FREQUENCY OF THYROID DYSFUNCTION DURING TFT IN INTERFERON AND RIBAVIRIN THERAPY IN PATIENTS WITH CHRONIC HEPATITIS C


PNS Shifa Karachi Pakistan, *Combined Military Hospital Rawalpindi Pakistan, **Baqai Medical University Karachi Pakistan

ABSTRACT

Objective: To determine the frequency of thyroid dysfunction among patients of chronic hepatitis C (HCV) infection receiving combination of interferon-alpha and ribavirin therapy.

Study Design: Cross-sectional study.

Place and Duration of Study: Department of Medicine, PNS Shifa Naval Hospital Karachi, from September 2012 to March 2013 over a period of six months.

Patients and Methods: In this study, 170 diagnosed patients of chronic HCV (confirmed by anti-HCV and HCV RNA-positive) presenting to medical OPD with normal thyroid functions were recruited. All patients fulfilled inclusion and exclusion criteria. They were prescribed IFN-alpha 2b (3 million units subcutaneously 3 days a week) and oral preparation of antiviral drug ribavirin (800 to 1200 mg daily in divided doses according to weight). At the end of 12 weeks of combination antiviral therapy, their thyroid profile was worked up. Serum TSH, free T4 and T3 levels were determined by chemiluminescence technique in chemical pathology lab of the hospital. Statistical analysis was done on SPSS 17.

Results: Out of 170 patients, 83 (48.82%) were females and 87 (51.18%) were males with the age ranging from 22–46 years (mean ± SD: 33.86 ± 5.32). After 12 weeks of antiviral therapy, thyroid functions were normal in 156/ 170 (91.76%) patients, whereas in 14/ 170 (8.24%) cases thyroid dysfunction was observed. Out of those patients having thyroid dysfunction, 10/ 14 (71.42%) were hypothyroid whereas 4/ 14 (28.58%) had hyperthyroidism.

Conclusion: Managing patients of chronic HCV with combination antiviral therapy comprising IFN-alpha 2b and ribavirin can cause thyroid dysfunction. These patients should be monitored before and during treatment to avoid complications and poor compliance.

Keywords: Chronic hepatitis C, Interferon, Ribavirin, Thyroid dysfunction.

INTRODUCTION

Hepatitis C virus (HCV) is currently the chief cause of chronic liver disease, including chronic hepatitis and cirrhosis, and hepatocellular carcinoma worldwide. Almost 170 million people are likely to be infected with HCV around the world with a global prevalence of 3%. Major cause of HCV infection includes transfusion of blood and blood products, sharing needles and injections and other parenteral contamination. On the other hand, frequency of HCV tends to stabilize or have downward trend in recent years. However, HCV remains the most common chronic blood borne infection in the United States. Current therapy for treatment of chronic HCV includes combination of INF and ribavirin for 6 months. The biochemical and virological response with this therapy is achieved in about 40% cases.

Thyroid dysfunction is a recognized side effect of interferon therapy particularly in women. Anti-thyroid antibodies were found in 5% to 17% of patients with HCV infection and thyroid disorder, however primarily hypothyroidism occurs in about 2% to 13% of patients and up to 25% have detectable thyroid antibodies.

However, it is still controversial that whether or not the occurrence is greater than in age and sex-matched control. Patients with chronic hepatitis due to other causes also reported with thyroid antibodies and thyroid disorders but the occurrence appears greater in those with chronic HCV infection. Only a few patients (1% to 7 %), who were treated with IFN...
therapy, also developed painless thyroiditis.
An increase in serum concentration of anti-
thyroid antibodies and having normal thyroid 
functions was also observed with an estimate 
relative risk of 4.4% and an incidence of 5-12% 
in HCV patients.

It was also noticed that genetically 
susceptible individuals were more prone to 
develop IFN induced thyroid disease. Most 
of the patients having INF induced hypothyroidism recover after the completion of 
therapy and treatment can be continued with 
regular monitoring and follow up. However, 
treatment must be stopped in patients with 
marked derangement in thyroid profile and 
having severe symptoms. All the patients, 
having chronic HCV, taking antiviral therapy 
must be explained regarding risk of developing 
thyroid abnormalities and necessary screening 
for thyroid antibodies and thyroid profile is 
suggested before starting, during the course 
and after the completion of antiviral therapy.

PATIENTS AND METHODS

This cross-sectional study was conducted 
at PNS Shifa Naval Hospital, Karachi from 
September 2012 to March 2013 over a period of 
6 months after seeking approval from hospital 
ethical committee. Before the commencement 
of interferon and ribavirin therapy, all patients 
had persistently raised serum alanine 
transferase (ALT) by International Federation of 
Clinical Chemistry (IFCC), positive anti-HCV 
antibodies by ELISA and positive HCV-RNA by 
polymerase chain reaction (PCR) with normal 
thyroid functions (TSH, T3 and T4 were within 
normal range). Exclusion criteria included 
decompensated liver disease, previous 
treatment with interferon or ribavirin, history of 
pre-existing goiter, thyroid or any other 
endocrine disorder, any autoimmune disease, 
severe cardiac or pulmonary disease, history of 
malignancy or using immunosuppressant and 
steroids or pregnancy. One hundred and 
seventy diagnosed patients of non-cirrhotic 
chronic HCV were selected by consecutive non-
probability sampling technique after getting 
informed consent. All patients were given 
standard antiviral treatment with conventional 
interferon alpha 2b (in a dose of 3 million units 
subcutaneously 3 days in a week) and oral 
ribavirin (1000-1200 mg) daily in divided doses 
according to patient’s weight and were asked to 
report back for repeat thyroid profile analysis 
after 12 weeks.

Venous blood samples were collected for 
thyroid profile including serum thyroid 
stimulating hormone (S. TSH), serum free 
thyroxine (S. Free T4) and serum 
triiodothyronine (S.T3) using full aseptic 
measures. Samples were immediately 
transported to pathology department, PNS 
Shifa hospital and were kept in closed bottles 
held in vertical position. Thyroid profile 
analysis was done by chemiluminescence 
technique. The tests were carried out under 
supervision of chemical pathologist and the 
results were entered in a designated proforma. 
Patients with serum TSH in the range of 0.72-
4.2 iuu/ ml, serum free T3 in the range of 2.57 -
4.43 pg/ ml and serum free T4 in the range of 
0.93-1.7 ng/ dl were labelled as euthyroid. 
Patients with serum TSH levels less than 0.72 
uiu/ ml, serum free T3 more than 4.43 pg/ ml and 
serum FT4 more than 1.7 ng/ dl were labelled as 
hyperthyroid. Patients with serum TSH levels 
more than 4.2 iiu/ ml, serum FT3 less than 2.57 
pg/ ml and serum FT4 less than 0.93 ng/ dl were 
diagnosed as hypothyroid.

All data collected was entered in SPSS 
version 17. It comprised of quantitative 
variables like age of patient, serum TSH, T3 and 
T4 levels at baseline and 12 weeks; and 
qualitative variables i.e. gender and thyroid 
disorder (outcome).

Descriptive statistics, mean and standard 
deviation were calculated for quantitative 
variables (age of patient, serum TSH, T3 and T4 
levels at baseline and 12 weeks). Frequencies 
and percentages were presented for qualitative 
variables (gender and thyroid dysfunctions 
associated with interferon alpha and ribavirin 
therapy). Results were presented with the help 
of tables. Paired sample t test was applied for 
basal and 12 weeks post treatment thyroid 
profile levels (TSH, T3 and T4). Chi-square test 
was used for gender and thyroid dysfunction 
association. p value <0.05 was taken as 
significant.
RESULTS

In our study, a total of 170 patients were selected. Of those, 83 (48.82%) were females and 87 (51.18%) were males. The age among all subjects ranged from 22 – 46 years (mean ± SD= 33.86 ± 5.32). Thyroid profile was assessed at baseline and 12 weeks of anti-viral therapy. Mean and standard deviation for TSH, T3 and free T4 at baseline and after treatment are displayed in (table-1). The results were found in significant (p>0.05).

At 12 weeks of interferon alpha and ribavirin therapy, thyroid function was normal in 156/170 (91.8%) patients, whereas in 14/170 (8.2%) cases thyroid dysfunction was observed. Out of these 14 patients, 10 (71.4%) were hypothyroid whereas 4 (28.6%) were found to have hyperthyroidism.

Out of 10 (71.4%) hypothyroid patients, 3 (30%) were males and 7 (70%) were females. Whereas, out of 4 (28.6%) hyperthyroid patients, 1 (25%) was male and 3 (75%) were females. Cross tabulation of gender and thyroid dysfunction as shown in table-3 showed no difference.(p>0.05)

DISCUSSION

The development of thyroid disease during interferon and ribavirin therapy in patients with hepatitis C virus has been well-established. Significant research has been carried out to study the relationship of thyroid dysfunction and interferon therapy14. Interferon related thyroid dysfunction can be mediated by immune and non-immune mechanism15. Interferon causes immune modulation and also has direct damaging effects on thyroid gland. HCV infection also causes thyroid dysfunction. Ribavirin adds to thyroid disease, caused by interferon, by modulating T helper 1 (Th 1) and T helper 2 (Th 2) subset balances, by activating type 1 cytokine in HCV specific immune response. In literature, the incidence of abnormal thyroid function ranges from 25% to 34.3% with a mean incidence of 6.6%16. In a local study, thyroid dysfunction was observed in 18.69% patients receiving antiviral therapy with interferon and ribavirin17. These studies concluded that frequency of hypothyroidism was more than hyperthyroidism (3.8 vs. 2.8%), and females were more affected than males (13.0 vs. 3.0%) 16.

In this study, the incidence of thyroid dysfunction among 170 patients of chronic hepatitis C, undergoing 12 weeks of anti-viral treatment was 8.24%. According to previous studies the incidence was in between 3.9–33.33%. Our results were consistent with most of the studies carried out in the past. Moreover, 5.9% of patients had hypothyroidism and 2.36% of patients had hyperthyroidism. Hypothyroidism was found to be more common in this study as is the case in most of the studies both local and international19,20.

Important risk factors associated with increased probability of INF induced thyroid dysfunction were female gender and the presence of thyroid auto antibodies before the initiation of therapy21.
Hence, it is suggested to perform a routine screen for thyroid disease in all chronic hepatitis C patients, before starting antiviral therapy.

Despite the development of thyroid disorders (overt and sub-clinical), patients completed their antiviral therapy with interferon alpha and ribavirin. Although these findings suggest that antiviral therapy can be continued despite the development of thyroid disorder, however the impact of continuing the antiviral therapy on the quality of life is still to be determined.

CONCLUSION

Standard anti-viral treatment of chronic HCV that is interferon-alpha (IFN-alpha) and ribavirin causes thyroid dysfunction (both hyperthyroidism and hypothyroidism). These patients should be closely monitored with thyroid profile before the start of therapy, during and after completion of the treatment to detect thyroid disorders and complications related to it. This can result in improved patient compliance.

CONFLICT OF INTEREST

This study has no conflict of interest to declare by any author.

AUTHORS CONTRIBUTION

Intizah Ali, Muhammad Umer Siddiqui, Muhammad Rashid Ahmed and Ghulam Hussain Ibrahim, data collection, analysis and manuscript. Syed Parvez Asghar and Muhammad Zafar Ali, technical advisor and supervision

REFERENCES