BRIEF COMMUNICATION

Interferon –alpha 2b (PDferon B®) in Treatment of HBeAg-negative Chronic Hepatitis B; Preliminary Report

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Abstract

Aims: In this report we aim to assess therapeutic efficiency and safety of particular brand of IFN-alpha 2b (PDferon B®) in patients with HBeAg negative-CHB in Iran.

Patients and Methods: 28 patients (23 male, 5 female, mean age 28^{+-} 12.4 years) with HBeAg-negative Chronic Hepatitis B enrolled. All of them received Interferon-alpha 2b (PDferon B®) 5-6 MU per dose and totally 15-35 MU per week for six months. Demographic characteristics, sex, age time of diagnosis, histological scoring and family history of HBV infection considered in analysis.

Results: All except one received the drug until finishing the course of treatment. 10.7 %determined as not responsive neither biochemically nor virologically. 85.7 were responder by considering one of the criteria. 60.7 % patients had complete response (HBV DNA negative and normal ALT) and 4.6% HBsAg seroconvert.

Conclusions: Considering high response rate of the current study, the efficacy of PDferon B®) is similar to other Interferons in different studies.

Key Words: Hepatitis B, PDferon B, Treatment

Introduction

Chronic hepatitis B virus (HBV) infection affects an estimated 350 million persons globally.[1] Chronic hepatitis B (CHB) virus infection is a leading cause of serious liver disorders such as cirrhosis and Hepatocellular carcinoma, which now it accounts for more than 1 million deaths per year.[2, 9]All patients with chronic HBV infection, defined in clinical practice by positive HBsAg for at least 6 months. Regarding to HBeAg status the CHB divided to two groups. In HBeAg negative CHB there is persistent or intermittent HBV replication [4] and it is potentially severe and progressive form of CHB prevailing in certain parts of world such as Southern Europe and Area, the middle east and asia.[3, 6] The long term outcome of CHB infection depends on the severity of liver disease at the time when virus replication is permanently suppressed.[9]

Interferon was the first agent shown to be effective in causing sustained suppression of HBV replication and the first treatment approved for CHB in most countries.[2, 7, 10] Response to interferon alpha therapy was reviewed in several report from different countries and it is accepted that 25-40 percent of CHB patients globally may benefit from treatment. [2,8]In HBeAg negative-CHB patients it is shown that end-treatment virologic response ranged from 38-90 percent in patients treated with IFN-a compared with 0-37 percent response rate in controls.[3]

The aim of CHB treatment is to suppress viral replication and eliminate the virus and endpoints of treatment are normalization of ALT (Alanine aminotranferase) level and elimination of HBeAg and HBV DNA from the blood.[8] In HBeAg negative CHB treatment response cannot be assessed by HBeAg loss and is usually defined as undetectable HBV DNA along with normalization of ALT level.[10]

In this report we aim to assess therapeutic efficiency and safety of particular brand of IFN-alpha 2b (PDferon B®) in patients with HBeAg negative-CHB in Iran.

Methods

Twenty-eight naive patients with HBeAg negative CHB were enrolled to the quasi-experimental interventional study from Feb 2003 to Sep 2004. All patients received IFN-alpha 2b (PDferon, Pooyesh Darou, Tehran, Iran) 5-6 MU per dose (Mean±SD: 5.3±0.86 MU) and totally 15-35MU per week (Mean±SD: 19.2±6.6 MU) at least for six months by intramuscular injection. Routine biochemical and virological tests made at start of trial, 1,3 and 6 months after treatment including: ALT, hepatitis B virologic profiles (HBsAg, HBsAb, HBeAg, HBeAb and HBV DNA with qualitative measurements). Complete response to the therapy was defined as presence of both biochemical response (normalization of ALT serum levels) and virological response (elimination of HBV DNA from serum samples) and presence of one of them separately was considered as either biochemical or virologic response during treatment course. The chi square test or Fisher's Exact test was used to comparisons in study groups according to baseline characteristics of them. Independent factors that might have influence the response to IFN-alpha therapy were studied using multiple logistic regression analysis and the following variables were evaluated as prognostic factors for the response: sex, age, , outcome of previous IFN-a therapy, time from diagnosis, development of HBeAb in serum during treatment. Data analysis was performed using SPSS soft ware considering $P<0.05$ as statistical significance level.

Results

Twenty-eight patients known to have HBeAg negative CHB infection enrolled to the study to receive IFN-alpha 2b. Patients diagnosed to have HBV infection ranging from 1 to 8 year prior to start of treatment. Demographic characteristics of patients were shown in table 1.

Three patients were determined as not responsive neither biochemically nor virologically and one patients have been expired because of causes other than related to CHB. Twenty-four patients (85.7 percent) were responder by one of the criteria, from those, 17 patients (70.8 percent) have complete response (virologic and biochemical response), 5 patients (20.8 percent) just had virologic response and finally 2 patients (8.4 percent) just had biochemical response alone.

Eithy five point seven percent of patients were diagnosed to have HBV infection via Blood Donation and Routine Examination of donated bloods. Fifty percent of patients have history of infection in their mother, 10.7 percent in their father and 39.3 percent in their sisters or brothers. Altogether 82.1 percent of patients have family history of HBV infection at least in on member of their family. At the end of follow up period time we determined that 96.4 percent of study subject were serologically HBsAg positive and HBsAb negative. All non responsive subjects along with the expired one were HBV DNA positive in their serum samples. At the regression analysis to determine the prognostic factors affecting response to the treatment non of the independent variables evaluated such as sex, age, time of diagnosis, histological scoring and family history of HBV infection have statistically significant effect on response status to the treatment.

Discussion

There are increasing evidences supporting the efficacy of IFN-a on chronic hepatitis B infection [4,9,11]. and in meta-analysis four RCTs with 84 treated and 84 untreated patients conducted between 1989 and 1997 it is shown that the response rate of IFN-alpha in CHB patients have a wide range between 38-90 percent [3], and more other report showed the effects of IFN therapy on slowing progression of CHB [11] and decreasing mortality due to CHB or development of Hepatocellular carcinoma [12]. Considering response rate of the current study (85.7 percent), the calculated response rate is in the range of response rate reported from authors in similar subjects of HBeAg negative CHB patients and even it is close to upper limit of the reported response rate and it would be because of considering only virologic elimination of HBV DNA or ALT normalization each alone as treatment response. So considering the complete virologic and biochemical response as treatment goal the response rate will be 60.7 percent (17/28). The results of this study in response to IFN issue is go with the other similar studies published in the literature but potential side effects of IFN may limit their administration in CHB patients specially HBeAg negative ones. The reported results of the current study regarding prognostic factors and correlation of independent factors to the response status of patients may be less satisfactory because of having no control and small sample size so we are continuing the study to follow patients in more wide time period and to study the impact of long term administration of IFN-a more than 6 month in HBeAg negative CHB.

Table 1
Baseline characteristics of HBeAg negative CHB patient treated with 6 month IFN-alpha 2b

	Total (n=28)	Responsive (n=24)	Non-responsive (n=4)	P.Value
Age (Mean±SD)	38.4±12.4	39.26±11.9	33.1±16.1	0.095*
Sex (M/F)	23/5	20/4	3/1	0.568**
Family History (n)	23	20	3	0.605**
Stage (Mean±SD)	2.2±0.9	2.2±0.9	2±1	0.762*
Grade (Mean±SD)	6.5±2.5	6.7±2.4	6±3.6	0.762*
Knodell Score (Mean±SD)	8.7±2.9	8.9±2.8	8±4	0.648*

*Mann-Whitney U test; ** Fisher's Exact test

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