Study of Therapeutic Efficiency and Efficient Factor of Interferon for Chronic Hepatitis B

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ABSTRACT Objective: To investigate the influencing factors of the efficacy of interferon α (IFN-α) on patients with chronic hepatitis B (CHB). Methods: 46 cases of CHB patients were chosen in this study, who were treated with IFN-α for 48 weeks in Qingdao Hospital for Infectious Diseases from January 2006 to June 2009, which were divided into responding group and non-responding group according to the efficacy of IFN-α. The influence of host factors, viral loads and biochemical factors on the efficacy of IFN-α was detected. Results: The proportions of sex and the mean ages and courses of disease were similar in the two groups (P> 0.05). The pre-treatment HBV-DNA loads were lower and the ALT levels were higher in responding group than those in non-responding group (P <0.05), while the responding rate of the patients with HBeAg positive was higher than that with HBeAg negative (P <0.05). The rate of HBV-DNA load decreased more than that of 2 log at the 12 weeks of treatment was significantly higher in the responding group than that in the non-responding group (P <0.05). Conclusion: The lower HBV DNA load, higher ALT level and HBeAg positive before treatment and the response of HBV DNA at the week 12 of treatment may be the predicting factors of the response at week 48 of IFN-α treatment in the CHB patients.

Key Words: Chronic hepatitis B; Efficiency; Interferon-α; Influencing factors

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Introduction

Chronic Hepatitis B (CHB) has become a serious global health problem, and it can easily develop into cirrhosis or even liver cancer [1]. IFN-α is one of drugs which are widely used in the treatment of CHB. It has the dual role of immunoregulation and anti-virus, and compared with other nucleoside (acid) analogue treatment, it has superiorities such as the treatment is fixed, no virus resistance, the serum conversion rate of HBeAg and HBeAb is high and the response is long[2]. However, the responding rate of IFN-α treatment is lower, in order to improve the response rate in treatment of IFN-α and guide treatment on CHB patients with the choice of anti-viral drug in the future, this essay aims to discuss the IFN-α treatment of CHB on the clinical efficacy and impact factors.

1 Materials and methods

1.1 Research Subjects

According to clinical diagnosis standard《Diagnostic criteria for viral hepatitis》[3]which was castiqated in The National Conference on Infectious and Parasitic Diseases in 2000, 46 cases of CHB patients were chosen, who were treated by IFN-α over one year in the Qingdao Municipal Hospital for Infectious Diseases in 2006.6 to 2009.1, excluding hepatitis infected by other virus, drug-induced hepatitis, alcoholic liver disease and autoimmune hepatitis. Before their treatment they all did not take any anti-virus or immunoregulation drugs, satisfy the indications curatives of IFN-α, and they had been continuously treated with IFN-α for more than 48 weeks and had completely related clinical information.

1.2 Therapy Methods

IFN-α 500 million IU a time, subcutaneous or intramuscular injection every two days, the treatment lasted 48 weeks.

1.3 Observation items and Methods

ALT, AST, HBeAg, HBeAb, HBVDNA load and adverse reactions of the patients were detected before treatment, ALT and AST are detected by application automatic biochemical analyzer and test reagents. HBeAg and HBeAb are detected by enzyme-linked immunosorbent assay (ELISA), which is proved by the kehua Biotechnology Co., Ltd of Shanghai. HBV-DNA is detected by fluorescent real-time quantitative polymerase chain reaction (RT-PCR), the reagents are offered by piji biological engineering company Ltd of Shenzhen.

1.4 Efficacy Evaluation

Virological response: after 48 weeks of treatment, HBV-DNA has reduced below 10^3copies/ml, no virological response: after 48 weeks of treatment, HBV-DNA has not reduced below 103copies/ml.

1.5 Statistical analysis

SSPS13.0 statistical software was used to analysis the data. Measurement data was detected by t test and Chi-square test was used to analysis enumeration data.

2 Results and analysis

2.1 The relationship between the host factors and treatment

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response

After 48 weeks of treatment, there were 30 cases (65.2%) in the 46 cases with the response and 16 patients (34.8%) without response. The sex, age and duration of treatment had no relationship with IFN-α response: the mean age for the responding group was 31.9 years old, and which was 32.7 years old for the non responding group. Duration for the responding group was 5.7 years, and which was 3.2 years for the non responding group; t = 0.357 and t=1.869 reparately, P= 0.723 and P=0.068 reparately, the difference was no significant. For the responding group the ratio of female was 6 / 24, and for the non responding group the female ratio was 7 / 9, $x^2 = 1.850$, P = 0.174, no significant difference.

2.2 The relationship between ALT, AST, HBV DNA load and treatment response

After 48 weeks of treatment, for the responding group, ALT and AST levels before the treatment were significantly higher than that of the non-responding group, while the HBV DNA load before treatment was lower in the responding group, the differences were statistically significant (Table 1).

Table1 The cooperation two groups, ALT, AST and HBV DNA load

Group (number)	ALT	AST	HBV-DNA
Responding group (30)	162.6± 76.3	101.1± 48.0	6.1± 0.9
Non responding group(16)	104.9± 41.7	79.1± 39.8	6.8± 1.1
t	2.800	1.566	2.381
P	0.008	0.125	0.022

2.3 The relationship between the characteristics of HBeAg and the treatment response:

The responding rate in the HBeAg -positive was 75.8%, while the responding rate in the HBeAg-negative was 38.5%, x^2=4.193, P=0.041, the differences were statistically significant (Table 2).

Table 2 The responses of HBeAg-positive and HBeAg-negative

Group (number)	Responding group	Non-responding group
HBeAg-positive (33)	25	8
HBeAg-negative (13)	5	8

2.4 After 12 weeks of treatment, the relationship between HBV DNA and treatment response

After 12 weeks of treatment there were a total of 18 cases whose DNA had decreased over 2log, of which 15 cases were in the responding group and 3 cases were in the non-responding group. $x^2 = 4.2783$, P = 0.0386, HBV-DNA load was lower in responding group than that in the non responding group, the differences were statistically significant

3 Discussions

At present, there are two major categories drugs used to anti-HBV in clinical: one is the α -interferon, and the other is the nucleoside (acid) analogues, such as adefovir, entecavir and so on[4,5]. After 6 months the rate of complete response was only 30% -50% with the former treatment, while the latter one has a better virological response rate, but it requires a long-term user, and often has the virology variation or resistance. So to select the appropriate antiviral therapy for chronic hepatitis B is very important. IFN-α as one of the main drugs to treat CHB[6], and its mechanism of action include anti-viral and immune regulation [7-11], many studies have shown that different patients had largely different responses to interferon[12,13]. This essay is a retrospective study of 46 cases of CHB who treated by α -interferon, analyzed their age, gender, disease duration, characteristics of HBeAg and HBV-DNA load, HBV DNA level after 12 weeks and other factors on the efficacy of α -interferon, so as to provide a basis for choosing the methods of clinical treatment. After 48 weeks of treatment, there were 30 cases (65.2%) had response and 16 patients (34.8%) did not have response, the virological responding rate after 48 weeks of treatment was higher than which reported in the other literatures [14-17], it may be related with the standard for choice and patients, exclusion who were treated less than 48 weeks. This study showed that patients, gender, age, duration of efficacy had no significant effect (P> 0.05). Before treatment their differences in HBV-DNA load, ALT and AST levels, characteristics of HBeAg were significant (P <0. 05). Before the treatment CHB patients who had low viral load, high aminotransferase level and with HBeAg-positive often had a better result, treatment for 12 weeks, HBV-DNA load declined over 2log correlated with the virologic response, and could be the indicators to predict the efficacy of 48 weeks. The efficacy of IFN treatment of CHB is determined by host and virus [18], patients, pretreatment serum ALT levels and HBV-DNA load, viral load dropped over 2log after 12 weeks treatment and other indicators are the better predictors of 48 weeks, efficacy. Therefore, considering the indicators mentioned above, it was necessary to choose the right patients who are appropriately treated with interferon a, and the related indicators should be observed in the treatment of chronic hepatitis B.

This study analyzed the influence of IFN efficacy to improve the forecast level of IFN therapy, and choose the appropriate treatment patients, by which to reduce the patients' financial burden. The study did not observe the liver histology and the impact of genetics on the efficacy and the sample size was limited, so it remains to be further accumulation of clinical data for scientific analysis.

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干扰素 -α 治疗慢性乙型肝炎的疗效及其影响因素的研究

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摘要 目的:分析影响干扰素 -α (IFN-α) 治疗慢性乙型肝炎(CHB)疗效的因素。方法:选择 2006 年到 2009 年青岛市传染病医院住院的 CHB 患者 46 例,应用 IFN-α 治疗 48 周,根据 IFN-α 治疗的疗效将其分为应答组与无应答组,评价患者的宿主、病毒载量及生化指标等因素对疗效的影响。结果:两组间的性别比例、年龄和病程无显著差异 (P>0.05),应答组治疗前 HBV-DNA 载量低于无应答组,ALT 水平高于无应答组,HBeAg 阳性患者的应答率高于 HBeAg 阴性患者,差异均具有统计学意义 (P<0.05),应答组在治疗 12 周时 HBV-DNA 载量下降>2log 的比例高于无应答组,差异具有统计学意义 (P<0.05)。结论:治疗前 HBV DNA 载量低、ALT 水平高和 HBeAg 阳性以及治疗 12 周时的 HBV DNA 应答可以作为干扰素 -α 治疗慢性乙型肝炎 48 周时应答的预测因素。

关键词:慢性肝炎,乙型;干扰素 -α 治疗;影响因素

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