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ORIGINAL ARTICLE

Comparing the Efficacy of Double Dose Hepatitis B Vaccine with Conventional Dose Hepatitis B Vaccine in Chronic Liver Disease Patients

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ABSTRACT

Aim: To compare the efficacy of double dose hepatitis B vaccine with conventional dose hepatitis B vaccine in hepatitis C related chronic liver disease patients.
Study design: Interventional study (randomized controlled clinical trial)
Place and duration of study: Outpatient Department of Medicine, Services Hospital, Lahore from 12th August 2019 to 12th February 2020.
Methodology: One hundred and ten patients of both male and female age group 30 to 70 years diagnosed with chronic liver disease on the basis of changed liver echo texture on ultrasound were included. Patients were divided into two groups, each group having 55 patients. One group was given double dose (2ml) while the other was given conventional dose (1ml). Both groups were compared for efficacy in terms of prevention of CLD.
Results: The mean age of conventional group was 33.8±9.6 years while 33.7±9.1 years in the double dose group with male predominance (69.10%). Hypo-responsiveness was detected in 23.6% and 32.7% of conventional low dose group and double dose group respectively. There were gender variations in mean Anti-HBs levels. It was 129.80±70.53 mIU/mL in males and 113.26±75.57 mIU/mL in female patients (*P*= 0.039). Mean titers of anti-HBs in conventional dose group and high dose group were 127.82±67.59 mIU/mL and 121.56±77.00 mIU/mL, respectively (*P*= 0.52).
Conclusion: Double dose hepatitis B vaccination in chronic HCV infected patients efficiently increases the response rate and hence protection against chronic hepatitis B.
Keywords: Double dose hepatitis B vaccine, conventional hepatitis B vaccine, chronic hepatitis.

INTRODUCTION

Hepatitis refers to inflammatory status of the liver with viruses and hepatotoxic drugs as the most common etiopathogenic agents. Hepatitis B virus is the most common among viruses responsible for significant burden of chronic liver disease worldwide. Liver trauma induced by hepatitis B ranges from minor inflammation to fatty configuration to cirrhotic liver and sometimes malignancy. Approximately 350 million people around the globe (7% of the world's population) are infected with HBV and millions among these suffer from chronic liver disease[1].

Hepatitis B is endemic in majority of the world countries and depending upon the endemicity rate, world can be categorized into low, medium and high endemicity. Sub-Saharan Africa is the worst affected continent among all with 8% HBV carrier rate[2]. As hepatitis B and C share their modes of transmission, hence co-infection with both the viruses at the same time is possible with rapidly worsening chronic liver disease.[3] Common modes for HBV transmission are contaminated blood, urine, saliva, semen, body fluids, or transplacental mothers to infants peripartum. Transfusing HBV-contaminated blood, sharing HBV contaminated needles, sharing toothbrush of affected patient, unsafe sex with affected partner, dental procedures, shaving from outside, nose and ear pricks for wearing ornaments, contaminated injections during medical procedures, and through injection drug use are common modes of transmission in our society[4].

Chronic liver disease (CLD) is a spectrum of disorders and consists of comprises of chronic hepatitis, cirrhosis of liver, and hepatoma[5]. Approximately 14 lac people succumb to death annually worldwide with majority of deaths related to complications (portal hypertension) of chronic liver disease and malignancy.

Disease related mortality due to HBV associated chronic liver disease is significant contributing about 1-2 million deaths annually worldwide. Sub-Saharan Africa is the region known for large number of people having HBV carrier state[6]. Hepatitis B disease prevalence varies among different parts of the world ranging from 0.1%–20% in various studies[7]. In Africa, significant number of peoples suffering from chronic liver disease were attributed to infection with HBV. A study in Ethiopian population revealed that about 12% of the hospital admissions and 31% of the mortality in medical wards was due to chronic liver disease[8]. Other studies from the same population revealed 2%[9] and another population-based study 0.9% prevalence[10].

Optimum management of chronic liver disease involve knowing the aetiology and focusing on the cause. Therefore, knowing the hepatitis B, C status of the patients is of utmost importance in order to be able to optimally treat the chronic liver disease. Majority of hepatitis B affected patient poorly respond to antiviral medication, therefore prevention of the disease through vaccination is the best available strategy.

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The aim of the study was to compare the efficacy of double dose hepatitis B vaccine with conventional dose hepatitis B vaccine in hepatitis C related chronic liver disease patients.

MATERIALS AND METHODS

This randomized control clinical trial was carried out in outpatient department of Medicine, Services Hospital Lahore from 12th August, 2019 to 12th February 2020. Permission was obtained from institutional Ethical Review Board. Both male and female patients in the age group 30 to 70 years diagnosed with chronic liver disease on the basis of changed liver echotexture on ultrasound were included. HBsAg positive patients determined by laboratory test, Individuals already immunized against HBV determined by history and patients taking steroids and immunosuppressants were excluded. A total of 110 patients were enrolled and divided into two equal groups. Fifty five selected patients were given double dose vaccine (2ml, 40µg) I/M 3 doses different times at 0, 1 and 2 months, and 55 patients were administered conventional dose (1ml, 20µg) similarly. Included patients were followed for three months and quantitative anti-HBs will be measures to document response. All variables of interest like age, sex, and outcome variable (effectiveness) were recorded. Data was entered and analyzed using SPSS version 20. Chi square test was used to determine the significant difference in both groups regarding effectiveness of vaccination. P-value ≤0.05 was taken significant.

RESULTS

In the present study, mean age of our studies population in the standard conventional group was 33.8±9.6 years and 33.7±9.1 years in the double dose group with male predominance (69.10%). The seroprotection rate in both groups was almost similar (65.5%). However, non-responders were significantly high in standard conventional group (1ml, 20µg) as compared to double dose group (2ml, 40µg) (10.9% vs 1.8%). Hypo-responsiveness was detected in 23.6% and 32.7% of conventional low dose group and double dose group respectively.

Table 1: Comparison of effectiveness between conventional dose hepatitis B vaccine and high dose hepatitis B vaccine

Effectiveness	Double dose	Conventional dose
Yes	54 (98.2%)	49 (89.1%)
No	1 (1.8%)	6 (10.9%)

Table 2: Comparison of anti-HBs level between conventional dose hepatitis B vaccine and high dose hepatitis B vaccine

Anti-HBs level	Double dose	Conventional dose
<10	1 (1.8%)	6 (10.9%)
11-99	18 (32.7%)	13 (23.6%)
>100	36 (65.5%)	36 (65.5%)

Table 3: Comparison of effectiveness according to genders

Gender	Group	Effectiveness		P value
		Yes	No	
Male	Double dose	34	-	0.123
	Conventional dose	38	4	
Female	Double dose	20	1	0.544
	Conventional dose	11	2	

There were gender variations in mean Anti-HBs levels. It was 129.80±70.53mIU/mL in males and 113.26±75.57mIU/mL in female patients (*P*=0.039). Mean titers of anti-HBs in conventional dose group and high dose group were 127.82±67.59mIU/mL and 121.56±77.00mIU/mL respectively (*P*=0.52) [Tables 1-4].

Table 4: Comparison of age effectiveness in both groups according to age

Age (years)	Group	Effectiveness		P value
		Yes	No	
30-40	Double dose	12	-	N/A
	Conventional dose	11	-	
41-50	Double dose	16	-	0.429
	Conventional dose	11	1	
51-60	Double dose	12	-	1.000
	Conventional dose	11	1	
61-70	Double dose	14	1	0.365
	Conventional dose	16	4	

DISCUSSION

Recombinant Hepatitis Bvaccine is safest vaccine in terms of efficacy. Shaw et al[11] showed rare neurologic phenomena but the incidence of the neurologic sequalae were insignificant when compared to general population. The only significant neurological adverse effect noted was Guillain-Barre' syndrome that exceeded the incidence in general population (9 cases in vaccinated group vs.3.6 cases in general population) when >850,000 vaccinated individuals were followed up across USA.

It goes without saying that development of hepatitis B vaccine is a major breakthrough in terms of disease prevention. Vaccinating against hepatitis B is not only cost effective but also helps in preventing hepatitis B in majority of cases along with its long term sequalae. Simultaneous infection with chronic hepatitis B and C endangers the risk of more fatal chronic liver disease along with liver cirrhosis and development of hepatoma at an earlier stage.[12] Also the response rate to antiviral medications is low in such cases. Wiedmann et al[13] revealed that HBV vaccine immunogenicity drops down significantly in CLD patients.

The present study was carried out to determine whether the use of high dose hepatitis B vaccine is more efficacious in terms of hepatitis B prevention in comparison with conventional low dose hepatitis B vaccine routinely administered. Patients were divided into two groups. Conventional hepatitis B vaccine group was given 3 doses of 1ml (20µg) vaccine at 0, 1 and 6 months while the high dose group was given 3 doses of 2ml (40µg) vaccine. Both groups were compared in terms of efficacy for disease prevention. Our results were in accordance with a randomized, controlled trial conducted on 110 HCV infected patients where double dose vaccine proved more efficacious in terms of disease prevention[14].

In the current study, rate of non-responsiveness to standard 3-dose hepatitis B vaccine was noted in 10.9% of 55 chronic HCV infected patients in comparison with non-responsiveness of 0.0% among 55 healthy adults. This observation was 5-10% higher than reported in the available literature. In contrast, only 1.8% chronic HCV patients were non-responders in high dose hepatitis B vaccine group.

In another study conducted by Mattos et al[15] on 85 chronic HCV patients and 46 healthy adults, rate of non-responsiveness to 3-dose hepatitis B protocol was 45% in chronic HCV infected group and 2% in healthy adults. Response rate was between 69% and 100% in other studies[16-17]. Impaired HBV immunogenicity has been reported in alcohol related chronic liver disease[18] post-liver transplant and in pts waiting for liver transplantation[19-20].

CONCLUSION

There were six non-responders (10.9%) in chronic HCV infected patients with conventional dose vaccination compared with 98.2% response rate in double dose vaccination group. The use of double dose vaccination in these patients is an effective way to increase the response rate.

Conflict of interest: Nil

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