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ORIGINAL ARTICLE

Hepatitis B virus e antigen-negative chronic infection. Treatment based on glutamic pyruvic transaminase and hepatitis B virus deoxyribonucleic acid cut-off values[☆]

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Abstract

Objectives: To identify glutamic pyruvic transaminase (GPT) and hepatitis B virus DNA (HBV-DNA) cut-off values at diagnosis in patients with hepatitis B virus e antigen-negative chronic infection (HBeAg(−)), which may be predictors of clinical course, prognosis and/or the need for antiviral therapy.

Methods: A retrospective and observational cohort study of patients diagnosed with HBeAg(−) chronic infection (2005–2012). A normal GPT cut-off value at diagnosis that predicts abnormal GPT values in the clinical course of the infection, a baseline HBV-DNA cut-off value that predicts an increase in HBV-DNA above 2000 IU/ml, and GPT and HBV-DNA as predictors of the need for treatment were investigated using ROC curves.

Results: 126 patients were enrolled (follow-up: 42.1 ± 21.5 months), 93 of which had normal GPT levels at diagnosis. In the ROC curve analysis, 900 IU/ml was found to be the HBV-DNA cut-off value that best predicted this value's increase above 2000 IU/ml (sensitivity: 90%; specificity: 88%; PPV: 79%; NPV: 100%; diagnostic precision: 89%), while 25 mU/ml was the normal GPT cut-off value at diagnosis that best predicted subsequently elevated GPT levels (sensitivity: 95.4%; specificity: 81.6%; PPV: 67%; NPV: 96%; diagnostic precision: 80.6%). Patients with GPT

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26–40 mU/ml at diagnosis presented with more complications or required more treatment than subjects with GPT ≤ 25 mU/ml ($p < 0.05$). The combined GPT and HBV-DNA values that elicited the highest treatment need were 38 mU/ml of GPT and 6000 IU/ml of HBV-DNA (sensitivity: 75%; specificity: 93.4%; PPV: 60%; NPV: 96.6%).

Conclusion: HBeAg(−) patients with GPT < 25 mU/ml and HBV-DNA < 900 IU/ml at diagnosis have positive outcomes and may not require such stringent follow-up in the first years after diagnosis.

PALABRAS CLAVE
Virus de la hepatitis B;
Glutámico-pirúvica transaminasa (GPT);
Ácido desoxirribonucleico;
Antígeno e de la hepatitis B;
Hepatitis B crónica

Infección crónica por virus de la hepatitis B antígeno e negativo. Manejo en función de puntos de corte de glutámico-pirúvica transaminasa y ácido desoxirribonucleico del virus de la hepatitis B

Resumen

Objetivos: Buscar puntos de corte de la glutámico-pirúvica transaminasa (GPT) y de ADN del virus de hepatitis B (ADN-VHB) al diagnóstico, en pacientes con infección crónica VHB antígeno e negativo (AgHBe(–)), que puedan ser predictores de la evolución, pronóstico y/o de la necesidad de terapia antiviral.

Métodos: Estudio observacional de cohortes retrospectivo de pacientes diagnosticados de infección crónica por VHB AgHBe(–) (2005-2012). Se investigó un punto de corte de GPT normal al diagnóstico que predijera la alteración de esta en la evolución, de ADN-VHB basal que predijera la elevación de este por encima de 2.000 UI/ml, y de GPT y ADN-VHB como predictores de la necesidad de tratamiento, mediante curvas ROC.

Resultados: Se incluyeron 126 pacientes (seguimiento: 42,1 ± 21,5 meses), de los cuales 93 tenían GPT normal al diagnóstico. En el análisis de curvas ROC el punto de corte de ADN-VHB que mejor predijo la elevación de este por encima de 2.000 UI/ml fue 900 UI/ml (sensibilidad: 90%; especificidad: 88%; VPP: 79%; VPN: 100%; precisión diagnóstica: 89%), y el que mejor predijo la alteración de GPT normal al diagnóstico posteriormente elevada fue 25 mU/ml (sensibilidad: 95,4%; especificidad: 81,6%; VPP: 67%; VPN: 96%; precisión diagnóstica: 80,6%). Los pacientes con GPT 26-40 mU/ml al diagnóstico presentaron más complicaciones o necesidad de tratamiento que aquellos con GPT ≤ 25 mU/ml (p < 0,05). La combinación de GPT y ADN-VHB que maximizó la necesidad de tratamiento fue 38 mU/ml de GPT y 6.000 UI/ml de ADN-VHB (sensibilidad: 75%; especificidad: 93,4%; VVP: 60%; VPN: 96,6%).

Conclusión: Los pacientes VHB AgHBe(–) con GPT < 25 mU/ml y ADN-VHB < 9.000 UI/ml al diagnóstico presentan buena evolución y podrían no requerir un seguimiento tan estrecho en los primeros años desde el diagnóstico.

Introduction

Chronic hepatitis B virus (HBV) infection is a public health problem worldwide. It is estimated that 350–400 million people in the world have chronic HBV infection[1] and that some 620,000 people die each year in connection with this infection.[2,3]

Chronic HBeAg(−) infection occurs after hepatitis B e antigen (HBeAg) seroconversion, with loss of HBeAg and the development of anti-HBeAg antibodies during the immune-reactive phase, representing one of the final stages of the natural history of the infection. In 75% of cases, individuals change from the immune-reactive HBeAg(+) state to the inactive HBV carrier (IC) state, characterised by persistently normal glutamic-pyruvic transaminase (GPT) levels, low deoxyribonucleic acid (DNA) levels and little or no histological involvement. In the remaining 25%, HBeAg seroconversion leads to chronic hepatitis due to HBeAg(−) HBV (HBc), or directly, largely due to mutations in the nucleotides of the precore and/or core promoter region; or, secondarily, to reactivation from IC, characterised by reactivation with fluctuating levels of HBV DNA (HBV-DNA), aminotransferases and active hepatitis.[4]

The chronic HBeAg(−) infection stage was first reported in Mediterranean countries,[5,6] but is currently reported worldwide.[7] Recent studies in Europe, Asia and the United States describe an increasing prevalence of these types of patients,[8–11] currently accounting for 85–90% of patients. In our recently published series,[12] such patients account for 87.61% of all patients, similar to other studies recently published in Spain[13,14] and in other areas of the world.[15–24]

At present, any patient recently diagnosed with chronic HBV HBeAg(−) infection needs close monitoring for the first few months after diagnosis to determine the stage