ORIGINAL ARTICLE

EFFICACY AND COST EFFECTIVENESS OF BIOSIMILAR PEGYLATED INTERFERON α2a 180 µg/RIBAVIRIN IN NON-CIRRHOTIC TREATMENT NAÏVE GENOTYPE 3 PATIENTS

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Background: Due to poor socio-economic status majority of the patients cannot afford the cost of investigations and treatment of chronic active hepatitis C which has compelled the local physicians to find cost effective ways of managing chronically infected hepatitis C patients. The objective of this study was to evaluate the efficacy and cost-effectiveness of biosimilar pegylated interferon α2a 180 µg and weight-based ribavirin, compared to pegylated interferon and ribavirin in treatment naïve GT3 patients. **Methods:** A total of 45 patients were recruited for the study out of which 39 patients completed the study protocol at Hepatology Clinic of Gujranwala Liver Foundation, Siddique Sadiq Hospital, Sheikhupura Road, Gujranwala, from Nov 2012 to Apr 2014. Patients with history of previous interferon-based therapy, liver cirrhosis, non GT3, hepatitis B co-infection, and organ transplant recipients were excluded. All patients were treated with biosimilar pegylated interferon α2a 180 µg and weight-based ribavirin in a response guided manner. **Results:** Out of the 39 patients who completed the study as per protocol, 92.3% achieved sustained virological SVR. Relapse rate was 13.1% and non-responders were 6%. **Conclusion:** Biosimilar pegylated interferon α2a 180 µg/ Ribavirin had a high SVR rate in carefully selected treatment naïve GT 3 non-cirrhotic patients. The results are comparable to Direct Acting Antiviral agent (DAA) which has higher cost.

Keywords: Hepatitis C, Antiviral therapy, Pegylated interferon, Biosimilar pegylated interferon, Ribavirin, Efficacy, Cost-effectiveness

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INTRODUCTION

Hepatitis C virus (HCV) infection results in a chronic carrier state in 80% of those infected. Approximately 20% of those chronically infected will ultimately progress to develop cirrhosis and death due to end-stage liver disease or hepatocellular carcinoma (HCC). Cure from the infection is known as sustained virologic response (SVR). SVR is associated with reversal of long-term outcomes of chronic liver disease, reduction in incidence of HCC and lowered HCV related mortality. According to one estimate nearly 10 million Pakistani people are affected with hepatitis C.[1] The most prevalent is Genotype 3 (GT3).[2] Although it is more sensitive to IFN than GT 1 but it is also associated with more aggressive clinical course due to faster fibrosis progression.[3]

Due to poor socio-economic status majority of the patients cannot afford the cost of investigations and treatment of chronic active hepatitis C which has compelled the local physicians to find cost-effective ways of managing chronically infected hepatitis C patients. There is limited published data on HCV GT 3 patients' responsiveness to interferon from Pakistan.[4] Response guided therapy with pegylated interferon has led to improved response rates along with early stoppage of treatment in non-responders.[5,6] Before the arrival of sofosbuvir, pegylated interferon in combination with ribavirin has remained the standard of care for treatment of HCV GT3 infection. SVR rates have been 70–80% for GT 2/3.[7–9] SVR has also been noted to be affected by host and viral factors namely age, gender, obesity, IL28B genotype, viral genotype, baseline viral load, and fibrosis stage. On-treatment virological response has led to improved outcomes with peg/Riba therapy and rapid virological response (RVR) has shown to be an excellent predictor of SVR.

Two varieties of pegylated interferon (peg IFN) are currently available. Peg IFN α2a 40 KDa in which branched PEG moiety is attached to IFN α2a by a stable amide bond that consists of six positional isomers. The other is peg IFN α2b which is 12 KDa. Biosimilar pegylated interferon α2a 180 µg/Ribavirin are new versions of existing biotech products and are similar biotechnology medicinal products. They are produced using the same core genetic material and are approved on the basis that they are equal to the reference product in terms of safety and efficacy for the treatment of chronic HCV infection.

In lower-resource countries, the total cost of HCV treatment with peg IFN/Riba, including diagnostic tests, physicians' fees etc. is up to US $ 2,000 (Approximately Rs. 200,000) representing more than half of the country's annual *per capita* income, which is approximately $ 2,800. The high cost of antiviral therapy is the main obstacle to treatment in 3rd world

countries. The rationale of this study was to test the efficacy of biosimilar pegylated interferon α2a 180 µg/Ribavirin in non-cirrhotic treatment naïve GT3 patients keeping within cost constrains.

PATIENTS AND METHODS

This single centre study was conducted at Hepatology Clinic of the Gujranwala Liver Foundation, Siddique Sadiq Hospital, Gujranwala, Pakistan from Nov 2012 to Apr 2014. The Institutional Review Board and Ethics Committee of the Gujranwala Liver Foundation approved the research protocol. It was an observational study based on analysis of the response rates of chronic hepatitis C GT3 treatment naïve non-cirrhotic patients who received biosimilar pegylated interferon α2a 180 µg subcutaneous once weekly and daily weight-based ribavarin. A total of 45 patients were included in the study aged 18–55 years, any gender, with detectable viral load, genotype 3 and non-cirrhotic. Patients with previous interferon therapy, pregnant or lactating women, suspected cirrhosis (AST, ALT >1, PLT ≤150, splenomegaly on ultrasound), organ transplant recipients, HBV or HIV co-infection were excluded. Patients with co-morbid illnesses like psychiatric illness, congestive cardiac failure, chronic renal failure, auto-immune disease, ischemic heart disease, and untreated thyroid disease were also excluded.

All patients were treated with biosimilar pegylated interferon α2a 180 µg subcotaneously once weekly, and weight-based ribavirin in 2 or 3 divided doses. HCV RNA by PCR qualitative (QL) was checked at week 4. Those with negative PCR, i.e., RVR-positive received 24 weeks of therapy and HCV RNA (QL) was repeated at the end of treatment and 6 months after completion. The patients whose HCV RNA QL was detected at week 4, i.e., RVR-negative, HCV RNA by PCR quantitative (QN) was checked at week 12. Antiviral therapy was continued in patients who had undetectable virus (complete EVR) and who showed >2 log reduction compared to baseline viral load (partial EVR). In these patients HCV RNA qualitative was repeated at week 24. Therapy was discontinued in patients whose HCV RNA was detected (ETR-negative). In patients who had HCV RNA undetectable at week 24 (ETR-positive), antiviral therapy continued till week 36. HCV RNA qualitative was checked 24 weeks of completion of therapy in all patients.

RESULTS

A total of 45 HCV treatment-naïve patients were included in the study. Out of these, 39 patients completed the duration required to assess sustained virologic response (24 weeks after cessation of treatment). Among 39 HCV treatment-naïve patients who had completed duration to assess sustainability of virus response, there were 18 (46%) males and 21 (54%) females. The mean age of patients was 38.47±8.7 years, (Rang 20–55 years). The mean pre-treatment HCV viral load was 4.03×10^6 IU/ml ranging from 11,889 to 8×10^7 IU/ml.

The RVR was found in 23 (59%) patients. Of the 16 (41%) patients who did not achieve RVR, 1 patient was null responder at week 12 whose therapy was discontinued and rest of the 15 patients achieved complete EVR. All RVR-positive and cEVR-positive patients showed ETR at week 24. All RVR-positive patients received antiviral therapy for 24 weeks, while patients who did not achieve RVR but showed complete EVR at week 12 were treated for another 24 weeks. SVR was checked 6 months after completion of treatment in all patents. All RVR-positive patients achieved SVR, while 2 patients showed virological relapse in the complete EVR group. Overall 36 (92.3%) patients achieved SVR, 2 patients (5.1%) were relapsers and 1 (2.6%) was non-responder.

DISCUSSION

An estimated prevalence of hepatitis C in Gujranwala is 6.3%,[1] though unpublished reports point to much higher prevalence in the local population. The average annual income of patients reporting to the Gujranwala Liver Foundation (GLF) clinic was Rs. 95,000 (US $ 950). Until now a total of 9,300 patients are registered with the GLF and approximately 90% of these are HCV positive. Offering quality antiviral therapy to this segment poses an enormous challenge and the GLF is continuously working to find cost-effective ways to cure maximum number in a cost-effective way. Injection of a local biosimilar peg IFN α2a is available at nearly 50% of the cost of other pegylated interferons available in Pakistan. High SVR was seen in our patients using the biosimilar peg IFN α2a with excellent efficacy.

Beside excellent treatment response, the cost incurred on such patient was much less, i.e., Rs. 64,800 for 6 months when treated with biosimilar pegylated IFN and ribavirin as compared to branded product (available at Rs. 132,000 for the same duration). It is important to note that the patients included in this study were all good risk patients, as non-GT3 patients, suspected cirrhotic, and patients with co-morbid illnesses were excluded. It is also interesting to note that the SVR rates with biosimilar peg IFN α2a are also comparable to reported results of sofosbuvir plus ribavirin and peg/Riba plus sofosbuvir. This points to the fact that dual therapy with pegylated interferon/ ribavirin will remain an excellent choice in carefully selected GT3 treatment naïve patients. In patients infected with HCV genotypes 2 and 3, the reported SVR is 76% and 82% of cases treated with peg-IFN-α2a plus RBV, and peg-IFN-α2b plus RBV, respectively.[10,11] A study in Brazil showed that the combination of

peginterferon α2a (40KD) plus ribavirin produced an SVR in 51% of relapsers and 26% of non-responders to conventional interferon plus ribavirin.[12]

Over the next 5–10 years, the spectrum of treatment available for HCV infection will expand (three new classes of antiviral drugs have entered phase III clinical trials) and it is very likely that interferon-free regimens will become a reality within this time. These will result in a substantial improvement in treatment success rates, shortened duration of therapy and a substantially improved side-effect profile. The key to success in low and middle income countries will be based on pricing decisions made by pharmaceutical companies and the availability of generic compounds.[13]

CONCLUSION

Biosimilar pegylated interferon α2a 180 µg/Ribavirin had a high SVR rate in carefully selected treatment naïve GT3 non-cirrhotic patients. The results are comparable to Direct Acting Antiviral agent (DAA) which has higher cost.

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