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EFAVIRENZ INCREASES DYSLIPIDEMIA AND HEPATOMEGALY, AND ALTERS GENE EXPRESSION IN ADIPOSE TISSUE OF MICE.

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OBJECTIVE: Previously, it has been suggested that efavirenz (EFV) may alter lipid levels in humans. While the effect of PIs on fat metabolism in mice has been reported, the effect of EFV in rodents has not been described. Thus, the effect of EFV on lipid metabolism in mice was investigated.

METHODS: AKR/J mice were fed a low fat diet and treated for two weeks with 50 mg/kg/d EFV or placebo. The effects on gene expression, liver weight, serum lipids, alkaline phosphatase, and β -hydroxybutyric acid were measured.

RESULTS: EFV treated mice had greater serum levels of triglycerides (29% or 42 mg/dL, $p=0.011$), free fatty acids (26% or 0.23 mEq/L, $p=0.0006$), alkaline phosphatase (26% or 24 U/L, $p=0.001$), and total cholesterol (11% or 8 mg/dL, 0.007) than control mice. Moreover, in epididymal fat of EFV treated mice the ratio of fatty acid synthase (FAS) to tumor necrosis factor (TNF- α) increased by >2 fold relative to control mice. Similarly, liver weight was 22% greater in EFV treated mice than control mice ($p=0.0004$). However, serum levels of β -hydroxybutyric acid (ketone bodies), glucose, glycerol, HDL cholesterol and expression of HMG CoA synthase in liver (an enzyme controlling ketone and cholesterol biosynthesis) remained unchanged in mice treated with EFV ($P>0.05$).

CONCLUSION: In contrast to the reported effects of PIs (e.g., amprenavir) in AKR/J mice fed a low fat diet, EFV treatment results in elevation of serum lipid levels. These effects may be due to altered production of proteins in fat (e.g., FAS and TNF- α) or liver that regulate lipid metabolism. EFV does not affect ketogenesis or HMG CoA synthase expression, suggesting EFV may not cause hyperlipidemia by altering mitochondrial function.

Keywords: AEGIS, Adipose Tissue, Brown Fat, Gene Expression, Hyperlipidemia, Oxazines, Hepatomegaly, Fats, Obesity, Dietary Fats, Triglycerides, Liver, Body Weight, Fatty Acid Synthetase Complex, Hydroxymethylglutaryl-CoA Synthase, Cholesterol, Dietary, Lipoproteins, HDL Cholesterol, Mice, Obese, efavirenz, Mice, Animal, Human, genetics, AIDS

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41

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