ORIGINAL ARTICLE

Patterns of Spirometry in patients of Chronic Hepatitis C While on Conventional Interferon and Ribavirin Treatment

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ABSTRACT

Background: Serious pulmonary toxicities of combination interferon therapy have been reported in literature.
Aim: To monitor the pulmonary function test while on interferon therapy.
Methods: Single center study was done on 90 patients taking conventional interferon therapy. Spirometry of these patients were done who were at baseline (n=30), 2nd month (n=30) and 6th month of treatment (n=30)
Results: Significant obstructive pattern is observed at 6 months of therapy as compared to baseline in patients of chronic hepatitis C while on conventional therapy.
Conclusion: All patients with chronic hepatitis C infection along with respiratory disease must have the monitoring of respiratory function test before and during the course of therapy.
Keywords: Spirometry, Hepatitis C, interferon, ribovirin

INTRODUCTION

The combination of Interferon and ribavirin for treatment of chronic hepatitis C has produced 88.57% biochemical, 85.14% end of treatment virological response and 78.85% sustained virological response in a study done in our population with few side effects[1]. Respiratory complications have been observed in 14% of patients treated with combination therapy[2]. Direct toxic effect of interferon on the lungs as well as indirect damage through autoimmune mechanisms are thought to play a role in producing pulmonary complications with an incidence rate of less than 1 %[3]. With the frequent use of interferon in the treatment of chronic hepatitis C, it is important to keep in mind the unusual but common pulmonary side effect of this regime in order to treat this condition effectively[4].

These adverse effects include interstitial pneumonitis, pulmonary sarcoidosis, pleural effusion, exacerbation of bronchial asthma, bronchiolitis obliterans organizing pneumonia and acute respiratory distress syndrome[5].

Different spirometric findings have been described in patients taking combination therapy. Restrictive pattern[6], no effect on spirometric pattern[7] and improvement of FEV1 in COPD[8] and asthmatic patients[9] have been shown by various international studies.

Because of the high prevalence of hepatitis C infection in Pakistan and still conventional treatment in use in the various Government Hospitals, the study was designed to evaluate the patterns of spirometry as markers of respiratory complications in patients of hepatitis C while on interferon therapy and its comparison with international studies.

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METHODOLOGY

Patients having hepatitis C and already receiving conventional interferon treatment were enrolled at Punjab Employee's Social Security Institute affiliated with University of Lahore by using simple random sampling technique. Spirometry was performed by each patient under supervision of a chest specialist. Observational cross sectional study design was employed. The duration of this study was six month. Data was recoded on questionnaire in first phase then entered into SPSS for analysis. Mean and standard deviation calculated for quantitative variables. Frequency with percentage and chi-square test was performed for qualitative categorical variables. Student t-test, Pearson chi square test for comparing two factors and Fisher test was performed to diagnose the prominent category in relation to the quantitative variable.

Inclusion criteria: Total 90 patients with chronic HCV who were receiving the standard combination therapy for HCV were included in the study. They had the following criteria to be candidate for IFN/RBV therapy:

1. Patients aged 18–60 years, normal renal function tests (RFTs)
2. Hemoglobin ≥12 g/dl for men and ≥11 g/dl for women, WBCs >4000/mm^3, neutrophil count >1500/mm^3 and platelets >150,000/mm^3.
3. Prothrombin time prolongation <2 s, albumin >3.5 g/dl.
4. Positive HCV RNA by PCR

5. Normal abdominal ultrasound

Patients were divided according to duration of their therapy

30 patients at baseline of therapy
30 patients at 2 months of therapy
30 patients at 6 months of therapy

Exclusion criteria:

1. Patients with history of a known chest disease for example COPD/Asthma ,occupational or interstitial lung disease, pulmonary tuberculosis, pneumonia or autoimmune pulmonary diseases before enrollment in the study.
2. Patients with systemic illness and patients non HCV related chronic liver diseases.
3. Smokers

The severity of reductions in the forced vital capacity (FVC) was graded by the following scheme as per recommendations by Cleveland clinic [10]:

- Mild: Predicted FEV_1 <100% and ≥70%
- Moderate: Predicted FEV_1 <70% and ≥60%
- Moderately severe: Predicted FEV_1 <60%& ≥50%
- Severe: Predicted FEV_1 <50% and ≥34%

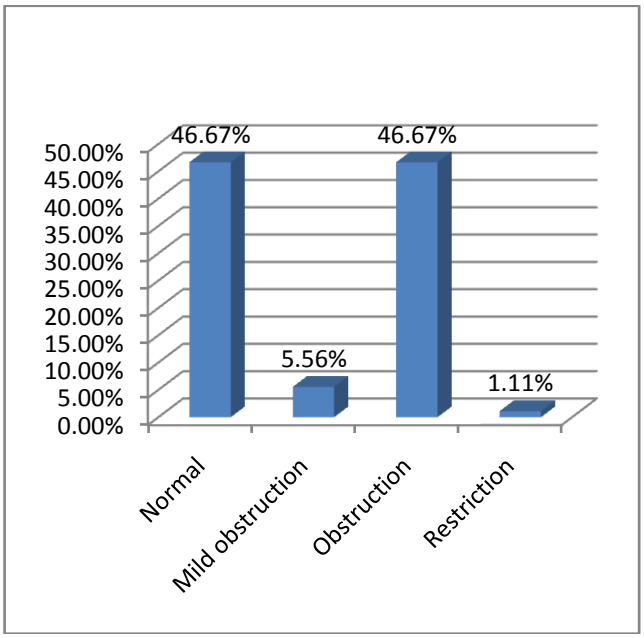
RESULTS

Out of 90 enrolled patients, 36(40%) were male and 54(60%) were female. Equal number (33.33%) of participants was enrolled in three groups who were at zero month, 2nd month and 6th month of their therapy with conventional interferon. The mean age was 35.46 with standard deviation 9.16 and mean of hemoglobin 10.8 with standard deviation 1.36. The minimum hemoglobin level of patient was 8.4 and maximum was 14. The mean and standard deviation of forced expiratory volume (FEV) in one minute was 72.56 and 6.34 and the mean and standard deviation of forced vital capacity (FVC) was 101.43 and 6.84 respectively. The mean of FEV_1/ FVC ratio was 70.28 however standard deviation was 6.84.

The graph shows that 46.67% people have normal spirometry pattern, 46.67% have moderate to severe obstructive spirometry pattern where 5.56% have mild obstructive spirometry pattern and only 1.11% have restrictive spirometry pattern.

The above table shows that female participants have more percentage than male participants at o month, 2nd month and 6th month. P-value of gender in study group is 0.38 which calls that gender preferences for enrollment does not exist and all patients were taken randomly who fulfilled the inclusion criteria. Although female participants are more in number in all groups of spirometric patterns (Normal , mild obstruction, moderate to severe obstruction and restriction), the p-value is 0.65 which shows that male and female patients suffer equally.

Regarding spirometric patterns, 22 patients showed normal spirometry results at baseline of therapy with conventional interferon, mild obstructive pattern was observed in 2 patients and moderate to severe obstruction was noted in 5 patients while restriction was noted in only 1 patient in same group



At 2 months, 11 patients had normal spirometric examination, only 1 patients showed mild obstruction while 18 patients demonstrated moderate to severe spirometric obstructive pattern. At the end of 6 months, only 9 patients were normal on spirometry while 2 patients showed mild obstruction and 19 patients demonstrated moderate to severe obstruction.

Restrictive spirometric pattern was not present in any patient at 2 months and 6 months of therapy.

The p-value of spirometry pattern and study groups is 0.006 which concludes that the spirometry pattern is not same at 0 month, 2nd month and 6th month and it changes with the passage of time. These results show that obstructive pattern on spirometry is getting worse with the passage of time with conventional interferon therapy.

Another important finding in our study is the significant difference between FEV1/FVC ratio in patients at baseline of therapy as compared to patients at 6 months of therapy with a p value of 0.00.

Table:

Characteristics		Categories	Frequency/Mean	Percentage/SD	Pvalue
Study Group	0 Month	Male	9	10	0.38
		Female	21	23.3	
	2nd Month	Male	14	15.6	
		Female	16	17.8	
	6th Month	Male	13	14.4	
		Female	17	18.9	
Spirometry Pattern	Normal	Male	17	18.9	0.65
		Female	25	27.8	
	Mild Obstruction	Male	1	1.1	
		Female	4	4.4	
	Moderate to severe Obstruction	Male	18	20	
		Female	24	26.7	
	Restriction	Male	0	0.0	
		Female	1	1.1	
Spirometry Pattern	Normal	0 Month	22 (73%)	24.4	0.006
		2nd Month	11(37%)	12.2	
		6th Month	9(30%)	10	
	Mild Obstruction	0 Month	2(7%)	2.2	
		2nd Month	1(3%)	1.1	
		6th Month	2(7%)	2.2	
	Moderate to severe Obstruction	0 Month	5(17%)	5.6	
		2nd Month	18(60%)	20	
		6th Month	19(63%)	21.1	
	Restriction	0 Month	1(3%)	1.1	
		2nd Month	0	0.0	
		6th Month	0	0.0	
FEV/FVC	Quantitative	Male	69.75	4.74	0.55
		Female	70.63	7.97	
FEV/FVC	Quantitative	0 Month	73.97	8.35	0.00
		2nd Month	69.41	4.84	
		6th Month	67.44	5.2	

DISCUSSION

Our study demonstrated the worsening pattern of spirometry mainly of obstructive type with increasing duration of treatment with conventional interferon. This is similar to spirometric results obtained by Garib in which decrease in FEV1 and decrease in FEV1/FVC ratio was noted in patients taking interferon and having advanced stage of liver fibrosis. However, these changes were noted at 12th week of therapy in contrast to our study in which abnormal spirometric pattern were present mostly at 24th week.[11] our study results are contrary to the spirometric values of interferon treated patients of Ezzeldin et al who found improvement in pulmonary function tests with the treatment. Their study suggests the improvement in FEV1,Total lung capapcity and DLCO with the passage of on treatment time with interferon therapy[12].

In our study, At the start of treatment, we noted abnormal spirometry pattern in 8(27%) patients of chronic hepatitis C which is close to the study population of Foster et al who were able to find abnormal spirometric pattern in 13% of patients only[13] as compared to the study of Ezzeldin et al who found abnormal spirometric pattern in 76.5% of their study participants at baseline. Most of these patients had reduced DLCO and reversible airway obstruction[12].

Our study also demonstrated significant obstructive spirometric pattern in 32% of our study group at 8 weeks of treatment which is much similar to study done by Foster et al who noted that at 12 weeks of treatment there is a clinically relevant decline in DLCO[13]. However, this finding is in contrast to the results obtained by Shirai who did not find any significant difference in pulmonary function test parameters at 12 weeks of treatment[14].

35% of patients at 24 weeks of treatment still showed obstructive pattern of spirometry in our study which is similar to Foster et al who demonstrated decline in DLCO at 24 weeks of therapy with interferon therapy which persisted even after 6 months post treatment in their study[13].

Limitations: Our study has several limitations

Firstly, this is not a prospective study so we do not know what were the results of spirometry at the mid or end of treatment for the patients at baseline of therapy and vice versa

Secondly, most of our patients were relatively younger so these results are not generalizable. Moreover, because of lack of proper equipment , we were unable to measure DLCO which might have been an important component in our patients.

Lastly, these tests were not repeated 6 months after discontinuation of therapy so reversibility of spirometric pattern is not known

CONCLUSION

Conventional antiviral therapy leads to obstructive pattern in most of the patients which is contrary to results of other international studies.
Recommendations:
All patients with chronic hepatitis C infection along with respiratory disease must have the monitoring of respiratory function test before and during the course of therapy.

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