HEPATITIS B VIRUS INFECTION IN THAI HEMODIALYSIS PATIENTS

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INTRODUCTION

Hepatitis B virus (HBV) infection occurs more often in patients with severe renal insufficiency or renal transplant than in other healthy individuals. Renal patients also respond with lower but more prolonged elevation of serum transaminases and less icteric diseases than hemodialysis staff members (Garibali *et al.*, 1973; Sopko and Anuras, 1978). It has been known that hepatitis B antigen (HBAg) carriers represent a reservoir for HBV infection, up to 60% of these patients are unable to eliminate the virus totally, and may become chronic hepatitis. This altered reactivity to HBV is due to immunodeficiency associated with end stage renal disease (Revillard, 1979) and factors inherent to hemodialysis (Goldblum and Reed, 1980).

Epidemiolgic patterns and modes of transmission of dialysis associated hepatitis is well known and established in developed countries. In a 1967 through 1968, survey of dialysis facilities in the United States, conducted by the Center for Disease Control, 41% of the centers reported single case or outbreaks of hepatitis. Attack rate per one hundred persons at risk was estimated to be 10% for patient and 3% for medical staff (CDC, 1969).

In Thailand, the prevalence of HBAg among healthy Thais is about 5-10% (Pongpipat *et al.*, 1971; Grossman *et al.*, 1975), among Thai medical students is 7% (Pongpipat *et al.*, 1978). The pattern which occurs in hemodialysis units in Thailand has not been explored. The purpose of this survey is to establish the incidence of HBV exposure by studying the HBAg and HBAb of hemodialysis patients in several hemodialysis centers during the past three years.

MATERIALS AND METHODS

The hemodialysis centers are located in the Bangkok Metropolitan area, three centers are in private hospitals and one center in a government hospital. All patients who underwent chronic hemodialysis would have blood tested for HBAg, HBAb and liver function test at the first time to have hemodialysis. The tests were repeated on a six monthly basis unless a change in status was observed, in which case the intervening monthly specimens were all tested. All 68 patients' sera were tested by reverse plasmaphoresis hemeagglutination method as described previously (CDC, 1977) and solid phase radioimmunoassay, (reagent from Abbott Laboratories, North Chicago, Illinois) commercial kit for HBAg (AUSRIA II)(R) and HBAb (AUSAB(R)). No test was done for core antigen (anti HBc), e antigen or e antibody.

For the purpose of this study, hepatitis was defined as (1) two consecutive aminotransferase values greater than 40 IU/l (normal 5-35) over a week period if the first test was found abnormal (2) new development of HBAg, (3) conversion of HbAb from negative to positive with abnormalities of liver function. Non A-Non B hepatitis was defined as an abnormal aminotransferase exclusive of hepatitis B, hepatitis A, drugs or disease

known to cause abnormalities of the enzymes. No fluoxymesterone was given to our patients.

RESULTS

There were 68 patients who had hemodialysis during this peroid of study from 1981 to 1984; 37 males and 31 females. Fifty-six had chronic renal failure from glomerulonephritis and interstitial nephritis, 10 had end stage kidney disease from diabetic nephropathy; and 2 had polycystic kidney disease. Detection of HBAg, HBAb according to age and sex distribution at the beginning and time of survey is shown in Table 1.

Ten out of 68 hemodialysis cases were positive for HBAg, thus the carrier rate was 14.7%. The exposure rate of HBV (HBAg+ve and HBAb+ve) was 28 out of 68 (41.2%) at the beginning of dialysis. There was one who had HBAg positive and HBAb negative at the beginning of hemodialysis, converted to HBAg negative and HBAb positive after 4 months on the programme. There were six with HBAg and HBAb negative, converted to be HBAb + ve at the time of survey. This made the exposure rate of HBV to be 50% (34 out of 68) at the time of survey.

Five cases with abnormal liver function test died while being on the hemodialysis programme (Table 2). One patient was HBAg negative and HBAb positive to start with normal liver function tests. After being on hemodialysis for about 5 months, he developed hepatitis symptoms with jaundice. The total serum bilirubin was 4.35 mg%, direct bilirubin 1.65 mg%, SGOT 2400 IU/1, SGPT 1260 IU/1. He expired three weeks later from liver failure in addition to renal failure.

Table 1

HBAb and HBAg findings in patients at the beginning of hemodialysis and at the time of survey.

	Begin hemodialysis			Survey		
	HBAg – ve HBAb – ve	HBAg – ve HBAb + ve	HBAg + ve HBAb – ve	HBAg – ve HBAb – ve	HBAg – ve HBAb + ve	HBAg + ve HBAb – ve
Age Group						
20-29	5	2	1	5	2	1
30-39	8	3	4	7	4	4
40-49	12	1	1	10	3	1
50-59	5	1	4	4	3	3
60-69	5	9	–	4	10	–
70+	5	2	–	4	3	–
Male	19	12	6	16	15	6
Mean age	49.2	50.7	43	49.4	50.2	43
Female	21	6	4	18	10	3
Mean age	47.1	60.5	44	45.3	58.9	41.3
Total	40	18	10	34	25	9
	58.8%	26.5%	14.7%	50%	36.8%	13.2%

Table 2

HBAg and HBAb findings in 5 cases with abnormal liver function test.

	HBAg – ve HBAb – ve	HBAg – ve HBAb + ve	HBAg + ve HBAb – ve
At the beginning of hemodialysis	2	1	2
At the time of death	1	2	2
	(3)*	(12.6)	(18.2)

*Number in parenthesis indicate duration in months of patient on hemodialysis.

Two cases were HBAg negative and HBAb negative when entering the dialysis programme. One had slight elevation of liver enzymes (SGOT 197 IU/1 and SGPT 202 IU/1) with HBAb conversion to be positive. Unfortunately, he died of sudden cardiac arrest in the hospital the day after hemodialysis. The other was HBAg negative and HBAb negative throughout the course. After being on hemodialysis for 3 months, he developed elevation of liver enzymes; SGOT 184 IU/1, SGPT 239 IU/1 and expired. The possibility of non A and non B hepatitis was considered for this case.

There were two cases who were HBAg positive and HBAb negative at the beginning of hemodialysis. After being on hemodialysis for about 6 months, one patient became lethargic, developed jaundice with SGOT 450 IU/1, SGPT 178 IU/1, total bilirubin 7 mg%, direct bilirubin 3.42% mg%, The other also had hemodialysis for 2 months, his liver enzymes started to rise with SGOT 180 IU/1, SGPT 165 IU/1, total bilirubin 3.6 mg%, direct bilirubin 1.4 mg%. Both expired shortly but HBAb remain negative.

DISCUSSION

Acute viral hepatitis plays a major role compared to other microbial infections in patients on hemodialysis or with transplants. This virus accounted for 1.7% (1978) and 1.1% (1979) of total mortality respectively, according to two European Dialysis and Transplant Association studies in successive years (EDTA, 1978). Our data showed a mortality of 7.8% (5 out of 64 patients) in a period of three years. The reason for a higher mortality rate in this survey is that most of our dialysis patients were "under dialysed". All of them became critically ill when there was liver damage in addition to their original end stage kidney disease.

The clinical consequences of chronic HBV infection are still not clearly ascertained (Ribot *et al.*, 1979; Goldblum and Reed, 1980). However, these consequences may well be underestimated. Most patients do not show any disturbances of liver function. Several observations suggest that the HBAg carrier state might ultimately result in chronic hepatitis, but that symptoms occur only late in the course of the disease and remain mild for a long time.

Acute and chronic HBV infection in hemodialysis patients are an important cause of HBV infectivity. In 1974, there was one infected staff member for every 25 patients on hemodialysis treatment and more than 70% of all centers had patients with HBV infections. Subsequently, the incidence of staff member levelled off. In 1978, there was one staff member case per 60 dialysed patients. In our present study, although all the staff members' sera were not screened, no obvious

hepatitis occurred in the staff members during the peroid of survey.

In this study, 10 of 68 (14.7%) hemodialysis patients were hepatitis carriers. The incidence was slightly higher when compared to the hepatitis carrier in healthy Thais, (Pongpipat *et al.*, 1971; Grossman *et al.*, 1975). A higher incidence in this study is probably due to sensitive tests used than in the previous studies, or that most chronic renal failure patients might have immunological alterations in the host defense (Pongpipat *et al.*, 1979) and previous blood transfusions. The incidence of HBAg carrier and serologic evidence of HBV infectivity among hemodialysis patients in this study is similar to Grob's report (Grob, 1981). In this study, the number of patients with sign of HSV infection increased from 28 (41.2%) to 34 (50%) thus 58.8% were eligible for vaccination at the beginning of hemodialysis to 50% at the time of survey.

Awareness of the problem of HBV infection in hemodialysis centers, vigorous hygiene and organizational measures have been taken throughout the world. The HBV infections almost disappeared from dialysis units (Polakoff, 1981, PHLS, 1974). However, in most countries of intermediate or high prevalences of HBV infections, the problem remains unsolved despite great efforts.

Among those high risk groups of individuals such as renal patients, nursing staff and laboratory personnels, vaccination should be the first priority to be considered.

In recent years, non A- non B hepatitis has become a growing problem, as have other causes of liver disorders, such as infections with other viruses or drugs. In this study there was one patient who had elevation of aminotransferase with negative HBAg and HBAb. At the time of enzymes elevation, no obvious clinical signs of hepatic congestion from heart failure nor hepatotoxic drugs were present. By exclusion, this case could likely be a non A- non B hepatitis and this is the only case of possible non A- non B hepatitis in this survey. We did not encounter high incidence of non A- non B hepatitis in chronic dialysis patients as reported by Seaworth *et al.*, (1984). The exclusion of anti HBc testing and the long interval between aminotransferases determinations, will certainly decrease the detection of hepatitis B exposure and non A-non B hepatitis incidence in this survey.

SUMMARY

The prevalence of hepatitis B virus infection in chronic hemodialysis patients in Bangkok was surveyed. There were 14.7% (10 out of 68 patients) HBAg carriers; 26.5% (18 out of 68 patients) positive for HBAb. Total exposure rate of HBV (28 out of 68 patients) was 41.2% at the beginning of dialysis. The exposure rate converted to be 50% (34 out of 68 patients) at the time of survey. Five cases with abnormal liver function expired while being on the hemodialysis. Acute viral hepatitis was thought to be the cause. One case of possible non A- non B viral hepatitis was discussed.

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