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RESEARCH ARTICLE

Response to Recombinant Hepatitis B vaccine (Engerix-B) and *TWINRIX* [*Hepatitis A & Hepatitis B Vaccine*] In Health care Workers at Prince Sattam Bin Abdul Aziz University Hospital, Al-Kharj Saudi Arabia

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Abstract

Background/Aims: Hepatitis B virus (HBV) infection is a major cause of liver-related morbidity and mortality. Infection with HBV can be prevented by vaccination with several forms of HB surface antigen (HBsAg) based vaccines. In the current study we assessed the efficacy and safety of both monovalent vaccine (Engerix) and HBV/HAV combination vaccine (Twinrix).

Methodology: Health care workers from Prince Sattam Bin Abdul Aziz University Hospital, Al Kharj with undetectable antibody to HBsAg were given 3 doses of either Engerix-B, 20 µg (1 mL),or Twinrix (720 ELISA units of inactivated hepatitis A virus and 20 µg of recombinant HBsAg protein) at 0, 1, and 6 months The route of administration was intramuscular injection. The primary outcome was the difference in proportion of patients achieving an anti-HBs antibody titer >10 IU/mL at 7 months.

Results: Out of 989 participants, 617 had HBsAb titers less than 10 IU/ml. Therefore, HCWs were randomly assigned to receive either Engerix B (n=309), or Twinrix (n=309). In Engerix recipients, 83.7% developed a protective antibody response after vaccination versus (94.7%) in participants who received Twinrix. With Engerix, the antibody titers ranged between 50 mIU/ml, and 683 mIU/ml versus 106 to 964 with Twinrix after the complete vaccination schedule. Antibody response was significantly higher among non-Saudis compared to Saudis.

Conclusion: Both HBV monovaccine and combination vaccines are effective and safe. However, given the higher immunogenicity of HBV/HAV combination vaccine, it may be more suitable for adults in regions where HAV is not endemic.

INTRODUCTION

Hepatitis B virus (HBV) infection is one of the major public health problems worldwide and is the tenth leading cause of death. More than two billion individuals have evidence of past or recent HBV infection and there are more than 350 million chronic carriers of HBV (1). Acute hepatitis B results in multiple symptoms such as fever, jaundice, and right hypochondrial pain that occur 1 to 4 months after exposure to the virus (2). In most people with acute hepatitis, symptoms resolve within several weeks. However, a minority of infected individuals develop a very severe, life-threatening fulminant hepatitis (3). About 15% of infected persons develop chronic hepatitis B is with persistence of HBV viremia beyond 6 months. Once the infection becomes chronic, it leads to chronic hepatitis,

cirrhosis of liver cancer (4,5). About two-thirds of people with chronic HBV infection are chronic carriers who do not develop symptoms, even though they harbor the virus and can transmit it to other people (6).
Most infected adults recover the infection spontaneously. A low percentage of adults infected with HBV go on to develop chronic infection (7). Children are at much higher risk for chronic infection. A majority of infected young children will fail to clear the virus and go on to develop chronic infection (8,9).

Healthcare workers (HCW) are at high risk of acquiring HBV through daily activities and exposure to patients through needle-stick or cut with a sharp objector contact with mucous membrane (10,11). It has been shown that HCWs with injuries from needles contaminated with blood containing HBV may get HBV in about 33% of cases (12,13). The potential for HBV transmission through contact with environmental surfaces has been demonstrated in investigations of HBV outbreaks among patients and staff of hemodialysis units (14).

Therefore, hepatitis B vaccine is essential requirement for healthcare to avoid transmission, and prevent the sequences of HBV infection. The hepatitis B vaccine is safe and effective and is usually given as 3-4 shots over a 6-month period (15, 16). There are several HBV vaccines available. The recombinant DNA vaccines are is developed by genetic engineering (17). Another vaccine, TWINRIX, is a vaccine indicated for active immunization against disease caused by hepatitis A virus and infection by all known subtypes of hepatitis B virus. TWINRIX is approved for use in persons 18 years of age or older (18).

In the current study done in Prince Sattam Bin Abdul Aziz University hospital, in AL Kharj, Saudi Arabia, we measured the response to HBV monovalent vaccine (Engirex) and HBV with HAV vaccine (Twinrix) in healthcare workers.

PATIENTS and METHODS

The current study was conducted to compare the response to among health care workers and patients at Prince Sattam Bin Abdul Aziz University Hospital, AL Kharj. The study was conducted between January 2013 until September 2014 to assess the response of physicians, nurses, laboratory technicians and medical students, to HBV monovalent vaccine (Engirex) and Twinrix. Patients were randomly classified into two groups. One group was vaccinated with Engirex and the other with Twinrix both vaccines were given according to the schedule 0, 1, 6 months.

All individuals were subjected to the following;

1. Careful history
2. Thorough clinical examination
3. Laboratory investigations including
    a. Complete blood picture
    b. Liver enzymes (AST and ALT)
    c. Serum albumin
    d. Prothrombin time
    e. Total and direct bilirubin
    f. Hepatitis A IgM and IgG antibodies
    g. Hepatitis B surface antigen and HBV s antibody
    h. Hepatitis C antibodies

RESULTS

989 HCWs were enrolled in the study. None was positive for HBsAg or HBeAg or HCV core antibodies before vaccination. Also, none was positive to HCV. Of the enrolled individuals, 617 had HBV surface antibody titers less than 10 IU/. These HCWs were classified into 2 groups. Group A (209 patients) received Engerix vaccine and Group B received Twinrix.

Table (1): Demographics of the two groups:

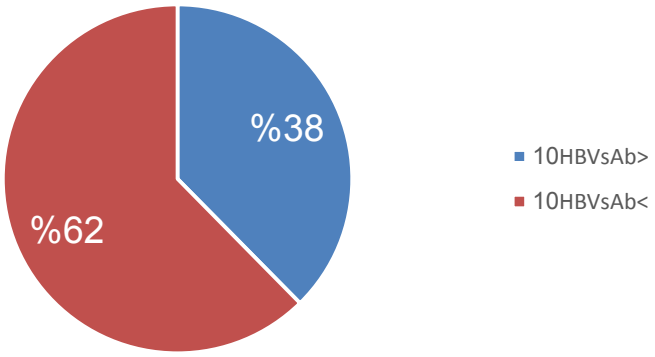
Variable	Health care workers receiving Engerix n=309		Health care workers receiving Twinrix n=308		P-value	Sig.
	N	**%**	**N**	**%**		
Gender: • **Male** • **Female**	158 151	(51.1) (49.9)	152 156	(49.35) (50.64)	0.17	**NS**
	Mean	**SD**	**Mean**	**SD**		
Age	32.99	7.40	32.54	9.63	2.04	**NS**
Nationalities (n,%) Saudis Filipinos Egyptians Sudanese Syrian Yemini	162 (52.4) 89 (28.8) 53 (17.2) 2 (0.64) 1 (0.32) 2 (0.64)		158 (51.3) 85 (27.6) 56 (18.2) 3 (0.97) 2 (0.65) 1 (0.32)		0.0447	**NS**

Table (3): Laboratory findings of the two studied groups:

Investigation	Health care workers receiving Engerix n=309		Health care workers receiving Engerix n=309		P value	Sig.
	Mean	**SD**	**Mean**	**SD**		
AST *Up to(40 IU/L)*	34.46	17.94	41.71	11.60	0.09	**NS**
ALT *Up to(37 IU/L)*	28.94	14.01	24.32	10.15	0.17	**NS**
Triglycerides *Up to(180mg/dl)*	143.6	15.4	149.8	30.8	**1.25**	**NS**
Cholesterol *Up to(250mg/dl)*	137.2	12.7	149.6	29.0	**0.78**	**NS**
Fasting blood sugar *(80-110mg/dl)*	97.4	16.3	105.2	18.1	0. 69	**NS**
Hemoglobin *(12-16g/dl)*	14.2	2.1	13.9	1.8	0.3509	**NS**
RBCs ($x10^6$)	4,3	0.2	4.1	0.3	0.5449	**NS**

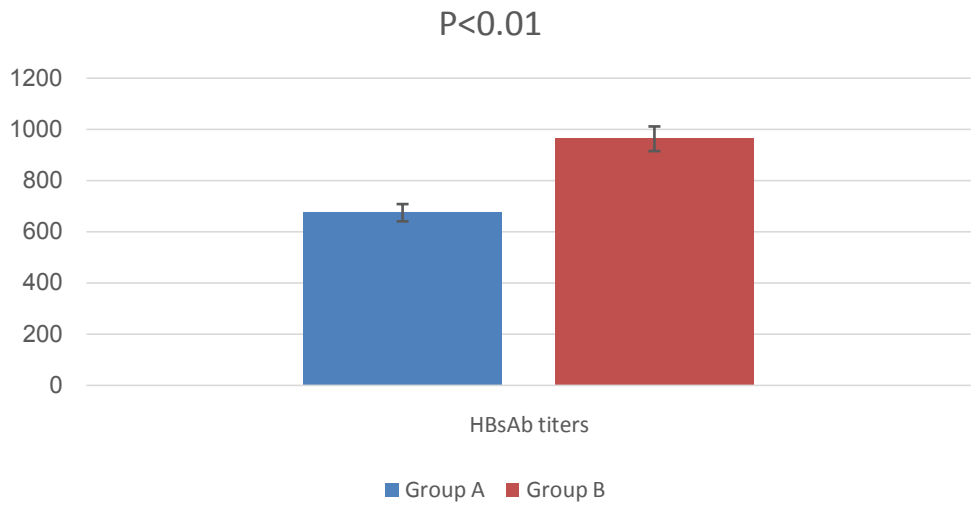
WBCs ($x10^3$)	7.4	1.1	6.5	2.2	0.2948	**NS**
Platelets x 1000 *(150 - 400/mm3)*	195.54	37.6	198.15	63.6	1. 15	**NS**

Figure 1: Patients with HBV surface antibody titers less than 10 IU/ml during screening



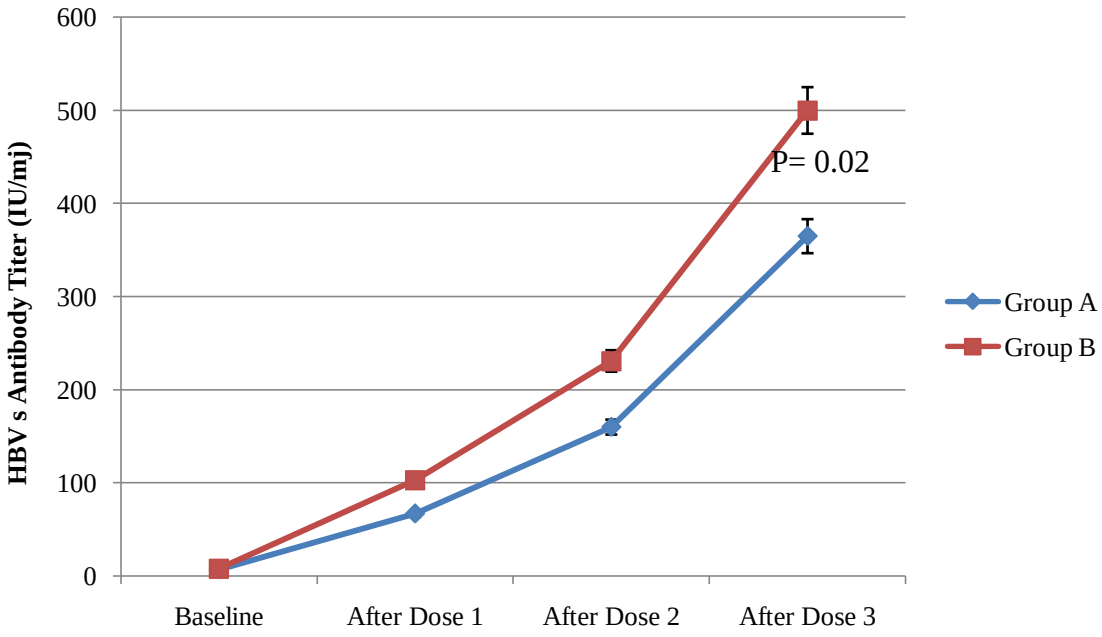
During screening, 617 HCWs showed HCV s AB titers less than 10 IU/ml and were randomized to receive either Engerix or Twinrix.

Figure 2: Post-vaccination hepatitis surface Antibody titers in the two studied groups



A significant difference was detected between HCWs who received Engerix and those who received Twinrix

Figure 3 : Mean Pre and Post immunization HBs Antibody titers in the 2 groups



This Line diagram show compare the Antibody titers in pre and Post immunization between Twinrix and mono-vaccine. The red line represent group B (those are the individuals who receive the Twinrix vaccine), and the blue line represent group A (individuals who receive Engerix B))
X axis represent the different doses (the vaccine is given in three doses), and the Y axis represent the response after each dose (antibody titer)

DISCUSSION

We conducted our study to compare between antibody response of Twinirix (Hep.A,B) and antibody response to the Engerix- B in addition to compare between the response of Saudis and Non Saudis to each vaccine.

In our study, the response of individual to Twinrix vaccine (antibody titer is more than 10 IU) was significantly higher compared to Engerix B. Our findings regarding the efficacy of both vaccines are comparable to the study by Al-Faleh et al, 2002 (19) who reported a response rate of 88% in individuals vaccinated by Engerix B. Furthermore, detecting antibodies in a subset of HCWs after completion of vaccination schedule in our study showed persistent HBV surface antibody titers. Our findings are in concordance with the findings of Al Ghamdi et al, 2013 who found persistent positive titers in 75% of previously immunized medical students[20]. Alfaleh et al, also showed that antibody titers are preserved several years after primary immunization. Western studies reported response rates ranging from 70%-90% with Engerix B and Twinrix (20).

The higher response rates and anti-body titers among individuals receiving Twinrix compared to those vaccinated by Engerix has also been reported by Bradley et al, 2007 (21) who showed that the response of individual combined vaccine resulted in a statistically significantly ($p < 0.001$) better anti-hepatitis B seroprotection compared to monovalent hepatitis B vaccine, 63.2% versus 43.5%, respectively.
Interestingly, the antibody response among Saudis was lower than the titers of HBsAb in non-Saudis. This difference may be due to difference of ethnic background genetic factors and differences in rates of compliance. In our study compliance was lower among Saudis.

Our studies and many previous studies showed that Engerix B and Twinrix vaccine were safe and there were no significant adverse events reported by the patients. Thus, both HBV monovaccine and

combination vaccines are effective and safe. However, given the higher immunogenicity of HBV/HAV combination vaccine, it may be more suitable for adults in regions where HAV is not endemic.

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