Early Virologic Response to Pegylated Interferon in Chronic Hepatitis B Infection

Ladep, N G** *FWAP,* ****Ugiagbe, R A** *MBBS*,**Okonkwo, U** *MBBS*, ***Okeke, E N** *FWACP,* ***Malu A O** *FMCP, FWACP*

*Department of Medicine, University of Jos/JUTH, **Department of Medicine, UBTH, Benin City *** Department of Medicine, UNTH, Nnewi.

Abstract

Background*: Early virologic response to pegylated interferon in the treatment of chronic hepatitis B infection is not frequently reported.*

Method: *The case notes of the patients was retrieved and relevant data extracted, literature review was done using Medline.*

Result: *A report of a case of early virologic response in a 62 year old man with chronic hepatitis B infection, receiving pegylated interferon is presented with a review of the relevant literature. He had HBV DNA level assessed by PCR and histology of liver biopsy specimen.*

Conclusion: *Clinicians should be on the lookout for early virologic response to pegylated interferon and the eventual outcome of such early response*

Words*: Virologic response; pegylated interferon; Nigeria; Jos.*

Date Accepted for publication: 11th June 2009
Nig J Med 2009; 330 - 331

Introduction

Chronic hepatitis B affects 350 million people worldwide.[1] For the clinicians who are confronted with diagnosis and management of hepatitis B, there is increased availability of newer antiviral agents. At present five approved drugs exist for the treatment of the disease: interferon alfa-2b, lamivudine, adefovir dipivoxil, entecavir and pegylated interferon alfa-2a.[2] Amongst these drugs, pegylated interferon alfa-2a is promising as it is administered once weekly and gives early response to therapy and has better defined period of therapy. Our experience with a case is here presented.

Case Report

A 62 year old man presented to our regular clinic of the Jos University Teaching Hospital because he had gone for a surgery outside Nigeria and found to be reactive to hepatitis B surface antigen. He was not symptomatic. He had uvulectomy as a child through unsterilized means and was transfused with blood when he had left lung resection in 1959. He does not take alcohol and has no history of multiple sexual exposures. He is not a known hypertensive or diabetic. On examination he was not jaundiced and had no stigmata of chronic liver disease. The liver span was 6cm and there was no ascites. Results of investigations showed his blood was reactive for HBs Ag and non reactive for anti HCV with slightly elevated liver enzymes (ALT 52 IU/L, AST 49 IU/L and ALP 115 IU/L. Normal reference ranges are 0-40 IU/L for ALT and AST, 21-92 IU/L for ALP) and deranged clotting profile (The prothmbin time was prolonged by 14 seconds with a PTR of 2 and INR of 2.83). He was assigned to child Pugh class B. HBV DNA read 62,400 copies/ml(4.8 log copies). Histology of trucut biopsy of the liver reports "severe necro inflammatory activity with minimal fibrosis, features are in keeping with chronic hepatitis and a Knodell score of 15/22". A diagnosis of chronic liver disease following HBV infection was made. He was commenced on pegylated interferon SC 180µg weekly and by the tenth week of treatment , repeat HBV DNA showed a sharp decline to 844 copies/ml (2.9 log copies). Liver enzymes rose to 103 IU/L, 72 IU/L and 191 IU/L for AST, ALT and ALP respectively.

Discussion

Interferon-alfa was approved by the US Food and Drug Administration for the treatment of hepatitis B in 1992, lamivudine in 1998 and adefovir dipivoxil in 2002.[3] Due to the side effects of interferon and inconvenience of frequent injections, lamivudine soon become the drug of choice worldwide. The disadvantage with the use of this agent includes development of lamivudine resistance as a result of YMDD mutations and concerns regarding the durability of response.[4] It was noted that adefovir seemed to be an effective antiviral agent and no resistant mutations were found in patients treated for up to 48 weeks . Recently, studies with pegylated interferon have demonstrated better results compared with conventional interferon.[3,5,6] Interferon acts by activating intracellular enzymes such as 2'5 Oligodenylate synthetase resulting in degradation of HBV mRNA. It also increases the cell mediated immune respons to HBV by augmenting expression of

Correspondence to: ***Rose A Ugiagbe*** *E-mail: rosierosekes@yahoo.com*

HLA class I antigen presenting molecules on the surface of infected hepatocytes. A number of studies have shown that the best independent predictors of a response to interferon therapy are the serum HBV DNA and alanine aminotranferase (ALT) levels at baseline. Perrilo et al demonstrated that virologic response (defined as sustained disappearance of HBV DNA and hepatitis B envelope antigen (HBe Ag) seroconversion) occurred in only 17% of patients with baseline ALT values < 2.5 times the upper limit of normal (ULN) but in 50% of those with baseline ALT >5 times ULN. In contrast, there was an inverse relationship between serum HBV DNA and virologic response with no response observed in patients whose baseline HBV DNA levels were >56 million copies by polymerase chain reaction.[7] This result suggests that interferon is more effective in patients who have a relatively well preserved cellular immune response to HBV. This is further supported by a study in which high necro inflammatory scores on liver biopsy correlated with higher rates of virologic response.[8] Higher rates of response to interferon have also been shown to correlate with ALT flares during therapy.[9] Our patient had high HBV DNA levels(62,400 copies/ml) at baseline, severe necro inflammation and only marginal elevations of ALT (52 IU/L) and a flare of ALT (72 IU/L) during therapy. Goals for treatment include suppression in HBV DNA levels, histologic improvement and ALT normalization. We were fascinated by the drop of HBV DNA from 62,000 copies/ml to 844 copies/ml at 10th week and are hopeful that our end points will be realized. We therefore encourage clinicians in Nigeria to use this drug for patients who meet the criteria for treatment but not for those with decompensated cirrhosis.[10]

References

1. 1.World Health Organization. Hepatitis B fact sheet. Available at :www.who.int/mediccentre/factsheet/fs204/en/Accessed June 30, 2006.
2. Naoky T. Diagnosis and management of chronic hepatitis B in the primary care setting. Postgraduate Medicine 2006 ; 119(2):1-8
3. Graham WE. The role of interferon therapy in hepatitis B. MedGenMed. 2004; 6: 16:1-2
4. Liaw Y-F, Chien RN, Yeh CT et al. Acute exacerbation and hepatitis B clearance after emergence of YMDD motif mutation during lamivudine therapy. Hepathology 1999; 30: 567-572.
5. Cooksley WGE, Piratvisuth T, Wang YJ, Mahachi V, Chao Y-C, Zahm FE et al. 40kd Peg-interferon alfa-2a(Pegasys) efficiency and safety results, from a phase II randomized actively controlled, multi-center disease in the treatment of HBeAg positive chronic hepatitis B. American Association for the study of liver disease, October 27-31, 2001, Dallas, Texas, USA.
6. Cooksley WGE, Piratvisuth T, Wang YJ, Mahachi V, Chao Y-C, Zahm FE et al. Evidence for the efficacy of Peg-interferon alfa-2a (40kd), Pegasys in the treatment of HBeAg positive chronic hepatitis B and impact of baseline factors. European Association for the study of the liver. Madrid. 19 April,2002
7. Perrilo RP. Schiff ER, Davis GL et al. A randomized, controlled trial of interferon alfa-2a alone and after prednisone withdrawal for the treatment of chronic hepatitis B. The Hepatitis interventional therapy group. N. Engl J Med. 1990; 323(5): 295-301.
8. Thomas HC, Karayiannis P, Brook G. Treatment of hepatitis B virus infection with interferon. Factors predicting response to interferon. J Hepatol 1991; 13 S1: S4-7.
9. Nair S, Perrillo RP. Serum alanine aminotransferase flares during interferon treatment of chronic hepatitis B; is sustained clearance of HBV DNA dependent on level of pretreatment viremia? Hepathology 2001; 34(5).1021-1026.
10. De Franchis R, Hadengue A, Lau G et al. EASL International Consensus Conference on Hepatitis B 2002. Geneva Switzerland. Consensus statement(long version). J Hepathol 2003,39:S3-25.