8th to the end of protocol. Weight was recorded on weekly basis. Insulin tolerance test was performed at the end of treatment. Dual channel microarrays were hybridized to the Mus musculus genome version with 22,000 genes using hepatic mRNAs. Liver and fat histological analyses were carried out, and liver proteins were analyzed by western blot and Chromatin immunoprecipitation (ChIP). Molecular docking was used to validate binding of PFD to JMJD2BBBBB.

Results: Compared with HF group, mice treated with PFD reduced weight gain, hepatic fat accumulation, and epididymal fat. In addition, treatment drastically decreased cholesterol, triglycerides and VLDL, ALT and AST. Inflammatory nodules, fibrosis, and steatosis in liver tissue were also reduced. Besides, PFD modified expression of genes, such as, Jmjd2b, Pparg, Fasn and Srebp1. Likewise, PFD restored the repressive marks in H3k9, suggesting its capacity as an epigenetic regulator by decreasing Jmjd2b protein activity and interacting with its catalytic site (JmjC).

Conclusions: PFD played an important role as an epigenetic regulator modifying Jmjd2b activity and improving NASH features.

https://doi.org/10.1016/j.aohep.2023.101189

P-3 PIRFENIDONE PREVENTS OBESITY-ASSOCIATED NONALCOHOLIC STEATOHEPATITIS AND CARDIAC FIBROSIS THROUGH HORMONAL REPROGRAMMING

Jorge Gutiérrez, Daniel López, Ana Soledad Sandoval, Ángel Omar Vázquez, Jonathan Samael Rodríguez, Juan Armendáriz

Department of Molecular Biology and Genomics, CUCS, Institute for Molecular Biology in Medicine and Gene Therapy, University of Guadalajara, Guadalajara, México

Introduction and Objectives: Obesity is now a worldwide epidemic, associated with insulin resistance, nonalcoholic steatohepatitis (NASH), and cardiovascular diseases (CVDs), being the latter main cause of global death. NASH is common among Hispanics, characterized by fatty infiltration, inflammation, with or without hepatic fibrosis, and shows hormonal dysregulation. Pirfenidone (PFD) is an anti-inflammatory, and anti-fibrotic drug. Previously, we reported that PFD has anti-steatosis effects on hepatic and cardiac tissues in mice with NASH, but its mechanisms involved are not completely known. The aim of this study was to investigate the effects of PFD on hormonal regulation in high-fat/high-carbohydrate (HFHC)- diet-induced obese male C57BL/6J mice.

Materials and Methods: At the age of 19-20 weeks, mice were fed with normal diet (ND, 6.2% lipids, 44.2 carbohydrates, 18.6% proteins, n=7) and normal water. Other mice were fed with HFHC (60.3% lipids, 21.4% carbohydrates, 18.3% proteins, n=14) and water with carbohydrates (2.31% fructose and 1.89% sucrose) diet for 16 weeks; at 8 weeks of feeding, seven mice with HFHC diet were administered PFD (300 mg/kg/day) by gavage. Experiments were performed according to the ARRIVE guidelines. Insulin tolerance test (4 h of fasting), ELISA, Hematoxylin-Eosin and Masson staining, and morphometric analysis were performed. Data analysis were evaluated using one-way ANOVA with Tukey post hoc test.

Results: HFHC mice showed NASH with an increase in resistin and aspartate aminotransferase (P0.05). Parameters significantly elevated in HFHC were prevented by PFD such as weight (body, liver, and heart), tibia length, epididymal fat, hepatic steatosis, insulin resistance, hormones (insulin, glucagon, leptin, plasminogen activator inhibitor 1) (Table), triglycerides, total cholesterol, LDL, and VLDL, including inflammatory foci and fibrosis in hepatic and cardiac tissue (P0.05). PFD decreased alanine aminotransferase (P0.05).

Conclusions: PFD decreases metabolic hormones and could be a promising drug for the prevention of obesity-induced NASH and CVDs.

Male C57BL/6J			
Hormones (pg/mL)	ND	HFHC	HFHC+PFD
Adiponectin	11,094.2 ± 718.8	9,308.3 ± 1603.7*	12,752.6 ± 335.5
Glucagon	2,368.1 ± 592.7	5,184.4 ± 584.8*	1,601.3 ± 624##
GIP	135.5 ± 14.3	193.2 ± 54.6	135.3 ± 15.5##
GLP-1	136.9 ± 13.1	207.4 ± 18.8	179.2 ± 48.6
Insulin	5,753.9 ± 449.1	18,029.7 ± 2,749.3***	9,191.9 ± 968.7##
Leptin	1,470 ± 192.5	14,678.8 ± 2,094***	4,475.7 ± 846.4###
Resistin	55,051.6 ± 4,168.4	89,032.2 ± 10,975.5*	85,795.1 ± 5,184.5
PAI-1	715.3 ± 111.3	2,424 ± 301.8***	1,058.4 ± 152.9##
Ghrelin	18,293.9 ± 2,347.1	20,636.8 ± 3120.7	16,557.8 ± 2,428.6

Table. Serum hormones levels. Data are expressed as mean ± SEM. *P < 0.05, ***P < 0.001 vs. ND; ##P < 0.01, ###P < 0.001 vs. HFHC. Abbreviations: GIP, Glucose-dependent insulinotropic peptide; GLP-1, Glucagon-like peptide-1; PAI-1, Plasminogen activator inhibitor-1.

https://doi.org/10.1016/j.aohep.2023.101190

P-4 HETEROGENEITY OF PRE-LIVER TRANSPLANT EVALUATION PRACTICES IN LATIN AMERICA COUNTRIES: THE LIVER TRANSPLANT ALEH SPECIAL INTEREST GROUP, INTERNATIONAL SURVEY 2023

Victoria Mainardi[1], Josemaría Menéndez[1], Solange Gerona[1], Alejandra Villamil[2], Josefina Pages[3], Manuel Mendizabal[3], Sergio López[4], Adriana Varon[5], Alfeu De Medeiros[6], Jhon Abad[7], Juan Carlos Restrepo[8], Liana Codes[9], Paulo Lisboa[9], Norma Marlene Perez[10], Pablo Coste[11], Graciela Castro-Narro[12], Martin Padilla[13], Débora Raquel B. Terrabuio[14], Mario Guimaraes[14], Marcos Girala[15], Leonardo Lucca[16], Edgard Aguilera[17], Álvaro Urzúa[18], Marcia Samada[19], Kenia Valenzuela[19], Rodrigo Zapata[20]

[1] *Programa Nacional de Trasplante Hepático, Hospital Central de las Fuerzas Armadas, Montevideo, Uruguay*
[2] *Trasplante Hepático, Hospital Italiano, Buenos Aires, Argentina*
[3] *Trasplante Hepático, Hospital Austral, Buenos Aires, Argentina*
[4] *Trasplante Hepático, Hospital Vivian Pellas, Managua, Nicaragua*
[5] *Lacardio Fundación Cardioinfantil, Lacardio Fundación Cardioinfantil, Bogotá, Colombia*
[6] *Trasplante Hepático, Hospital Santa Casa, Porto Alegre, Brasil*
[7] *Trasplante Hepático, Hospital Carlos Andrade Marín, Quito, Ecuador*
[8] *Trasplante Hepático, Hospital Pablo Tobón Uribe, Medellín, Colombia*
[9] *Trasplante Hepático, Hospital Portugues, Salvador De Bahía, Brasil*
[10] *Trasplante Hepático, Hospital General Plaza De La Salud, Santo Domingo, República Dominicana*
[11] *Trasplante Hepático, Hospital R.A. Calderón Guardia, San José, Costa Rica*

[12] *Trasplante Hepático, Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán y Hospital Medica Sur, México, México*
[13] *Unidad De Hígado, Hospital Nacional Guillermo Almenara. Universidad Nacional De San Marcos, Lima, Perú*
[14] *Trasplante Hepático, Hospital Das Clinicas Da Faculdade De Medicina Da Universidade De Sao Paulo, Sao Paulo, Brasil*
[15] *Trasplante Hepático, Hospital De Clínicas De La Universidad Nacional De Asunción, Asunción, Paraguay*
[16] *Trasplante Hepático, Hospital Universitario UFSC, Florianópolis, Brasil*
[17] *Gastroenterología, Honduras Medcal Center, Tegucigalpa, Honduras*
[18] *Trasplante Hepático, Hospital Clínico Universidad De Chile, Santiago, Chile*
[19] *Trasplante Hepático, Centro De Investigaciones Médico Quirúrgico, La Habana, Cuba*
[20] *Trasplante Hepático, Clínica Alemana De Santiago, Santiago, Chile*

Introduction and Objectives: Latin America (LA) includes 20 countries, with significant cultural and economic diversity. In order to develop regional liver transplant (LT) guidelines, the LT ALEH special interest group (SIG) made a survey aimed at investigating the current status of pre- LT evaluation in LA.

Materials and Methods: A 150 questions-survey was distributed to LT-SIG members in 01-05/2023. A descriptive analysis was performed.

Results: 20 answers from 14 countries were obtained. All countries performed LT except one. Financing was private in 5%, public in 32% and mixed in 63%. Allocation system was MELD-Na/MELD in 70 and 30%, respectively. Hepatocellular carcinoma granted supplementary points except in one country. Expansion of Milan criteria was acceptable in 9 centers (UCSF, Up to 7, AFP model, Milan/Brazil). Effective downstaging applied to LT except in 2 centers and AFP>1.000 was a contraindication in 10 centers. Three centers performed LT for cholangiocarcinoma and 4 for colorectal liver metastasis. Acute Liver failure had emergency prioritization in all but 2 countries. Age>65 was a contraindication in 1, >70 in 2 and >75 in 4 centers. Body Mass Index>40 was a contraindication in 8, and <18 in 2 centers. Fragility score7 was a contraindication in 1 center. A period of alcohol abstinence was required by 14 centers (3-6 months), as well as for tobacco in 4, cannabis in 7 and cocaine in 14. VIH was a contraindication in 7 centers and portal thrombosis in 3. Other contraindications were: coronary artery disease requiring surgery (8 centers), dynamic intraventricular gradient>80 mmHg (8 centers), hepatopulmonary syndrome with severe hypoxemia (14 centers), severe or moderate portopulmonary hypertension (7 and 10 centers, respectively).

Conclusions: Pre-LT evaluation in LA is very heterogeneous. The collaborative sharing of experiences between countries and the development of regional guidelines will be relevant in order to unify criteria and improve LT access.

https://doi.org/10.1016/j.aohep.2023.101191

P-5 APACHE STUDY DESIGN TO EVALUATE THE EFFICACY AND SAFETY OF PLASMA EXCHANGE WITH HUMAN SERUM ALBUMIN 5% ON SHORT-TERM SURVIVAL IN PATIENTS WITH ACUTE-ON-CHRONIC LIVER FAILURE AT HIGH RISK OF HOSPITAL MORTALITY.

Nikolaos Pyrsopoulos[1], Giovanni Perricone[2], Jasmohan S. Bajaj[3], Thierry Gustot[4], Thomas Reiberger[5], Mireia Torres[6], Peter Nelson[6], Javier Fernandez[7], On Behalf of the Apache Study Investigators [8]

[1] *Division of Gastroenterology and Hepatology, Rutgers-New Jersey Medical School, New Jersey, Estados Unidos (EEUU)*
[2] *Hepatology and Gastroenterology Unit, ASST GOM Niguarda, Milan, Italia*
[3] *Division of Gastroenterology, Hepatology, and Nutrition, Richmond VA Medical Center and Virginia Commonwealth University, Richmond, Virginia, Estados Unidos (EEUU)*
[4] *Department of Gastroenterology, Hepato-Pancreatology, HUB Erasme Hospital, Université Libre de Bruxelles, Brussels, Bélgica*
[5] *Division of Gastroenterology and Hepatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria*
[6] *Clinical Operations, Scientific Innovation Office, Grifols, Barcelona, España*
[7] *Liver Unit, EF Clif, EASL-CLIF Consortium and Grifols Chair, Hospital Clínic, IDIBAPS and CIBERehd, Barcelona, España*
[8] *Apache Study Investigators, Barcelona, España*

Introduction and Objectives: Acute-on-chronic liver failure (ACLF) in cirrhotic patients is characterized by acute deterioration of liver function and severe organ injury with high short-term mortality. Liver transplantation is the only treatment to improve survival. A pilot study suggested that plasma exchange with human serum albumin 5% (PEA5%) as a replacement fluid is feasible and safe in ACLF patients and may improve organ function and survival. This study aimed to assess PE-A5% as a treatment for patients with ACLF in a pivotal study.

Materials and Methods: A phase 3, multicenter, randomized (1:1), controlled, parallel-group, open-label study (APACHE) compares standard medical treatment (SMT) + PE-A5% (treatment arm) to SMT alone (control arm). PE-A5% is performed using Albutein 5% (Grifols). Treatment schedule consists of two initial PE-A5% sessions on consecutive days followed by every other day PE-A5% (min-max 4-9 PE-A5%). Patients receive IVIG (200mg/kg) after every 2 PE-A5% to prevent hypogammaglobulinemia-associated infections, and FFP after each PE-A5% to prevent coagulopathy. Eligible patients are adult (18-79 years old), with ACLF-1b, ACLF-2, or ACLF-3a at admission or during hospitalization. Main exclusion criteria are patients with ACLF-1a or ACLF-3b, ACLF >10 days