Available online at http://www.advancedscientificjournal.com

IJMASRI, Vol. 1, Issue 2, pp. 49-54, April 2021

INTERNATIONAL JOURNAL OF MULTIDISCIPLINARY ADVANCED SCIENTIFIC RESEARCH AND INNOVATION (IJMASRI)

RESEARCH ARTICLE

UNFAVORABLE EFFECTS OF PEG- IFN (INTERPHERON) ALPHA+ RIBAVIRIN[B] DEVELOPED IN 24 WEEKS OF TREATMENT BESIDE HEPATITIS C

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Abstract

Almost 5.3% people are being ill with (hepatitis C virus HCV) in Pakistan. The therapy allotted to most of genotypes is a mixture of interferon and ribavirin. The patients received some side effects. The study was consisted of 25 people. Peg-Interferon alpha+ Ribavirin[b] treatment was prescribed for constant hepatitis C from September 2015 to February 2016 for 24 weeks. Those patients noted down in our questionnaire and updated us about side effects which they had faced during the whole period. Overall, side effects were fatigue, nausea, anemia, rashes, decreased appetite, chills, influenza like symptoms, neutropenia and hair loss. Most common side effect was hair loss (87%). It is concluded that combined therapy of peg-Interferon alpha+ Ribavirin[b] also have side effects. Further approaches with fewer side effects are needed for the treatment of hepatitis C.

Key words: Hepatitis C virus HCV, treatment, Peg-Interferon, Side effects, Sustained Virological Response

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Introduction

Hepatitis C virus (HCV) is a particular feature of liver diseases and is a key health problem worldwide (Asselah *et al.*, 2016; Alter, 2007). Hepatitis C has about 175 million Global Disease loads which show about 3% of population in the world, 3 to 4 million new patients with HCV are discovered yearly. HCV persists extensive in the world (Butt, 2005; Soriano *et al.*, 2009; Koziel and peters, 2007). Common healthy population studies depicted that HCV has 5.3% occurrence in Pakistan, 2.2% in Turkey and 7.7% in Zimbabwe (Demirturk,

2006; Gangaidzo *et al.,* 1997; Khokhar *et al.,* 2004). Hepatitis C virus disease is not a main reason of death in the first decade of infection (Harris *et al.,* 2008). Although, the biological features of HCV are exposed to an immense level in recent years, an utmost medication of hepatitis C is intricate in most of patients (Jawaid and khuwaja 2008).

Almost 50% HCV patients does not get steady virological Responses (Manns *et al.,* 2001; Baldick *et al.,* 2010; National Institutes of Health Consensus Development Conference Statement). Sustained virological response is different due to different genotypes of HCV (Mohamed *et al.,* 2013). A well-built correlation is present between hepatitis C viral genotypes and reaction of treatment. HCV is sorted into six genotypes on the basis of nucleotides sequence variation (Safi *et al.,* 2010). HCV genotypes 1-3 are common worldwide and their rate is different in different regions of the world. HCV genotype 4 is most common in Middle East and North Africa. HCV genotype 5 and 6 are present mainly in South Africa and Hong Kong in this sort (Idress and Riaz uddin, 2008). The prevalent genotype in Pakistan is 3 (Safi *et al.,* 2010; Idress and Riaz uddin, 2008). Now there is no vaccine accessible for HCV (Washeed, 2012). About 20 years ago, HCV management was begun with interferon- α (Lindsay *et al.,* 2001). A significant quantity of viral RNA is reduced with the help of α-interferon, but its application alone produces numerous side effects. The addition of a polyethyleneglycol side chain (pegylation) to the interferon provides it a much longer bioavailability, permitting for weekly injections rather than three injections per week. Pegylated interferon increases the sustained viral response rate (Hoofnagle *et al.,* 1986). When pegylated interferon is combined with ribavirin response rate is also improved. Ribavirin increases the viral mutation rate upto huge level due to which feasible genomes and weak off springs are produced. It is a purine analogue of HCV.

The production of cellular IMP (Inositol Monophosphate) dehydrogenase enzyme down regulated by Ribavirin which leads to declined cellular GTP levels. It also normalizes the host's immune system and improves the polymerase mutation velocity, expressing to damaged catastrophe (Duffy *et al* 2008; Feld and Hoofnagle 2005; Mansky and Bernard 2000; Waheed *et al* 2013; Young *et al.,* 2003). Combination of interferon and ribavirin is accessible for treatment against most of genotypes. This treatment is feasible but it produces a number of side effects. These side effects sometimes become bothersome, which can lead to dose decline or discontinuation of therapy. This study was designed to assess the range of combination (peg-Interferon alpha+ Ribavirin[b]) therapy in patients who had treated to cure chronic hepatitis C.

Materials and Methods:

This study was carried out in THQ (Tehsil headquarter) hospital Burewala from January 2016 to February 2016. There were 25 patients. 7 female and 18 male patients were present. Inclusion criteria was that all people who were treated with peg-Interferon alpha+ Ribavirin[b] therapy for chronic hepatitis C from August 2015 to January 2016 for 24 weeks. The age of all those people was between 25 years to 39 years. A response form was given to all those people. They were inquired about part effects during treatment. They were requested to mark in relevant column of bad results. All side consequences were included in the form. After completion of all forms, the data was evaluated with respect to the percentage of side effects in all people. Then, we drew a graph on MS Excel 2007 to test the ratio of side effects in all people.

Results:

A sum of 25 people who were treated with peg-Interferon alpha+ Ribavirin[b] therapy for chronic hepatitis C were included in this study. Mean age of people were 35 years. Majority of people had age between 31- 38 years. Gender division exhibited male majority. This treatment had many side effects. Among these side effects, 20(80%) out of 25 people had fatigue, while 11(44%) people developed headache. Nausea occurred in 8(32%) people. Hematological disorder such as Anemia took place in 10(40%) people and Neutropenia in 3(12%) people. Other most common side effect was skin rashes which occurred in 16(64%) people. Decreased appetite was observed in 6(24%) population. Chills

arose in 6(24%) people. Influenza like symptoms was seen in 5(20%) people. Hair loss which is a major problem was examined in 22(88%) people (Table 1).

Table1: Side effects of combined therapy (peg-Interferon alpha+ Ribavirin[b]) of 24 weeks during treatment of Hepatitis C.

Sr. No.	Side Effects	Answered Yes in %age (N=25)	Answered No in %age (N=25)
1.	Fatigue	80	10
2.	Headache	44	6
3.	Nausea	32	20
4.	Anemia	40	43
5.	Rash	64	13
6.	Decreased Appetite	24	43
7.	Chills(Fever)	24	10
8.	Influenza like symptoms	20	6
9.	Neutropenia	12	67
10.	Hair loss	88	9

Discussion:

The incidence of Hepatitis C is high worldwide and is rapidly increasing in Pakistan. The only accessible cure for most of genotypes is the combination of interferon and ribavirin. The remedy proved miscellaneous response in patients living with different HCV genotypes along with a number of side outcomes. In recent times two protease inhibitors were supported by FDA for the cure of patients living with HCV genotype 1 infection. The protease inhibitors were continued unsuccessful due to quick appearance of opposing mutants (Waheed *et al* 2013). Our dosage varying observations show that genotype 3 patients who were taking 800mg of Ribavirin regardless of their weight for 24 weeks, experienced good rate of treatment response. It is stated that peg- IFN and ribavirin therapy of 24 weeks leads to fatigue in 80%, headache in 44% people in HCV patients (Hafsa *et al.,* 2012). The side effects of peg-interferon and ribavirin therapy affect commonly all organ systems, while accumulation of protease inhibitor can intensify these side effects mainly anemia (Mark *et al.,* 2011), and/or may goes to new ones such as anemia in 40% people (Aftab *et al.,* 2013; Veronique *et al.,* 2016; Komal *et al.,* 2015) or thyroid dysfunction in 18% people (Amna and Muhammad, 2012).

Diarrhea is also a common side effect of peg-IFN + Ribavirin dose in 48% people (Lok *et al.,* 2012). Dermatological side effects e.g. rashes were happened in 64% patients. Dermatological side effects lead to mucocutaneous demonstration e.g. common skin Pruritus and skin Xerosis etc. (Patrice *et al.,* 2012]. Hair loss irregularity also occurs in 88% people (Lubbe, 2008). Neutropenia is common during cure of hepatitis C with interferon and ribavirin, but it is not typically associated with Hepatitis C infection. Neutropenia is perceived in 12% people [34]. Influenza like symptoms occurs in 20% patients during early weeks of treatment (Manns *et al.,* 2006). Symptoms of Myalgia occurred in 16% people as observed by (Nissen *et al.,* 2005) during interferon and methotraxate therapy.

Other unfavorable effects of this therapy includes nausea (32%), decreased appetite (24%), Chills or fever (24%), hematological parameters(Haemoglobin, Neutrophils, Thrombocytes) were also decreased. Certain parameters such as Bilirubin, Creatin Kinase and Lipases were also elevated in these patients

Conclusion:

It is concluded that Interferon plus ribavirin remedy turns out a good effect in patients having HCV of genotype 3. The chief disadvantage of the therapy is a number of side effects. Interferon free Abbott's triple therapy and GS-7977 drug are good alternative for HCV patient. While interferon free course of therapy of Sofosbuvir (Sovaldi + Ribavirin) includes better result with improved SVR rates and fewer side consequences. Among these interferon free regimes, the drugs having a elevated genetic barrier to resistance such as nucleotide NS5B inhibitors in addition to medicines with a high antiviral effectiveness such as NS3/4A or NS5A inhibitors shown to be important. More investigation is needed to choose which treatment is significant in conditions of defense and efficiency in patients.

Acknowledgement:

We would like to thank Dr. Najam ul Haq: the Chairman, Department of Biochemistry, Bahauddin Zakariya University Multan Punjab Pakistan for providing us a platform to conduct this study.

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