ORIGINAL ARTICLE

Early Virological Response in Hepatitis C Patients with Insulin Resistance

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ABSTRACT

Aim: To determine the frequency of early virological response (EVR) in chronic hepatitis C insulin resistant (IR) patients being treated with conventional interferon.

Methods: This descriptive case series study was conducted in Medical Outpatient Department of University College of Medicine & Dentistry from December 2013 to June 2015.One hundred and fifty patients with HCV RNA detected by PCR and insulin resistance (IR) were included. Homeostasis model assessment (HOMA-IR) was used to determine IR and HOMA-IR >2 were considered to have IR. EVR was defined if HCV RNA had not been detected by PCR after 12 weeks of antiviral treatment Data was collected on a structured proforma and analyzed using SPSS 21. Chi square and t test were used for categorical and continuous variables respectively.

Results: Among 150 patients, 92(61.3%) were male while 58(28.7%) were female. Early viral response in the sampled population came out in 55(43.3%) individuals. Early viral response was significantly associated with gender and genotype of chronic hepatitis C.

Conclusion: It is concluded that frequency of early viral response in chronic hepatitis C patients with insulin resistance is quite low (43.3%). Hence pegylated interferon should be used preferably.

Keywords: Insulin resistance, Interferon therapy, Chronic Hepatitis C, Pegylated interferon

INTRODUCTION

Every year 350 000 people die from hepatitis C-related liver diseases and 3-4 million people are infected with the hepatitis C virus[1]. Hepatitis C virus (HCV) infection is associated with insulin resistance (IR) and subsequent poor response to antiviral therapy[2]. The clinical relevance of IR in HCV arises from its ability to promote hepatic inflammation and fibrosis and to impair response to antiviral therapy. Several studies are focused on the relationship of insulin resistance and chronic hepatitis C (CHC). Different lines of evidence have found that IR is a common feature in patients with CHC[3,4,5].

In a study using homeostasis model assessment for insulin resistance (HOMA-IR) it was concluded that IR is a major determinant of both early and sustained viral response (odds ratio: 14.29; P=0.004)[6]. Similarly in another study to assess the effect of insulin resistance, IR was increased (>2 IU) in 31(40.7%) of patients and early virological response was achieved among 37 patients (48.7%)[3]. There is difference in response rate in different genotypes and populations[3,4,5].

Our population is suffering double burden of disease i.e., both infectious and noninfectious diseases. The rationale of this study is that there is no local study available showing effect of insulin resistance on treatment outcome of chronic Hepatitis C i.e., early viral response among Pakistani population being treated for chronic hepatitis C. As our population differs from other populations regarding circulating genotype, use of conventional interferon and dietary habits. An accurate early predictor of a patient's response to interferon therapy may reduce or eliminate unnecessary and ineffective treatments, permit greater flexibility in tailoring therapy on an individual basis, and enhance the cost-effectiveness of treatment[6].

PATIENTS AND METHODS

This descriptive case series study was comprised 150 patients and conducted at Medical Outpatient Department of University College of Medicine & Dentistry from December 2013 to June 2015.Patients either gender with age 16-60 years, HCV RNA detected by PCR and insulin resistance were included. End stage renal disease with blood urea more than twice the upper normal limits (100-150 mmol/L), fatty Liver determined by ultrasonography , any sign of decompensated chronic liver disease determined by ultrasonography i.e., ascites or more than 80%, coarse echo texture of liver or prothrombin time double the normal and taking euglycemics like metformin or hypoglycemic like glicliazide or insulin were excluded.After 12 hours overnight fasting, under aseptic measures phlebotomy was done and blood

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was sampled in standard serum vial and sent immediately to pathology laboratory for measurement of insulin and fasting glucose levels. Insulin resistance was recorded. All variables of interest like age, sex, genotype of HCV and insulin resistance by HOMA-IR were recorded. Genotype was recorded to stratify the results later on as it modified the effect. Patients were treated according to standard protocols i.e. conventional interferon and oral ribavirin and followed up to 12 weeks then early viral response was determined by PCR for HCV RNA. Data collected was entered and analyzed in the SPSS version 17.

RESULTS

One hundred and fifty patients were included. There were 92 (61.3%) males while 58 (28.7%) females with mean age of the patients were 37.76±6.06 years. According to early viral response, 55 (43.3%) patients have early viral response while 45 (66.7%) have no early viral response. The genotype of the higher percentage among all the patients 106 (70.7%) were genotype III while next common was genotype II then the genotype I and in the last the Untypable type of hepatitis C virus was circulating (Table 1). When we cross tabulated the gender versus early viral response we found a significant difference [p= 0.02] (Table 2). Similarly genotype has an effect on early viral response, statistically the difference was significant (p=0.009) [Table 3]. The mean age was compared to early viral response group there was a non-significant difference showing that the age has no effect on result regarding early viral response in insulin resistant patients (Table 4).

Table 1: Demographic information of the patients (n=150)

Variable	No.	%
Gender		
Male	92	61.3
Female	58	38.7
Early viral response		
Yes	65	43.3
No	85	56.7
Genotype		
Genotype 1	8	5.3
Genotype 2	32	21.3
Genotype 3	106	70.7
Untyable	4	2.7

Table 2: Comparison of gender according to early viral response

Gender	Early viral response		Total
	No	Yes	
Male	59	33	92
Female	26	32	58
Total	85	65	150
Using Pearson Chi-Square, p Value=0.02 (significant)			

Table 3: Comparison of genotype according to early viral response

Genotype	Early viral response		Total
	No	Yes	
Genotype I	7	1	8
Genotype II	12	20	32
Genotype III	62	44	4106
Untypable	4	-	4
Total	85	65	150
Using Fisher's Exact Test, p Value=0.009 (Significant)			

Table 4: Comparison early viral response according to age

Early viral response	Age
No (n = 85)	37.52±6.42
Yes (n = 65)	38.08±5.58
Using Independent Samples Test, p value=0.577 (Non-significant)	

DISCUSSION

Hepatitis C virus infection is associated with insulin resistance and subsequent poor response to antiviral therapy.[2] The clinical relevance of IR in HCV arises from its ability to promote hepatic inflammation and fibrosis and to impair response to antiviral therapy. Several studies are focused on the relationship of insulin resistance and chronic hepatitis C (CHC). Different lines of evidence have found that IR is a common feature in patients with CHC[3,4,5].

Table I showed that male were more in our sampled population showing that it may be due to health seeking behaviour or change in pattern for seeking advice in our sampled population but on the other hand they are more at the risk of contracting this disease by trauma, by infected blood transfusion having shaves from infected barbers etc. Early viral response was low as compared to report other studies. It was only 43.3%. Showing that the conventional interferon are not as efficacies as the pegylated interferon due to cost effectiveness and the cost of pegylated interferon we are still depending on the conventional interferon for the treatment of hepatitis C as in poor countries like us can't afford pegylated interferon for all the patients suffering from hepatitis C virus. These early viral response patients will have more chances of sustained viral response at 6 months so more care should be taken if there is no early virus response we may shift to pegylated interferon. Secondly the results may be due to insulin resistance present in our sampled population. Insulin resistance has previously shown that it highly effect the outcome i.e., early virus response and sustained virus response in case of chronic hepatitis. Similarly here this low percentage of those who have clear the virus shows that in patient with insulin resistance we should shift to pegylated interferon. Then comes a genotype table here showed that the most common genotype in our circulating population is genotype III which is easily treatable as compared to genotype II, I and untypable.

The second most common was genotype II. Prevalence of genotype II also demand for further study so we may be able determine that different intervention needed in our population. In last but not the least the age of patient shows that more are in their working age group ranging from 23-48 years. These are the young lords which are the future of our generation and presence of chronic hepatitis may lead to disturb working conditions. Then we stratify the patients for gender and when cross tabulated the gender with early viral response we found that there is a difference in response of male and female patients.

Female patients have relatively good response as significant results. Male with insulin resistance are less likely to achieve an early viral response when treated with conventional interferon treated with chronic hepatitis C. similarly genotype III, it has previously shown that genotype III is quite responsive to conventional interferon but in our study the patients with insulin resistance and chronic hepatitis C have shown that there is less likely a chance of getting an early response with genotype III and same maximum people didn't get an early viral response with untypable genotype of chronic hepatitis C. To see either there is effect of age the early viral response we applied independent t-test and after resuming equal variance we found that there is no significant difference of age in our sampled population as mean age in both groups were 37-38 years so far.

CONCLUSION

Frequency of early viral response in chronic hepatitis C patients with insulin resistance was found in 55 (43.3%) individuals. It was not seen in 66.7 % of the sampled population in the study. We hereby suggest the use of pegylated interferon in patients with insulin resistance. Further studies should be encouraged in this regard.

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