Review paper

Use of diet supplements, synthetic drugs and herbal remedies with immunotropic activity during pregnancy. III. Conjugated linoleic acid

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Abstract

This mini-review summarizes some experimental and clinical data about effects of conjugated linoleic acid (CLA) supplementation during pregnancy. Some studies prove its positive effects on immunologic variables in lactating sows and piglets and reduction the incidence of pregnancy-induced hypertension (PIH). However, there is a number of negative effects of CLA, namely reduced growth rates and an increase in mortality of suckling pups.

Key words: *conjugated linoleic acid, pregnancy, breastfeeding, sows, human studies.*

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Despite the fact that some herbs are widely used in everyday life (as spices etc.), there has been no agreement on taking them during pregnancy and breast-feeding, especially in the form of highly concentrated extracts [1].

Most vitamins and minerals are generally accepted as safe and they are recommended during pregnancy and nursing. However, the role of other substances, such as conjugated linoleic acid (CLA), is debatable [1].

Conjugated linoleic acid refers to a group of positional and geometric isomers of the omega-6 essential fatty acid – linoleic acid. It plays an important role within the framework of the food economy sector. The main source of CLA is meat (veal, beef, lamb) and dairy products of ruminating animals. It is formed (primarily the c-9, t-11 isomer, ruminic acid) by endogenous bacteria present in the rumen, from unsaturated fatty acids (mainly linoleic) as a result of the isomerisation and desaturation reactions. An average amount of CLA in milk fat obtained from a cow varies from 3.38 mg to 6.39 mg on 1 g of fat. A quantity of CLA can be changed depending on conditions in which cows are kept. The closer the conditions on a farm are to the natural environment (cows allowed to pasture feed naturally) the more CLA is observed in a fat of milk products. Supplementing the cows diet with polyunsaturated oils that contain either linoleic acid (like corn oil or sunflower oil), linolenic acid (fish oil) or algae increases CLA content of milk fat substantially.

Its role has been explored widely in both animal and human models, nevertheless, no consensus has been reached. Despite CLA intake influence on health is not entirely known today, it is currently believed, that it has multidirectional positive impact on human body. A number of scientific analysis allow assuming that CLA has an anti-inflammatory, immunomodulatory, and anti-cancer properties. Inhibitory effect of CLA on the development of a cellulite and advantageous influence on weight management has been also observed. Conjugated linoleic acid supports burning fat without effect of losing a muscular mass [2-4].

It has been agreed that CLA is probably safe for women who are breastfeeding (and their infants) if obtained through natural dietary sources (dairy products, beef). Whether synthetic supplements are equally safe, it remains unclear [5].

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Bontempo *et al.* studied the effects of CLA on metabolism and immunologic variables in lactating sows and piglets. Half of each group of sows were assigned to 0% CLA or 0.5% CLA. Supplementation started in late pregnancy and continued throughout lactation. Conjugated linoleic acid affected the fatty acid composition of colostrum fat; sows fed CLA had higher serum leptin, IgG and lysozyme. Nursing piglets from CLA-fed sows had significantly higher serum lysozyme and IgG [6].

The other study reveals the effect of calcium and linoleic acid therapy on women with pregnancy-induced hypertension (PIH). Forty-eight healthy primigravidas with a family history of preeclampsia and with diastolic notch were randomized to daily oral doses of calcium and CLA or lactose-starch placebo from week 18 to week 22 of gestation until delivery. The results showed significantly reduced occurrence of PIH among women receiving the supplement. The women who developed PIH presented a significant increase in the concentrations of intracellular calcium after interventions. There were no significant differences in the plasma concentrations of ionized calcium, prostaglandin E2, renin, angiotensin II, parathormone and calcitonine [7].

The study analysing the influence of CLA in late pregnancy on blood thyroid hormone and cholesterol levels in piglets was conducted on 8 lactating sows.

From day 90 of pregnancy to delivery, the sows received a 4% addition of sunflower seed oil or CLA oil. The addition of CLA to the rations of the experimental sows late in pregnancy increased the level of conjugated linoleic acid in colostrum in comparison with the control group. Significantly higher levels of thyroxine and triiodothyronine, lower total cholesterol and HDL and LDL levels were found in the blood plasma of piglets in the experimental group in comparison with those in the control group [8].

Studies executed by scientists from Barcelona revealed the impact of CLA supplementation on immunoglobulin production during gestation and suckling in rats. It revealed that CLA increased IgG and IgM concentrations [9].

The same scientists showed the impact of CLA feeding during suckling and early infancy on mucosal IgA level (a period when mucosal immunoglobulin production is poorly developed, as is also the case in humans). It has been found that IgA mucosal production was enhanced in animals supplemented with CLA during suckling and early infancy. In addition, gene expression of PPARγ, which is a possible mediator of CLA's effects, was also up-regulated in animals receiving CLA during early life [10, 11].

It is important to know whether CLA reaches the same concentration in maternal and neonatal organism. Müller *et al.* tried to determine the proportions of CLA in total plasma lipids, lipoproteins and erythrocytes from maternal blood and from venous cord blood of 20 pregnant women consuming conventional western diets after delivery. Cis-9, trans-11 CLA was the only isomer detected. Mean proportions in plasma, lipoproteins and erythrocytes of mothers were higher than proportions in cord blood lipids. In addition, there was some significant linear relationship between CLA in maternal lipids and neonatal lipids [12].

Ringseis *et al.* have found that dietary CLA consumption during pregnancy and lactation influences growth and tissue composition in weaned pigs [2]. It reduces triacylglycerol concentrations in the milk via reduced de novo fatty acid synthesis in the mammary gland and an impaired uptake of fatty acids from lipoproteins into the mammary gland. The authors claim this might be the reason for reduced growth rates and an increased mortality of suckling pups [13]. In Bee trial [4] sows were fed with diets supplemented with CLA or linoleic acid (LA). Weaned offspring of both sow groups were offered either a CLA- or LA-enriched starter diet for 35 days (2 g CLA or LA per 100 g feed). As a result piglets reared on the CLA sows had greater final body and warm carcass weights ($p < 0.01$), and greater feed intake ($p = 0.02$) than piglets reared on the LA sows. The dietary effect on the fatty acid composition was similar for the adipose and muscle tissues. Conjugated linoleic acid increased the level of total saturated fatty acids.

Despite the availability of some data regarding safety and effects of CLA supplementation, the impact of enriched diet for pregnant women is still uncertain.

Quoted articles highlighted its positive effects on immunologic variables in lactating sows and piglets [6], reduction the incidence of PIH, and intracellular concentration of ionized free calcium in peripheral blood lymphocytes [7] or increase plasma thyroid hormone levels in the blood of piglets and lowers the levels of total cholesterol and cholesterol fractions [8]. What is more CLA supplementation during gestation and suckling with an 80 : 20 cis-9, trans-11-trans-10, cis-12 CLA mix is claimed to enhance the production of the main *in vivo* and *in vitro* Ig isotype in Wistar rats [11]. However, there is a number of negative effects of CLA, namely reduced growth rates and an increase in mortality of suckling pups [13]. The two major reasons for the slower growth rate are availability and composition of the milk. In humans maternal supplementation with CLA decreased milk fat [14].

Another explanation may be an anti-angiogenic activity of CLA. Inhibitory effect of CLA on cutaneous angiogenesis induced in mice by syngeneic sarcoma cells was reported [15]. On the contrary, plant-derived LA presented stimulatory effect on angiogenesis and tumor growth [16]. Other authors demonstrated inhibitory effect of CLA on new vessels growth in the mammalian brain [17].

Vascular endothelial growth factor (VEGF) and basic fibroblast growth factor (bFGF) are known as the most potent angiogenesis promoters. These growth factors play a crucial role in organogenesis and take part in placentation and cytotrophoblast proliferation during pregnancy [18-20]. Moon *et al.* [21] have found that CLA decreased bFGF – induced endothelial cell proliferation and DNA synthesis *in vitro*, in a dose-dependent manner, and exerted a potent inhibitory effect on embryonic vasculogenesis and bFGF-induced angiogenesis *in vivo*.

Conclusions

Clearly, further investigation is required to determine whether additional CLA supplementation is safe for pregnant or breast-feeding woman. According to the present knowledge, these women should consume CLA obtained through natural dietary sources only. Consumption of ruminant meat (beef and lamb) and dairy products (milk and cheese) is the main source of dietary exposure to CLA (0.4-1% of total lipids, respectively) [22]. Then, a balanced diet rich in all natural ingredients, rather than expensive synthetic substances with debatable effects are recommended.

In our opinion, diet supplements which contain synthetic CLA are not recommended for pregnant and breast-feeding women.

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