IGFBP2: a possible molecular link between liver, heart, and bloodstream during metabolic dysfunction-associated steatotic liver disease

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Introduction and Objectives: Metabolic dysfunction-associated steatotic liver disease (MASLD) is highly prevalent worldwide, the concomitant presence of fibrosis is considered the most important risk factor of cardiovascular death. IGFBP2 is expressed mainly in the liver and at very low levels in heart. This peptide is associated with metabolic affection including obesity and type 2 diabetes. IGFBP2 role in MASLD is not clear. We aimed to assess the expression of IGFBP2 protein in the liver and associate it with its blood levels and cardiac expression in a rodent model of MASLD.

Materials and Patients: Male C57BL/6 mice weighing 23±2g were included and fed a high-fat diet with water added with sugar (HF-SF) or control diet up to 30 weeks. Liver damage was assessed by biopsy. IGFBP2 was assayed by ELISA in serum, liver, and heart. Data is shown as Mean±SD, analyzed by ANOVA, $p<0.05$.

Results: HF-SF mice exhibited increased bodyweight, visceral adiposity, and fasting glycemia compared to controls. HF-SF group developed steatosis with or without fibrosis. Mice showing fibrosis were assessed as F1C, portal fibrosis. IGFBP2 was significantly lower in steatosis regardless of the presence of fibrosis, both in serum and liver. Cardiac expression of IGFBP2 was diminished in steatosis with fibrosis compared with controls. Significant, moderate, positive correlations were observed between serum IGFBP2 and its hepatic expression, as well as IGFBP2 cardiac expression. IGFBP2 in serum negatively correlated with visceral adiposity and bodyweight.

Conclusions: IGFBP2 expression in liver and heart depends on the stage of MASLD and is associated with visceral adiposity. IGFBP2 in the bloodstream is produced mainly by the liver, and with lower contribution from heart. Serum IGFBP2 can be considered as a marker of its hepatic and cardiac expressions which are closely related with the stage of MASLD. IGFBP2 might be considered a molecular link between liver and heart during MASLD.

Ethical statement

All procedures were approved by CICUAL-FM-UNAM (002-CIC-2022).

Declaration of interests

None

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Endoscopic ultrasound guided portal pressure gradient: safety aspects, clinical relevance and technical issues to improve the procedure

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Introduction and Objectives: Endoscopic ultrasound guided portal pressure gradient measurement (EUS-PPGm) would provide useful clinical information in patients with liver diseases. However, there is yet scarcely data on the clinical relevance of this EUS-guided procedure.

We report our experience on EUS-PPGm focus on safety, clinical relevant findings, technical drawbacks and how to overcome them, aiming to make this procedure more safe, accurate and available.

Materials and Patients: EUS-PPGm was performed with a therapeutic echoendoscope and a dedicated 25G needle in 30 consecutive patients. Assessment of NAFLD 25; idiopathic portal hypertension 3; evaluation for curative therapy in hepatocellular carcinoma (HCC) 2. EUS-guided bilobar liver biopsies (EUS-BLB) were also immediately performed in 26 patients (87%) with a 19G needle

Results: EUS-PPGm was obtained in 25/30 patients (83%) being >5 mmHg in 10/22 NALFD patients (45%) without endoscopic and/or ultrasonographic signs of portal hypertension neither liver fibrosis on EUS-BLB. Mean time to obtain EUS-PPGm was 21±2 minutes.

EUS-PPGm was not obtained in 5 cases. In 4 cases for excesive use of the elevator and up&down wheel and bending of the needle. In another case for exacerbating breathing movements. The hepatic and portal vein were difficult to punction in one and two cases, respectively having to transverse the vessels and reposition the needle.

A self-limited bleeding from the cardias and a mild epigastric pain 2 day after a combined procedure were observed without other adverse events one month later.

Conclusions: EUS-guided PPGm, even when combined with EUS-BLB, seems safe providing useful clinical information. Almost half of patients affected with NAFLD have portal hypertension diagnosed precociously in reversible stages providing a useful tool in precision Medicine, especially in the setting of obesity pandemic. There are technical aspects related to the needle and the position of the echoendoscope that should be known to improve the safety, accuracy and availibility of this procedure.

Ethical statement

The protocol was registered and approved by the Ethics Committee. The identity of the patients is protected. Consentment was obtained.

Declaration of interests

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