fat and sugar (HF n=8) for 18 weeks, or a diet high in fat and sugar for 10 weeks, plus 8 weeks of HF diet + methyl group donor supplementation (HFMS n=8). Insulin Tolerance test was performed before sacrifice. Liver, epididymal and visceral fat, and serum samples were collected. Biochemical and histological analyzes were performed. In the liver, global DNA methylation was quantified and the transcriptome was analyzed using dual-channel microarrays. Proteomic analysis was carried out by immunoblotting.

**Results:** The supplemented animals (HFMS) showed a decrease in body weight epididymal and visceral fat ($p<0.001$). The HFMS group showed reduced serum levels of triglycerides and glucose and increased insulin sensitivity. Histological analysis of livers from ND and HFMS animals did not show characteristic MAFLD damage. Global DNA methylation was increased in the HFMS animals. Transcriptome analysis in the HFMS group showed a decrease in metabolic pathways associated with the development of MAFLD and an increase in lipid and cholesterol metabolic pathways. The proteomic analysis revealed an increase of the expression of H3K9 and DNMT1 and a decrease of H3K4, MJD2B and EZH1 proteins involved in the development of the disease.

**Conclusions:** Supplementation with methyl group donors has beneficial effects on weight and body composition, improves hepatic metabolism of lipids, and increases the expression of molecules that regulate DNA methylation and histones, even when consumption of a high-fat diet is continued.

### Ethical statement

The protocol was registered and approved by the Ethics Committee.

### Declaration of interests

None

### Funding

None

**Table 1**
Differences between diet groups

| | ND | HF | HFMS |
|---|---|---|---|
| **Final weight (gr)** | $30.25 \pm 2.25^{**}$ | $46 \pm 4.39^{**,\#}$ | $33.83 \pm 2.92^{\#}$ |
| **Feed consumption (gr)** | $3.417 \pm 0.37$ | $3.37 \pm 0.53$ | $3.164 \pm 0.36$ |
| **Liver weight (gr)** | $1.918 \pm 2.27^{*}$ | $2.3 \pm 0.36^{*}$ | $2.12 \pm 0.15$ |
| **Visceral fat weight (gr)** | $1.027 \pm 0.12^{*}$ | $1.433 \pm 0.39^{*,\#}$ | $0.98 \pm 0.19^{\#}$ |
| **Epididymal fat weight (gr)** | $1.58 \pm 0.31^{***}$ | $3.4 \pm 0.85^{***,\#}$ | $2.24 \pm 0.41^{\#}$ |
| **Glucose (mg/dL)** | $116.6 \pm 10.93^{*}$ | $137.13 \pm 19.19^{*,\#}$ | $132.9 \pm 13.3^{\#}$ |
| **Global Methylation (%)** | $0.6033 \pm 0.061^{*}$ | $0.5200 \pm 0.062^{*,\#\#}$ | $0.8967 \pm 0.17^{\#\#}$ |
| **Triglycerides (mg/dL)** | $82.67 \pm 5.508^{*}$ | $104.4 \pm 6.841^{*,\#\#}$ | $81.2 \pm 6.017^{\#\#}$ |

All the results are expressed as the mean ± SD. Statical analysis were performed using One-Way Anova and Tukey Post hoc test. The "#" symbol represents (#p<0.05) (##p<0.01) differences between HF vs. HFMS and "*" is used for HF vs. ND differences (*p<0.05) (**p<0.01) (***p<0.001).

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## Methyl-group donor supplementation beneficial effects on metabolic, histological, and inflammatory parameters in a murine model of alcoholic steatohepatitis

Carolina Diaz-Canul[1], Angel O. Vázquez-Esqueda[1], Rebeca Rosas-Campos[1], Marina Galicia-Moreno[1], Armendariz-Borunda Juan[1,2], Ana Sandoval-Rodriguez[1]

[1] *Departamento de Biología Molecular y Genómica, Instituto de Biología Molecular en Medicina y Terapia Génica, Centro Universitario de Ciencias de la Salud, Universidad de Guadalajara, Guadalajara, México*
[2] *Tecnológico de Monterrey, Escuela de Medicina y Ciencias de la Salud*

**Introduction and Objectives:** Chronic alcohol consumption is the main cause of alcohol-related liver disease (ARLD) ranging a spectrum characterized by inflammation and progressive fibrosis. Currently, abstinence is the main treatment for ARLD; for this reason, it becomes indispensable to evaluate therapeutic alternatives as methyl group donors which have the potential to influence the development and progression of the disease. To evaluate the effect of chronic alcohol consumption coupled with methyl-group donor supplementation on metabolic and histologic features and gene expression of proinflammatory cytokines in a murine model of ARLD.

**Materials and Patients:** : 24 male C57BLC/6J mice divided into groups with conventional diet (ND n=8); alcohol-induced liver-injury induced with *ad libitum* consumption of a 20% ethanol-aqueous drink and a 45%-fat diet (OH n=8) for 18 weeks; or latter diet for 10 weeks, plus 8 weeks of this diet and methyl group (OH +METMIX n=8). This protocol is in the process of being approved by the CUCS Ethics, Research and Biosafety Committees.

**Results:** Serum biochemical studies and histological analysis performed in the methyl-donor supplemented group (OH+ METMIX) -zinc sulfate, methionine, vitamin B12, folic acid, betaine and choline- showed a significant decrease in body weight, epididymal and visceral fat ($p<0.05$), and serum levels of cholesterol, HDL and LDL. Whilst, serum levels of AST, ALT, TG and VLDL, as well as IL-6 and TNF-$\alpha$ mRNA from hepatic tissue, and the hormones insulin, leptin, glucagon, and resistance, demonstrated a tendency to decrease their concentrations compared to the OH group.

**Conclusions:** Treatment with methyl-group donors improves body weight, body composition, cholesterol, LDL and HDL concentrations, exerting beneficial and protective effects even when consuming an ethanol-aqueous drink.

### Ethical statement

The protocol was registered and approved by the Ethics Committee.

### Declaration of interests

None

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## Passenger lymphocyte syndrome, an unusual cause of anemia after liver transplantation

Alejandro Gutierrez-Castillo[1], Héctor Cabrera-Larios[1], Fernando Segovia-Rivera[2], Rafael Valdez-Ventura[1], Nayelli C. Flores-García[3]

[1] *Internal Medicine, National Institute of Medical Sciences and Nutrition Salvador Zubirán, Meixico City*
[2] *Geriatrics, National Institute of Medical Sciences and Nutrition Salvador Zubirán*
[3] *Gastroenterology, National Institute of Medical Sciences and Nutrition Salvador Zubirán*

**Introduction and Objectives:** The prevalence of anemia after liver transplantation ranges from 4.3% to 28.2%. Causes that occur in the first two weeks include bleeding, sepsis, medications, and hemolysis. Immune hemolysis represents less than 1% of the cases and includes graft-versus-host disease and hemolysis associated with ABO incompatibility. We present a case of passenger lymphocyte syndrome as a cause of immune hemolytic anemia two weeks after a liver transplant.

**Materials and Patients:** A 43-year-old woman, blood group A+, with a history of HCV-related liver cirrhosis and BCLC-A hepatocellular carcinoma, was chosen for a liver transplant. Surgery was uneventful, requiring the transfusion of an O+ blood unit. The postoperative evolution was carried out without complications. On day 10, after the transplant, she presented a drop of 3 g/dL in hemoglobin, leukocytosis, elevated acute phase reactants, and mixed hyperbilirubinemia. An esophagogastroduodenoscopy and colonoscopy showed no active bleeding. The hemolysis profile showed a decrease in the haptoglobin value and an increase in DHL, negative Coombs, without schistocytes. An MRCP was requested, with no evidence of bile leakage or active bleeding. Because of the suspicion of hemolysis due to drugs, tacrolimus was changed to mycophenolate mofetil, and because of possible hemolysis due to sepsis, broad-spectrum antibiotic coverage was added without improvement. On day 14, there was a suspicion of transient lymphocyte syndrome. Isohemagglutinin levels were requested and became positive, and two O+ blood units were transfused. The following day, she presented a significant improvement in all laboratory parameters, and on day 20 she was discharged from the hospital without any abnormality in her laboratory parameters.

**Results:** In our management of hemolytic anemia after liver transplantation, two theories initially emerged: 1) Hemolysis due to tacrolimus, for which it was suspended and changed to mycophenolate mofetil, and 2) Hemolysis due to sepsis, due to leukocytosis and inflammation, initiating coverage with meropenem and vancomycin. But without improvement after both interventions. Finally, due to suspicion of transient lymphocyte syndrome, isohemagglutitins were requested and were positive, and after the transfusion of 2 O+ blood units, containing anti-A+ antibodies, she showed improvement, confirming the diagnosis.

**Conclusions:** In the passenger lymphocyte syndrome, there is a donor B lymphocyte production of antibodies causing a primary or secondary response to recipient erythrocytes. The incidence is higher in the heart-lung transplant, followed by liver transplantation. The risk also increases according to the donor-recipient ABO mismatch, being more common with group O donors and group A recipient (61%), followed by group O donors and group B recipients (22%). The clinical picture is characterized by fever, diarrhea, rash and hemolysis. The hemolysis usually occurs on days 3 to 24 after the liver transplantation and tends to be mild and self-limited. The diagnosis is made when the recipient had a positive direct antiglobulin test and there were donor antibodies in the serum against the recipient's red blood cell antigens. Treatment options include the transfusion of O red blood cell units and, in cases of severe hemolysis, immunosuppressors or plasmapheresis.

**Ethical statement**

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

**Declaration of interests**

None

**Funding**

None

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## Effect of the combination of orlistat and l-carnitine on the quality of life (sf-36) in 16 overweigth patients. a preliminary result

Saúl A. Vera-Nungaray[1], Miguel Y. Carmona-Castillo[1], María F. Higuera-de la Tijera[1], Livan Delgado-Roche[2], Evelyn Altamirano-Castillo[3], Nancy G. Vega-López[4], Uriel Gutiérrez-Estrada[4], Santiago Camacho-Hernández[1]

[1] *Gastroenterology Service, General Hospital of Mexico, Mexico City, Mexico*
[2] *Clinical Research Manager, Liomont Laboratories, Mexico City, Mexico City, Mexico*
[3] *General Hospital Of Zone 8, Mexican Social Security Institute, Mexico City, Mexico*
[4] *National Polytechnic Institute, Mexico City, Mexico*

**Introduction and Objectives:** Orlistat is a drug widely used in overweight/obese patients, while the combination with l-carnitine could offer an improvement in its effectiveness. To our knowledge, the effect of this combination on the quality of life of overweight patients has not been determined.

To evaluate the effects on the quality of life of patients who took the combination of orlistat and l-carnitine at 4 and 8 weeks of treatment.

**Materials and Patients:** : We evaluated the quality of life (Short Form-36) in 16 patients [41.81±8.26 (37.77-45.86) years, 81% women] undergoing pharmacotherapy of the combination of orlistat and l-carnitine (once a day) at 4 and 8 weeks of treatment. Data express mean±SD and 95%IC or percentages as correspond. We use paired Student t Test, two tails with an alpha=0.05.

**Results:** Patients lowered their weight by about 3%. Patients show improvement in body pain, general health, vitality and in both Mental [45.68±6.51 (42.49-48.86) vs. 49.88±3.21 (48.31-51.46), p=0.02] and Physical [59.4±8.92 (55.03-63.77) vs. 63.36±9.64 (58.63-68.08), p=0.01) summaries.

**Conclusions:** These results suggest a beneficial effect of the combination of Orlistat and l-carnitine on the treatment of overweight. Further studies compared with placebo and standard care are required.

**Ethical statement**

The protocol was approved by the local research and ethical committees.

Registration number: DECS/JPO-CT-1944-2023.

**Declaration of interests**

None

**Funding**

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## METS-IR and its correlation with the diagnosis of nonalcoholic fatty liver disease corroborated by elastography.

María E. Hernández-Ortega[1], Scherezada M.I. Mejía-Loza[2], Otto P. González-Guzmán[3]

[1] *Medicina Interna, Hospital Juárez de México, Ciudad de México*
[2] *Gastroenterología, Hospital Juárez de México, Ciudad de México*
[3] *Endocrinología. Hospital Juárez de México, Ciudad de México*

**Introduction and Objectives:** Nonalcoholic fatty liver disease (NAFLD) has become the leading cause of chronic liver disease worldwide, with a prevalence ranging from 25% to 40% (1,2). Its increase