cadherin and Occludin was observed; conversely, mesenchymal-type features such as N-cadherin and Snail decreased with GDF11 treatment, confirming that this growth factor-induced a mesenchymal to epithelial transition. Furthermore, our group reported the effect of GDF11 in reducing lipid content, especially cholesterol and triglycerides. It was also confirmed that GDF11 reduced mevalonate pathway proteins in Huh7 and Hep3B liver cancer cell lines. Additionally, they reported that GDF11 was able to impair mitochondrial functionality and its structure. Moreover, GDF11 treatment induced an alteration of glycolytic capacity and oxygen consumption rate in these models.

Objectives General: To determine the sensitizing effect of GDF11 in the Hep3B cell line. Specific: To determine the capacity of GDF11 in the reduction of the EC50 of cisplatin.

Methods: We used the HCC cell line Hep3B (ATCC). A 72-h pretreatment with GDF11 or without was performed; then we treated the cells with cisplatin at various concentrations (0, 2.5, 5, 10, 15, 15, 25, 50, and 100 μM), incubated for 48 h, and cell viability assay was performed by crystal violet.

Results: In our experiments, GDF11 has shown an increased sensitivity of Hep3B cells to cisplatin treatment by significantly reducing the mean effective dose (EC50) from 22.26 μM to 8.11 μM this result was observed by crystal violet assay and by light microscopy.

Discussion: Results demonstrate that GDF11 has sensitizing effects against cisplatin treatment on the liver tumor cell line Hep3B. This agrees with previous results of our group where a detrimental impact in liver tumor cells is observed by the GDF11 treatment and contrast with other works where TGF-β family members have chemoresistance effects.

Conclusions: GDF11 pretreatment sensitizes the HCC cell line Hep3B by reducing the cisplatin EC50.

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The authors declare that there is no conflict of interest.

https://doi.org/10.1016/j.aohep.2021.100634

HGF AND PROTECTIVE ROLL IN THE INTESTINAL COLLATERAL DAMAGE BY A-NAFTILISOTIOCIANATO- INDUCE CHOLESTASIS.

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Introduction and Objectives: he prevalence of cholestasis has been increasing in recent years; The excretion of bile acids via basolateral has been demonstrated to prevent the excessive accumulation in the hepatocyte, and the liver-intestine axis has been seen affected by enterohepatic circulation deregulation. The epithelial permeability loss caused by the tight junction ruptures leads to inflammation and reactive oxygen species (ROS) production. The hepatocyte growth factor is an essential cellular redox regulator and repair growth factor; it has been reported in its relevance in the intestinal mucosa regeneration and proliferative proprieties. This study aims to evaluate the protective effect of HGF in the intestine of animals subjected to cholestatic damage induced by ANIT. Material and methods: Twenty 10-12 weeks-old male CD-1 mice were used. ANIT (60mg/kg) was administrated at the beginning, 24 h later HGF (10 μg/kg) was injected, and 48 h later, the animals were subjected to euthanasia under anesthesia, and serum and intestines were collected. According to the National Institutes of Health of United Stated (NIH) guide, All mice have been cared for and the Norma Oficial Mexicana (NOM), NOM-062-ZOO-1999. The intestinal tissue was fixed and embedded in paraffin for the histological assessment, followed by routine H&E staining. The expression analysis of TNF- alpha, IL-1b and IL.6 were performed by RT-qPCR using a CFX96 Touch thermocycler with 5μg 2x SYBER Green, which included 1000ng of cDNA and 2μl of forward and reverse primers. The protein quantification was evaluated by Western Blot analysis; using 12% polyacrylamide gels, and the primary antibodies for anti-SOD-1, anti-GPx4, anti-Catalase were incubated. Data are presented as the average $\pm$ standard error media (SEM) using GrandPad (Prism 8) software. Variance analysis (ANOVA) was used for the statistical analysis and was considered $p<0.005$ to indicate a statistical significance.

Results and Discussion: Macroscopic changes reveal no apparent effect. Microscopic studies carried out by H&E staining showed a reduction of the intestinal lumen diameter in mice under ANIT treatment compared with Not treated control (NT). Interestingly, ANIT + HGF-treated group showed protective effects preserving lumen and tissue architecture. To corroborate the potential repair effect of HGF treatment to maintain the tissue and thus digestive process, the excreted stool for every group was addressed. The stools excretion level of ANIT- treated mice was significantly reduced compared with the control and co-treated mice. These results indicate that ANIT-cholestasis induce damage in the small intestine. However, results also found a vulnerability in the colon and ileum to cholestasis damage. To determine whether these sections received damage in ANIT- acute cholestasis model, by RT q-PCR, we examined the mRNA expression of inflammatory cytokines, which were increased in ANIT- treatment. By comparison, HGF co-treatment decreases inflammation like the control group. To check if this regulation of inflammation was for the HGF-induced redox regulation we evaluated, the protein expression of SOD-1, GPx4, and catalase. The treatment with HGF increased the expression of antioxidant enzymes of the intestine tissue. These results suggest that the damage in the intestine is supported by the regulation of ROS induced by cholestasis disease.

Conclusion: The current study demonstrated how HGF exerts a protective effect in the intestine triggered by ANIT. This effect seems to be the cellular redox regulation seen in the liver and renal tissue.

CONACYT: CB-A1-S-38154.

The authors declare that there is no conflict of interest.

https://doi.org/10.1016/j.aohep.2021.100635

IGFBP-1 TO 7 AS BIOMARKERS IN STAGES OF LIVER FIBROSIS DURING VIRAL HEPATITIS C

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Introduction and Objectives: Diagnosis of liver disease (LD) is essential for the treatment and management of patients. The use of non-invasive methodologies is necessary despite the availability of direct-acting antivirals, some reports has been showed that treated patients can progress to cellular hepatocarcinoma (HCC). Continuous sampling that will evaluate liver tissue before and after treatment are essential for the prognosis of LD. Objective: To determine the sensitivity and specificity of insulin-like growth factor binding proteins (IGFBP) in the different stages of fibrosis in hepatitis C

Material and methods: A prospective, cross-sectional, observational study. The study included patients with CHC that were treatment naïve. The stages of fibrosis were classified as F0, 16 F1, F2, F3, or F4, according to international guidelines, through the FibroTest® and/or FibroScan® Patients with at-risk alcohol consumption (AUDIT>8), and without concordance between fibrosis diagnostic methods employed, and comorbidities were not included. Serum was obtained and multiple suspension array technology (Millipore®) was used to evaluated IGFBP-1,2, 3, 4, 5, 6, 7. Chi-square test, Mann-Whitney U test. Logistic regression models, odds ratios (ORs) and 5% confidence intervals were determined.

Results: A total of 128 patients diagnosed with CHC and 123 CT were included. Fibrosis stages were classified as follows: F0 (n=18), F1 (n=16), F2 (n=20), F3 (n=25), and F4 (n=48). IGFBP-1 to -7 showed an evident increment in patients mainly at F3 and F4. IGFBP-7 allows discriminate F3 vs F4 (72% sensibility, 62.5% specificity and cut of value of 2.74), whereas IGFBP-4 discriminates F3 vs F4 (83% sensibility, 68% specificity and cut of value of 14.68). P<0.001 was consider in statistical analysis.

Discussion: Although HCV treatment is available the progression from cirrhosis to HCC has been reported after clearance of HCV. Post-treatment studies evaluating the different stages of fibrosis should be performed. Therefore, the use of IGFBPs could be a tool in the continuous sampling previous and after treatment.

Conclusion: IGFBPs can be used as additional strategy for the diagnosis and discrimination of fibrosis stages in HCV.

Conflict of interest: The authors declare that there is no conflict of interest.

This work was partially financed by CONACyT SALUD-2016-272579 (GRG) and PAPIIT- UNAM TA200515 (GRG).

https://doi.org/10.1016/j.aohep.2021.100636

LYMPHOCYTE PROFILE ON PATIENTS WITH CHRONIC AND ACUTE ALCOHOL CONSUMPTION

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Introduction and Objectives: Several mechanisms participate in the physiopathology of chronic alcohol consumption and Alcoholic Liver Disease (ALD), such as deregulation in the immune system.

Aim: To analyze the lymphocyte subpopulations from patients with chronic and acute alcohol consumption.

Material and methods: A Cross-sectional study that included: G1: Controls with alcohol consumption <10g/day (CT); G2: Alcoholism, without clinical or biochemical stigma of liver damage (OH); G3: Patients with cirrhosis by alcohol (CiOH) and G4: Patients with Alcoholic Hepatitis (AH). Determination of T-CD3, T-CD4, T-CD8, NK and NKT lymphocytes from peripheral blood was performed by flow cytometry. Statistical analysis was performed by U-Mann Whitney test, p<0.05 was considered significant.

Results: 570 participants were included, the mean of age was: 29.5±10.8, 31±12.6, 47.6± 7.7 y 41.2±9.2 years for CT, OH, CiOH and AH respectively (p<0.001). Alcohol consumption was higher in CiOH 240(320,120) and AH 320(480,160) (p<0.001, p<0.05). Liver function test showed alterations in patients with CiOH and AH, AST 49.5 (75.3,38) for CiOH and 155 (177,121) for AH (p<0.001, p<0.001); ALT 32.5 (47.3,24) in CiOH and 49 (75,35.3) in AH (p<0.001, p<0.001), whereas GGT was 91.5 (191.8, 48) for CiOH, and 224 (525.5, 104) for AH (p<0.001, p<0.001). Cell percentages are described in Table 1.

Data expressed as the median and quartiles (Q3-Q1). a) Alcoholism vs. Control; b) Cirrhosis vs. Control; c) Alcoholic Hepatitis vs. Control; d) Alcoholism vs. Cirrhosis; e) Alcoholism vs. Alcoholic Hepatitis; f) Cirrhosis vs. Alcoholic Hepatitis.

Discussion: Changes in the proportion of innate cells affect their ability to repair tissues, which can be exacerbated when damage is perpetuated and chronic inflammation is established. To compare CiOH vs. CT groups we found the suppression of adaptive response and increase in innate population. Furthermore, when CiOH was compared vs. OH increased CD4+ cells and decreased the cytotoxic population, which could be explained due to factors such as active alcohol consumption or advanced cirrhosis. In AH, the innate responses are suppressed compared to other groups. When we compare acute damage (AH) vs. alcoholism (OH) cytotoxic populations decrease, while CD4+ cells increase. However, during acute damage (AH) vs chronic damage (CiOH) increase T and CD8+ cells.

Conclusions: The immunological abnormalities that occur during alcoholism, cirrhosis and alcoholic hepatitis are different, the most significant changes were observed in CD4+, CD8+, NK and NKT cells promoting an imbalance that could be related to progression of liver damage.

The authors declare that there is no conflict of interest.

This work was partially financed by CONACyT SALUD-2016-272579 y PAPIIT-UNAM TA200515.

Table 1
Lymphocytic profile in patients with different types of liver damage

	Control (n=300)	Alcoholism (n=102)	Cirrhosis (n=121)	Alcoholic Hepatitis (n=47)
T-Cells (CD3+) %	66.5 (71.7, 61.1)	62.3 (67.6, 56.2) a+	57.1 (66.5, 51.6) b*,d€	66.4 (78.3, 60) f€
Helper Cells CD4+ (%)	39.6 (45.4, 34.7)	35.1 (42.1, 30) a+	42 (47.7, 32.6) d+	47.4 (51.5, 34.7) e€
Cytotoxic Cells CD8+ (%)	21.2 (27, 17)	24.7 (30.8, 16.6)	14.1 (18.9, 8.8) b*,d*	18.9 (23.6,12.3) e€,f€
CD4+/CD8+ Cells (%)	1.87 (2.56, 1.37)	1.5 (2.2, 1) a+	2.7 (4.1, 2) b*, d*	2.7 (3.4, 1.7) e+
NK Cells (%)	11.1 (15.9, 8.4)	15.5 (20.9, 10.7) a*	13.2 (22.1, 8.1) b€	1.7 (12, 0.9) c+,e*,f*
NKT Cells (%)	1.7 (2.8, 1.1)	2.6 (4.5, 1.2) a+	1.4 (2, 0.7) d*	0.5 (1.1, 0.3) c+,e*,f*

https://doi.org/10.1016/j.aohep.2021.100637

IL-10 Y TNF-α IN SERUM OF PATIENTS WITH CHRONIC HEPATITIS C AND HEPATIC DAMAGE CHRONIC AND ACUTE FOR ALCOHOL CONSUMPTION

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