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EFFECT OF IRON DEPLETION ON INSULIN RESISTANCE IN PATIENTS WITH CHRONIC HEPATITIS C AND HYPERFERRITINEMIA

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Background and Aims: Hyperferritinemia, a surrogate marker of iron overload, is a frequent finding in hepatitis C that has been related with liver inflammation and insulin resistance (IR). In fatty liver disease, it has been observed a decrease in transaminases level as well as an improvement in IR after iron depletion with phlebotomies. This effect, however, has not been specifically studied in hepatitis C. Our main objective was to investigate the effect of iron depletion by phlebotomies on IR in patients with chronic hepatitis C and hyperferritinemia.
Methods: Patients with chronic hepatitis C and hyperferritinemia (serum ferritin >300 ng/ml in men and >200 ng/ml in women) were considered for inclusion. Those patients with cirrhosis, co-infection with human immunodeficiency virus or with other liver diseases were excluded. Therapeutic phlebotomies were performed every two weeks until achieving a ferritin level lower than 30 ng/ml without concomitant anemia (Hb > 11 g/dl). IR was evaluated, before and after iron depletion, calculating the HOMA2 index.
Results: 30 patients, 28 (93%) men, mean age of 49±1.5 years, were included. 16 (53%) of them were previously non responders to antiviral treatment and 23 (77%) were infected by genotype 1. Only three patients (10%) were heterozygotes for the C282Y mutation of HFE gene. Basal HOMA was higher than two in 15 (50%). Iron depletion was achieved (mean of 5.3±0.3 phlebotomies; estimated extracted iron of 1.325±67g) in all cases, without any adverse event. Iron depletion was associated with a decrease in transaminases level in 26 (90%) patients, achieving normalization in 6 (20%), and being the decrease of mean ALT statistically significant (124±15 vs. 79±8 UI/L, P < 0.001). By contrast, no significant differences in viral load level (6.1±0.1 vs. 5.9±0.1 log UI/ml) and in HOMA index (2.7±0.3 vs. 2.6±0.4) were observed before and after iron depletion.
Conclusions: Iron depletion is associated with a significant decrease on transaminases in the majority of patients with chronic hepatitis C and hyperperritinemia. However, in contrast with previously described in fatty liver disease, a relevant effect of iron depletion on IR evaluated by HOMA index has not been observed.

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CIRCULATING FIBROCYTES AS A POTENTIAL NON INVASIVE MARKER OF LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C VIRUS INFECTION

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Background and Aims: Chronic hepatitis C virus (HCV) infection often leads to fibrosis and cirrhosis. Liver biopsy is currently the gold standard technique to quantitate liver fibrosis but it is an invasive procedure with even life-threatening complications. Direct and indirect markers of liver fibrosis have been studied although no accepted method is currently available to monitor disease progression.
Peripheral blood fibrocytes are bone marrow-derived cells capable of producing extracellular matrix molecules, therefore considered to be potentially involved in fibrotic processes. The aim of the present study was to investigate whether the level of circulating fibrocytes is increased in patients with chronic hepatitis C as compared with healthy controls and whether it correlates with the histological stage of fibrosis.
Methods: Between January 2006 and January 2007 we enrolled 70 patients affected with chronic HCV infection, without other known causes of liver disease, not on interferon or ribavirin. All patients underwent liver biopsy (Metavir score F0 to F4) and Fibroscan (liver stiffness measured in kilopascal units) for fibrosis measurement. Peripheral blood fibrocytes were measured on all patients by flow cytometry as positive for CD34, CD45 and collagen-I expression.
Results: Patients with chronic hepatitis C had significantly higher levels of circulating fibrocytes as compared with healthy individuals (31.3% versus 17.59%, p = 0.04). Patients in the F0–F1 group had a percentage of circulating fibrocytes of 23.3±4 %, whereas the mean rate of circulating fibrocytes in the F2 and F3 group was 38.4±4 % and 44.8±2% respectively (p < 0.001 versus F0–F1). Patients in the F4 group had a mean rate of circulating fibrocytes of 50.6±2% (p < 0.001 versus the F0, F1, F2 stages). The percentage of circulating fibrocytes correlated positively with both the Metavir score and the liver stiffness. No correlation was found with serum ALT and HCV RNA levels.
Conclusions: Peripheral blood fibrocytes are increased in patients with HCV infection and correlated with HCV-related liver fibrosis. Fibrocytes not only could be involved in the pathogenetic mechanisms of liver fibrosis but they also may act as a surrogate marker of liver fibrosis. Further studies are needed to thoroughly investigate their role in chronic HCV infection.

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EVALUATION OF ANTIBODIES TO MULTIPLE CORE PEPTIDES IN PATIENTS WITH OCCULT HCV INFECTION

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Background: HCV RNA may be detected in the liver either of patients with persistently abnormal liver function tests of unknown etiology whose serum anti-HCV and HCV RNA are repeatedly negative by commercial assays (primary occult HCV infection) and among anti-HCV-positive patients who apparently have resolved HCV infection (secondary occult HCV infection). Antibodies to HCV core5–19 peptide epitope can be detected in 40% patients with primary occult HCV infection (J Hepatol 2009;50:256–63).
Aim: To evaluate the detection of antibodies to multiple HCV core-derived peptides in sera from occult HCV-infected patients.
Patients and Methods: Antibodies to three non-overlapping HCV core-derived peptides were investigated by ELISA (patent ES/P200800493 & PCT/ES2009/000019) in sera from:
1. 126 anti-HCV/HCV RNA-negative patients with altered transaminase values and a biopsy-proven occult HCV infection (HCV RNA-positive);
2. 75 anti-HCV-positive patients including 11 asymptomatic carriers (serum anti-HCV-positive/HCV RNA-negative but liver HCV RNA-positive) and 64 chronic hepatitis C patients (serum anti-HCV/HCV RNA-positive).

Results: Among 126 patients with primary occult HCV infection, 52 (41%) tested positive against core5–19; 19 patients reacted to core21–40 (15%) whereas 31 resulted antibody-positive to core101–120 (25%). Thus, combining antibody reactivity to the three peptides, a total of 67/126 (53%) patients with primary occult HCV infection reacted in the anti-core assays, including 15 non-reactive patients to core5–19 epitope.
Anti-core antibodies were detected in all anti-HCV-positive patients: 11 (100%) with secondary occult HCV infection and 64 (100%) patients with chronic hepatitis C.