Short-term Administration of Conjugated Linoleic Acid Reduces Liver Triglyceride Concentration and Phosphatidate Phosphohydrolase Activity in OLETF Rats

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The present study explored the short-term effects of dietary conjugated-linoleic acid (CLA) on liver lipid metabolism in starved/refed Otsuka Long Evans Tokushima Fatty (OLETF) rats. Male OLETF rats (12 weeks old) were starved for 24 hours, then refed for 48 hours with either a CLA diet [7.5% CLA and 7.5% Safflower oil (SAF)] or a SAF control diet (15% SAF). The results demonstrated a 30% reduction of hepatic triglyceride (TG) concentration in the CLA group when compared to the control group. Liver cholesterol concentration was also 26% lower in the CLA fed rats. The activity of mitochondrial carnitine palmitoyltransferase, the rate-limiting enzyme of fatty acid oxidation, was moderately elevated by 1.2-fold in the livers of the CLA group when compared to the control. In contrast, phosphatidate phosphohydrolase, the rate-limiting enzyme for TG synthesis, was found to be 20% lower in the livers of the CLA-fed rats. Therefore, dietary CLA evidently lowers liver lipid concentrations through a reduced TG synthesis and enhanced fatty acid oxidation in starved/refed OLETF rats.

Keywords: Carnitine palmitoyltransferase, Conjugated-linoleic acid, Phosphatidate phosphohydrolase

Introduction

Conjugated linoleic acid (CLA) refers to a group of positional (9/11 or 10/12 double bonds) and geometric (various cis/trans combinations) isomers that are derived from linoleic acid (cis-9, cis12-octadecadienoic acid). They are found in edible foods, such as ruminants meats, pasteurized dairy products, and processed cheeses (Ha et al., 1989; Chin et al., 1992). CLA exhibits several beneficial effects, such as a protective effect against cancer and heart disease (Ip et al., 1991; Ip et al., 1994; Lee et al., 1994), and reduced body fat mass in experimental animals (Park et al., 1997; West et al., 1997; Park et al., 1999). Furthermore, Houseknecht et al. showed that CLA is capable of improving glucose tolerance in hyperglycemic Zucker rats (Houseknecht et al., 1998).

Re-feeding after starvation leads to a significant increase in lipogenesis in the liver and white adipose tissue in experimental animals (Owens et al., 1979; Kochan et al., 1997). This physiological alteration may have some advantages for survival by directing the newly-synthesized fatty acids to form triglycerides as a high-energy source; this increases weight and lipid accumulation in the liver and adipose tissues (Nace et al., 1976; Baltzell et al., 1985). Belury et al. observed that CLA can modulate hepatic lipid composition in rats. However, it is unclear whether or not the short-term feeding of CLA influences the hepatic lipid metabolism in the starved/refed animal model.

In the present study, we employed Otsuka Long-Evans Tokushima Fatty (OLETF) rats, which develop obesity, non-insulin dependent diabetes mellitus with early hypertriglyceridemia, and hyperinsulinemia in adulthood (Kawano et al., 1992; Kawano et al., 1994). We, therefore, evaluated the dietary influences of CLA on hepatic lipid metabolism in this animal model.

Materials and Methods

Animals and diets Male OLETF rats were a generous gift from the Tokushima Research Institute (Otsuka Pharmaceutical Co. Ltd., Tokushima, Japan). The rats were individually housed in metal cages in a temperature-controlled (24°C) room under a 12-hour light/dark cycle. All of the animals were fed chow powder ad libitum until they were given the experimental diet. At 12 weeks of age (body weight 440-450 g), the rats were divided into control and
RESULTS AND DISCUSSION

The present study investigated the effect of the short-term feeding of the dietary CLA on hepatic lipid metabolism in starved/refed OLETF rats. The results demonstrated a 31% reduction of hepatic triglyceride content in the CLA-fed OLETF rats when compared to the control rats (Table 1). Similarly, the liver cholesterol concentration was 26% lower in the CLA fed rats.

The investigation then researched what leads to the reduction of hepatic lipid after the CLA administration. We measured the activities of two key enzymes; CPT for fatty acid oxidation and PAP for TG synthesis in liver. The present study found that there was a tendency to increase the CPT activity in the livers of the CLA-fed rats when compared to the control rats (Table 2). Short-term CLA feeding also enhanced the CPT activity in the brown and white adipose tissues of CLA-fed OLETF rats. Regarding the CPT activity increase in the CLA-fed OLETF rats, it may be assumed that CLA might alter the cellular expression of CPT mRNA. Another possibility is the involvement of peroxisome proliferator-activated receptors (PPARs). It was reported that CLA has structural and physiological characteristics that are similar to PPARs (Moya-Camarena et al., 1999). It is known that liver fatty acid catabolism is regulated by PPAR-alpha.
regulating PP AR-alpha, may enhance the PAP activity in liver. It was reported that the Mg2+-dependent P AP concentration confirms earlier reports, where the dietary CLA reduced the serum total and HDL-cholesterol concentrations (Fig. 1). Our data (so far the first of this type) shows that CLA reduces liver TG, as well as blood cholesterol, after 48 hours of feeding. In addition, none of the previous studies showed the lipid-lowering effects of CLA on the liver and blood. From this point-of-view, it is reasonable to say that the effect is unique in this type of rat model. However, no study on the short term CLA effect on normal rats has been undertaken. Therefore, further study will be necessary to clarify this point.

In conclusion, a 48-hr supplementation of CLA to the diet caused a significant reduction of hepatic TG and cholesterol concentration in starved/re-fed OLETF rats. This reduction may be attributed to both the enhanced β-oxidation of fatty acids and the reduced triglyceride synthesis in the livers of starved/re-fed OLETF rats.

**References**


