ORIGINAL ARTICLE

To Study the Frequency of Various Side Effects of Alpha Interferon Therapy during Treatment of Hepatitis C in DHQ Hospital Gujranawala

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ABSTRACT

Aim: To see the frequency of various side effects of alpha interferon therapy of hepatitis C patients.
Methods: This prospective observational study was conducted in Medical unit DHQ Hospital, Gujranawala medical college. A total of 200patients of chronic hepatitis C with positive Anti HCV (hepatitis C virus) antibodies and HCV RNA by polymerase chain reaction (PCR) were enrolled in the study, who presented in OPD from Dec 2013 to June 2014.
Result: Out of 200 patients 82 were males and 118were females.107(53.5%) patients presented with various flu like symptoms like body aches, headache, fever and fatigue. 34(17%) patients presented either with bruises or petechiea or sore throat. On peripheral blood examination there was either neutropenia or thrombocytopenia. 24(12%) presented with depressive symptoms, 2(1%) patient presented with deranged renal function test 9(4.5%) presented with deranged thyroid function tests. 12(6%) patients presented with various gastro intestinal complaints like fullness, nausea, anorexia etc 11(5.5%) presented with various dermatological side effects.
Conclusion: Side effects during interferon therapy are very common. Early detection and then management of the side effects lead to better success rate of treatment and a good survival.
Keywords: Chronic hepatitis C, combination therapy, side effects.

INTRODUCTION

Hepatitis C virus (HCV) infection is problem which is increasing day by day. It is effecting 3% world s population, it means that 170 million people are at risk for having chronic liver disease due to hepatitis C[1]. Out of these patients substantial proportion of the individuals, if not all develop chronic infection[2,3]. Side effects of interferon and ribavirin are well known. These side effects may be treatment limiting and require dose reduction or drug discontinuation[4,5,6,7,8]. In our area too, frequency of hep c infection is increasing day by day. People are very eager to get treatment but compliance is not up to the mark because of side effects, leading to dose reduction or discontinuation[9] or intolerability to medicine and self abundance of medicine. It is therefore essential to monitor the patients at regular interval during treatment to detect the undesirable effects timely and to manage them properly. This study was designed to assess the spectrum of the side effects of combination therapy (interferon and ribavirin).

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MATERIAL AND METHODS

This prospective observational study was conducted in DHQ hospital OPD department Gujranwala from DEC2013 to June 2014. A total of 252patients were initially enlisted in the study, there age was ranging from 35-50 years. Out of these 52 patients were lost in follow up. Inclusion criteria was that all Patients with chronic hepatitis C, positive anti HCV antibody by ELISA, positive HCV RNA by polymerase chain reaction (PCR) were included in the study. Exclusion criteria was that patients with evidence of decompensated liver disease; serious underlying medical illness and patients who had other contraindication to combination therapy. After verbal consent and base line investigations, the patients were given injection Interferon 3 MIU subcutaneously thrice weekly & ribavirin 800 to 1200mg/day, as per their body weight i.e., those less than 50kg received 800 mg/day, 50-75kg received 1000mg/day and more than 75kg received 1200 mg/day. These patients were evaluated on monthly basis for various side effects. Patients were also told to report any side effects anytime during the course of treatment. These unwanted effects were graded as mild (not requiring consultation and not affecting quality of life),

moderate (requiring consultation, reassurance and symptomatic treatment) and severe (requiring reduction or discontinuation of treatment). Finally data was analyzed to analyse side effects of combination therapy of interferon plus ribavirin in chronic hepatitis C patients

RESULTS

Two hundred chronic hepatitis C patients, who got both interferon and ribavirin entered the study.82 were males and 118 were females. Their age ranges between 35 to 50 years. There were a number of mild side effects observed during the treatment. Flu like symptoms were observed in 107 out of 200 (53.5%) patients. They included fatigue in 43(40%), fever in 56(52%), body aches and pains in 8(7.5%) patients respectively. All of this flu like symptoms were mild to moderate and were resolved on simple reassurance and simple medicine like paracetamol. These side effects were by far most common among all side effects and luckily were resolved easily. Hematological side effects were noted in 34 out of 200(17%) patients.21 patients (61.7%) presented with mild to moderate anemia (Hb= or <8g/dl).8 (23.5%) patients presented with decrease white cell count. Range was between 2500-3500cell/mm3 in 6 out of 8(75%) patients. Only 2(25%) patients presented with sever leucopenia (1000-1500/mm3). Interferon therapy has to be discontinued in these patients. 5 patients presented with decreased platelet count. Out of these 5 four (80%) presented with asymptomatic thrombocytopenia (platelet count =or >50,000/mm3). Only 1(20%) patient presented with severe bleeding. 24(12%) patients presented with neuropsychiatric symptoms. 11(45.5%) presented with insomnia, 6(25%) presented with mood changes, 5(20.8%) presented with anxiety, 2(8.3%) patients presented with restlessness. Nobody presented with serious depression or suicidal thoughts for which interferon therapy has to be discontinued. 2(1%) patients presented with deranged renal functions. In both there was steady rise of kidney function tests which did not improve without discontinuing therapy. They were of serious nature and with ureic symptoms too. 12(6%) patients presented with various GI side effects. 5(41.6%) presented with dyspepsia, 6(50%) presented with anorexia.1(8.3%) patient presented with nausea. All these GI side effects were mild to moderate.11(5.5%) patients presented with various dermatological side effects. 5(45.5%) presented with alopecia. 3(27.27%) patients out of total 11 presented with skin rashes and 3(27.27%) presented with photosensitivity. All these dermatological effects were mild to moderate and reversible. 9(4.5%) patients presented with thyroid dysfunctions. Out of these 9, 7(77.77%) patients presented with mild to moderate thyroid abnormalities. 3(33.33%) presented with severe thyrotoxicosis which eventually led to discontinuation of therapy. So total 8 out of 200 patients presented with severe side effects either leading to discontinuation or dose reduction of the combination therapy along with supportive management. 2 presented with serious renal functions impairment needing discontinuation along with hemodialysis. 3 presented with severe thyrotoxicosis. 2 patients presented with severe leukopenia along with evidence of infection. Only 1 patient presented with serious thrombocytopenia leading to major bleeding.

DISCUSSION

Different varieties of interferon have been widely used in treatment of hepatitis c. They are usually given subcutaneously. A wide spectrum of side effects have been noted in different large trials of treatment of hepatitis C. Side effects are common; most of the time they are minor but can be serious in some of patients. Major adverse events can occur, but life-threatening adverse events have been rare in large trials[10]. Tolerance of interferon therapy is same in elderly patients and children[11,12,13].

Treatment of hepatitis C with combination therapy is not without unwanted effects in our study too. Most of these side effects are attributed to interferon and some to ribavirin. The adverse effects noted in this study were generally mild to moderate

except in few patients in whom treatment had to be withdrawn due to serious side effects. Influenza like symptoms occurred in most of the patients (53.5%) during the first month of treatment. They were usually alleviated by explanation and simple analgesics like paracetamol[14]. Giuseppe B et al[15] have reported influenza like symptoms in 77.7% of the patients with combination therapy and 65% of the patients with Interferon alone, various body pains and aches including headache, myalgia and arthralgias etc. So in our study fever was most prominent flu like symptom, after which comes fatigue. Hematological side effects were noted in 34 out of 200(17%) patients. 21 patients (61.7%) presented with mild to moderate anemia (Hb= or <8g/dl). Mean drop in haemoglobin was almost 1.5g/dl. Anaemia is caused both by interferon due to myelosupression and ribivirin causing haemolysis. Haemoglobin ranged between 7.5-12g/dl. The dose of ribavirin was decreased inpatients in whom the haemoglobin fell below 10g/dl.A reduction in the dose resulted in an increase in haemoglobin concentration and it remained stable through out treatment. The 8 (23.5%) patients presented with decrease white cell count. Range was between 2500-3500cell/mm3 in 6 out of 8(75%) patients. Only 2(25%) patients presented with sever leucopenia (1000-1500/mm3). Interferon therapy has to be discontinued in these patients.5 patients presented with decreased platelet count. Out of these 5 four (80%) presented with asymptomatic thrombocytopenia (platelet count =or >50,000/mm3). Only 1(20%) patient presented with severe bleeding. In contrast in another Pakistani study conducted at Peshawer[14], 70%patients presented with anemia, 64% with leukopenia and 61% with asymptomatic thrombocytopenia and 1% with sever thrombocytopenia. In this study 8% patients of anemia required dose reduction of ribavirin and 8.5% required discontinuation of drug .While 14 neutrophil count returned to normal on stopping therapy. 24(12%) patients presented with neuropsychiatric symptoms. 11(45.5%) presented with insomnia, 6(25%) presented with mood changes, 5(20.8%) presented with anxiety, 2(8.3%) patients presented with restlessness. Nobody presented with serious depression or suicidal thoughts for which interferon therapy has to be discontinued. While in a study conducted by Khalid Mehmood and Noor Rehmat in Peshawar[14] showed neuropsychiatric features in 71% patients. They are mostly attributed to interferon. Hauser and J Khosla et al[16] conducted a study in which 13 out of 39 patients (33%) developed major depressive disorders but were fully controllable with citalopram[17].

The exact mechanism is unknown. These effects include fatigue, asthenia, drowsiness, confusion, depression and apathy. Severe depression was observed in six patients and two had suicide ideation with suicide attempt. Depression has been reported to be as high as 30% in patient receiving combination therapy for chronic hepatitis C[18] Dieprink E et al[19] have reported a suicide in patients with out a previous psychiatric history. These neuropsychiatric side effects respond to selective serotonin reuptake inhibitor and regress after discontinuing therapy, albeit after some weeks. None of our patient had major depressive symptoms which is otherwise very common in other trials. 11(5.5%) patients presented with various dermatological side effects. 5(45.5%) presented with alopecia. 3(27.27%) patients out of total 11 presented with skin rashes and 3(27.27%) presented with photosensitivity. All these dermatological effects were mild to moderate and reversible. While in a local study conducted in Peshawar showed[14]. Dermatological side effects were noted in 81% patients and ranged from photosensitivity, dry skin, pruiritis, itching and alopecia. Out of these 9, 7(77.77%) patients presented with mild to moderate thyroid abnormalities. 3(33.33%) presented with severe thyrotoxicosis which eventually led to discontinuation of therapy. While in Pakistani study[14] thyroid function abnormalities were noted in 16(4%) of the patients. Hyperthyroidism occurred in two patients in whom there was diffuse enlargement of the thyroid gland with increase in T3 and T4 and suppression of TSH. The mechanism seems to be related to immunomodulatory properties of interferon, which induces non-organ specific antibodies causing autoimmune thyroiditis. Thyroid disorders have been reported in 2.5 to 20% of patients. Both hypothyroidism and hyperthyroidism can occur[1]. 12(6%) patients presented with various GI side effects. 5(41.6%) presented with dyspepsia, 6(50%) presented with anorexia. 1(8.3%) patient presented with nausea. All these GI side effects were mild to moderate while Khan PM et al[20] showed various GI side effects in 50% patients.

CONCLUSION

Combination therapy is not without side effects. Most of the unwanted effects are well tolerated by the patients. If we properly re-assure and educate

patients and start timely treatment, this can lead to better compliance to interferon therapy.

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