Prevalence of Hepatitis B In 27 Michigan Hemodialysis Centers

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Abstract: A large epidemiological survey of in-hospital chronic hemodialysis patients was conducted in 27 (93 per cent) of the 29 dialysis centers in Michigan. Serum was collected from 699 patients on chronic maintenance hemodialysis for periods from one month to eight years. Hepatitis B surface antigen (HB_sAg) was determined in all patients by radioimmunoassay and positive samples were confirmed by specific neutralization. Antibody against HB_sAg (anti-HB_s) was determined by radioimmunoassay in 110 HB_sAg negative patients from six dialysis units with a high prevalence of hepatitis B.

HB_sAg was detected in 80 (11.4 per cent) patients distributed among 21 (78 per cent) of 27 dialysis units and anti-HB_s in 34 (31 per cent) patients from the selected dialysis units. The prevalence of HB_sAg was related to duration of dialysis, number of blood transfusions, and to a history of bilateral nephrectomy, but not to age, sex, race, nor the underlying renal disease. Twenty-one (26 per cent) of the 80 HB_sAg positive patients had not been previously identified by the clinical laboratories of their institutions. Since preventive measures were not taken in the care of these inapparent carriers of HB_sAg, they represent an unrecognized risk. (*Am. J. Public Health* 69:581-584, 1979.)

Introduction

Hepatitis B infection is recognized as a common and serious hazard to patients and staff in hemodialysis units. The high prevalence of hepatitis was noted from the very onset of this treatment. Previous investigators have reported that this infection occurs among dialysis patients and staff with attack rates up to 100 per cent for patients[1-6] and from zero[2] to 36 per cent[3] for staff. In both patients and staff, hepatitis infection may cause death.[2] Since there are approximately 37,000 patients on chronic maintenance hemodialysis in the United States, hepatitis associated with hemodialysis is a major public health problem and a serious threat to patients and their contacts. The scope of this potential problem is emphasized by several studies which report Hepatitis B surface antigen (HB_sAg) in saliva,[7,8] semen,[7] urine,[9] breast milk,[10] menstrual blood,[11] and vaginal secretions.[12] These observations suggest that these body fluids may be potential vehicles for the transmission of hepatitis B and indicate the difficulty of adequately containing this infection to dialysis units. Indeed, a previous study demonstrated that family members of dialysis patients had a high prevalence of hepatitis B.[4]

The observation that hepatitis B can be transmitted by frozen red blood cells[13] suggests that this means of blood preservation will not prevent this disease from remaining a major complication of chronic hemodialysis.

We surveyed, in cooperation with the Michigan Department of Public Health, 699 long-term dialysis patients from 27 centers in the State of Michigan to determine the current prevalence of HB_SAg and antibody against Hb_SAg (anti-HB_s). Special emphasis was given to those patients who were considered HB_sAg negative by their respective dialysis units. The presence of a substantial population of false-negative HB_sAg carriers might be a particular public health hazard because usual precautions would not be applied. Furthermore, the finding of false-negatives might apply to several other epidemiologically important populations.

Methods

This study includes 699 (100 per cent) patients from 27 hospitals in Michigan. Two of the 29 regular hemodialysis units (7 per cent) were not willing to cooperate and were not included. Both of these non-participating units were located in a metropolitan area; however, several of the 27 units which did participate were located in the same metropolitan area.

The majority of the hemodialysis units operate two shifts per day, six days weekly. The time spent on dialysis and the frequency of dialysis varied from center to center and among patients within a given center. Four of the 27 units included in this study had a separate facility for dialyzing HB_sAg positive patients. All patients were screened for HB_sAg at intervals of one to three months by the clinical laboratories of their institution. HB_sAg was determined in 24

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TABLE 1—Prevalence of HB_sAg in relation to sex, race, age, number of blood transfusions and duration of dialysis

Category	Number of Patients Tested	Number of Patients With HB_sAg	Per Cent with HB_sAg
Sex			
Male	410	48	11.7
Female	289	32	11.1
Race			
White	463	61	13.2
Black	233	18	7.7
Age (years)			
10-19	68	10	14.7
20-39	162	17	10.5
40-59	322	38	11.8
≥60	147	15	10.2
Number of Transfusions			
0	462	40	8.7
1	105	10	9.5
≥ 2	132	30	22.7*
Duration of Dialysis			
0-12 months	298	24	8.1
13-24 months	165	28	10.9
25-48 months	174	27	15.5
>48 months	62	11	17.7**

*Significantly different from 0 transfusions ($P < 0.001$)
**Significantly different from 0-12 months ($P < 0.05$)
All other intragroup comparisons not significantly different

of the 27 laboratories by radioimmunoassay (Ausria II 125, Abbott Laboratories) and in three by counter-immunoelectrophoresis.

For the purpose of this study a single serum sample from each patient was tested for HB_sAg by radioimmunoassay (Ausria II 125, Abbott Laboratories) at the Michigan Department of Public Health by the same technician. Positive samples were confirmed by a specific neutralization test (Ausria II-125, Abbott Laboratories). Anti-HB_s was determined by radioimmunoassay (AUSAB, Abbott Laboratories) in 110 HB_sAg negative samples obtained from the six units with the highest known prevalence of HB_sAg.

The medical records of all 699 patients were reviewed. Data concerning age, sex, race, duration on dialysis, serum transaminase activities, total serum bilirubin level, previous history of transfusions, bilateral nephrectomy, and underlying renal disease were obtained. Chronic HB_sAg carrier status was determined by reviewing the serial hepatitis screening performed by the respective institution. Statistical analysis was performed by the chi-square test.

Results

HB_sAg was detected in 80 (11.4 per cent) of the 699 sera analyzed. Fifty-nine (74 per cent) of these positive patients had previously been identified as carriers of HB_sAg by the institutions where dialysis was performed. Twenty-one (26 per cent) of the HB_sAg positive cases were discovered to be antigenemic during this survey. All 21 had been negative on serial screening performed by their institutions for the previous six or more months. Serum transaminase levels and total bilirubin of these 21 patients were normal.

Anti-HB_s was detected in 34 (31 per cent) of the 110 patients screened. Retrospective review of the medical records of these 34 patients revealed a previous report of HB_sAg in only three patients (9 per cent). The remainder showed no serologic evidence of HB_sAg or history of abnormal liver function tests.

The prevalence of HB_sAg varied widely in the units surveyed. In six units (20 per cent) no patients were found to be antigenemic, while in others up to 50 per cent were positive. This wide variation in prevalence could not be related to the geographic location, population density, or size of the various dialysis units. Conversely, low staff/patient ratios, high staff turnover, and inexperienced staff tended to be related to a higher prevalence of HB_sAg. In the four units which had a separate facility for dialysis of HB_sAg positive patients, the prevalence of HB_sAg was from one to 35 per cent. This wide range could be explained by the duration that these separate facilities had been used. In the two units using separate facilities for less than one year, the prevalence of HB_sAg positive patients was 30 and 35 per cent, and in the two units using separate facilities for more than three years, the prevalence of HB_sAg positive patients was only 1 and 3 per cent. No new cases were found in any of the four units since implementing these separate facilities, either by history or at the time of this study.

Table 1 depicts the prevalence of hepatitis B in relation to sex, race, age, duration of dialysis, and number of transfusions. There were no significant differences between male and female patients nor among the several age groups. The frequency of HB_sAg was higher in whites (13.2 per cent) than blacks (7.7 per cent), but the difference was not significant.

Thirty-three per cent of the patients surveyed had received at least one unit of blood since beginning dialysis and more than one-half of these had received two or more units of blood. At the time of this survey, all dialysis units were using frozen red blood cells. HB_sAg was detected in 22.7 per cent of patients who had received more than two transfusions and in 8.7 per cent of the non-transfused patients ($P < 0.001$). Furthermore, the presence of HB_sAg was related to the duration of dialysis—17.7 per cent of patients being treated for more than four years were HB_sAg positive, compared with 8.1 per cent for those dialyzed for less than one year ($P < 0.05$). However, no significant differences were noted among patients dialyzed for less than 48 months. We were unable to distinguish whether the high prevalence of HB_sAg among patients on longer dialysis was related to the duration of treatment or to a larger number of blood transfusions. Patients on dialysis for longer periods of time are more likely to receive multiple transfusions and also have increased opportunity for exposure to the virus. Finally, the prevalence of HB_sAg was related to a history of bilateral nephrectomy (Table 2). Twenty-one per cent of patients with a history of bilateral nephrectomy were antigenemic, compared to 10.4 per cent of non-anephric patients ($P < 0.05$). However, 58 per cent of anephric patients and

TABLE 2—Prevalence of HB_sAg in Relation to Bilateral Nephrectomy

	Number of Patients Tested	Number of Patients With HB_sAg (per cent)	Number of Patients with More than One Transfusion (per cent)
ANEPHRIC	66	14 (21)*	38 (58)*
NON-ANEPHRIC	633	66 (10.4)	199 (31)
TOTAL	699	80	237

*Significantly different from non-anephric ($P < 0.05$)

only 31 per cent of the non-anephric patients had received at least one blood transfusion ($P < 0.05$).

Discussion

The detection of hepatitis B surface antigen in 11.4 per cent of 699 dialysis patients and of anti-HB_s in 31 per cent of 110 HB_sAg seronegative patients together with the demonstration of HB_sAg and anti-HB_s in 60 to 70 per cent of patients in certain units supports the conclusions of others that hepatitis B is a serious endemic problem in hemodialysis centers.[4–6] Despite precautionary methods recommended to reduce the risk to hemodialysis patients, the prevalence of this infection remains high. The finding of a positive relationship between the prevalence of HB_sAg and the duration of dialysis is in agreement with other investigators[4, 5] and suggests that a prolonged antecedent exposure to the virus is important. Other investigators, too, have found that the prevalence of HB_sAg among black dialysis patients is lower than whites.[4] Males and females demonstrated a similar prevalence of HB_sAg in respect to point prevalence and chronic carrier status. This finding that the prevalence of HB_sAg did not differ substantially between male and female subjects nor among age groups is at variance from others.[14] These differences may be explained by population differences. In a normal population HB_sAg was detected more frequently among males than among females, and most frequently among 20 to 40 year-old males. Perhaps these young males have a greater exposure to hepatitis B because of their life styles. However, dialysis patients of all ages have a similar exposure to hepatitis that seems related primarily to the duration of dialysis.[4]

Data obtained from these 27 centers suggest that blood transfusions continue to be associated with a high prevalence of hepatitis B even though, at the time of this survey, all units were using frozen blood. This observation combined with the recent observation that frozen red blood cells can transmit hepatitis B[13] suggests that blood transfusions remain a source of transmission of hepatitis B to transfused patients, although a direct causal relationship could not be proven in this survey. Fifty per cent of patients positive for HB_sAg did not receive a transfusion within one year prior to detection of hepatitis B surface antigen in their sera. Therefore, other factors such as the spread of infective particles in urine,[9] or other body fluids[7, 8, 10–12] may also play an important role in the transmission of this disease.

Of interest is the finding of 21 additional positive patients undetected by periodic screening at the dialysis units, although most dialysis patients were tested for HB_sAg by a radioimmunoassay (Ausria II, Abbott Laboratories). This finding suggests that the prevalence of hepatitis B infection in hemodialysis units may be considerably higher than might be inferred from the laboratory of the institution. In order to explain the discrepancy between these results and those of the various institutions, these 21 previously unrecognized carriers were classified into several groups:

1. Patients (n = 5) from units using counter-immunoelectrophoresis to detect HB_sAg, which under optimal conditions does not detect more than 75 per cent of HB_sAg detected by radioimmunoassay.
2. Patients (n = 4) from units which screened their patients at quarterly intervals. Subsequent to this study all four patients were found to be sero-positive by their institution's screening program.
3. Patients (n = 3) from units which screened their patients at monthly intervals. Following this study all three were found to be carriers by their institution's screening program.
4. Patients (n = 2) who were reported by their institutions to be sero-negative for at least six months preceding this survey but who had a past history of HB_sAg sero-positivity.
5. Patients (n = 7) from various units where the detection of HB_sAg was performed by the same radioimmunoassay but by different technicians. Follow-up of these patients three months later, revealed that five were reported as HB_sAg and anti-HB_s sero-negative and two had expired.

Unidentified positive patients might account for some cases of hepatitis B infection among other patients or among staff, particularly when hepatitis B occurs without a definite history of transfusion, or other parenteral exposure to blood or other body fluids from sero-positive patients.

Of additional interest is the finding that patients who are anatomically anephric seem to have a significantly higher prevalence of HB_sAg sero-positivity. These differences can be explained partly by blood transfusions as our data demonstrated that anephric patients are more likely to receive blood transfusions. Unfortunately, the population of anephric patients without history of blood transfusions was too small to study the effect of the anephric state on the prevalence HB_sAg. Alternate explanations for the higher prevalence of HB_sAg among anephric patients might include more

frequent dialysis and therefore greater exposure to the virus or a role of the kidney in maintaining the carrier state. We favor the role of increased exposure either via more transfusions or more frequent dialysis.

If one assumes that 37,000 dialysis patients are currently being dialyzed in the United States and uses the 11.4 per cent carrier prevalence reported here, then approximately 4,250 such patients can be expected to carry HB_sAg at any one time. Furthermore, about 26 per cent (1100) of these seropositive patients may be unrecognized carriers. Thus, it is probable that precautionary measures recommended by the Center for Disease Control and the Committee on Viral Hepatitis[15] to prevent the spread of hepatitis would probably not be utilized in management of these potential high-risk carriers.

In view of recent studies which suggest that the presence of DNA polymerase and e antigen in serum of HB_sAg positive patients are indicators of relative infectivity,[16, 17] it is probable that positive carriers are not equally infectious. Thus, until such tests of infectivity are available to all dialysis centers, methods to prevent hepatitis should include regular, accurate, and frequent screening for HB_sAg, the minimal use of blood transfusion, high staff/patient ratios, low staff turnover, and the use of separate facilities for dialysis of HB_sAg positive patients. The argument for the use of separate facilities is supported by our finding that no new cases of HB_sAg were seen in the four units using separate facilities. Further support for the use of separate facilities will require careful prospective studies.

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