

Weight loss with Interferon and Ribavirin therapy in Chronic Hepatitis C patients

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Abstract

Recommended treatment of chronic Hepatitis C virus (HCV) infection is interferon and ribavirin. Most patients develop side effects during treatment. Weight loss is one of the side effects of interferon therapy. Present study was conducted at Pakistan Medical and Research Centre (PMRC), Jinnah Postgraduate Medical Centre (JPMC), Karachi from January 1998 - December 2010, to find out the frequency, extent of weight loss, its recovery after interferon therapy and the impact of weight loss on treatment response. Body weight was recorded on regular outpatient visits i.e initially, then at 1, 3 and 6 months of treatment and six months post treatment. Out of 260 patients, 176 (67.7%) observed statistically significant weight loss ($p < 0.05$), on completion of therapy as compared to initial visit. Weight loss during interferon therapy was found to be independent of age, gender, treatment outcome, serum albumin, haemoglobin, white blood cell (WBC) and platelet count. Body weight returned to baseline within six months after completion of treatment in most cases.

Keywords: Chronic hepatitis C, Interferon, Side effects, Weight loss.

Introduction

Hepatitis C is a global health problem. About 170 million people i.e. 3% of the world's population are infected with HCV.¹ Long term sequel of disease is cirrhosis which may later lead to hepatocellular carcinoma.² The treatment of choice is combination of interferon and ribavirin. This treatment results in viral clearance in about 62% patients.³ One of the side effects of interferon therapy in this study is weight loss. Patients expect improvement after the commencement of treatment and on the contrary side effects like weight loss may deteriorate their well being. If these patients are not properly counseled before starting treatment sometimes it results in discontinuation of therapy leading to relapses of disease. The side effects experienced by patients on pegylated interferon are similar to patients on conventional interferon.⁴ Our patients with HCV infection are generally not well nourished to start with, either due to poor nutritional status or due to taboo of food resulting in traditional dietary restrictions. Poor appetite, fatigue, depression after starting interferon therapy; makes the situation more complex in our scenario. The present study was conducted to assess the pattern of

weight changes and its association with treatment response to create awareness among the treating physicians to vigilantly observe and counsel patients on treatment.

Patients and Methods

This study was conducted in the outpatient department of PMRC, JPMC, Karachi, from January 1998 to December 2010. The study was approved by the ethical committee of PMRC. All patients of chronic HCV infection, who were HCV RNA positive, had raised alanine aminotransferase (ALT) twice the upper limit of normal for more than six months treated with interferon and ribavirin were included. All the baseline parameters including complete blood count (CBC), liver function tests (LFTs), serum protein/ albumin and HCV RNA were noted. Patients with any signs of decompensation or concurrent Hepatitis B virus (HBV) infection were excluded. Follow up of patients were done with Blood CBC and ALT. Body weight in kilograms was recorded as base line before starting therapy and at each outpatient visit i.e. 1, 3 and 6 months and at six months after cessation of therapy.

Conventional Interferon:

Three million units subcutaneously thrice weekly, with ribavirin orally according to body weight ($\leq 70\text{kg}$ 800mg, $>70\text{kg}$ 1200mg) was given in divided doses for adults. Seven patients ≤ 18 years of age were given ribavirin in the dose of 15mg/kg/day. No dietary restriction or supplementations were advocated before, during or after the treatment period.

Statistical Analysis:

The data was fed and analysis was done on computer

package SPSS (Statistical Package for Social Science) version 11.0. Statistical analysis was performed using the Chi-square test for the comparison of discrete variables and the t-test for the comparison of continuous variables (weight in kg). In all statistical analysis, only p-values < 0.05 are considered significant.

Results

A total of 260 patients were treated with combination therapy for 6 months and followed for six months post treatment. Out of them 165 (64%) were males, 95 (36%) females. Age ranged from 15 to 66 years with a mean of 36.4 ± 10.25 years. At baseline mean weight was 65.3 ± 13.7 kg. In males it was 63.6 ± 14.7 kg while in females average weight was 66.3 ± 13.7 kg, which was not statistically significant ($p = 0.147$). On completion of therapy average weight was 62.7 ± 13.6 kg. In males the mean weight was 63.7 ± 12.6 kg while mean weight in females was 60.9 ± 15.0 kg which did not reach statistical significance ($p = 0.107$) (Figure-1).

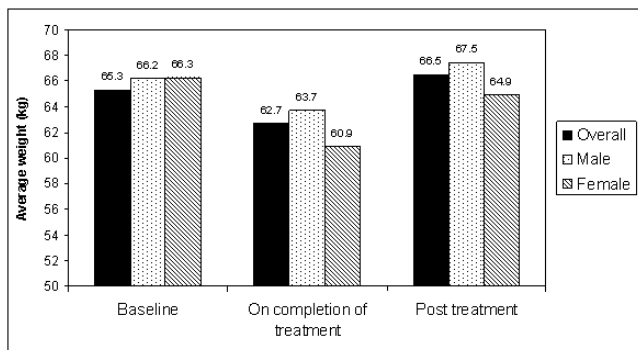
Decrease in weight was observed in 176 (67.7%) patients as compared to the initial baseline weight, which was statistically significant ($p < 0.05$), while weight increased in 64 (24.6%) patients and 20 (7.7%) patients showed no change at completion of therapy (Figure-2).

Weight loss pattern in patients less than 40 years and more than 40 years of age had no statistically significant difference. No significant difference in weight loss was noted among patients with haemoglobin 10-12 g/dl or > 12 g/dl. In patients with WBC < 4000 and those with > 4000 , difference in weight loss did not reach statistical significance. Patients with platelet count > 150000 and less than 150000 did not show any significant difference in

Table-1: Weight status on completion of treatment and post treatment according to gender, age, Albumin, platelet, hemoglobin and WBC (n=260).

Variables	No. of Subjects	Weight decreased On completion	Weight regained 6-months post treatment
Gender	n=260		
Male	165	106 (64.2%)	105(63.6%)
Female	95	70 (73.7%)	66(69.4%)
Age in years	n=260		
Under 40	64	46 (71.8%)	44(68.7%)
40 & above	196	131 (66.8%)	127(64.7%)
Haemoglobin (g/dl)	n=243		
10 - 12	40	30 (75.0%)	24(60%)
> 12	203	136 (67.0%)	133(65.5%)
WBC	n=245		
< 4000	9	7 (77.8%)	5(55.5%)
> 4000	236	164 (69.5%)	156(66.1%)
Platelet	n=223		
Normal ($>150,000$)	182	128 (70.3%)	123(67.5%)
Abnormal (150,000)	41	27 (65.9%)	22(53.6%)
Albumin (g/dl)	n=222		
< 4.0	85	53 (62.4%)	58(68.2%)
> 4.0	137	101 (73.7%)	86(62.8%)

No significant difference in weight loss on completion and 6 months post treatment according to gender, age, platelet, albumin, WBC, haemoglobin $p > 0.05$.



Weight decreased significantly due to Interferon (from baseline to completion of treatment) $p < 0.05$ and on post treatment increased, and reached to baseline ($p > 0.05$).

Figure-1: Weight status of Interferon patients on baseline, completion of treatment and after 6 months post treatment (n=260).

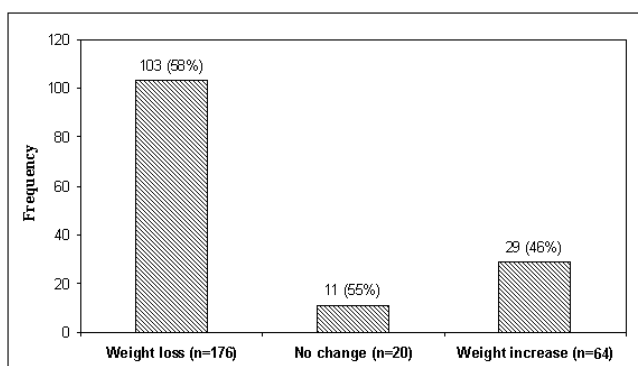


Figure-2: Effect of weight on Sustained Virological response (SVR).

weight loss. Similarly weight loss patterns among patients with albumin > 4.0 g/dl and those with albumin > 4.0 g/dl were not significantly different (Table). Thus no significant difference in weight loss pattern was found during therapy and its recovery after completion of therapy, in relation to above mentioned treatment variables ($p > 0.05$) (Table).

Out of 176 patients who experienced weight loss, 103 (58.2%) achieved sustained virological response (SVR). Out of 20 patients who maintained their weight during therapy 11 (55%) achieved SVR and out of 63 patients who observed weight gain during therapy 29 (46%) achieved SVR, however the difference was not statistically significant $p > 0.05$.

One hundred forty three patients who achieved sustained virologic response, forty six non responders and fifty four patients who relapsed, had similar pattern of weight loss during therapy and regained their weight after the completion of therapy, the difference was statistically not significant.

Six months post treatment 147 (56.5%) not only

regained their baseline weight but also put on weight, 24(9.2%) patients simply regained their baseline weight within 6 months, while 89 (34.2%) patients could not regain their baseline weight.

Discussion

Weight loss is an important side effect of interferon therapy and a major concern for the patients. According to a French study weight loss has been reported in more than 20% patients on combination therapy⁵ which is quite low as compared to the present study in which 67% patients experienced weight loss, which could be due to racial difference or poor baseline nutritional status in our patients. Our study included seven children who showed the same pattern of weight loss as adults similar to earlier studies.⁶ The exact mechanism of weight loss during interferon and ribavirin therapy is not known. Some studies show that interferon decreases appetite by stimulating tumour necrosis factor (TNF) but others indicate that changes in levels of leptin and insulin are responsible.⁷ Weight loss may be related to a number of other side effects of combination therapy such as nausea, altered taste sensation, mouth ulcers and anorexia. Another factor which could play a major role in weight loss especially in our society are the dietary restrictions commonly known as perhez or food taboos (hot/cold things), very commonly practiced in our community in which all the high caloric diet like meat, fish, oil and dairy products are restricted in patients with liver disease irrespective of their disease severity and without any justification. It is the responsibility of the physician to counsel the patients to maintain a normal diet thus minimizing weight loss.

Weight loss was slightly higher in females as compared to males. The reason for this difference is that females are much more prone to side effects during interferon therapy.⁸ It is not known as to why females develop more side effects but females generally weigh less than males so the higher cumulative dose of interferon and ribavirin in females as compared to males may be the cause.⁹

In this study it was observed that SVR was achieved in 103(58.2%) patients who lost weight which was higher than in patients who maintained or increased weight during therapy but did not reach statistical significance ($p > 0.05$). These results are consistent with previous studies.¹⁰ This study also shows that increased weight loss during therapy was not associated with age, gender, serum albumin, haemoglobin, WBC and platelet count.

Weight loss during interferon therapy is usually reversible and majority of patients regained their pretreatment weight within six months after treatment completion.¹¹

This study is limited as it is retrospective and complete data of all parameters is not available. Also it is not known as to how many patients observed dietary restrictions. Another limitation of the study is that BMI cannot be calculated because of its retrospective nature.

Hence weight loss is an important side effect of interferon therapy which is still poorly addressed; treating physicians need to be aware of this side effect for proper management of the patient.

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