REVIEW OF CLINICAL PHARMACOLOGY AND
PHARMACOKINETICS, INTERNATIONAL
EDITION 20: 88-89 (2006)

T-lymphocyte Subpopulations in Patients with Chronic Hepatitis B and C and the Effect of Lamivudine on the Immune Function

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Key words: T-cells, CD4, CD8, NK-cells, hepatitis B, hepatitis C

S u m m a r y. T-cell subsets in naïve patients with chronic viral hepatitis B and C, before any kind of anti-viral treatment, were investigated. We also studied the effect of the antiviral agent lamivudine on T-cell subsets in patients with HBV infection. A significant increase of total lymphocytes, total T-cells and suppressor-cytotoxic T-cells in chronic hepatitis C and an increase in natural killer cells in chronic hepatitis B were detected. No effect of antiviral treatment on the above immune parameters was shown. This indicates that immune responses in chronic hepatitis B and C have different patterns and suggests a different pathogenesis for chronicity, while lamivudine has only antiviral and no immunomodulating effect.

INTRODUCTION

T-cell response is critical in viral diseases and necessary for viral clearance and avoidance of chronicity. Cytotoxic responses in patients with chronic hepatitis B (CHB) and C (CHC) vary. Concerning chronic hepatitis B, it seems that inappropriate T-cell responses are a major mechanism for chronicity, while even in low viremia cases of CHB there is a mild cytotoxic effect. In a recent study with patients suffering from Hbe(-) CHB an increase in peripheral CD8(+) cells was noted, consistent with an ongoing viral replication.

HCV infection is characterized by a high rate of chronicity (65-85%) as a result of an inappropriate immune function necessary for the final viral clearance. On the other hand, cellular immune function may be responsible for the necro-inflammatory liver damage. There is data to suggest that, in CHC, virus-specific CD8 (+) T-cells have a functional paralysis and a decrease in interferon-gamma production leading to viral persistence and chronic liver disease. In the present study we investigated the effect of chronic hepatitis B and C on peripheral T-lymphocytes and their main subpopulations, as well as the effect of lamivudine on the immune function in patients with complete therapeutic response.

PATIENTS AND METHODS

The study included 20 patients with HbeAg(-) CHB and 20 patients with chronic hepatitis C. All patients had the disease for >6 months, elevated liver function tests (LFTs: AST, ALT >2 times upper limits for two consecutive measures), and viremia (HBVDNA or HCVRNA + as detected with PCR). All patients had a positive liver biopsy. Patients with HBV+HDV, HCV+HIV and HBV+HCV co-infection, as well as patients with co-existing liver disease (steatohepatitis, autoimmune disease or drug induced hepatitis) were excluded from the study.

Blood tests were performed in all patients before the initiation of any kind of treatment and, in 12 patients 6 months after the initiation of lamivudine (100 mg/day) in CHB patients with a complete response to therapy (i.e. HBVDNA – anf LFTs normal 6 months during treatment). Flow cytometry was used for the detection of T-cell subsets (XL-2 software, EPICS, Coulter). Statistical evaluation was done by the use of SPSS12 for windows.

RESULTS

There was a statistically significant increase in the absolute number of total lymphocytes, T-lymphocytes (CD3) and suppressor – cytotoxic T lymphocytes in patients with chronic hepatitis C in comparison to CHB patients. In the contrary, we found a significant increase in the percentage number of patients with chronic hepatitis B. The results are shown in the Table 1.

Table 1

T-cell subset	HBV	HCV	p
Total lymphocytes	2076	2653	0.024
Total T-lymphocytes (CD3)	1368	1877	0.009
Helper T-cells (CD4)	918	1101	0.132
Suppressor T-cells (CD8)	493	745	0.006
CD4/CD8	1.56	2.15	0.347
Natural killer (NK) cells (%)	13.2	6.82	0.005

No statistically significant differences in all measured T-cell subsets were detected one year after the initiation of therapy with lamivudine in patients with chronic hepatitis B (Table 2).

Table 2

T-cell subset	*Before lamivudine*	*After lamivudine*	*p*
Total lymphocytes	2040	1900	NS
Total T-lymphocytes (CD3)	1416	1352	NS
Helper T-cells (CD4)	915	875	NS
Suppressor T-cells (CD8)	488	453	NS
CD4/CD8	2.10	2.17	NS
Natural killer (NK) cells (%)	13.2	12.4	NS

DISCUSSION

HBV and HCV are both hepatotropic viruses that can cause acute and chronic liver disease. The liver damage and chronicity during HBV and HCV infections is believed to be mostly immune mediated. Therefore comparative analysis of immune response during the course of the above viral infections may provide important insights into the pathogenetic mechanisms which are involved in viral clearance or viral persistence. In this report, we describe the immune profile, regarding T-lymphocyte subsets in patients with chronic hepatitis B or C, in order to focus on the pathogenesis of chronicity. It seems that the human immune response is different in the above diseases. Insufficient cellular immune response is critical for the ineffective virus clearance in chronic hepatitis B, while in chronic hepatitis C CD3(+)CD8(+) immune response is present. However, there is an immunological escape of HCV, which seems to survive in the presence of an adequate immune response. As expected, therapy with lamivudine has an antiviral effect, but not any kind of immuno-modulation. More studies investigating features of the different immune cells may provide further evidence on the underlying mechanisms of chronic disease and liver damage in patients with chronic viral hepatitis.

REFERENCES

1. Maini M.K., Boni C., Lee C.K., et al.: The role of virus-specific CD8+ cells in liver damage and viral control during persistent HBV infection. *J. Exp. Med. 191*: 1269-1280 (2000)
2. Panasiuk A., Prokopowicz D., Zak J., et al.: Peripheral blood T, B and NK cells in relation to histological hepatitis activity and fibrosis stage in chronic hepatitis C. *Hepatogastroenterology 50*: 178-82 (2003)
3. Tang T.J., Kwekkeboom J., Mancham S., et al.: Intrahepatic CD8+ T-lymphocyte response is important for therapy induced viral clearance in chronic hepatitis B infection. *J. Hepatol. 43*: 45-52 (2005)
4. Neau-Cransac M., Foucher J., Ledinghen V., et al.: Modifications of T-lymphocyte subsets before and during interferon treatment for chronic hepatitis C infection. *Viral Immunol. 18*: 197-204 (2005)
5. Jiaren S., Kui L., Shata M.T., et al.: The immunologic basis for hepatitis C infection. *Curr. Opin. Gastroenterol. 20*: 508-602 (2004)
6. Bertoletti A., Maini M., Williams R.: Role of hepatitis B virus specific cutotoxic T-cells in liver damage and viral control. *Antiviral Res. 60*: 61-66 (2003)