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ORIGINAL ARTICLE

Characteristics and course of chronic hepatitis B e antigen-negative infection☆

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KEYWORDS
Hepatitis B virus;
Negative HBe antigen;
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Glutamic pyruvic transaminase;
DNA

Abstract
Objective: To describe the epidemiological, analytical and histological characteristics and clinical course of hepatitis B virus (HBV) carriers with negative HBe antigen.
Materials and methods: Observational, retrospective cohort study of HBV carriers with negative HBe antigen (2005–2012), with no other causes of liver disease.
Results: One hundred and thirty-eight patients were included, with mean age 40.5 ± 12.2 years; 54% were women, and 38% were of foreign origin; the number of foreign patients significantly increased ($p < .001$) over the years. Transaminases were normal in nearly 75% and HBV-DNA was <2000 IU/mL in 56% of patients at diagnosis. There was a gradual decrease in HBV-DNA levels in inactive carriers over the study period. Fibrosis study was performed in 47% of patients by Fibroscan® or liver biopsy: 55.4% normal histology and 6.1% cirrhosis. Just over three quarters of patients (77.77%) were inactive carriers. Treatment was required in 15.5% of patients (20% because of cirrhosis and 80% HBeAg-negative chronic hepatitis B). Five patients cleared HBsAg (annual rate .94%), all of whom presented HBV-DNA <2000 IU/mL at diagnosis. Five patients developed complications (3.6%), 4 of them hepatocellular carcinoma (HCC), of which only 2 had cirrhosis. There was 1 HBV-related death (.72%).

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Conclusion: Among HBV carriers with negative HBe antigen, inactive HBs-Ag carriers are predominant. HBV-DNA gradually decreases in the first few years after diagnosis. Morbidity and mortality are low, especially if glutamic pyruvic transaminase (GPT) is normal and HBV-DNA levels are low at diagnosis. Treatment is needed in a considerable number of patients. HCC is the most frequent complication, even in the absence of cirrhosis.

PALABRAS CLAVE
Virus de la hepatitis B;
Antígeno HBe(−);
Hepatitis crónica antígeno HBe(−);
Glutámico pirúvico transaminasa;
ADN

Características y evolución de la infección crónica por virus de la hepatitis B antígeno e negativo

Resumen
Objetivo: Describir las características epidemiológicas, analíticas, histológicas y evolutivas de pacientes con infección crónica por VHB AgHBe-negativo.
Material y métodos: Estudio observacional de cohorte retrospectivo de pacientes diagnosticados de infección crónica VHB AgHBe-negativo (2005-2012) sin otras hepatopatías.
Resultados: Se incluyeron 138 pacientes con edad media de 40,5 ± 12,2 años, de los cuales el 54% eran mujeres. El 38% eran extranjeros, con incremento de estos en los últimos años (p < 0,001). Las transaminasas en el momento del diagnóstico eran normales en casi el 75% y el ADN-VHB < 2.000 UI/ml en el 56%. En los portadores inactivos existe una disminución progresiva de los niveles de ADN-VHB en el periodo de estudio. En el 47% se evaluó la fibrosis hepática por Fibroscan® o biopsia hepática: el 55,4% resultó normal y el 6,1% reportó cirrosis. El 77,77% eran portadores inactivos. Precisaron tratamiento el 15,5% (20% por cirrosis y 80% por HBC AgHBe-negativo). Aclararon el AgHBs 5 pacientes (tasa anual 0,94%), presentando todos al diagnóstico ADN-VHB < 2.000 UI/ml. Cinco pacientes desarrollaron alguna complicación (3,6%), 4 de ellos carcinoma hepatocelular (CHC) (solo 2 presentaban cirrosis). Hubo un fallecimiento relacionado con el VHB (0,72%).
Conclusión: Entre los enfermos con infección crónica por VHB AgHBe-negativo predominan los portadores inactivos. Se produce un progresivo descenso de ADN-VHB en los primeros años tras el diagnóstico. Desarrollan poca morbimortalidad, especialmente si existe GPT normal y ADN-VHB bajo al diagnóstico. Un número no despreciable de pacientes precisa tratamiento. El CHC es la complicación más frecuente, incluso en pacientes sin cirrosis.

Introduction

Chronic hepatitis B virus (HBV) infection is a global public health problem. An estimated 350–400 million people worldwide have chronic HBV infection,[1] and around 620,000 people die annually from HBV-related causes.[2]

Chronic HBV infection can present as hepatitis B e antigen (HBeAg) positive (+) or negative (−). HBeAg(−) chronic infection occurs after HBeAg seroconversion. In 75% of cases, the patient seroconverts from an HBeAg(+) chronic hepatitis state to an inactive HBV carrier (IC) state, characterised by persistently normal transaminases and low HBV deoxyribonucleic acid (DNA) (generally <2000 IU/mL), with little histological damage. In the remaining 25%, HBeAg seroconversion gives rise to HBeAg(−) chronic hepatitis, either directly, mostly as a result of mutations that occur in the precore and/or core promoter region, or secondary to reactivation from the IC state, in which there are periods of reactivation with a pattern of fluctuating HBV DNA (HBV-DNA) and aminotransferase levels, and active hepatitis.[3]

The HBeAg(−) chronic infection phase was first described in Mediterranean countries,[4] but has now been reported worldwide.[5] Studies from Europe, Asia and the United States describe an increase in the prevalence of these types of patients,[6] mainly due to ageing of the infected population, and it is the most common form of chronic hepatitis B not only in Europe, but worldwide,[7] currently affecting 85–90% of patients. In our published series of patients with chronic HBV infection,[8] those with HBeAg(−) chronic infection represented the largest group (87.61%), similar to other studies recently published in Spain,[9,10] other Mediterranean countries,[11] and more remote regions, such as Asia[12] and South America.[13] Since HBeAg(−) patients are the largest HBV infection group, we set out to study the characteristics and clinical course of this patient group in our healthcare area.

Materials and methods

Observational, retrospective cohort study of patients diagnosed with HBeAg(−) chronic HBV infection at the time of