Annals of Hepatology 29 (2024) 101187

Contents lists available at ScienceDirect

Annals of Hepatology

journal homepage: www.elsevier.es/annalsofhepatology

Abstracts of the 2023 Annual Meeting of the ALEH (Asociación Latinoamericana para el Estudio del Hígado)

P-1 EFFECTIVENESS AND SAFETY OF BARIATRIC SURGERY IN PATIENTS WITH ADVANCED HEPATIC FIBROSIS SECONDARY TO METABOLIC ASSOCIATED FATTY LIVER DISEASE IN A TERTIARY REFERENCE HOSPITAL

Ana Luiza Gomes Reis,
Marcella Motta Lucindo Duarte, Renato Gama Altike,
Patrícia Momoyo Youshimura, Danilo Razente,
Miller Barreto de Brito e Silva, Marco Aurélio Santo,
Mário Guimarães Pessôa, Claudia Pinto Oliveira

Departamento de Gastroenterologia, Hospital das Clínicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brasil

Introduction and Objectives: There is limited knowledge regarding the outcomes of patients with Metabolic Associated Fatty Liver Disease (MAFLD) and hepatic fibrosis who undergo bariatric surgery. We aimed to evaluate the benefits and safety of bariatric surgery in patients with MAFLD and advanced hepatic fibrosis (F3-F4).

Patients and Methods: An observational and prospective study that included participants from the MAFLD outpatient clinic of a Brazilian tertiary hospital, who had grade 3 or 4 hepatic fibrosis on biopsy or transient hepatic elastography and underwent bariatric surgery for obesity treatment.

Results: A total of 25 patients were included, with 80% being female. The mean age was 54 years and the surgical procedures performed included gastric bypass (44%) and sleeve gastrectomy (56%). The body mass index ranged from 35 kg/m^2 to 63 kg/m^2, with a median of 41 kg/m^2. Regarding comorbidity, 68% had hypertension, 80% had type 2 diabetes or insulin resistance, and 48% had dyslipidemia. Furthermore, 64% were diagnosed with grade 3 fibrosis and 36% already had cirrhosis, with 4 of them presenting portal hypertension with esophageal varices, but Child-Pugh A. After the procedure, weight loss ranged from 18% to 47% with a median follow-up of 3 years, with higher percentages achieved with gastric bypass (Table 1). Regarding hepatic fibrosis, 50% showed regression to less advanced stages. Among patients with portal Hypertension, 2 of them had subsequent endoscopic examinations without detection of esophagogastric varices. There were no complications related to hepatic decompensation; however one patient developed postoperative pulmonary thromboembolism without severity.

Conclusions: Bariatric surgery, either gastric bypass or sleeve gastrectomy, resulted in significant weight loss in patients with advanced hepatic fibrosis and regression of fibrosis, without serious outcomes or hepatic decompensation in a small cohort in a tertiary reference hospital.

TABLE 1
WEIGHT LOSS BY TYPE OF SURGICAL PROCEDURE PERFORMED

Weight Loss	Gastric bypass	Sleeve gastrectomy
<30%	5	11
>30%	6	3
Total	11	14

https://doi.org/10.1016/j.aohep.2023.101188

P-2 NASH IS IMPROVED THROUGH MODIFICATIONS IN H3K9 METHYLATION BY PIRFENIDONE ACTING AS JMJD2B DEMETHYLASE ANTAGONIST.

Samael Rodríguez[1], Rebeca Rosas[1],
Angel Omar Vazquez[1], Ivonne Palacios[2],
Ricardo De la Rosa[1], Rebeca Escutia[1], Josep Jiménez[2],
Luis Felipe Jave[3], Arturo Santos[4], Ana Sandoval[1],
Juan Armendariz[1]

[1] *Biología Molecular y Genómica, Universidad de Guadalajara, Guadalajara, México*
[2] *Biochemistry and Physiology, Universitat de Barcelona, Barcelona, España*
[3] *Inmunología, IMSS/CIBO, Guadalajara, México*
[4] *EMCS, Tecnológico de Monterrey, Guadalajara, México*

Introduction and Objectives: NASH is characterized by hepatic lipid accumulation and inflammation and Jmjd2b up-regulation has been linked with this illness progression. Pirfenidone is an antifibrotic agent with anti-inflammatory and antioxidant effects recognized to decrease NASH features. Here, we report epigenetics mechanisms related to PFD-induced histone modifications involved in experimental NASH. This study aimed to investigate PFD as an epigenetic regulator in the Jmjd2b pathway by demethylating H3k9me3 in a NASH animal model.

Material and Methods: Male C57BL/6J mice were fed with either normo-diet, or high fat/carbohydrate-containing diet (HF) for 16 weeks. A HF-subgroup was treated with PFD 300 mg/kg/d from week

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*