The Professional Medical Journal
www.theprofesional.com

ORIGINAL PROF-0-3791

DOI: 10.29309/TPMJ/2019.26.07.3791

ASSESSMENT OF EFFECTS ON HEMATOLOGICAL PARAMETERS AFTER INTERFERON AND RIBAVIRIN THERAPY AMONG HEPATITIS C PATIENTS IN KARACHI.

Zubia Zia[1], Naim ul Hasan Naqvi[2], Ayaz Mustafa[3], Muzammil Hussain[4], Aysha Zia[5], Rehana Perveen[6], Hira Naeem[7], Zuneera Akram[8]

1. Ph.D.,
Assistant Professor,
Baqai Institute of Phamaceutical Sciences.
2. Ph.D., D.Sc.
Professor,
Baqai Institute of Phamaceutical Sciences.
3. Ph.D.
Centre Incharge,
PMRC, Specialized Research Centre on Child Health,National Institute of Child Health, Karachi, Pakistan.
4. M.Phil
Lecturer
Baqai Institute of Phamaceutical Sciences.
5. M.Phil
Baqai Institute of Pharmaceutical Sciences.
6. Ph.D.
Professor
Baqai Institute of Pharmaceutical Sciences.
7. M.Phil
Lecturer
Baqai Institute of Phamaceutical Sciences.
8. M.Phil
Lecturer
Baqai Institute of Phamaceutical Sciences.

Correspondence Address:
Dr. Zubia Zia
Baqai Institute of Phamaceutical Sciences.
dr_zubia@baqai.edu.pk

Article received on:
06/08/2018
Accepted for publication:
15/12/2018
Received after proof reading:
25/06/2019

ABSTRACT… This study aims to evaluate the hematological abnormalities treated with interferon and ribavirin therapy in hepatitis C patients of Pakistan. **Study Design:** Descriptive cross sectional study. **Setting** Gastroenterology and Hepatology Department of JPMC, Karachi, Pakistan. **Period:** 2 years from August 2014 to July 2016. **Materials and Methods:** All the patients with positive HCV RNA test were enrolled in the study and their HB, WBC`s and platelets level were assessed. Standard treatment (interferon and ribavirin) against HCV were started. Then after 6 months of therapy, their levels of HB, WBC`s and platelets were again evaluated to examine the current status. **Results:** 88 Cases of HCV were enrolled in the study, of which 52(59%) were females patients and 36 (41%) were male patients. 33(37.5%) patients were those who had age below than 40 years while 55(62.5%) patients were those who had above 40 years age. In these 88 patients 49(55.68%) patients were those who respond toward the therapy and 39(44.31%) patients were those who did not respond toward the therapy. Only 2(2.27%) patients from Non-Responder groups was found with increase WBC'S count, while 17% patient of both groups in case of hemoglobin and 19.3% Patients of both group in case of platelets was found with decreased level after treatment. **Conclusion:** Interferon plus ribavirin therapy induces anemia due to decreasing hemoglobin level, as well as increases the WBC'S count in case of not responding the therapy and decrease platelet counts have been observed as side effect of therapy.

Key words: Hemoglobin, Hematological, Hepatitis C, Interferon, Platelets, WBC`S.

Article Citation: Zia Z, Naqvi N, Mustafa A, Hussain M, Zia A, Parveen R, Naeem H, Akram Z. Assessment of effects on hematological parameters after interferon and ribavirin therapy among hepatitis c patients in Karachi. Professional Med J 2019; 26(7):1162-1166. **DOI:** 10.29309/TPMJ/2019.26.07.3791

INTRODUCTION

Globally, hepatitis C is considered as a major cause of concern and its chronic nature is a leading cause of cirrhosis, which is responsible for end-stage liver disease and hepato-carcinoma.[1] Mostly, treatment with interferon along with ribavirin is prescribed for eradication of virus, which produces good effects on liver histology.[2] The therapy is also involved in reducing risk of developing cirrhosis and liver cancer.[3] Recently, a lot of advancement in the treatment against HCV have been developed but interferon based treatments are still the mainstay of therapy in Pakistan, with a cure rate of 50-80%.[4] Besides the effectiveness of therapy against HCV, the therapy also possess severe side effects including bone marrow depression, hematological disturbances and pulmonary difficulties.[5,6] For any of the unwanted event that occur due to interferon therapy, dose reduction is suggestive.[7] Myelosuppresion has also been reported as a side effect of interferon treatment. The count of WBCs, platelets and Hemoglobin level have been observed which is decreased during the therapy but could be manageable, if their levels were normal before initiation of the therapy. This decrease in blood count is reversible and could be manage with the reduction in dose.[8]

MATERIAL AND METHOD

Patients visiting the Gastroenterology and Hepatology department of JPMC was approached to participate in the study. Their HCV status was confirmed with PCR and patients with positive

HCV status were selected. Before enrollment, a written consent was obtained from them. Data from 88 patients were included in the study as they properly followed the treatment. Their demographics and socioeconomic status were recorded on a pre-designed proforma which was pre coded in order to maintain confidentiality and other clinical details, including levels of Hb, WBC`s and platelets count were also evaluated. Afterwards the standard treatment against HCV consisting of interferon and ribavirin was started. After 6 months of therapy patient`s post treatment HCV status was again assessed and the effect of treatment on the levels of Hb, WBC`s and platelets were also assessed. On the basis of results patients were categorized into two groups. One group was named as treatment responder and the other group was named as treatment non-responder group. Patients with negative HCV status were placed in first group i.e. treatment responder group while patients with still positive HCV status after treatment were placed in second group i.e. treatment non-responder group.

RESULTS

A total of 88 cases of HCV have been included in the study. Among these 88 patients, females were 52 and males were 36. The patients age below than 40 years were 33 and 55 patients were of about 40 years of age or above. Education status of patients showed that only 18 patients have completed their matric whereas 70 patients have not completed matric. The socio-demographic detail of study population are presented in Table-I.

Eighty eight patients have completed the 6 months treatment with interferon and ribavirin and maintain follow up checkups. After 6 months of therapy, their HCV status was again evaluated to monitor the status of the disease. It was observed that a total of 49 patients responded to the therapy positively and classified into `RESPONDER` group whereas 39 patients did not responded towards the therapy positively and therefore placed into `NON-RESPONDER` group. The effect of therapy on patient`s WBC`s, platelets and hemoglobin was observed concisely.

The effect of therapy on WBC`s was evaluated which revealed that patients with normal count of WBC`s in both responders and non-responders group are upto 80.68%. Whereas 19.31% patients are those who does not showed normal count of WBC`s in both groups before and after therapy. Only 2.27% patients from the non-responder group showed an increase in count of WBC`s after therapy (Figure-1).

On evaluating the effect of therapy on hemoglobin levels, it was observed that 37.5% patients in responder and non-responder group presented with normal levels of Hb both before and after receiving interferon therapy. Whereas 45.5% patients showed low levels of Hb in both groups before as well as after treatment. Although, only 17% patients in both groups with levels of Hb in normal range before treatment showed that their levels of Hb reduced after receiving therapy (Figure-2).

When platelets were evaluated against the treatment of HCV, the results showed that the platelet count of 75% patients in responder as well as non-responder group remain same within the normal range. Further we observed that 5.6% patients in both group was those who had normal level of platelets before treatment while their platelet count decreased when the patient received the therapy and 19.3% patients in both groups were those who already had decreased levels of platelets count which further decreased after the therapy (Figure-3).

Characteristics	Number of Patients (N)	Percentage (%)
Gender		
Male	36	40.9
Female	52	59.1
Age		
Less than 40 years	33	37.5
40 or above 40 years	55	62.5
Educational Status		
Below Matric	70	79.6
Completed Matric	18	20.4

Table-I. Socio-demographic characteristics of patients (N=88)

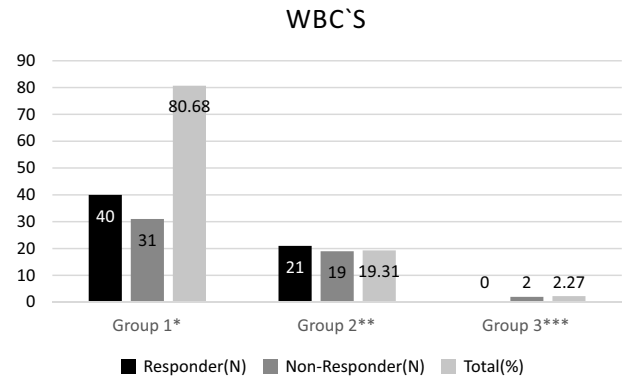

Figure-1. Effect of Interferon and ribavirin therapy on WBC's

*Normal WBC'S levels (Before and after treatment)
**Abnormal WBC'S Levels (Before and after treatment)
***WBC'S normal (Before treatment) and WBC'S decreased (After treatment)

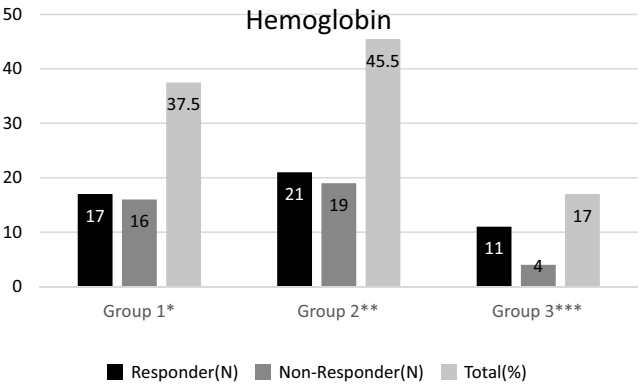

Figure-2. Effect of Interferon and ribavirin therapy on hemoglobolin

*Normal Hb levels (Before and after treatment)
**Abnormal Hb Levels (Before and after treatment)
***Hb normal (Before treatment) and Hb decreased (After treatment)

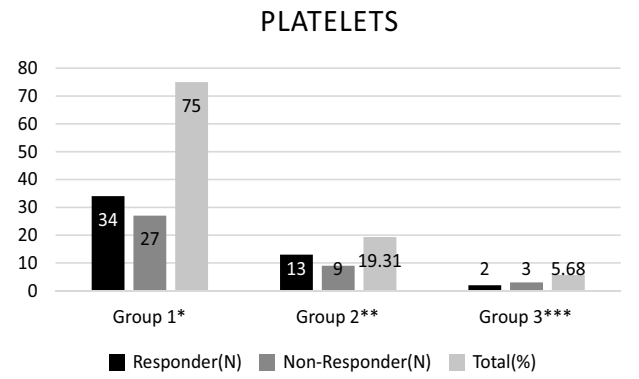

Figure-3. Effect of Interferon and ribavirin therapy on Platelets

*Normal Platelets levels (Before and after treatment)
**Abnormal Platelets Levels (Before and after treatment)
***Platelets normal (before treatment) and Platelets decreased (After treatment)

DISCUSSION

Hepatitis C virus has produced a greater health burden in current scenario leading towards the progression of the disease and causes liver abnormalities.[9] Around 200 million peoples are affected with the disease globally, among which 7.5 million peoples belongs to the region Pakistan.[9,10]

According to Takeuchi *et al*., high incidence of the disease have been reported at age of above 45 years. Similarly, in our study, it was also observed that majority of HCV patients (62.5%) reporting the disease belongs to age above 40 years.[11]

A study in China, reported the dominance of the disease in females as compared to males.[12] Our study also demonstrate the supremacy of the disease in females as 59.1% patients that have reported the incidence of hepatitis C virus were females.

The literacy rate plays an important role in combating the disease prevalence. A study identified inverse association of the disease with high education status.[13] The incidence rate of HCV in current study population showed that majority of patients (79.6%) had low level of education as they have not passed the matric level whereas with the increase in education, the incidence rate of the disease has decreased.

The known side effects of interferon therapy on hematological parameters including WBC`s, Hb and platelets were observed in this study. A study designed to evaluate the hematopoietic components, namely WBC`s, platelets and hemoglobin after the administration of complete INF-α therapy. Researchers concluded that levels of Hb, WBC`s and platelets count were prominently decreased in all patients taking various combinations of therapy.[14]

The established side effects of interferon therapy against HCV including WBC`s, Hb and platelets were observed showing reduction in Hb and platelet count, while increase in WBC`s count of 2 patients.

A study conducted by Dourakis *et al*., reported that alpha interferon causes drug induced thrombocytopenia.[15] In another study conducted by Colombatto *et al*., indicated the decreasing effect of platelets by interferon therapy, which can be reduced by treating the patient with N3 leukocytic interferon which show least effect on haemopoietic system and is used as a drug of choice in patients already suffering from low levels of leukocyte and platelets.[16]

This study also demonstrated that the number of patient in non-responder group with high WBC`s count has increased which reflecting that these patients are unresponsive towards therapy. In responder group, number of patients with normal WBC`s count remains same after receiving interferon and ribavirin therapy that which is 80.6%.

Findings of this study showed that majority of HCV patients presented with normal platelet count prior to treatment. After provision of HCV treatment, a slight shift was observed from normal to decrease platelet count, which could be explained as a side effect of interferon therapy. Although in responder group there are more number of patients with decreased platelet count which shows the effect of treatment.

In previous study, a decrease in mean Hb level of 2.05gm/dl was observed after HCV treatment.[17] Effect of interferon therapy on levels of Hb showed significant variation, according to current study i.e. after provision of therapy against HCV, there is decrease in number of patients with normal Hb level and increase in number of patients with decrease Hb level. This decreasing effect of Hb by interferon is supporting the fact that interferon therapy has declining effect on hematopoietic lineages.

CONCLUSION

It is concluded that the therapy including interferon and ribavirin significantly affects the levels of Hb and platelets count. However, the therapy does not affects level of WBC`s in the studied population and the WBC`s level remains same in responder group, whereas in non-responder group patients are with increase WBC`s count.

REFERENCES

1. Alter MJ, Mast EE. **The epidemiology of viral hepatitis in the United States.** Gastroenterol Clin North Am. 1994; 23: 437-55.

2. Lau DT, Kleiner DE, Ghany MG, Park Y, Schmid P, Hoofnagle JH. **Ten-year follow-up after interferon-alpha therapy for chronic hepatitis C**. HEPATOLOGY 1998; 28: 1121-27.

3. Camma C, Giunta M, Andreone P, Craxi A. **Interferon and prevention of hepatocellular carcinoma in viral cirrhosis: An evidence-based approach**. J Hepatol 2001; 34:593-602.

4. Rosen HR. **Clinical practice: Chronic hepatitis C infection**. N Engl J Med. 2011; 364(25):2429–38.

5. Wong S, Kaita K, Gauthier T, Jones S, Minuk GY. **A comparative trial of recombinant interferon alpha 2a versus alpha 2b on myelosuppression in healthy adult volunteers**. Hepatogastroenterology 1996; 43: 301-5.

6. de-Araujo ES, Campos AF, Yamashiro J, Mello ES, Takagaki T, Barone AA**. Expectoration of large bronchial casts secondary to the treatment of chronic hepatitis C with pegylated interferon and ribavirin**. Clinics. 2010; 65:745-8.

7. McHutchison JG, Poynard T. **Combination therapy with interferon plus ribavirin for the initial treatment of chronic hepatitis C**. Semin Liver Dis 1999; 19 (S~ppl 1):57-65.

8. De Salvo L, Plumacher Z, Gomez O, Weir-Medina J, Paz L, Salas D. **Hypertriglyceridemia following treatment with interferon alpha in essential thrombocythemia**. Invest Clin 1996; 37:177-81.

9. Umar M, Khaar HT, Khurram M, Hasan Z. **Anti-HCV antibody positivity of various sections of Pakistani patients.** J Coll Physicians Surg Pak. 2009; 19(11):737-741.

10. Averhoff FM, Glass N, Holtzman D. **Global Burden of Hepatitis C: Considerations for Healthcare Providers in the United States**. Clin Inf Dis. 2012; 55:10–5.

11. Takeuchi LC, Pham TK, Katz AR. **Hepatitis C virus antibody prevalence, demographics and associated factors among persons screened at Hawai'i community-based health settings, 2010-2013**. Hawaii J Med Public Health. 2015; 74(1):9-15.

12. Niu Z, Zhang P, Tong Y. **Age and gender distribution of Hepatitis C virus prevalence and genotypes of individuals of physical examination in WuHan, Central China**. Springerplus. 2016 Sep 13; 5(1):1557. doi: 10.1186/s40064-016-3224-z.

13. Wang CS, Chang TT, Yao WJ, Chou P. **Comparison of hepatitis B virus and hepatitis C virus prevalence and risk factors in a community-based study**. Am J Trop Med Hyg. 2002; 66(4):389-93.

14. Schmid M, Kreil A, Jessner W, Homoncik M, Datz C, Gangl A, Ferenci P, Peck-Radosavljevic **M. Suppression of haematopoiesis during therapy of chronic hepatitis C with different interferon alpha mono and combination therapy regimens**. Gut. 2005; 54(7):1014-20.

15. Dourakis SP, Deutsch M, Hadziyannis SJ. **Immune thrombocytopenia and alpha-interferon therapy**. J Hepatol. 1996; 25: 972–75.

16. Colombatto P, Oliveri F, Leandro G, Baldi M, Capalbo M, Rocca G, Brunetto MR, Bonino F. **Platelet and white blood cell counts during therapy with different types of alpha interferon in patients with chronic viral hepatitis. Investigators of the Alpha Interferon Study Group of Piemonte, Italy.** Ital J Gastroenterol Hepatol. 1997; 29: 441-47.

17. Shakeel Ahmad J, Ashfaa A, Habib Ahmad J. **Effect of standard interferon and ribavirin on haemoglobin level in hepatitis-C patients.** J Ayub Med Coll Abbottabad. 2014 Oct-Dec; 26(4):510-2.

AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Zubia Zia	Study design, Data collection, Data analysis, Data interpretation, Literature review, Manuscript writing.	
2	Naim ul Hasan Naqvi	Research Proposal, Concept of study, Final and Critical review.	
3	Ayaz Mustafa	Research Proposal, Concept, Study design.	
4	Muzammil Hussain	Tabulation, Graphing, Manuscript writing, Data interpretation.	
5	Aysha Zia	Data collection and analysis.	
6	Rehana Perveen	Data collection and corrections.	
7	Hira Naeem	Data collection and analysis and formatting of article according to journal format.	
8	Zuneera Akram	Data collection and analysis and formatting of article according to journal.