Research Review

Does Conjugated Linoleic Acid Increase Insulin Resistance in Humans?

Conjugated linoleic acid (CLA) refers to a group of linoleic acid-derived isomers with conjugated double bonds, typically found at carbon atoms 9 and 11 or 10 and 12. While there are many *cis* and *trans* combinations, the *cis*-9, *trans*-11 and the *trans*-10, *cis*-12 isomers are considered to be the major biologically active forms of CLA.

CLA naturally occurs in foods such as dairy products and ruminant meat. Research on CLA was spurred in the 1980s after its isolation as a proposed anticarcinogen in beef.[1] Since that time, numerous and ever-increasing numbers of studies using synthetically prepared CLA have been performed in humans, animal models, and in vitro cell culture systems. CLA has been suggested to possess the following beneficial health effects:

- Promotes anticarcinogenic and antimutagenic activity[1,2]
- Reduces body weight and improves body mass index (BMI) by enhancing lean mass[3-5]
- Supports healthy glucose and insulin metabolism by activating insulin sensitizing receptors known as peroxisome proliferator-activated receptors (PPARs)[6,7]
- Prevents the progression of hyperglycemia and diabetes by normalizing glucose tolerance and improving hyperinsulinemia[6,8]
- Enhances immunologic function[9]
- Promotes a healthy blood lipid profile and decreases risk of atherosclerosis[10-12]
- Reduces arachidonic acid content of phospholipids and prostaglandin E2 (PGE2) biosynthesis[13,14]

Recently, a few studies have raised some concern in regards to increasing insulin resistance among subjects taking CLA. When addressing these concerns, it is important to note that positive effects on blood glucose and insulin levels have been observed in the vast majority of animal research and in recent human studies. CLA has even been studied as an intervention for type 2 diabetes.[6,8]

In two separate studies, Riserus et al. demonstrated that men receiving 3.4 grams per day of CLA for 12 weeks had increased insulin resistance upon conclusion of the respective study.[15,16] While these results may seem significant upon first glance, a more thorough examination reveals that the subjects in these studies were limited to obese men with metabolic syndrome. According to the National Institutes of Health, the chances of developing insulin resistance greatly increases if a patient has been previously diagnosed with metabolic syndrome and/or has a waist measurement greater than 40 inches (this waist measurement applies to men).[17]

Furthermore, it is important to recognize that the observations regarding insulin resistance in these studies were seen only in subjects who were given the pure *trans*-10, *cis*-12 CLA isomer. While this isomer has been shown to be the most effective CLA isomer in reducing body fat, many CLA products available today contain a mixture of the *trans*-10, *cis*-12 isomer and the *cis*-9, *trans*-11 isomer. Interestingly, the *cis*-9, *trans*-11 isomer has been shown to prevent insulin resistance in humans without affecting the beneficial qualities of CLA. In fact, there is no evidence for increased insulin resistance in humans consuming CLA preparations containing *both* biologically-active isomers (M.W. Pariza, personal communication, October 16, 2002).

An animal study conducted in 2000 concluded that the reduction of fat mass by CLA resulted in significant insulin resistance in mice.[18] Similar to the studies discussed above, mice were given a widely variegated CLA mixture that did not include the *cis*-9, *trans*-11 isomer. As mentioned above, the *cis*-9, *trans*-11 isomer has been shown to prevent insulin resistance and is found in a large majority of products available today.

DeLany and West reported that CLA supplementation increased plasma insulin levels in mice.[4] However, the dosage (1% of the diet) in this study is worth stressing. If mice eat roughly 25% of their body weight per day (a normal amount), this means they were eating 0.25% of their body weight in CLA per day. This would translate, in human terms, to 175 grams per day for a 154 lb. (70 kg) white male. Current human research uses only 2.7 to 7.2 grams per day.

In 1999, Stangl et al. reported a 37% increase in insulin levels in CLA-fed (1% of the diet) swine.[19] In regards to percentage increase, this value seems significant. Upon closer look, however, it appears that this value may be overstated. In fact, the difference in insulin levels between the control and CLA groups was only 21.4 μU/mL at the end of the study. Interestingly, the total amount of insulin in non-diabetic swine (and humans) generally fluctuates 15-20 μU/mL per day depending on diet and activity level. Thus, while these results may indicate the beginning of insulin insensitivity, the difference in insulin levels between the control and CLA groups is not significant enough to confirm the hyperinsulinemic role of CLA.

While it is obvious that more human studies need to be conducted, it is important to keep in mind that the human data we have to date, as well as the overall trends seen in animal models, indicate that the consumption of CLA containing both the *cis*-9, *trans*-11 and *trans*-10, *cis*-12 isomers is safe at levels found to be effective in available research.

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