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Research Article

Comparison between hepatitis C patients treated with interferon alpha and pegylated interferon in term of thyroid disorder

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ABSTRACT:

Objectives: To compare the frequency of thyroid disorders in patients of chronic hepatitis C being treated with interferon alpha versus pegylated interferon.

Materials & Methods: This randomized Controlled Trial was conducted Department of Medicine, Sheikh Zayed Hospital Rahim Yar Khan from January 2017 to March 2017. A total of 340 diagnosed case of chronic hepatitis C by PSR HCV RNA of both genders, having age range between 25 years to 60 years, were included in the study.

Results: The average age of cases in group A& B was as35.73 ± 7.31years and 35.91 ± 8.24years respectively. Out of these 340 patients, 201 (59.12%) were male and 139 (40.88%) were females with ratio of 2.09:1. Mean thyroid stimulating hormone level was 2.31 ± 1.12 in group A and 2.46 ± 0.98 in group B. Thyroid disorder was seen in 15 (8.82%) patients in conventional interferon therapy group and 31 (18.24%) patients in pegylated interferon therapy group with p-value of 0.011.

Conclusion: This study concluded that the frequency of thyroid disorders is lower in patients of chronic hepatitis C being treated with interferon alpha compared to pegylated interferon with higher frequency among females in both groups.

Keywords: Hepatitis C, interferon therapy, hypothyroidism, hyperthyroidism.

INTRODUCTION:

Hepatitis C virus belongs to Flaviviridae family. The HCV virion is made of a single-stranded positive RNA genome.[1] Chronic hepatitis C (CHC) is defined as infection with the hepatitis C virus persisting for more than 6 months based on the presence of its RNA.[2] About 150 million people are chronically infected with hepatitis C virus. Its highest prevalence (15–20%)[3] has been found in Egypt while the United Kingdom has lowest prevalence (0.01–0.1%). Pakistan is one of the worst afflicted nations of the world havingCHC infection in 4.8% population.[4,5]

The risk factors for transmission of hepatitis C infection are transfusion of blood and blood products, use of unsterilized sharp instrument or needle stick injuries and tattooing.[5] Interferon and ribavirin combination therapy has been the mainstay of hepatitis C treatment.[2] Thyroid dysfunction (TD) is one of the common side effect of interferon-based antiviral treatment for CHC, which may lead to dose reduction or discontinuation of therapy.[6] Although conventional interferon no more used in developed countries but it still is use in Pakistan because of cost-effectiveness.[6] Rate of development of thyroid dysfunction vary from population to population and type of treatment i.e. conventional versus pegylated interferon.

There are two local studies available regarding thyroid dysfunction during treatment with conventional interferon, one showing that 20/107 patients (18.69%) developed thyroid dysfunction.[7] While other showed that thyroid disorders developed in 18/100 (18.0%).[8] Both of which are different from those reported in studies for different population e.g. 10.0% for French population.[9] No study exists for pegylated interferon in our local context. In another study, it was concluded that pegylated interferon are associated with higher rates of thyroid disorder than conventional one (14.1% vs 6.0%, P=0.0029).[10]

The current study was aimed to compare the frequency of thyroid disorders in patients of chronic hepatitis C being treated with interferon alpha versus pegylated interferon in our population. Our population of subcontinent differs from other populations in terms of environment, dietary life style, genotype and rate of development of thyroid disorders as described previously for interferon (18% vs 6%). Similarly there may be difference in rate of thyroid disorder for pegylated interferon which this study has attempted to find. Pegylated interferon is in use due to better efficacy and convenient dosing although they are not cost-effective. Current study would help to develop local evidence regarding thyroid aspect of complication profile associated with interferon treatment so this would help physicians to understand and choose better treatment options in Pakistani context. So, we had planned this study to find out which of these two treatment modality is better in preventing thyroid disorders due to interferon therapy, so it may be advocated as treatment of choice.

MATERIAL AND METHODS:

This randomized Controlled Trial was conducted at Department of Medicine, Sheikh Zayed Hospital Rahim Yar Khan from January 2017 to March 2017.

Inclusion Criteria:

- Diagnosed case of chronic hepatitis C by PSR HCV RNA (Qualitative).
- Both genders.
- Age range between 25 years to 60 years.
- With normal thyroid stimulating hormone levels (0.4-4.0 mU/L).
- Duration of interferon therapy for 6 months.

Exclusion Criteria:

- Previously treated for thyroid disorders determined by history.
- Patients of decompensated chronic liver disease i.e. cirrhosis, ascites and Splenomegaly determined by ultrasound and laboratory examination.
- Previously treated with interferon determined by history.
- Patients with connective tissue disorder like SLE, rheumatoid arthritis determined by history.

Data collection procedure:

After approval from the hospital ethical committee, 340 patients fulfilling the inclusion criteria were included in the study. Informed written consent was taken from each patient.

Selected patients were randomly divided into two group A & B. Patients of Group A were treated with conventional interferon therapy. Patients of Group B were treated with pegylated interferon. Final outcome (the development of thyroid disorders) was measured at 6 months following the start of interferon therapy.

Thyroid disorders: included the presence of any of these;

Hypothyroidism: was defined as serum thyroid stimulating hormone level > 4.0mU/l.

Hyperthyroidism: was defined as serum thyroid stimulating hormone level <0.4mU/l.

Data collection was done with predesigned proforma. The patient's demographics were recorded at the time of admission. A baseline assessment of the thyroid function tests was recorded before the start of therapy.

Data analysis procedure:

Collected data was analyzed by using SPSS version 20. Age and thyroid stimulating hormone level was presented as mean and SD. Gender and

presence of thyroid disorders was presented as frequency. Chi square was used to compare the frequency of thyroid disorder in both groups and p-value ≤0.05 was taken as significant. Stratification for age and gender was done and post stratification chi-square test was applied. P ≤ 0.05 was taken as significant.

RESULTS:

Total 340 patients were recruited for this study. Mean age of the cases was 35.79 ± 7.86 years. In group A and group B, mean age of the cases was 35.73 ± 7.31 years and 35.91 ± 8.24 years respectively.

Most 110 (32.35%) of the patients were between 25 to 35 years of age as shown in Table I.

Male patients were 201 (59.12%) and female patients were 139 (40.88%) as shown in Figure I.

Mean thyroid stimulating hormone level was 2.31 ± 1.12 in group A and 2.46 ± 0.98 in group B.

Thyroid disorder was seen in 15 (8.82%) patients in group A (conventional interferon therapy) and 31 (18.24%) patients in group B (pegylated interferon therapy) with p-value of 0.011 as shown in Figure II. Stratification of the patients in relation to age and gender was done. In age group 25-35 years, TD was noted in 07 (12.96%) patients of group A and 11 (19.64%) patients of group B. The difference of TD was insignificant with p value 0.344. in age group 36-45 years, TD was noted in 04 (8.16%) patients and 08 (16.0%) patients of group A & B respectively. Difference of TD was also insignificant with 0.232. In age group 46-55 years, TD was develop in 02 (4.88%) patients of group A and 05 (11.90%) patients of group B with insignificant (P = 0.249) difference. In age group 56-60 years, significant (P = 0.033) difference between the TD rate was observed. (Table 2)

TD was found in 91 (90.10%) and 81 (81.0%) male and in 64 (92.75%) and 58 (82.86%) female patients of group A & B but the difference was insignificant with p value 0.066 and 0.075. (Table 3)

Table-I: Age distribution for both groups

Age (years)	Group A (n=170)		Group B (n=170)		Total (n=340)	
	N	%	N	%	N	%
25-35	54	31.76	56	32.94	110	32.35
36-45	49	28.82	50	29.41	99	29.12
46-55	41	24.12	42	24.71	83	24.41
56-60	26	15.29	22	12.94	48	14.12
Mean ± SD	**35.73 ± 7.31**		**35.91 ± 8.24**		**35.79 ± 7.86**	

Figure I: Gender distribution (n=340)

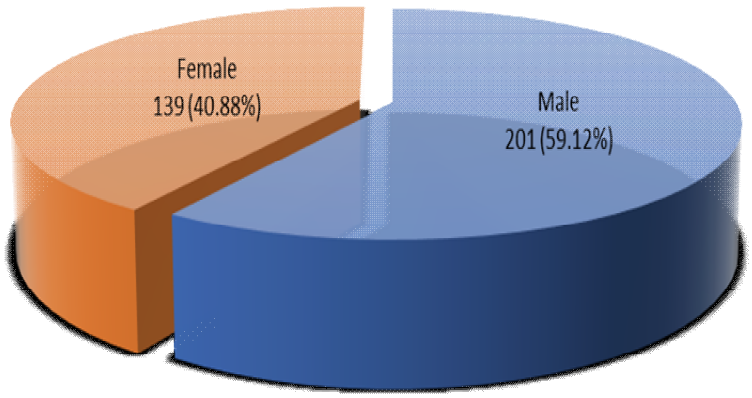
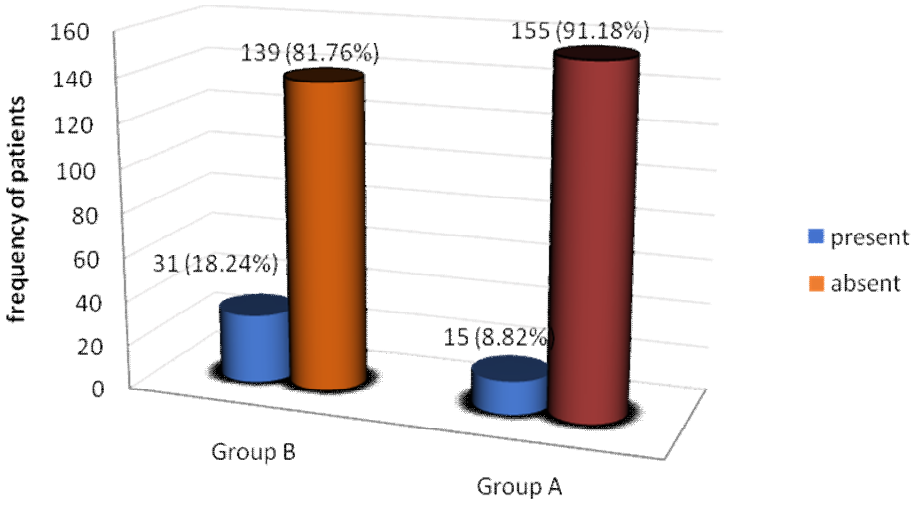


Figure II: Presence or absence of thyroid disorders in both groups



P-value = 0.011 which is statistically significant.

Table II: Stratification in relation to age

Age of patients	Group A (n=170)		Group B (n=170)		p-value
	Thyroid disorders		Thyroid disorders		
	Absent	Present	Absent	Present	
25-35	47 (87.04%)	07 (12.96%)	45 (80.36%)	11 (19.64%)	**0.344**
36-45	45 (91.84%)	04 (8.16%)	42 (84.0%)	08 (16.0%)	**0.232**
46-55	39 (95.12%)	02 (4.88%)	37 (88.10%)	05 (11.90%)	**0.249**
56-60	24 (92.31%)	02 (7.69%)	15 (68.18%)	07 (31.82%)	**0.033**

Table III: Stratification in relation to gender

Gender	Group A (n=170)		Group B (n=170)		p-value
	Thyroid disorders		Thyroid disorders		
	Present	Absent	Present	Absent	
Male	91 (90.10%)	10 (9.90%)	81 (81.0%)	19 (19.0%)	**0.066**
Female	64 (92.75%)	05 (7.25%)	58 (82.86%)	12 (17.14%)	**0.075**

DISCUSSION:

According to WHO, globally 180 million individuals are infected and 350000 die from hepatitis C infection every years.[11]FDA approved two 1st generation protease inhibitors, telaprevir and boceprevir for the management of HCV. Ribavirin and peg-IFN remain the integral part of the treatment but it has many side effect and TD is one of them.[12]Mechanisms of development of TD in interferon treated patient is still unclear.[13] Furthermore, IFN-α has direct inhibitory effects on thyroid hormone synthesis, release and metabolism, as well as abnormal expression of major histocompatibility antigens on thyroid cells.[14]

This randomized controlled study has compared the frequency of thyroid disorders in cases of chronic hepatitis C being treated with IFN-α versus peg-IFN. The average age of the cases in our study was 35.79 ± 7.86years.The average age of the cases in group-A was 35.73 ± 7.31years while in group B average age of the cases was 35.91 ± 8.24years and most 110 (32.35%) of the cases were between 25 years to 35 years of age in both groups. These findings are very much comparable with Aziz S et al[15] study who had a average age of the cases as 33 years but much lower than Yan Z et al[16] who had a mean age of 41 years. On the other hand, Othmane BM et al[17] had found mean age of 27 years in his study

which is much lower compared to our study. In this study, out of these 340 patients, 201 (59.12%) were male and 139 (40.88%) were females with ratio of 2.09:1. Many previous studies have also found higher incidence of male than female participants.[15,16]

In our study, thyroid disorder was seen in 8.82% patients in group A (conventional interferon therapy) and 18.24% patients in group B (pegylated interferon therapy) with p-value of 0.011. Yan Z et al[16] has reported that 8.0% patients who were treated with IFN-α developed TD, while 8.6% cases who were managed with IFN-α in combination with ribavirin and 13.8% cases who were managed with Peg-IFN-α with combination of ribavirin also developed TD.Insignificant(P = 0.145) difference for the rate of TD among the three treatment regimens was noted.

Kee KM et al[18] has shown no significant (P = 1.00) difference betweenrate of TD among the standard IFN and Peg-IFN-treated cases. There are two local studies available regarding thyroid dysfunction during treatment with conventional interferon, one showing that 20/107 patients (18.69%) developed thyroid dysfunction.[7] While other showed that thyroid disorders developed in 18/100 (18.0%).[8] Both of which are different from those reported in studies for different population e.g. 10.0% for French population.[9] It was concluded that pegylated interferon are associated with higher rates of thyroid disorder than conventional one (14.1% vs 6.0%, P=0.0029).[10]Another study reported TD as 2 % to 3% in cases treated with IFN-α.[19]Another study reported TD as 15% in cases treated with IFN-α.[20] In another study, TD rate was 21.3% in Peg-IFN-treated cases.[21]

CONCLUSION:

This study concluded that the frequency of thyroid disorders is lower in patients of chronic hepatitis C being treated with interferon alpha compared to pegylated interferon in our population with higher frequency among females in both groups. So, we recommend that interferon alpha should be used as a primary therapy for treating every patient of chronic hepatitis C for the prevention of thyroid dysfunction in these particular patients to reduce the morbidity of chronic hepatitis C patients.

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