Eur. J. Clin. Chem. Clin. Biochem.
Vol. 31, 1993, pp. 407–411

Increase of Serum α_1-Acid Glycoprotein Despite the Decline of Liver Synthetic Function in Cirrhotics with Hepatocellular Carcinoma

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(Received January 1/April 15, 1993)

Summary: α_1-Acid glycoprotein, an acute phase reactant synthesised by the liver, has been reported to be increased in neoplastic conditions and reduced in chronic liver disease. We measured serum α_1-acid glycoprotein by a nephelometric method in 186 subjects (112 males, 74 females): 55 had mild chronic liver disease (chronic hepatitis and steatofibrosis), 45 cirrhosis, 38 hepatocellular carcinoma, 15 extra-hepatic malignant disease; 33 healthy subjects were used as controls. Analysis of variance demonstrated a significant variability among groups ($F = 17.08$, $P = 0.0000$). Higher concentrations of α_1-acid glycoprotein were detected in malignant extra-hepatic disease than in all other groups ($P < 0.01$); concentrations of α_1-acid glycoprotein were higher in hepatocellular carcinoma than in cirrhosis ($P < 0.01$). Multiple regression analysis by groups (dependent variable = α_1-acid glycoprotein; group 1 = mild chronic liver disease + cirrhosis; group 2 = hepatocellular carcinoma) showed a significant correlation for both group 1 ($r = 0.6264$, $F = 8.005$, $P = 0.0000$) and group 2 ($r = 0.8947$, $F = 13.643$, $P = 0.0000$). The significant standardised regression coefficients were: cholinesterase, C-reactive protein, γ-glutamyltransferase and iron (negative) for regression upon group 1; C-reactive protein, α_1-antiproteinase, γ-glutamyltransferase, iron (negative) for regression upon group 2. A difference between the 2 regression equation coefficients was detected ($F = 5.209$, $P = 0.0002$). In conclusion, a raised α_1-acid glycoprotein concentration was found in patients with malignancies, both hepatic and extra-hepatic; however, patients with hepatocellular carcinoma had a lower α_1-acid glycoprotein concentration than patients with malignant extra-hepatic disease. In hepatocellular carcinoma, a good correlation existed between α_1-acid glycoprotein and other serum indices of the acute phase response. In some patients with hepatocellular carcinoma, α_1-acid glycoprotein was increased, despite the decrease of liver function.

Introduction

α_1-Acid glycoprotein is a circulating glycoprotein synthesized mainly in the liver. It has a relative molecular mass of about 41000 and is characterized by the presence of five glycosylation sites (1, 2). α_1-Acid glycoprotein has long been recognized as an acute phase reactant (3). Thus, its concentration increases 2–10 fold in serum, under conditions that promote the increase of other acute phase proteins such as α_1-antiproteinase and C-reactive protein; moreover, its synthesis in human adult hepatocytes is augmented by interleukin-1 and interleukin-6, cytokines that are considered the main mediators of the acute phase response (4).

Previous studies have shown that the α_1-acid glycoprotein concentration rises in serum during the course of several neoplastic diseases (5–7), including hepatocellular carcinoma in Asian patients (8).

However, hepatocellular carcinoma has a striking geographical variation and in industrialised countries, where its incidence is relatively low, hepatocellular