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Retinoic Acid Targeting DGAT2 in Non-Alcoholic Fatty Liver Disease Model

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Introduction: Nonalcoholic fatty liver disease (NAFLD) is caused by triglyceride (TG) accumulation in the hepatocyte. The initial reversible stage is steatosis, and if left untreated may progress to steatohepatitis, marked by necrosis and inflammation, eventually leading to cirrhosis. Currently, there are no approved therapeutics for NAFLD. Retinoic acid (RA), the active form of vitamin A, has been found to be reduced in individuals with NAFLD and animal models have shown that RA could mitigate TG accumulation in the liver. However, the mechanism of RA's action remains to be determined. Diacylglycerol acyltransferase (DGAT) catalyzes the final step in triglyceride synthesis in the liver. We aimed to evaluate the effect of RA on hepatic expression of DGAT2 in diet induced NAFLD rats. Materials and Methods: NAFLD was induced through a high cholesterol diet (HCD). Thirty-six rats were divided into four groups; a control group with a normal diet, HCD group treated with a vehicle, HCD group and a HCD group that received subcutaneous RA twice weekly for four weeks. The percentage of steatosis, ballooning and inflammation of the livers were compared between groups. Immunohistochemistry hepatic DGAT2 expression was determined using Image J software. The findings were analysed using one-way ANOVA followed by the post hoc Scheffe test. Results: The administration of RA significantly reduced TG accumulation in the liver. We observed improvement in steatosis (48.6+9.8 vs 22.1+12.4, P<0.001), ballooning, and inflammation in the livers of HCD group receiving RA compared to HCD group. The results also demonstrated a significant (P<0.0001) decrease in expression of DGAT2 enzyme in the liver of HCD animals received RA (12.1 ± 1.8) when compared to animals with HCD only (21.5 ± 1.9) . Conclusion: These findings reveal the potential therapeutic efficacy of RA in improving NAFLD possibly via inhibiting DGAT2.

Keywords: DGAT2; diacylglycerol acyltransferase; hepatic steatosis