

Effectiveness of Recombinant Hepatitis B Vaccine

Tahir Shafi, Jamila Iqbal and Shahid Ahmad

NHRC, Nephrology and Microbiology Department of Skaikh Zayed Hospital, Lahore-54600

SUMMARY

The study was carried out to see the efficacy of recombinant hepatitis B vaccine (Engerix 'B' by SK & F) in two high risk groups viz; chronic renal failure patients on maintenance haemodialysis (n=20) and medical staff (n=25). The prevaccination status of these individuals was assessed by HBsAg, Anti-HBs and LFTs. Only those subjects were included in this study who were negative for HBsAg & Anti-HBs. The patients were given 2cc while the staff 1cc dose of the vaccine intramuscularly at the schedule of 0,1 and 6 months. Quantitative estimation of antibody titre (seroconversion) was noted by ELISA method 15 days after the last dose. This became positive in 84 % of the medical staff members and 65% of the patients in a concentration of ≥ 10 IU/L.

No significant side effects were noted in any of the subject.

INTRODUCTION

Hepatitis B is a major public health problem throughout the world affecting several hundred of millions of people. It is a cause of appreciable morbidity and mortality in the human population both from acute infection and the chronic sequelae which include chronic active hepatitis, cirrhosis and primary liver cancer.

There is a striking correlation between the incidence of HCC and the prevalence of the chronic hepatitis B virus (HBV) carrier state. Globally, HBV is probably the etiologic agent for 75-90% of these primary liver cancers. HCC is one of the the most common cancer worldwide¹.

Hepatitis B virus is believed to account for almost 50% of all clinical cases of hepatitis. Although acute infection in the majority of patients is likely to result in a mild and apparently self limiting disease, about 1 per 1000 cases develop fulminant hepatitis, resulting in acute liver failure and death in 65-90% of cases. However the greatest problem lies in the development of the carrier state following infection (estimated to be 200 million cases worldwide)².

In the absence of effective methods of treating acute infection and controlling the long term results of the carrier state, the only viable alternative is to

prevent the original infection³. Before 1980 the only available measure was the use of hyperimmune gamma globulin in those persons who were at risk, such as babies of carrier mothers, surgeons suffering needle stick injuries and close contacts of known case of hepatitis B. Such passive immunization although effective is expensive, short lived and in limited supply. It however still has a place as prophylaxis in patients requiring urgent antibody cover.

There are two major vaccines which are currently being used. Plasma-derived vaccine and yeast derived recombinant hepatitis B vaccine. The yeast derived recombinant DNA hepatitis B vaccine contains the purified surface antigen of the virus. The surface antigen expressed in yeast cells is purified by several physiochemical steps and formulated as a suspension of the antigen adsorbed on aluminum hydroxide.

AIM AND OBJECTIVE

The objective of this study was to evaluate the immune response of haemodialysis patients and medical staff at high risk of acquiring hepatitis B infection to a recombinant vaccine prepared from HBs Ag expressed in yeast.

SUBJECTS AND METHODS

For study purpose, we selected subjects from two high risk groups.

1. Medical staff.
These include doctors, nurses, laboratory personnels, sweepers in the wards and staff working in haemodialysis unit.
2. Immunodeficient patients i.e; patients on continuous haemodialysis.

Both of the above cited groups were screened for hepatitis B surface antigen (HBsAg), antibodies to HBs Ag (anti-HBs). Their liver function tests were done. Only subjects with negative HBsAg, Anti HBs and having normal liver functions were included in the study. The recombinant yeast derived hepatitis vaccine (Engerix-Bx of SK & F) was given to both groups by deep intramuscular injection in the deltoid region, the schedule being 0,1 and 6 months. Medical staff members were given 1 ml (20 µg) of the vaccine while haemodialysis patients recieved 2 ml (40 µg) of the vaccine per dose. Post-vaccination status of the individuals for HBsAg, Anti-HBs and LFTs was evaluated 15 days after the last dose. The levels of antibodies to hepatitis B surface antigen were determined by ELISA using solid-phase immunoassay. Each batch of samples included positive and negative controls. After the completion of the test, the absorbance of the specimens and controls were measured using EIA photometer (Quantum II). Positivity of each sample for anti-HBs was evaluated against a cut off value calculated from positive and negative controls. The weak positive samples were redetermined. Seroconversion was defined as development of an anti-HBs concentration >1 IU/l in a post vaccination serum of an initially seronegative subject⁴.

RESULTS

Anti-HBs values above 10 IU/l or more indicate protection against hepatitis B virus infection⁴. 21 out of 25 (84%) healthy individuals and 13 out of 20 (65%) renal failure patients developed anti-HBs titre greater than 10 IU/L. These results are shown in Table 1.

Vaccination with recombinant hepatitis B vaccine did not induce clinically significant local or systemic adverse reactions in any of the subjects.

The most common complaint was mild or moderate local soreness at the injection site. No one experienced generalized reaction. During the seven months of observation, none of the subject became positive for HBs Ag. None of the individuals had abnormality of liver functions following vaccination.

Group	Subjects	Protective anti-HBs	Percentage
Medical Staff	25	21	84%
Haemodialysis Patients	20	13	65%

DISCUSSION

Active immunization against hepatitis B is required for groups which are at an increased risk of acquiring this infection. These groups included individuals requiring repeated transfusions of blood or blood products, prolonged inpatient treatment, patients who require frequent tissue penetration or need repeated access to the circulation, patients with natural or acquired immune deficiency and patients with malignant disease. Viral hepatitis is an occupational hazard among health care personnel and the staff of institutions for the mentally retarded people. High rates of infection with hepatitis B occur in narcotic drug addicts and drug abusers, homosexuals and prostitutes. Women in highly endemic areas of the world where the carrier state in that group is high also require immunization in light of the increased risk of transmission of the infection to their offspring. Patients in haemodialysis units are at high risk of getting hepatitis B infections⁵. If left unvaccinated, such patients may easily become carriers of the hepatitis B virus (60% of uremic patients), and thereby constitute an infectious reservoir for their treatment centers and community⁶.

A point of special concern is that haemodialysis patients develop a poorer response to the recombinant vaccine than do healthy people^{7,8}. Our results indicated that only 65% of the patients were seroconverted after full course of the vaccine. Hans Kohler et al showed that using plasma derived hepatitis B vaccine (MSD) 50% of male, 65% of female dialysis patients and 95% of medical staff members developed anti HBs antibodies⁹. In two other studies immunization rate of 60% was reported^{10,11}. Our results are comparable to these

reports. Steven et al reported much higher immunization rate in their patients 89%.¹² This poor response in dialysis patients is likely due to an immune deficiency of patients with chronic uremia, which predisposes them to become chronic carriers of HBs antigen as well¹³. Based on these observations, it is suggested that vaccine recipients should not be assumed to have always protective antibody level but the individual response to the vaccine should be checked. Some individuals are slow responders, whose response could have been known if sera were checked two months after the last dose or if they were given a booster dose with the same or another potent vaccine. The various studies conducted on young and healthy subjects show the antibody response close to 100%^{9,14,15}, which is higher than what was seen by us. The reasons for this are not clear.

CONCLUSION

A reduction in the incidence of hepatitis B can be expected only if significant proportions of persons at high risk receive vaccine. Increased efforts are needed to develop programmes to vaccinate persons in all high risk groups. This can only be achieved by lowering the cost of vaccination. Results indicated that the yeast - derived hepatitis B vaccine have a high immune response and sustained level of protection. Specific humoral antibodies against the surface antigen appeared in 84% of the healthy subjects and 65% of dialysis patients who received a course of vaccine. The vaccine was well tolerated and the subjects suffered with little side effects.

ACKNOWLEDGEMENT

We are thankful to Dr Iffat Yazdani Medical Director SK & F for providing us the test kits. We also acknowledge Mr. Majid Ehsan and Sabir ali for computerization this manuscript.

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The Authors:

Dr. Tahir Shafi,
Professor of Nephrology,
Shaikh Zayed Postgraduate Medical Institute,
Lahore.

Dr. Jamila Iqbal,
Associate Professor Microbiology,
Shaikh Zayed Postgraduate Medical Institute,
Lahore.

Dr. Muhammad Shahid,
National Health Research Complex,
Shaikh Zayed Postgraduate Medical Institute,
Lahore.

Address For Correspondence:

Dr. Tahir Shafi,
Professor of Nephrology,
Shaikh Zayed Postgraduate Medical Institute,
Lahore.