

O-22 DIFFERENTIAL MUTATION PATTERN ASSOCIATED WITH HEPATITIS B E ANTIGEN SEROCONVERSION BETWEEN SUBGENOTYPE F1b CLUSTERS: POTENTIAL ROLE IN PATHOGENESIS

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Introduction and Objectives: Two clusters of the subgenotype F1b (basal and cosmopolitan) have recently been described. The basal cluster has been associated with the early occurrence of hepatocellular carcinoma in chronically infected patients from Alaska and Peru. In Argentina, where the cosmopolitan cluster is the most prevalent, this relationship has not been observed. In the course of chronic hepatitis B infection, mutations occur in different regions. In particular, mutations in the basal core promoter (BCP) and the preC/C regions are associated with HBeAg seroconversion, an event related to the severity of chronic HBV infection. This study aimed to determine the HBeAg status and to characterize the molecular mutation patterns associated with HBeAg seroconversion in both subgenotype F1b clusters.

Materials and Methods: Serum samples from 68 patients with subgenotype F1b chronic hepatitis B infection were analyzed. The BCP and pC/C regions were amplified and sequenced.

Results: Twenty-one samples belonged to the basal cluster and 47 to the cosmopolitan cluster. No differences in age or gender were observed between the cases of both clusters. The basal cluster samples showed a lower frequency of positivity for HBeAg (38.1 vs. 57.4 %). In HBeAg negative samples, the basal cluster showed significantly higher rates of A1762T/G1764A (92.3 vs. 50.0, p:0.013) and G1896A (92.3 vs. 20.0, <0.001) mutations in relation to the cosmopolitan cluster.

Conclusions: The disparity observed in HBeAg positivity frequency suggests that the basal cluster would be associated with earlier HBeAg seroconversion than the cosmopolitan cluster. The frequency of mutations associated with a worse clinical outcome was significantly higher in the basal cluster samples.

Overall, this study provides new insights into the role of viral variants in the pathogenesis of chronic HBV infection and contributes to identifying molecular determinants associated with the pathogenesis of chronic HBV infection.

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O-23 HEPATITIS B VIRUS STATUS OF ORGAN DONORS IN ARGENTINA

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Introduction and Objectives: Argentina is considered an area with a low prevalence of hepatitis B virus (HBV). However, the real

prevalence of the disease is unknown. We aimed to study the prevalence of HBV in potential cadaveric donors.

Materials and Methods: We performed a cross-sectional study to analyze data from the National Procurement of Transplantation in Argentina from all donors from 2006 to 2020. HBV serologic tests included hepatitis B virus antigen (HBsAg), core antigen-antibody (HBcIgG) and anti-HBs performed during the procurement process. HBV status was defined as 1) active HBV: donors with positive HBsAg; 2) Past HBV infection or false positive: isolated positive HBcIgG; 3) Cured infection anti-HBs+/HBcIgG+.

Results: Overall, 16140 deceased donors were denounced. The prevalence of HBsAg was 0.37% (n=60) and of isolated HBcIgG+ was 3.6% (n=575). Among organ donors only, 328 (3.8%) presented isolated HBcIgG-positive serology. Of these, 252 (77%) were effective organ donors. Solid-organ transplants performed using isolated HBcIgG+ donors were 220 kidneys, 124 livers, and 27 intrathoracic organs. There was no significant 5-year graft and patient survival difference between HBcIgG+ receptor (kidney transplant 65% and 81%, and for liver 65% and 83% respectively) and the general population. Anti-HBs data were available in only 4455 donors, of which 19% (N=847) were anti-HBs+. In those patients with positive anti-HBs, HBcIgG was positive in 8.3% (n=369), reflecting past HBV infection. Of the remaining 4086 AntiS available, only 11.7% were positive; that is, they were effectively vaccinated. The Patagonia region presented the highest prevalence of HBsAg, especially in the provinces of La Pampa (2.3%), Santa Cruz (2.2%), and Tierra del Fuego (2.1%).

Conclusions: The prevalence of HBsAg in deceased donors in Argentina is low. Since the probability of being a donor is random, the prevalence in this population could be close to the real one in the country.

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O-24 PIRFENIDONE PREVENTS NEOPLASTIC LESIONS DEVELOPMENT BY OXIDATIVE, FIBROGENIC, ANTIPROLIFERATIVE AND EPIGENETIC MECHANISMS REGULATION IN A MODEL OF CHEMICAL HEPATOCARCINOGENESIS

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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) determine whether PFD has antioxidative, antifibrogenic and antiproliferative effects and 2) determine PFD effects on epigenetic regulation mechanisms.

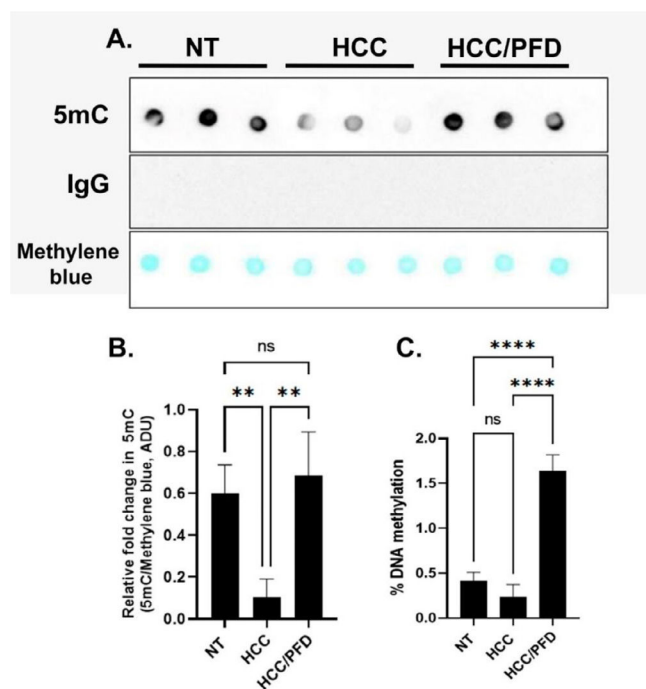
Materials and Methods: Male Fischer-344 rats were divided into three groups. Group 1. Control, NT; Group 2. Damage, HCC, generated by diethylnitrosamine weekly administration; (50mg/kg, i.p.) and 2-acetylaminofluorene (25mg/kg, p.o.) for 12 weeks; and Group 3. HCC/PFD: with the same treatment as Group 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 \pm 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)



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O-25 ASSESSMENT OF MODELS FOR PREDICTING RESPONSE TO CORTICOSTEROIDS TREATMENT IN ALCOHOL-ASSOCIATED HEPATITIS: A GLOBAL COHORT STUDY

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