HBV load in treated and untreated individuals

Yates, S.C.

Citation for published version (APA):
Summary

In this thesis, the effects of treatment for HIV and/or HBV on HBV load are described.

First of all, the association of HCC with HCV in Egypt was analyzed. Chapter 2 describes how HCV and HCV/HBV double infection but not HBV or HEV infection alone were correlated with hepatocellular carcinoma (HCC). We found no significant difference in mean HCV RNA load in HBV+ and HBV− samples. This indicates that in this setting, HBV infection does not have an impact on HCV load. Monitoring anti HCV therapy with interferon or other agents might be difficult in areas where HCV infection with genotype 4 is most prevalent.

Screening of samples by nucleic acid amplification is useful to narrow the infectious window in the early stage of acute HBV infection. An additional advantage is the possibility to detect HBV-DNA in persistently infected individuals with the extremely low concentrations of HBV antigen and antibody often observed during therapy.

In chapter 3 the detection and quantification method for HBV DNA we developed is discussed. This method is based on NASBA technology. NASBA is in principle more suited for RNA amplification. With modifications like primer design, sample extraction method, and template denaturation we developed a NASBA suitable for DNA target amplification resulting in RNA amplicons. This method is easy to use, accurate, specific and sensitive. This makes the assay well suited for routine serological screening for HBV.

In chapter 4, we investigated if HIV-1 infection influences the natural course of acute HBV infection.

Our study showed that HBV positive drug addicts were more often presenting with elevated aminotransferases than HBV positive homosexuals. Even more important, (con)current HIV-1 infection causes a more rapid clearance of HBV infection. This presents a significant effect of HIV-1 infection on the natural history of HBV infection, which could have an important impact on HBV infection in regions, or patient groups, with high HIV-1 seroprevalence. Differences in liver damage, HBV chronicity, length of the HBsAg positive period and T cell immunity were only minor when HIV-1 seropositives were compared to seronegatives.

During anti-HIV-1 HAART therapy in HIV/HBV coinfected patients, damage to the liver is
Summary

frequently observed. Up to now it is still not clear if the liver damage is caused by the medication, by HBV itself or by an interaction between HIV-1, HBV and the immune system.

Chapter 5 shows how we studied biochemical and virological determinants of LEE, among HBsAg positive HIV-1 infected individuals in the first year following administration of HAART regimens including 3TC. The hepatotoxicity observed in our patients does not seem to be related to the usage of antiviral drugs or other risk factors.

Our findings are in favor of the hypothesis that not 3TC therapy by itself, but rather the active clearance of virus particles from the blood by the host's immune system through the cytotoxic pathway may be causing damage to the liver.

Quantification of HBV RNA in serum or plasma might have diagnostic value. In chapter 6 we describe a quantification method for this HBV RNA based on NASBA technology. The presence of HBV RNA in serum might be a marker for active replication. Our assay can be used to easily monitor HBV replication in patients by quantifying the HBV RNA load in their serum.

Various studies suggest that the amount of HBV RNA in serum is related to the disease status or progression. In chapter 7 we monitored the clearance of HBV markers following lamivudine (3TC) therapy in chronic HBV carriers who are also infected with HIV-1.

Use of 3TC including highly active antiretroviral therapy (HAART) increased the probability of HBV RNA and DNA clearance, compared to patients using 3TC as mono- or dual therapy. HBV RNA was cleared more often from the serum of patients than DNA, and HBV RNA was cleared more rapidly to levels below detection level than HBV DNA. The effect of therapy on HBV may be measured best by monitoring HBV RNA, instead of HBV DNA.