Liver histology of chronic hepatitis C patients who relapsed or not responded to conventional interferon and ribavirin therapy

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Abstract
Objective: To evaluate liver histology of chronic hepatitis C patients, who were relapsers or non-responders to previous conventional therapy.
Methods: The descriptive case series was conducted in the Hepatology section of Medical Unit-III at the Jinnah Postgraduate Medical Centre, Karachi, Pakistan, from January to December 2008. The study had 109 hepatitis C patients who had relapsed or not responded to the conventional interferon and ribavirin for at least 24 weeks. All the patients were subjected to liver biopsy. The inflammatory activity and fibrosis shown by the liver biopsies were assessed according to the Batts-Ludwig classification. SPSS version 15 was used to analyse data.
Results: A majority (n=57; 52.3%) of the 109 patients were female with hepatitis C virus genotype 3. Among these, 100 (91.7%) patients were non-responders and 9 (8.3%) were relapsers. The mean age of the patients was 38.9±8.8 years. The non-responders had elevated levels of serum aminotransferase. According to Batts-Ludwig classification, Grade 0 inflammation was not present in the non-responders and relapsers; grade 1 in 51 (46.8%); grade 2 in 47 (43.1%); grade 3 in 10 (9.2%); and grade 4 in 1(0.9%). Stage 0 fibrosis was present in 10 (9.2%); stage 1 in 34 (31.2%); stage 2 in 36 (33.0%); stage 3 in 13 (11.9%); and stage 4 in 16 (14.7%).
Conclusion: Results suggested that even if it failed to eradicate hepatitis C virus, the conventional interferon and ribavirin therapy was able to halt the progress of necroinflammation and fibrosis.
Keywords: Hepatitis C, Non-responder, Relapser, Conventional interferon, Ribavirin. (JPMA 63: 231; 2013)
interferon monotherapy, age below 17 years, concomitant evidence of B or D virus infections, human immunodeficiency (HIV) infection, decompensated cirrhosis, alcohol or intravenous drug abuse, pregnancy, malignancy and autoimmune disease were not included. SPSS 15 was used to analyse data. Mean ± standard deviation was calculated for quantitative variables.

Results

Of the 109 patients, 57 (52.3%) were women and 52 (47.7%) were men. Mean age was 38.9±8.8 years (Table-1). Among these, 100 (91.7%) patients had never achieved undetectable HCV RNA (qualitative polymerase chain reaction [PCR] testing) during the first treatment, and were, thus, non-responders, while 9 (8.3%) patients had shown undetectable HCV RNA during the therapy, but had become HCV RNA positive after discontinuing medication and were, thus, relapers. Genotype 1 was seen in 29 (26.6%) patients and Genotype 3 in 78 (71.6%). Genotype of 2 patients was missing. Grade 1 inflammation were present in 51 (46.8%) patients; grade 2 in 47 (43.1%); grade 3 in 10 (9.2%); and grade 4 in 1 (0.9%). Stage 0 fibrosis was present in 10 (9.2%) patients; stage 1 in 34 (31.2%); stage 2 in 36 (33.0%); stage 3 in 13 (11.9%); and stage 4 in 16 (14.7%) (Table-2).

Discussion

Chronic hepatitis C patients who are non-responders and relapers to conventional interferon (IFN) and ribavirin represent one of the most difficult challenges in clinical routine in Pakistan. The current standard of care for chronic hepatitis C is treatment with combination therapy of pegylated interferon (PEG-IFN) plus weight-based ribavirin, with an overall SVR rate of 70-90% in Asian patients compared with 50-80% in Caucasian patients.\(^8,9\) In developing countries like Pakistan where the burden of chronic hepatitis C is increasing day by day, it is very difficult to prescribe PEG-IFN to every patient. In Pakistani patients with chronic hepatitis C, clinical observations indicate that SVR obtained with conventional IFN and ribavirin is higher than that in studies conducted in Western countries.\(^10\)

Hepatic fibrosis is a primary endpoint in the evaluation of the severity of chronic liver disease. Liver biopsy remains the gold standard for assessment of hepatic fibrosis.\(^11\) In the current study, HCV infection was higher among women. The mean age of the non-responders was 39.19±8.9 years and relapers 35.89±8.3 years, which is a very productive part of life.

In the current study, most of the patients were non-responders to conventional IFN therapy, and only 8.3% of the patients were relapers. The most common HCV genotype in both the relapers and the non-responders was Genotype 3 followed by Genotype 1. Shin et al. reported in a cohort of Korean chronic hepatitis C (CHC) patients that risk factors for relapse were age older than 50 years, Genotype 1
cases, higher baseline HCV RNA level, while lower adherence to treatment was important in Genotype 2 and 3 patients. Older age was not the risk factor in our patients. Treatment responses to antiviral therapy with IFN plus ribavirin have been shown to be influenced by the genotype, and the SVR is higher for patients with HCV Genotype 2 or 3 than for those with HCV Genotype 1. Majority of the non-responders and relapers in our study had HCV Genotype 3, which reflects the most common HCV genotype in Pakistan. Aminotransferase levels were high in the non-responders compared to the relapers. Basso et al. indicated that alanine aminotransferase (ALT) elevation in the later course of antiviral therapy of HCV RNA negative patients was associated with virologic relapse. In this study both mean ALT and aspartate aminotransferase (AST) levels were elevated in the non-responders compared to the relapers.

The current study had limitations as baseline liver biopsy was not done, baseline HCV RNA levels were not checked and, on treatment, virological responses were not available.

Conclusion

Even if not eradicating HCV, conventional anti-viral therapy is able to halt the progress of necroinflammation and fibrosis, and, hence, hepatocellular carcinoma. Although the number of patients in the study was very low; but stage IV fibrosis was not seen in the relapers and they also had less degree of inflammation that might be the histological response with conventional interferon and ribavirin therapy. Further studies are required to establish this relationship with certainty.

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References
5. Idrees M, Riazuddin S Frequency distribution of hepatitis C virus genotypes in different geographical regions of Pakistan and their possible routes of transmission. BMC Infect Dis 2008; 8: 69.