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 ± 0.37	3.37 ± 0.53	3.164 ± 0.36
Liver weight (gr)	$1.918 \pm 2.27^{*}$	$2.3 \pm 0.36^{*}$	2.12 ± 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

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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-α 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

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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.