Collagen matrix scaffold as vehicle of WP1066, STAT-3 inhibitors, in an in vitro hepatocellular model.

Moises Martinez-Castillo[1], Cristina Piña-Barba[2], Israel A. Núñez-Tapia[2], Marisela Hernandez-Santillan[1], Abigail Hernández-Barragán[1], Gabriela Gutiérrez-Reyes[1]

[1] *Laboratorio de Hígado, Páncreas y Motilidad (HIPAM), Unidad de Investigación en Medicina Experimental, Facultad de Medicina, UNAM, Hospital General de Mexico, Dr. Eduardo Liceaga*
[2] *Instituto de Investigaciones en Materiales, UNAM, Ciudad de México*

Introduction and objectives: Liver disease causes approximately 1.75 million deaths per year and chronic liver disease (CLD) and is usually detected in advanced stages (cirrhosis or hepatocellular carcinoma) that require partial ablation or transplant. STAT-3 has been identified as a therapeutic target in cancer. Moreover, collagen matrix scaffolds (CMS) can be used as carriers of antineoplastic drugs for hepatocellular carcinoma. The objective was to determine the capacity of CMS as vehicle of WP1066 (inhibitor of STAT3) in an in vitro HCC model.

Materials and Patients: WP1066 was incubated with HCC cell lines to determine the IC50 by the Resazurin method. After this, the IC50 concentration of WP1066 was added to CMS during 1, 3 and 7 days before the incubation with each HCC cell, then the WP1066 stability was evaluated by mass spectrometry. The pH of the RPMI medium was evaluated in all the experimental conditions using a potentiometer. Whereas the cell viability was compared with untreated cells and CMs without WP1066 by Resazurin method.

Results: The IC50 of WP1066 for HEPA 1-6 and HEPG2 was similar 1.54 uM $\pm$ 0.07 and 1.68 $\pm$ 0.16 uM, respectively. WP1066 showed stability after 7 days of preparation in DMSO. The pH evaluation of RPMI with WP1066, CMS and WP1066+CMS was similar (pH 7.2) at 72 h of incubation. Cell viability of both HHC cell lines was reduced 80% in the combination of CM plus WP1066 ($p<0.001$), however, CM alone also promotes the reduction of cell viability like WP1066 alone (50%) ($p<0.001$).

Conclusions: Previously, we reported that CM allows the survival and proliferation of mesenchymal stem cells. CM can be used as a vehicle of WP1066; moreover, CM alone or in combination with WP1066 promotes reduction of HCC cell lines. It is possible that hydroxyapatite from CM promotes reduction of cell viability of cancer cells but does not cause negative effects in mesenchymal stem cells.

Ethical statement

The protocol was registered and approved by the Ethics Committee.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

https://doi.org/10.1016/j.aohep.2024.101403

Segmental portal hypertension secondary to chronic pancreatitis

Karla Correa-Cedeño, Carlos M. Martinez-Escanamé, Carlos A. de-la-Torre-Cabral, Viviana Herrera-Muñoz, Graciela Rodriguez-Gonzalez, Diego A. Martinez

Hospital Central"Dr. Ignacio Morones Prieto"

Introduction and objectives: Case presentation of a male patient with portal hypertension secondary to chronic pancreatitis

Materials and Patients: This is a 38-year-old male patient, occasional drinker, risky consumption, history of diagnosis of diabetes mellitus, with adequate adherence to hypoglycemic treatment with metformin, presented a clinical picture of 3 years of evolution consisting of severe pain in the upper abdomen with irradiation to the back on the left side, which required emergency admissions with stabilization and discharge with subsequent recurrence, as well as significant weight loss of 10% over a period of 8 months. He was admitted to the emergency department with clinical symptoms compatible with upper gastrointestinal bleeding due to the presence of melaenic bowel movements on multiple occasions, associated with anemic syndrome, biochemically highlighting a Hb of 2.4 mg/dl, with normal liver function tests and other laboratories, with no changes of chronic hepatopathy by ultrasound.

Results: Regarding the approach to the digestive tract bleeding, Panendoscopy was performed, showing mucosa without alterations, without observing bleeding during the study, ruling out the presence of varices at esophageal level, proceeding to the realization of contrasted Angio Tomography, where findings of segmental portal hypertension with spleno-portal collateral vessels, splenic thrombosis and pancreatic calcifications suggestive of changes due to chronic pancreatitis were observed, with an area of enhancement at the level of the gastric fundus at the site of gastric varices, splenomegaly was not reported. For treatment selection, interventional radiology was evaluated, offering as a therapeutic option the recanalization of the splenic vein with stent placement; however, since Splenectomy was still considered as the definitive treatment for segmental portal hypertension, the latter intervention was chosen for resolution, with adequate evolution after the procedure, remission of bleeding and corroborating adequate flow redistribution after surgery by means of new Angio-CT. The patient attends his consultations on a regular basis, with good evolution, good glycemic control and improvement in nutritional status.

Conclusions: Segmental portal hypertension (SPH) is due to the presence of isolated obstruction of the splenic vein by thrombosis or extrinsic compression.

Pancreatitis conditions the development of thrombosis because the inflammatory state induces stasis and damage of the intima related to the contact of the splenic vein and the pancreas.

The presence of isolated gastric varices makes it necessary to rule out splenic venous thrombosis.

The definitive treatment continues to be splenectomy, reducing the flow to the varices and collateral circulation.

Ethical statement

The identity of the patients is protected. Consentment was obtained.

Declaration of interests

None

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

https://doi.org/10.1016/j.aohep.2024.101404