ORIGINAL ARTICLE

The Frequency of the Retinopathy in Patients of Chronic Hepatitis C Treated with Interferon Alpha - Ribavirin Combination Therapy

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ABSTRACT

Objectives: Chronic hepatitis C causes cirrhosis of liver in 20% of the total 170 million people affected and is the commonest cause of hepatocellular carcinoma as well. Treatment of hepatitis C with interferon-ribavirin combination therapy has proved to be effective in terms of biochemical and virological response. Retinopathy is a well-recognized side effect of interferon therapy. Cases have been reported where patients of chronic hepatitis C being treated with interferon suffered from blindness. Surveillance for this side effect of interferon has not been done strictly in the past. The objective of the study is to elucidate the frequency of retinopathy in patients of chronic hepatitis C who are on conventional interferon alpha-ribavirin combination therapy.

Design: Descriptive case series.

Place and duration of study: The study was conducted in Hepatitis Clinic, Medical Unit III Services Hospital Lahore**.** The study was carried out over a period of six months, from 25th August 2010 to 25th Feb. 2011.

Method: One hundred and fifty patients were included in the study. Interferon and ribavirin combination therapy was then started in the dose of 3 million units subcutaneously thrice a week and 400mg orally thrice a day respectively. Fundoscopy was done by a single ophthalmologist in every patient after the week 6 and 12 of the start of therapy. Presence or absence of retinopathy was documented.

Results: One hundred and fifty patients were enrolled in the study. Eighty eight patients (58.7%) were male and 62 (41.3%) female. Ages of the patients ranged between 20-50 years with the mean age 37 ± 7.907 years. One hundred and sixteen patients (77.3%) did not develop any retinal changes but remaining 34 patients (22.7%) suffered from retinopathy.

Conclusion: It is concluded that every patient on interferon therapy should have regular eye examination for surveillance of retinopathy to prevent blindness, a dreadful consequence

Key words: Interferon, retinopathy and chronic hepatitis C

INTRODUCTION

Hepatitis C virus (HCV) is a single-strand, positive sense ribonucleic acid (RNA) virus belonging to the flaviviridae family [1]. Incidence of end stage liver disease (ESLD) among HCV infected individuals is 3.1 /1000 person-year [2]. Chronic hepatitis C causes cirrhosis of liver in 20% of the total 170 million people affected and is the commonest cause of hepatocellular carcinoma as well [3]. Its prevalence in Pakistan is estimated between 3-13%[4, 5]. Treatment of hepatitis C with interferon- ribavirin combination therapy has proved efficacy in terms of biochemical and virological response[6]. Interferon is an anti-inflammatory, anti-tumor, antiviral, and immunomodulatory cytokine. Ribavirin is an antiviral agent with immunoregulatory activity [7]. Immune complex deposition in the retinal capillaries and ischemic insult similarly found in diabetes and hypertension are the proposed mechanisms underlying the development of interferon induced retinopathy [8]. Various adverse effects of interferon include flu like illness, bone marrow suppression, thyroid dysfunction, depression, arthralgias and significant retinal complications [9]. Interferon induced retinopathy is characterized by retinal hemorrhages, cotton wool spots around optic disc, and macular edema. Branch retinal vein occlusion, retinal rubeosis and ischemic optic neuropathy are its rare manifestations. Interferon induced retinopathy ranges from completely asymptomatic condition to permanent visual loss [10, 11]. These retinal changes most often develop within the first 12 weeks of interferon therapy7.Interferon induced retinopathy can result in permanent loss of vision [12,13] .Older

age of the patient, higher dose of INF, diabetes and hypertension are most commonly associated risk factors. Chronic hypertension and diabetes is associated with thickening of vessel walls, thus predisposing patients to interferon induced retinopathy. Aim of the present study is to determine the frequency of interferon induced retinopathy in patients of chronic hepatitis C in Pakistani population and if it is found high, routine fundoscopic examination of such patients should be undertaken during interferon treatment.

MATERIAL AND METHOD

The study was conducted in Hepatitis Clinic, Medical Unit III, Services Hospital Lahore, over a period of six months from 25th August 2010 to 25th Feb, 2011.

One hundred and fifty patients of chronic hepatitis C were included in this study. Non probability purposive sampling technique was used and it was a descriptive case series. Patients with chronic hepatitis C between the ages of 20-50 years with normal fundoscopic examination before the start of interferon therapy were included in this study. Patients with diabetes mellitus, hypertension, history of eye trauma, surgery or laser phototherapy and who had already on interferon alpha therapy were excluded from the study. After informed consent, 150 patients who met the inclusion criteria and were registered in the Hepatitis Clinic of Medical Unit III of Services Hospital Lahore were enrolled in the study. Informed consent was taken before fundoscopy. Interferon and ribavirin combination therapy was then started in the dose of 3 million units subcutaneously thrice a week and 400mg orally thrice a day respectively. Fundoscopy was done by a single ophthalmologist in every patient after the week 6 and 12 of the start of therapy. Data was analyzed on SPSS version 12.0.

RESULTS

During the study period, 150 patients of chronic hepatitis C were enrolled. INF-Ribavirin combination therapy was started and the patients were followed till the completion of 12 weeks of therapy. Out of total 150, 88 patients (58.7%) were male and 62 were female (41.3%), (table1). Age was broadly divided into two groups i.e. 20-35 years and 36-50 years (table 2). Out of total 150, 71 patients (47.3%) had their ages in the range of 20-35 years. The mean age for this group (20-35 years) was 29.80 ± 4.08 years. Second group comprised of 79 patients (52.7%) who had their ages between 36-50 years. The mean age for this group (36-50 years) was 43.36 ± 4.038 years. Mean age for the total sample size was 37 ± 7.907 years. Out of the total 150 patients, 34 (22.7%) developed retinopathy and 116 patients (77.3%) did not (table 3).

Table 1: Distribution of Patients by Gender

GENDER	Patients	Percentage
Male	88	58.7%
Female	62	41.3%

Table 2: Distribution of Patients by Age

Age in years	No of patients	Percentage
20-25	12	8
26-30	27	18
31-35	32	21.3
36-40	25	16.7
41-45	31	20.7
46-45	23	15.3

Table 3: Frequency of Retinopathy after Therapy

Retinopathy	No. of Patients	Percentage
Yes	34	22.7 %
No	116	77.3 %

DISCUSSION

Chronic hepatitis C affects more than 170 million people in the world [14, 15]. Its prevalence in Pakistan estimated by various studies is between 3-13% [16, 17]. The treatment of chronic hepatitis C (CHC) is now well established with conventional interferon or pegylated interferon in combination with ribavirin [18]. Ocular toxicity is one of the dreadful complications of interferon therapy. Out of 150 enrolled patients in the present study, 88 patients (58.7%) were male and 62 (41.3%) female. This difference in number of patients with respect to gender is reflected in various studies conducted worldwide, where male patients were in overwhelming majority [19, 18.] This difference may further strengthen the fact that male population seeks health care facilities with increased frequency in Pakistan [19]. In this study 34 patients (22.7%) developed retinopathy with INF therapy, supporting further the already established fact by different studies conducted worldwide [20, 21]. The incidence of reported retinopathy in patients receiving INF therapy is variable in different small

scale studies to large study groups [22]. In this study group most of the patients were asymptomatic. The patients who did experience subjective complaints spoke of reduced vision and watery eyes. This fact is well supported by different studies in which no patients were aware of any significant change in their vision but had retinopathy. Similar to previous studies, this study also showed that retinal changes usually develop within the first 12 weeks of INF treatment [20, 21]. Therefore, there is sufficient evidence to point out the first 3 months as the most likely time for its development. It is very unlikely that retinopathy occurs after the start of 3 months of therapy.

CONCLUSION

It is concluded that INF induced retinopathy develops in considerable number of patients and is most commonly detected during the first 12 weeks of therapy. Therefore, it is recommended that every patient on interferon therapy should have regular eye examination for surveillance of retinopathy to prevent blindness, a dreadful consequence.

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