EDITORIAL

What to Treat with Interferon?

Paucker for the first time in 1962 described that interferon (IFN) alpha had an anti-proliferative effect [1]. This focused interests on its possible use in treatment of neoplasia. Interferons are naturally occurring proteins with antiviral and antiproliferative properties that help in treatment of cancerous cells. Recently, it has been reported that the expression of IFN-alpha receptors in malignant urothelial cells is significantly higher than in normal urothelial cells. In vitro studies have indicated that IFN-alpha in combination with bacillus Clamette-Guerin (BCG) at very low concentrations inhibit the proliferation of human bladder cancerous cells. In vivo studies of intravesical BCG suggest that BCG induces IFN-gamma expression and that the level of induction correlates with clinical response. [2, 3, 4] In stage four of renal cell cancer the responses to cytotoxic chemotherapy generally do not exceed 10% for any regimen and interferon-alpha has been evaluated and approximately a 15% of selected individuals had objective response [5]. Other studies have shown that IFN-alpha can produce clinically meaningful tumor regression or disease stabilization in patients with hairy cell leukemia or AIDS-related Kaposi's sarcoma. In ph-positive Chronic Myelogenous Leukemia, interferon-alpha supplemented with intermittent chemotherapy has been shown to prolong overall survival and delay disease progression compared to patients treated with chemotherapy alone [6]. There is enough data regarding the use of IFN-alpha in treatment of Chronic Myeloid Leukemia (CML) and Multiple Myeloma (MM) [7]. Several studies have reported that interferon therapy improves the risk for developing hepatocellular carcinoma (HCC) and death.

Chronic hepatitis B (CHB) is the most prevalent cause of chronic liver disease in Iran [8]. HBeAg-negative CHB is a potentially severe and progressive and most common form in Mediterranean area. The beneficial effect of IFN-alpha in chronic hepatitis B was first reported in the mid 1970s [11] and after that the drug was approved by FDA over a decade ago. Suppression of HBV replication by Interferon alpha is almost always associated with remission in biochemical activity. Thus, an effective antiviral therapy is expected to improve its prognosis. [9] Unfortunately, although IFN-alpha has been reported to induce initial remission in almost 65% of the treated patients, but due to relapse after cessation of treatment the sustained virologic response rate appeared to range between 10 and 30% [10]. There are many publications regarding to long-term beneficial effect of IFN-alpha therapy in CHB, and about 66% of patients with sustained virological response lost HBsAg and some of them also developed anti-HBs. Papatheodoridis et al. had demonstrated that patients with sustained virological response were associated with lower rates of death and development of HCC [12]. For the time being, one year of IFN-a therapy appears to represent the most effective form of treatment for HBeAg-negative CHB and 4-6 months for HBeAg-positive CHB with a good rate of response and 20-40% of them going into sustained remission.[9]

Hepatitis C infection now comes to the top of virus-induced liver diseases in many parts of the world. In Iran, it seems that its prevalence in general population is less than 1 percent which is much lower than most of middle east countries. But the infection is emerging mostly due to problem of intravenous drug abuse and needle sharing in addicts [13]. In the past few years, the prevalence of HCC has increased in Western countries and currently cirrhosis related to the hepatitis C virus is the most common indication for liver transplantation worldwide [14].

Antiviral therapy for patients with chronic hepatitis C has the final objective of decreasing the mortality of infected patients by preventing HCC and decompensation of cirrhosis. Until 1998, Interferon alpha (monotherapy) was the only approved treatment for HCV infection.

Now, combination therapy with ribavirin should be considered as the initial treatment of choice among patients with chronic hepatitis C. The overall sustained virologic response (optimal response) with combination therapy is about 40%. Follow-up studies have shown that response is durable in the majority of patients and the progression of liver lesion is stopped. It has been shown that liver fibrosis diminishes when the inflammatory activity disappears; which is probably due to the antifibrogenic effect of interferon [15]. It is important to note that even in patients without a sustained virologic response, liver histology may improve by stopping the progression of fibrosis [16]. The results from Ikeda et al. showed that there is a significant beneficial effect of interferon by reducing the incidence of HCC in treated patients [17].

Treatment of hepatitis C is expensive and unfortunately is not affordable for all the patients in the world. Pooyesh Darou Company started its biotechnology plant in collaboration with the International Centre for Genetic Engineering and Biotechnology (ICGEB) in Triest, Italy and Tehran University of Medical Sciences at 1998. Interferon alpha (PDferon B®) is the first product that introduced to Iranian clinicians on 2000 after nearly 3 years of sustained and serious effort. In 2000, a clinical trial was designed to evaluate the effects and side effects of PDferon B® in patients with chronic hepatitis C in two centers in Tehran. The results by considering biochemical and virological response were excellent and PDferon B® had an efficacy equal to the products imported from other foreign countries [18].

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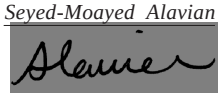

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