

论著

聚乙二醇干扰素治疗HBeAg阳性慢性乙型肝炎患者外周血NKT细胞的变化及疗效预测

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摘要:

目的研究聚乙二醇干扰素 $\alpha$  2a (Peg IFN $\alpha$  2a) 治疗乙型肝炎e抗原 (HBeAg) 阳性慢性乙型肝炎 (CHB) 患者, 其外周血NKT细胞表达率和疗效预测相关性。方法 选取 2010年1—12月在中南大学湘雅三医院住院和门诊接受治疗的HBeAg阳性CHB患者63例, 予Peg IFN $\alpha$  2a 18 MIU肌肉注射, 1次/周, 共48周。检测各时段外周血NKT数量占外周血T淋巴细胞的百分比、血清乙型肝炎5项定量及乙型肝炎病毒 (HBV) DNA载量。结果Peg IFN $\alpha$  2a治疗HBeAg阳性CHB患者48周后, 显效 (完全病毒学应答) 26例, 有效 (部分病毒学应答) 21例, 无效 (无病毒学应答) 16例。外周血NKT 细胞占T淋巴细胞百分比: 显效组治疗前及治疗后4、8、12、16、24周, 较有效组和无效组均明显升高 (均 $P < 0.01$ ); 在治疗48周和停药24周, 显效组较有效组NKT表达水平明显升高 (分别 $t = 32.0, P < 0.01; t = 27.6, P < 0.01$ )。显效组治疗后前4周, NKT表达水平上升速度最快, 12周时达最高峰, 其后逐渐下降, 到24周比治疗前水平稍高, 一直维持到48周; 有效组12周时NKT表达水平达最高峰, 较治疗前显著增高 ( $t = 12.83, P < 0.05$ )。显效组患者肝功能基本在12周左右完全恢复正常, 且持续维持在正常水平, 其HBV DNA载量亦逐步下降; 而有效组和无效组患者的肝功能波动在 (1~2)  $\times$  ULN。监测至停药24周后, 共有27例患者出现HBeAg血清学转换。结论Peg IFN $\alpha$  2a治疗HBeAg阳性CHB患者, 其外周血中NKT的表达对疗效有一定预测作用。

关键词: 肝炎 乙型 慢性 肝炎病毒 乙型 HBeAg 聚乙二醇干扰素 $\alpha$  2a 病毒学应答 NKT细胞

Correlation between natural killer T cell expression and virological response to treatment with peg interferon alfa 2a in patients with HBeAg positive chronic hepatitis B

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Abstract:

Objective To study the correlation between expression of natural killer T (NKT) cells and virological response to treatment with peg interferon alfa 2a (Peg IFN $\alpha$  2a) in patients with HBeAg positive chronic hepatitis B (CHB). Methods A cohort of 63 HBeAg positive CHB inpatients and outpatients in a hospital between January and December 2010 were treated with 18MIU Peg IFN $\alpha$  2a once a week for 48 weeks. The percentage of NKT cells in T lymphocytes, five serological markers of hepatitis B and HBV DNA load were assessed by flow cytometry and quantitative real time PCR. Results At the end of 48 week treatment, 26 cases achieved complete virological response, 21 achieved partial response, and 16 didn't achieve response. The percentage of NKT cells in T lymphocytes in complete virological response group before treatment and after 4, 8, 12, 16 and 24 weeks of treatment all increased markedly compared with partial and non response group (all  $P < 0.01$ ); At the end of 48 week treatment and 24 weeks after withdrawing from the treatment, the expression level of NKT cells of complete response group was also higher than partial response group ( $t = 32.0, P < 0.01; t = 27.6, P < 0.01$ ). Within 4 weeks after the start of treatment, the expression level of NKT cells in complete response group increased fastest and reached highest at week 12, then decreased slowly, and at week 24-48 was slightly higher than pre treatment; the expression level of NKT cells in partial response group reached highest at week 12, which was much higher than that before treatment ( $t = 12.83, P < 0.05$ ). Liver function in complete response group returned to normal at week 12, and continued to remain normal, HBV DNA level also decreased gradually, but in partial and non response groups, the liver function fluctuated at (1-2)  $\times$  ULN. Follow up to 24 weeks after stopping treatment, 27 cases appeared HBeAg seroconversion. Conclusion The expression of NKT cells in HBeAg positive CHB patients' peripheral blood can help predict response to Peg IFN $\alpha$  2a therapy.

Keywords: hepatitis B, chronic hepatitis B, virus HBeAg peg interferon alfa 2a virological response; natural killer T

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