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

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Introduction and Objectives: The 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-α, IL-1β, and IL-6 were performed by RT-qPCR using a CFX96 Touch thermocycler with 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 ± standard error media (SEM) using GraphPad (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 intestinal 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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