Assessment of immunological response of Hepatitis B vaccination in patients of Chronic Hepatitis C (HCV)

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ABSTRACT

Objective: To evaluate the synthesis of anti-Hbs in response to the Hepatitis-B vaccination in patients with Hepatitis C infection in comparison with healthy people.
Study Design: Interventional Study.
Place and Duration: Department of Medicine and Department of Gastroenterology, Nishtar Hospital, Multan, from May 20, 2016 to June 15, 2018.
Methodology: A total of 83 subjects were enrolled, 41 were patients of Hepatitis C infection (HCV) and 42 were normal healthy individuals. Baseline anti-Hbs was done before vaccination. All the enrolled subjects (healthy and HCV patients) were administered Hepatitis-B vaccine intramuscularly according to recommended schedule of 0, 1 and 6 months. Anti-Hbs were measured after one month of third injection.
Results: Sero-protective representation was almost equal (more than 90%) for both groups (i.e. HCV patients and healthy individuals). Males were more sero-protected than females for both HCV patients and healthy individuals. The representation of sero-protection for males in HCV patients and healthy individuals were 56.09 % and 50.00 % respectively while the representation of sero-protection for females were 36.58 % in HCV patients and 47.61 % in healthy individuals.
Conclusion: The standard dosage of hepatitis B vaccine gave sero-protective levels in both groups i.e. normal healthy individuals and HCV patients. The antibody titers were almost equal in both groups as HCV infection has little or no effect on immune response of body.
Keywords: Hepatitis C virus, Hepatitis B vaccination, Antibody titers, HCV patients, Humoral immunity

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INTRODUCTION

The most common enveloped RNA virus affecting liver is Hepatitis C virus (HCV), leading to Hepatitis C infection. Hepatitis C can be very fetal due to its progressive nature. The end result of hepatitis can be either cirrhosis or hepatocellular carcinoma[1]. The superadded infections like hepatitis A and B are also very common with hepatitis C. The patients with superinfections can develop serious complications and can lead to death[2,3]. Thus in these cases immunization against hepatitis A and B play an important role in preventing superadded infections. WHO recommends that hepatitis B (HBV) vaccine should be given to patients with chronic HCV and HIV infections[4]. Hepatitis B vaccine is considered potentially safe in HCV and HIV infection. Several studies show the recommended use of hepatitis B (HBV) vaccine in patients with hepatitis C (HCV) infection[5].

The antibody response is directly proportional to the protection provided by given vaccine. Many studies show the decreased response of hepatitis B (HBV) vaccine in patients with documented liver cirrhosis[6,7]. Hepatitis C patients are mostly immunocompromised, so the normal sero-protective levels of antibodies against hepatitis B (HBV) infection are not achieved as compared to normal healthy individuals[8]. This leads to the development of various formulations of hepatitis B vaccination[9,10]. Recombinant hepatitis B vaccine has shown maximum immunogenic activity and is most safe form of hepatitis B vaccine[11-14].

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Therefore, the objective of this study is the evaluation of production of anti-Hbs in patients with HCV in comparison with healthy people. The rationale behind this aim of study is to find out the best use and efficacy of hepatitis-B vaccine in patients of chronic hepatitis-C infection (HCV).

METHODOLOGY

This interventional study was conducted at the Department of Medicine and Department of Gastroenterology, Nishtar Hospital, Multan, Pakistan within a period of 2 years from May 20, 2016 to June 15, 2018. The total 83 subjects were enrolled in this study after obtaining informed consent, 41 were patients of HCV and 42 were normal healthy individuals. The age of enrolled subjects ranging from 20-65 years. The patients who were known cases of hepatitis C for more than 5 years and not treated previously for Hepatitis C infection (HCV) were included in study. Moreover, all the enrolled subjects (healthy and patients) were not previously vaccinated against hepatitis B (HBV). The patients suffering from hepatocellular carcinoma, cirrhosis, renal failure and any systemic illness were excluded from study. Patients with other form of hepatitis like Hepatitis A, Hepatitis B and auto-immune hepatitis were also excluded. Baseline investigations like complete blood count (CBC), prothrombin time (PT), serum electrolytes and abdominal ultrasonography (USG) were done before administration of hepatitis B vaccine. Baseline anti-Hbs was also done.

All the enrolled subjects (healthy and patients) were administered Hepatitis-B vaccine intramuscularly according to recommended schedule of 0, 1 and 6 months. The serum levels of Anti-Hbs were measured after one month of third injection. The titers < 10 mIU/mL labelled as non-responders, the titers 10-100 mIU/mL labelled as hypo-responders and titers > 100 mIU/mL labelled as sero-protected. There was also a controlled monitoring of side-effects of vaccine.

Data Analysis: The data were analyzed by using SPSS (23.0) version. Frequencies and percentages were calculated for both males and females, among both the groups i.e. HCV patients and normal individuals. The percentages of both the HCV patients and healthy individuals were compared and p-value was calculated independently for non-responders, hypo-responders and sero-protected showing no significant difference in antibody titers of Hepatitis-B vaccination in HCV patients and normal persons.

RESULTS

Among the total 83 enrolled individuals, 41 were HCV patients and 42 were normal healthy individuals. Among HCV patients, 15 were females and 26 were males. Among the normal individuals, there were 20 females and 22 males. The mean age was 41.24 ± 9.05 years in patients of HCV and 36.55 ± 8.53 years in healthy persons. After the three injections, the anti-HBs titers were 275 ± 82.49 mIU/mL in patients of HCV and 271 ± 42.87 mIU/mL in normal individuals. Among the total enrolled subjects of study there were 5 non-responders (i.e. <10 mIU/mL), 3 hypo-responders (i.e. 10-100 mIU/mL) and 75 sero-protected (>100mIU/mL). Among the HCV patients there were 3 non-responders (i.e. <10 mIU/mL), 1 hypo-responder (i.e. 10-100 mIU/mL) and 37 sero-protected (>100mIU/mL). Among the normal persons there were 2 non-responders (i.e. <10 mIU/mL), 2 hypo-responders (i.e. 10-100 mIU/mL) and 38 sero-protected (>100 mIU/mL). This is shown in Table-I. Sero-protected representation was almost equal (more than 90%) for both groups (i.e. HCV patients and healthy individuals). The representation of sero-protection for males in HCV patients and healthy individuals were 56.09 % and 50.00 % respectively while the representation of sero-protection for females were 36.58 % in HCV patients and 47.61 % in healthy individuals. No one suffered from any side effect of vaccine.

Table-I: Anti-Hbs response and titers in HCV patients and Normal persons n=83 (Number of subjects/individuals) (N=83)

Antibody Response	HCV Patients (n=41)			Normal Persons (n=42)			Total (n=83)	p-value
	Males n (%)	Females n (%)	Total (HCV) n (%)	Males n (%)	Females n (%)	Total (Normal) n (%)	n (%)	
Non-responders (<10 mIU/mL)	2 (4.87%)	1 (2.43%)	3 (7.33%)	0 (0%)	2 (4.76%)	2 (4.76%)	5 (6.02%)	0.624
Hypo-responders (10-100 mIU/mL)	1 (2.43%)	0 (0%)	1 (2.43%)	1 (2.38%)	1 (2.38%)	2 (4.76%)	3 (3.62%)	0.586
Sero-protected (>10 mIU/mL)	23 (56.09%)	14 (34.1%)	37 (90.24%)	21 (50.00%)	17 (40.76%)	38 (90.48%)	75 (90.36%)	0.451
	26 (63.41%)	15 (36.58%)	41 (100.0%)	22 (52.38%)	20 (47.61%)	42 (100.0%)	83 (100.0%)	0.421
Antibody Titers (mIU/mL)	275 ± 82.49			271 ± 42.87			273 ± 15.86	0.169

DISCUSSION

Hepatitis B vaccine is considered as a revolution in the field of immunization because of its efficacy in the prevention of hepatitis B. The efficacy of hepatitis B vaccine is almost 95 % after three recommended injections[15]. However on the other hand there is also a failure rate of this vaccine. A small percentage of individuals mainly 5-10 % fail to produce antibodies in response to hepatitis B vaccine, hence are called non-responders. A similar study conducted in Karachi to evaluate the efficacy of hepatitis B, showing that success rate of 98.7 % after three doses[16]. A similar study conducted in Iran demonstrated the sero-protection rate of 94.3 %[12]. If the efficacy had been extremely varied in multiple studies then, this would have raised questions on the usage and outcomes of hepatitis B vaccine.

In this study, the antibody titers after third dose in HCV patients are 275 ± 82.49 mIU/mL and in normal healthy individuals are 271 ± 42.87 mIU/mL. So, it clearly shows that the antibody titers in both HCV patients and normal persons are almost equal and these titers are suggestive of intact immune system and its responsiveness in both HCV patients and normal persons. 90.2 % HCV patients and 90.4 % normal persons were sero-protected. So, it can be clearly demonstrated that that the antibody response in both the HCV patients and normal persons is equal. From this study it can further be deduced that the failure rate of hepatitis B vaccine is almost equal in both HCV patients and normal persons as there are 7.32 % non-responders in HCV patients and 5 % non-responders in healthy persons. The similar study explained the decreased response against hepatitis B vaccine in 31 % of HCV patients[17]. However the exact mechanism of this decreased response is not well clear but it was suggested the involvement of both cellular and humoral immunity[5,17]. Males are more sero-protected than females for both HCV patients and healthy individuals.

Various investigators have suggested various methods to warrant the development of immune response in those patients who do not produce antibodies in response to hepatitis B vaccine up to sero-protective levels. The most commonly suggested method is double dose strength[18]. High dose of hepatitis B vaccine with short intervals can produce immune response in non-responders. Another commonly suggested method to boost up the immune response in non-responders is administration of combined hepatitis B and hepatitis A vaccine[15]. The results produced in view of administration of combined hepatitis B and hepatitis A vaccine are much more agreeable and acceptable as compared to the usage of double dose strength of hepatitis B vaccine[19].

Some authors have suggested the use of other drugs like Granulocyte-Macrophage Colony Stimulating Factor (GM-CSF), levamosole etc. along with hepatitis B vaccine, to boost up the immune system in response to hepatitis B vaccine, in non-responders[20]. But the studies have shown that the antibody titers produced as a result of combined usage of GM-CSF or levamisole with hepatitis B vaccine are not satisfactory. The other major problems in the usage of these drugs with hepatitis B vaccine are that these methods are not cost effective and they also lead to the development of various significant systemic side effects[21].

The debate about the immune response of patients with HCV infection to hepatitis B vaccine still remains contradicted as many investigators believe that the HCV infection results in poor immune response to hepatitis B vaccine. So, it is usually recommended the use of hepatitis B vaccine as early as possible in patients with HCV infection[21,22]. Laboratory assessment of anti-Hbs titers after immunization can help in making the decision about the usage of double dose strength and GM-CSF or levamosole[23,24]. This study does not cover all the aspects of relationship between hepatitis C (HCV) infection and hepatitis B vaccine. Limitations involve small sample size, availability of inadequate information about immune response of HCV patients and non-assessment of effect of various systemic and generalized body conditions on immune response. More extensive, detailed and elaborative studies are required to authenticate the results of this study.

CONCLUSION

The standard dosage of hepatitis B vaccine gave sero-protective levels in both groups i.e. normal healthy individuals and HCV patients. The antibody titers were almost equal in both groups as HCV infection has little or no effect on immune response of body.

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AUTHOR'S CONTRIBUTION

Abbas MW: Conceived idea, Designed research methodology, Manuscript final reading and approval
Javaid R: Literature search, Data collection
Iqbal MN: Literature review, Data interpretation
Iqbal MA: Statistical analysis, Manuscript writing

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