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Effectiveness of Low-Dose Intradermally Administered Hepatitis B Virus Vaccine

Tahir Shafi, Jamila Iqbal, Muhammad Shahid
Department of Nephrology, Microbiology, National; Health Research Complex,
Shaikh Zayed Postgraduate Medical Institute Lahore

SUMMARY

Hepatitis B vaccine is underutilized because of high cost. A study was performed to see the effectiveness of yeast derived recombinant vaccine in low dose (0.1 ml; 2 µg) given at 0, 1,2 and 6 months in 50 seronegative individuals. 39 (78%) of them developed anti hepatitis B surface antigen (anti HBs) in a concentration greater than 10 IU/l which is considered to be protective. None of them had any significant side effect except for minor local soreness at the site of injection.

INTRODUCTION

Hepatitis B (HBV) is a major public health hazard in the world. At least two million people die of acute or fulminant hepatitis, cirrhosis and hepatocellular carcinoma and chronic hepatitis each year. It is also responsible for significant morbidity from acute infection or its complications. Incidence of the disease varies from country to country. as demonstrated by the presence of hepatitis B antigens and antibody markers. The lowest incidence is reported from North America, Northern Europe, South Africa and Australia. On the other hand some areas of Africa, China, South East Asia show total marker rates of up to 80% and carrier rates of 10 to 20%[1]. Currant estimate is 300 million chronic HBsAg carriers worldwide and 75 % of them are Asians[2]. A carrier rates up to 10.7% have been reported from Pakistan[3,5]. It is estimated that 40% of the carriers of HBsAg will die of chronic liver disease and/or hepatoma[6]. 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 infection7 There are two major vaccines which are currently being used. Plasma-derived vaccine and yeast derived recombinant hepatitis B vaccine.

Recombinant hepatitis B vaccine is an effective and safe means of preventing hepatitis B virus infection when given as three intramuscular injections of 20 µg of hepatitis B surface antigen (HBsAg).

AIMS AND OBJECTIVES

Utilization of Hepatitis vaccines is limited due to its high cost. We carried out this study to see the immune response to recombinant hepatitis "B" vaccine in low dose by intradermal route.

SUBJECTS AND METHODS

50 subjects were included in this study. All were health care workers of Sheikh Zayed Hospital Lahore. Pre-vaccination status of these individuals was assessed by liver function tests, HBs Ag and Anti-HBs. Only those subjects were included in this study who were negative for HBs Ag and Anti-HBs and had normal liver function tests. The subjects were given 0.1 ml (2 µg) of recombinant hepatitis B vaccine by intradermal route at the schedule of 0, 1, 2 and 6 months. 15 days after the last dose, their sera was again checked for Anti-HBs. Liver functions tests were repeated during this period. They were asked about occurrence of fever, chills, nausea, vomiting, arthralgias, myalgias, malaise, wheezinging, itching, urticaria, dizziness and headache after each injection. They were also examined for the presence or absence of local reactions like erythema, swelling, tenderness, skin discoloration, skin breakdown, regional lymphadenopathy, and subcutaneous nodules at the site of injection.

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). Positivist 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.

RESULTS

Out of the 50 subjects included in this study, 39 showed seroconversion, while 11 were non-responders. Thus the seroconversion rate in our subjects was 78%. Quantitative estimate of Anti-HBs was as follows.

		No.	%
Excellent response	(> 270 IU/L)	11	22
High response	(100-270 IU/L)	24	48
Low response	(< 100 IU/L)	04	08
No response		11	22

Side effects like fever, rash, arthralgia and liver dysfunction were not seen. We noted local reaction at the site of injection in only ten subjects. It was in the form of small erythematous macule, usually less than 5 mm in diameter after 24-48 hr disappearing subsequently without leaving any scar.

DISCUSSION

Intradermal route is recognized strategy for inducing immunity with small amounts of antigen[8,9]. Presentation of antigen to the immune system intradermally results in a macrophage-dependent T-lymphocyte response via specific epidermal cells. Intradermal route has already been used for immunization against other diseases like TB, diphtheria, typhoid, cholera, influenza, rabies and other likely infections. Another reason for attempting to use hepatitis B vaccine intradermally is to accelerate the immune response in persons who suddenly become at high risk of infection-e.g; after accidental exposure to hepatitis B or infants born to carrier mothers.

Immunogenicity of low dose intradermal HBV vaccine has been demonstrated in other studies[10-12] Seroconversion rate in these studies reported has been higher than 78% seen in our study. However it is comparable to 84%, we have observed in our previous study with standard dose regimen by intramuscular route. Thus we have found no significant difference in seroconversion between the intradermal group and intramuscular group.

Although adverse reactions after 1/D injection were not marked, local reaction at the site of administration of the vaccine frequently included the development of an erythematons macule 5-10 mm in diameter after 24-48 hr; the lesion would subside after days or weeks, leading a small pigmented macule, occasionally overlying a small palpable nodule.

In most of the studies reported to date, those who received hepatitis B vaccine intradermally were young healthy subjects, in whom the antibody response is known to be good, and the vaccine was given by experimental staff under ideal conditions. Intradermal inoculation requires skill, and subcutaneous injection into fat will result in a poor immune response. There are no data on the longer term duration of anti-HBs on the subclass (es) of antibody induced, or an antibody specificity and affinity. Furthermore, protective efficacy studies of intradermal immunization against hepatitis B have not been conducted.

Many of the researchers, working on this topic are against intradermal route of vaccination, due to lower ultimate antibody response, more local reactions and early requirement for revaccination. A follow up study is required to see the long-term immunogenicity of the vaccine by intradermal route. As the dose of the vaccine (or more precisely, HBs Ag) is concerned, we think that 0.1 ml (or 2 μg) of the vaccine is satisfactory. If the required antibody response is not present, individual may be offered full dose course of the vaccine.

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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.