Introduction and Objectives: Chronic infection with hepatitis C virus (HCV) still affects millions of people around the world despite the recent development of very effective direct-acting antiviral (DAA) treatment. Even after a high cure rate, patients with advanced fibrosis should remain under surveillance due to the high risk of developing hepatocellular carcinoma. This study aimed to evaluate the prevalence and risk factors for hepatocellular carcinoma development in previously treated chronic HCV patients in an outpatient hepatology clinic at Clinic Hospital of the University of São Paulo of School Medicine in the city of São Paulo.

Materials and Methods: This is a retrospective, observational and descriptive study of a series of cases in which 410 HCV patients were treated with three different antiviral regiments: Interferon plus Ribavirin (INF + RBV) or Protease Inhibitors (PI) or DAA, were followed for up to ten years (2011-2021). Demographic, clinical and laboratory data were obtained for electronic medical records.

Results: the total sample of this study consists of 402 patients. Table 1 shows the patient demographic and clinical data. Of the 35 patients who developed HCC, 26 (74%) had F4-degree fibrosis. Logistic regression model was performed with the following variables: BMI (p=0.005), positive anti-HBC IgG (p=0.015), combination fibrosis and CHIILD-PUGH score A (p=0.001), B (p=0.012) and C(p< 0.001).

Conclusions: In our cohort, obesity and anti-HBc IgG were significantly associated with a high risk of developing HCC. The type of antiviral treatment (IFN or DAA-based) was not associated with the risk of HCC.

https://doi.org/10.1016/j.aohep.2023.100944

P- 43 PIRFENIDONE PREVENTS NEOPLASTIC LESIONS DEVELOPMENT BY OXIDATIVE, FIBROGENIC, ANTIPROLIFERATIVE AND EPIGENETIC MECHANISMS REGULATION IN A MODEL OF CHEMICAL HEPATOCARCINOGENESIS

Hipólito Otoniel Miranda-Roblero[1], Hugo Christian Monroy-Ramírez[1], Marina Galicia-Moreno[1], Ana Sandoval-Rodriguez[1], Arturo Santos[2], Juan Armendáriz-Borunda[1,2]

[1] *Institute of Molecular Biology in Medicine and Gene Therapy, University Center of Health Sciences (CUCS), University of Guadalajara, Guadalajara, Mexico*
[2] *School of Medicine and Health Sciences, Technological of Monterrey Campus Guadalajara, Zapopan, Mexico*

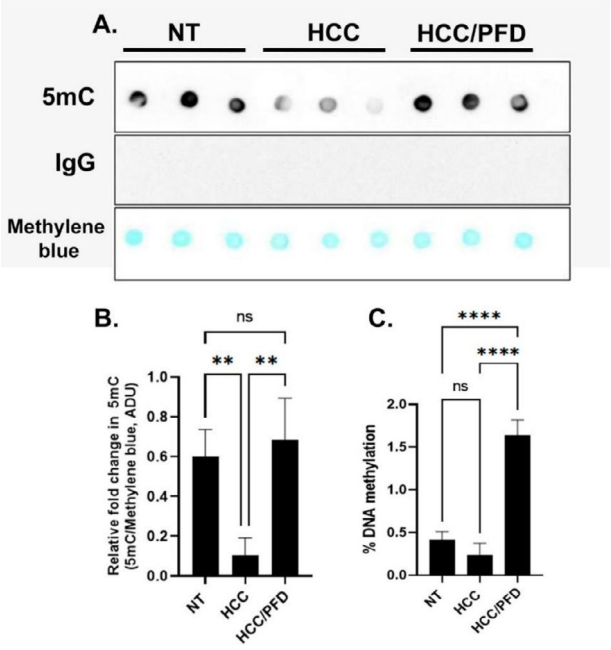
Introduction and Objectives: Hepatocellular carcinoma (HCC) is the most frequent hepatic neoplasia, where oxidative, fibrogenic, proliferative, and epigenetic processes are altered. Pirfenidone (PFD) has been shown to have important hepatoprotective properties. However, its efficacy in HCC development is unknown. This study aimed to 1) To determine whether PFD has antioxidative, antifibrogenic and antiproliferative effects. 2) To determine PFD effects on epigenetic regulation mechanisms.

Materials and Methods: Male Fischer-344 rats were divided into three groups. Group 1. Control, NT; Group 2. Damage, HCC, generated by diethylnitrosamine weekly administration; (50mg/kg, i.p.) and 2-acetylaminofluorene (25mg/kg, p.o.) for 12 weeks; and Group 3. HCC/PFD: with the same treatment as Group 2, plus PFD (300 mg/kg, p.o./day). Liver enzyme activity was quantified in serum; lipoperoxidation and GSH levels were evaluated in liver tissue samples; histopathological analyzes were performed. In addition, fibrogenic, antioxidant, anti-proliferative and epigenetic regulation markers were determined by Western blot. Finally, global DNA methylation was determined by Dot-blot and ELISA. The data obtained were analyzed using one-way ANOVA and a Tukey post hoc test.

Results: We demonstrate that PFD treatment reduces the number and size of neoplastic lesions, prevents damage to hepatic architecture and collagen deposition, and decreases the presence of the histopathological marker Glypican-3. On the other hand, it positively regulates antioxidant markers such as GSH, MDA, Nrf2, GSTP1 and Catalase. It was also effective to decrease c-Myc expression and β-catenin redistribution from the nucleus to the cytoplasm. Finally, PFD stimulated the nuclear transfer of several isoforms of PPARs, SIRT1 and DNMT1, increasing epigenetic mechanisms of global DNA methylation (figure 1).

Conclusions: PFD prevents neoplastic lesions development by modulating antifibrogenic, antioxidant, and antiproliferative processes and modulating epigenetic marks to reverse global DNA hypomethylation.

Figure 1. Analysis of global DNA methylation. A) Representative dot blot using anti-5mC which recognizes global methylated DNA, anti-IgG as negative control and methylene blue staining as total DNA loading control. B) Graphs shows mean ± standard deviation of 5mC densitometry brand intensity of study groups. C) Graph that represents the percentage of global methylation of the DNA analyzed with ELISA.A one-way ANOVA statistical test and a Tukey post hoc test were performed. Group NT: only received vehicle; Group HCC: damage group induced by weekly administration of DEN and 2-AAF for 12 weeks; and Group HCC/PFD: which received the same treatment as Group HCC, plus PFD (300 mg/kg) (**p<0.005)



https://doi.org/10.1016/j.aohep.2023.100945

P- 44 HEPATOCELLULAR CARCINOMA IN CIRRHOTIC PATIENTS IN A PARAGUAYAN LIVER REFERENCE CENTER: CLINICAL AND EPIDEMIOLOGICAL CHARACTERISTICS

Lorena Martínez[1], Amaya Ortiz[1], Rodrigo Pérez[1], Mirian Colarte[1], Sebastián Díaz[1], Martin Sánchez[2], Johana Silvero[2], Maisa Vallejos[3], Marcos Girala[1], Jesus Ortiz[1]

[1] *Department of Gastroenterology and Digestive Endoscopy, Clinics Hospital, National University of Asunción, San Lorenzo, Paraguay*