Role of tamsulosin in recovery from thioacetamide-induced subchronic liver damage in a Wistar rat model

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Introduction and Objectives: The liver is one of the most important organs in the organism due to its multifunctionality. For this reason, any damage affecting this organ can promote a systemic imbalance, starting from the formation of hepatic fibrosis to encephalopathy due to the increase of ammonium. This study aimed to evaluate the treatment with tamsulosin in the recovery of liver damage in a Wistar rat model.

Material and Methods: Induction of liver damage was by thioacetamide for five weeks. After induction, 5 groups (n=6) were formed: 1) cirrhotic, 2) tamsulosin 11 μg/kg, 3) tamsulosin 93 μg/kg, 4) vehicle and 5) intact. For the determination of liver damage, biochemical tests were performed. For tissue evaluation, H/E and Syrian red staining were performed, and immunohistochemistry NF-KB as an inflammatory marker. Biochemical and morphological tests were correlated with the degree of locomotor activity. The trial was approved by the research ethics committee.

Results: Rats treated with tamsulosin showed a significant improvement in weight recovery and locomotor activity due to decreased serum ammonium, about intact and vehicle. The 11 μg/kg dose of tamsulosin presented better results in the histological analyses since a greater recovery of the hepatic architecture was observed with a decrease in fibrosis and a decrease in NF-KB activation.

Conclusion: The use of tamsulosin at low doses can be considered a therapeutic option for the recovery of liver damage; however, further trials and tests are required to support its efficiency in patients.

Funding: The resources used in this study were from the hospital without any additional financing

Declaration of interest: The authors declare no potential conflicts of interest.

https://doi.org/10.1016/j.aohep.2022.100866

Hepatic MIR-122-3P, MIR-140-5P and MIR-148B-5P expressions are correlated with cytokeratin-18 serum levels in MAFLD

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Introduction and Objectives: This study aimed to investigate the expression and correlation of miR-140-5p, miR-148-5p and miR-122-3p in the liver with circulating levels of CK-18, APOB, IL-6, IL-32, TNF-α of patients with and without MAFLD who underwent laparoscopic cholecystectomy.

Material and methods: Cross-sectional study in patients scheduled for elective cholecystectomy, from whom anthropometric and biochemical variables, blood samples and liver biopsy were obtained with prior signed informed consent. A qRT-PCR assay was performed from the liver biopsies RNA, to determine the microRNAs expression levels. ELISA assay was used to measure circulating levels of CK-18, APOB, IL-6, IL-32, TNF-α. The patients were classified according to the histological report as control group and MAFLD.

Results: Circulating plasma levels of CK-18 showed a significant difference (p=0.001) between the control (46.5pg/mL) and MAFLD (230.2pg/mL) groups; the rest of the explored markers showed no difference. The results show a very strong correlation between, miR-122-3p (rho= 0.071 p= 0.001) and CK-18 levels, while with miR-140-5p (rho= 0.564, p= 0.023) and hsa-miR-148b-5p (rho = 0.689, p= 0.003) are strong.

Discussion: We show that the expression of the microRNAs studied is related to CK-18 circulating levels in patients with MAFLD, which makes these potential molecules biomarkers.

Conclusion: There is a very strong correlation between hepatic expression levels of miR-122-3p, miR-140-5P and miR-148-5P and circulating levels of CK-18 in patients with MAFLD.

Funding: The resources used in this study were from the hospital without any additional financing

Declaration of interest: The authors declare no potential conflicts of interest.

https://doi.org/10.1016/j.aohep.2022.100867

Serum determination of MMP-2 and MMP-9 in chronic liver disease according to alcohol consumption, non-alcoholic fatty liver disease and hepatitis C

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Introduction and Objective: This study aimed to evaluate serum concentration of MMP-2 and -9 in different etiologies of liver disease also according to fibrosis stages.

Materials and methods: Cross-sectional multicentric study, including subjects with no alcoholic fatty liver disease (NAFLD), chronic Hepatitis C (CHC), alcohol cirrhosis (CiOH) and alcoholism (OH), groups with alcohol drinking habits were classified according to OMS criteria, with clinical and biochemical evidence of alcoholic liver disease (ALD). Transitional elastography (Fibroscan) was performed in NAFLD and CHC, considering mild fibrosis (FL: F0, F1, F2) and severe fibrosis (FA: F3, F4). As controls, subjects without alcohol consumption (CT) were recruited. Multiplex®-MERCK© was used for MMP-2 and -9 quantification. Statistical analysis was performed by Mann Whitney-U test, p<0.05, with SPSS V.22.

Results: The groups included were: 27 NAFLD (mild fibrosis: F0, F1, F2), 36 NAFLD (severe fibrosis: F3, F4), 48 CHC (mild fibrosis: F0, F1, F2), 54 CHC (severe fibrosis: F3, F4), 45 (CiOH), 99 (OH), and 138

CT. Both gelatinases, MMP-2 y MMP-9, were found elevated in CHC (mild and severe fibrosis) vs. CT; and decreased in OH, CiOH, HGNA (mild and severe fibrosis) vs. CT, plus there are significant differences between all etiologies, p<0.001.

Discussion: In patients with CHC, MMP-2 y -9 serum concentration increases, particularly in severe fibrosis stages, although it has no effect on ECM (extracellular matrix) degradation, as they are inactive. Nevertheless, there is a significant decrease in these gelatinases in ALD and NAFLD.

Conclusions: MMP-2 y MMP-9 module depends on the etiological agent involved, which can be useful for the differential diagnosis of liver diseases.

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

Declaration of interest: The authors declare no potential conflicts of interest.

https://doi.org/10.1016/j.aohep.2022.100868

MMP-7 is a non-invasive biomarker of chronic liver diseases

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Introduction and Objectives: This study aimed to evaluate serum concentrations of MMP-7 in different liver etiologies and according to fibrosis stage.

Materials and methods: A cross-sectional and multicenter study was carried out, including subjects with alcoholism (WHO criteria), without (OH) and with liver injury (cirrhosis, CiOH); diagnosed by clinical, biochemical data, non-alcoholic fatty liver (NAFLD) and chronic Hepatitis C (CHC). Transitional elastography (Fibroscan) was performed in NAFLD and CHC, considering mild fibrosis (MF: F0, F1, F2) and advanced fibrosis (AF: F3, F4). As controls, subjects without alcohol consumption (CT) were recruited. For the quantification of MMP-7, Multiplex-MERCK© was used. Statistical analysis was performed using SPSS V.22 using Mann Whitney U, p<0.05.

Results: It was included 99 subjects (OH); 45 (CiOH); 48 (CHC, FL); 54 (CHC, FA); 27 (NAFLD, FL); 36 (NAFLD, AF) and 131 CT. MMP-7 was found to be elevated in CHC (FL and FA), vs. CT; and decreased in OH, CiOH, NAFLD (FL and FA) vs. CT, plus there are significant differences between all etiologies, p<0.001.

Discussion: MMP-7 is a matrilysin that degrades extracellular matrix products (proteoglycans); it increases significantly in subjects with CHC compared to CT, while in other pathologies with stages, even in advanced fibrosis, the levels are decreased compared to CT.

Conclusion: The increased MMP-7 in serum of chronic Hepatitis C and decreased in alcoholism and non-alcoholic fatty liver patients suggests that, according to the etiology, the levels can be useful to make a differential diagnosis. It is a potential non-invasive biomarker.

Funding: This work was partially financed by CONACyT SALUD-2016-272579 and PAPIIT- UNAM TA200515.

Declaration of interest: The authors declare no potential conflicts of interest.

https://doi.org/10.1016/j.aohep.2022.100869

Autoimmune hepatitis with superimposition of primary sclerosing cholangitis on non-specific chronic ulcerative colitis

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Introduction and Objetives: Chronic nonspecific ulcerative colitis can be associated with autoimmune hepatitis (AH) and Primary Sclerosing Cholangitis (PSC) as an overlap (prevalence 1.7-12.6%). The evolution depends on the clinical picture, biochemical pattern, and histological determination. The response to immunosuppressive treatment of inflammatory bowel disease and autoimmune hepatitis is good, but not Primary Sclerosing Cholangitis.

Case Summary: 26-year-old female resident of Mexico City. Family history of arterial hypertension and acute myocardial infarction. Smoking suspended, alcoholism denied, other history denied. Current condition: Begins 2013 with diarrhea with scant blood, bloating, abdominal pain, general malaise, weight loss; microcytic hypochromic anemia, thrombocytosis, hypertransaminasemia. Colonoscopy: Pancolitis Mayo 2. Biopsy: chronic ulcerative colitis, intense cryptitis, cryptic abscesses. Hypertransaminasemia and cholestatic syndrome persisted; viral hepatitis was ruled out, positive ANAP 1:80, and negative anti-smooth muscle. Liver biopsy: lymphoplasmacytic infiltrate without cholangiole damage or cholestasis, suggestive of HA. He received steroid, azathioprine, ursodeoxycholic acid and mesalazine. Treated latent TB. He received infliximab with improvement. August 2020: jaundice and direct hyperbilirubinemia. Cholangioresonance 2021: Primary Sclerosing Cholangitis. Liver biopsy 2021: lymphocytic infiltrate beyond the limiting plate, plasma cells, cholangiole proliferation, peripheral sclerosis, intracytoplasmic and canalicular cholestasis, focal necrosis, bridges of fibrosis (F3) compatible with AH and PBC. Biological therapy was suspended, Azathioprine was adjusted, and sent for transplant by MELD of 20. Fig. 1 y Fig. 2.

Results:

Conclusions: The patient debuted with moderate Montreal E3S2 UC and confirmed HA. She presented biochemical and clinical remission and intermittent cholestasis; She presented jaundice six years later, confirming PSC by MRI and Biopsy. The evolution of this overlap depends on age, gender and initial phenotype, regardless of the course of UC, representing a diagnostic and therapeutic challenge

Funding: The resources used in this study were from the hospital without any additional financing

Declaration of interest: The authors declare no potential conflicts of interest.