = <0.001
No	106	25 (24%)	81 (76%)	
Transaminase more than 2.5 times				
Yes	08	06 (75%)	02 (25%)	P = <0.01
No	108	28 (26%)	80 (74%)	
Anti HBc IgG Positive				
Yes	37	15 (41%)	22 (59%)	P = Not
No	79	19 (24%)	60 (76%)	Signifcant

Table II shows an overall association of Anti HO! to the history of jaundice, transaminases and Anti HBc IgG. Of 3 Anti HCV positive patients in the conservative group, all were females. One had biopsy proven cirrhosis and two received multiple blood transfusions. There were three patients, two in haemodialysis and one in conservative group who were never transfused and yet were Anti HO! positive.

Discussion

Hepatitis C infections have assumed an alarming proportion in haemodialysis units[10], especially after the adequate control of hepatitis B. HCV is now the leading cause of post-transfusion hepatitis worldwide[11]. The present study shows a HCV positivity of 46% in haemodialysis population. Similar results were reported from Singapore (45%)[12] Taiwan (50.2%)[13], Indonesia (46.8%)[14] and Brazil (50%)[7]. These figures are significantly higher when compared with those from Europe (Germany 10.1%[15], Italy 17.3%[16], Hungary 20%[17]) and USA 12%6 to 15.7%[18]. Majority of patients in this study had ESRD secondary to chronic glomerulonephritis of unknown etiology. It is possible that hepatitis C might be playing an etiological role in the development of immune complex nephritis leading to renal failure[19,20]. High Anti HO! positivity in female patients in the present study is different from studies conducted abroad[5,8,21]. The possible explanation might be a higher pregnancy rate with poor obstetric and gynaecological care requiring frequent blood transfusion at the time of delivery. A definite correlation of Anti HO! positivity was found between the frequency of blood transfusion and the duration on dialysis. Similar results are reported in other studies[2,5,7]. Similarly the percentage of Anti HCV positivity increases as the duration on dialysis increases reaching to almost 100% in those who are on dialysis for more than 3 years. Our figures are higher than those reported from Germany (14%)[15], Japan (14%)[22] and Italy (26%)[23]. Various factors implicated for this high frequency are the cross infection through the use of common equipment, extracorporeal hemocirculation, immune compromised state contact with an infected person and contamination of environmental surfaces gloves, clamps and dressing[5,22,24]. Three patients (two in haemo dialysis and one in conservative group) who had never received transfusion and yet were Anti HCV positive. suggest community

transmission of HCV[5,25,26]. For the first time we have found a strong correlation between the reuse of dialyzer and Anti HCV positivity. Though the mean pore size of the dialyzer membrane is much smaller than that of viral particle (and is considered a safe barrier against the passage of virus) but it is possible that during the procedure of reuse and cleaning especially when performed manually micro fractures occur leading to contamination of machine[27,28]. It was seen that most of the patients (although the number is small) with a history of jaundice or raised transaminase levels were Anti HCV positive but at the same time, a significant number of patients had no history of jaundice or raised transaminases and yet they were Anti HCV positive. This points towards the milder course of the disease with characteristic waxing and waning of transaminase levels[5,7,18,29]. Anti HBc IgG has long been considered as a surrogate marker for HCv[30,31]. In this study 24% patients were Anti HCV positive without and 40.5% with evidence of past HBV infection. Anti HBc IgG as a surrogate marker for HO! is less convincing in our study when compared to others[6,18]. There is a need to conduct further studies in high risk group[26] and blood donors[32,33] so that true incidence is established. We recommend routine estimation of showing persistently raised levels and are anti HCV positive to be dialyzed separately. Confirmatory assay like recombinant Immunoblot assay (RIBA) and Polymerase chain reactions (PCR) should be made available[34,35]. Instead of discontinuing reuse of dialyzer which has its own benefits like cost effectiveness and better biocompatibility[36], we recommend adaptation of strict disinfection protocols and universal precautions in every dialysis unit[27,28]. Automation in dialyzer reprocessing can go a long way in limiting the spread of hepatitis C viral infection.

References

1. Mayer, LA., Alter, M.J. and Favero, MS. Haemodialysis associated hepatitis B: revised recommendations for serologic screening. Semin. Dialysis. 1990;3:201-4.
2. Mioli, V.A., Balestra. E., Bibano, L et at. Epidemiology of viral hepatitis in dialysis centres: a national survey. Nephron., 1992;61:278-83.
3. Choo, Q.L. Kuo, G.. Weiner, AJ. et al. Isolation of cDNA clone derived from a blood-borne non-A Non-B viral hepatitis genome. Science, 1989:244:359-61.
4. Alter, M.J., and Sampliner, R.E. Hepatitis C and miles to go before we sleep. N.Engl.J.Med., 1989;321:1538-40.
5. Macbida.J., Yamaguchi, K., Ueda,S. etal. High incidenceof hepatitis C virus antibodies in bemodialysis patients. Nephron., 1992;60:117-18.
6. Zeldis, J.B., Depner, TA., Kuramoto, L.K. et aL The prevalence of hepatitis C virus antibodies amonghemodialysis patients. Ann. Intern. Med., 1990;112:958-60.
7. Yoshida, C.F.T., Takahashi, C., Gaspar, A.M.C. et at. Hepatitis C virus in chronic hemodialysis patients with Non-A Non-B hepatitis. Nephron., 1992;60:150-53.
& Consolo, F. and Freni. MA. Nosography and immunopatbogenesis of viral hepatitis. Nepbron., 1992;61:251-54.
9. Kew, M.C., Houghton. M., Choo, Q.L and Kuo, G. Hepatitis C virus antibodies in Southern African blacks with hepatocellutar carcinoma. Lancet, 1990;335:873-74.
10. Seaworth, B.J., Garret, L.E., Stead, W.W. and Hamilton, J.D. Non- A Non-B hepatitis and chronic dialysis. Another dilemma. Am J.Ncphrol.. 1984;4:235-39
11. Alter, H.J., Purcell. RH.. Shih. J.W. et at. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic Non-A Non-B hepatitis. N.EnglJ.Med., 1989;321:1494-1500.
12. Choong. H.L, Koh. L and Woo, K.T. Anti-HCV seropositivity in long term hemodislysis patients. Abstract. 9th Asian Colloquium in Nephrology: Seoul, Korea. The Korean Society of Nephrology:

1992, p91.
13. Yang. CS. and Huang CS. The high prevalence of hepatitis C virus antibodies and ribonucleic acid in hemodialysis patients. Abstract, 9th Asian Colloquium in Nephrology: Seoul. Korea,The Korean Society of Nephrology, 1992, p180.
14. Siregar, P., Hudoro, W., Junus, l. et al. Anti-hepatitis C virus in chronic hemodialysed patients. Abstract, 9th Asian Colloquium in Nepbrology; Seoul, Korea. The Korean Society of Nephrology: 1992, p 180.
15. Schlipkoter, U., Roggendorf, M.. Ernst, G. et at. Hepatitis C virus antibodies in hemodialysis patients. Lancet, 1990:335:140-9.
16. Gilli, P., Moretti, M., Soffritti, S. et at. Anti-HCV positive patients in dialysis Units? Letter, Lances, 1990;336:243-44.
17. Par, A. Antibody to hepatitis C virus in Hungary, Letter. Lancet, 1990;336:123.
18. Jaffers, Li., Perez, G.O., Medina, M.D. et at. Hepatitis C infection in two urban hemodialysis units. Kidney Int., 1990;38:320-22.
19. Johnson, RJ.. Gretch, DR., Yamabe. H. et al. Membranoproliferative glomerulonephritis associated with hepatitis C virus infection, N.Engl.J.Med., 1993;328:465-70.
20. Appel. GB. Immune-complex glomerulonephritis- deposits plus interest. Editorial. N.Engl.J.Med., 1993;328:505-6.
21. Dentico, P., Volpe, A., Buongiorno, R. et at. Hepatitis C virus in hemodialysis patients. Nephron.. 1992;61:307-8.
22. Yamaguchi, K., Nishimura, Y., Fukuolca. N. et at. Hepatitis C virus antibodies in hemodialysis patients. Letter. Lancet, 1990;335:1409-10.
23. Mosconi,G., Desanctis, LB.,Stefoni, S.et al. Epidemiology ofhepatitis Cina population of hemodialysis patients. Nephron., 1992;61:298-99.
24. Petrarulo, F.. Maggi, P., Sacchetti, A. et al. HCV infectionoccupational hazard atdialysis units andvirus spread, among relatives of dialyzed patients. Nephron., 1992;61:302-3.
25. Alter, M.J., Coleman, PJ., Alexander, W.J. et al. Importance of heterosexual activity in the transmission of hepatitis B and Non- A Non-B hepatitis. JAMA., 1989:262:1201-5.
26. Esteban, J.I. Esteban, R., Viladomiu, L et at. Hepatitis C virus antibodies among risk groups in Spain. Lances, 1989;2:294- 96.
27. Chiaramonte, S., Tagger, A.. Ribero, M.L et al. Prevention of viral hepatitis in dialysis units: isolation and technical management of dialysis. Nephron., 1992;61:287-89.
28. Alter, MJ.,Favero, MS. and Maynard,3.E. Impact of infection control strategies on the incidence of dialysis - associated hepatitis in the United States. i.lnfect.Dis.. 1986;153:1149-$1.
29. LaRussa, A., Bufano, G., Cauzzi, L and Pecchini, P. Non-A Non-B hepatitis: clinical laboratory course in patients on hemodialysis and its correlation with the presence of anti-hepatitis C virus antibodies. Nepbron, 1992:61:273-75.
30. Lai, K.N., Tam, iS., Lai, F.M. and Lin, H.). Isolated presence of antibody to hepatitis B core antigen in dialysis patients: occurrence of subclinical hepatitis? Am.J.Kidney Dis., 1989;13:370-76.
31. Elisaf, M., Tsianos, E., Mavndis, A. etal. Antibodies againsthepatitisCvirus (anti-HCV) in baemodialysis patients: association with hepatitis B serological markers. Nephrol. Dial. Transplant., 1991:6:476-79.
32. Hepatitis Cvirus upstanding. Editorial. Lances, 1990;335:1432,
33. Stevens, C.E., Taylor, P.E., Pindyck, J. et al. Epidemiology of hepatitis C virus. A preliminary studyin volunteer blood donors. JAMA., 1990;263:49-53.
34. Mazzotta. L, Landucci, G.. Planner, L. et al. Comparison between first and second generation tests to determine the frequency of anti-HCV antibodies in uremic patients in replacement dialytic therapy. Nephron., 1992;61:354-55.
35. Garson, J.A., Tedder, R.S., Briggs, M. et al. Detection of hepatitis C viral sequences in blood

donations by nested polymerase chain reaction and prediction of infectivity. Lancet, 1990;335:1419-22.
36. Kuinar, H., Alam, F. and Naqvi, S.A.J. Experience of hemodialysis at The KidneyCentre. J.Pak.Med.Assoc., 1992,42:234-36.