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"Short-Term High Fat, High Sucrose Diet Increases Markers Associated with Hepatic Lipid Accumulation in Rhesus Macaques"

Self-reported data collected from our clinical cohort, the New Orleans Alcohol Use in HIV (NOAH), shows that a significant number of people living with HIV (PLWH) consume a suboptimal diet as determined by the Dietary Guidelines for Americans. Consumption of a high fat, high sucrose diet (HFSD), known as a Western Diet contributes to metabolic dyshomeostasis and development of metabolic syndrome and non-alcoholic fatty liver disease. At-risk alcohol consumption, HIV-infection, and consumption of a HFSD independently can lead to liver disease. Thus, PLWH with at risk alcohol consumption and consuming a HFSD may have increased risk for liver pathology. Alcoholic and non-alcoholic fatty liver disease are the principal indications for liver transplantations. The difficulty of matching donors and the requirement of life-long anti-rejection therapy warrants elucidating the underlying pathophysiological mechanisms to develop preventive and therapeutic strategies to ameliorate liver pathology. The aim of this study was to characterize the impact of HFSD on liver pathophysiological adaptations in rhesus macaques. We hypothesized that a short-term HFSD (3 mo.) would increase markers of hepatic lipid accumulation. Histological analysis was performed using hematoxylin and eosin. Expression of genes associated with lipid accumulation, metabolic dyshomeostasis, inflammation, and apoptosis was determined using RNA extracted from livers of macaques fed a HFSD (N=8) and control-diet (N=8). Expression of mRNA was quantified using qPCR. Histological analysis revealed a qualitative increase in lipid accumulation, enlarged hepatocytes, and cells that either indicated cell death or mitosis in the HFSD group. Gene expression of perilipins 1 and 3 and peroxisome proliferator-activated receptor γ (lipid accumulation), glucose-6-phosphatase (gluconeogenesis), uncoupling protein 2, and interleukin-10 (anti-inflammatory/transforming growth factor β stimulated) was increased in macaques fed a HFSD. There were no significant changes in gene expression of pro-inflammatory (tumor necrosis factor α and interleukin 1β), apoptotic (B-cell lymphoma 2 and BCL2 associated X), or fatty acid synthesis (acetyl CoA carboxylase) markers. These results indicate that short-term HFSD results in alterations in gene expression reflecting hepatic metabolic dyshomeostasis and lipid accumulation in rhesus macaques. These animals are part of a longitudinal study determining the interactions of HFSD with chronic binge alcohol (CBA) and SIV-infection, and we predict that long-term HFSD consumption in combination with CBA and SIV infection will further exacerbate hepatosteatosis, metabolic dyshomeostasis, inflammation, and fibrosis predisposing these animals to liver injury.