Journal of Nutritional Disorders & Therapy

Food Summit 2020

Effect of Conjugated Linoleic Acids on some Bone Markers in patients with active Rheumatoid Arthritis who referred to the Rheumatology Research Center of Shariati Hospital: A double blind clinical control trial

Aryaeian Naheed

Abstract

Background & Objective: Rheumatoid arthritis (RA) is a chronic relapsing inflammatory multisystem disease with synovial proliferation and destruction of articular cartilage. It is the most common inflammatory arthritis, affecting approximately 0.5-1% of the general population worldwide. RA has served as a useful model for the study of many inflammatory and immune-mediated diseases. The exact explanation for RA isn't yet known. Recently, several studies have shown the possible role of reactive oxygen species (ROS) in the pathogenesis of RA. The destructive reactions by ROS can be improved by antioxidants. Antioxidants have beneficial effect for inhibition of inflammation related to neutrophil functions, Vitamin E as a potent antioxidant has an ability to modulate host immune functions, so it may be have positive effect on patients who suffer from RA.

Conjugated linoleic acids (CLAs) are naturally occurring isomers of linoleic acid found in meat and milk of grazing animals. Their anti-inflammatory effects that have been shown can protect bones from damage. The biological activities of CLAs, much attention has been due to their anticancer, antiatherogenic and antidiabetic effects, as well as their effect on increasing the bone mass. The role of CLAs in oxidative stress as an antioxidant has been investigated to elucidate its beneficial physiological effects. In previous articles we reported the effects of CLAs on RA by a randomized, double-blind placebo-controlled trial. Pain and morning stiffness were significantly lower in the group taking CLA or CLA plus Vitamin E, compared to placebo the group after 12 weeks of supplementation. We have concluded that CLAs may improve clinical outcomes; lower lipid peroxidation without negative effects on lipid profile and fasting blood sugar in patients with RA.

Materials & Methods: The present study may be a randomized double-blind clinical test. Subjects included 46 patients with active atrophic arthritis who were divided into two groups. Group I established normal behaviour plus 2 daily 1.25 gram capsules (containing about 2 grams of 9-cis 11-tans isomer and 10-cis 12-tans isomer in ratio of 50-50 CLAs in glycerinated form), Group II received standard treatment plus 2 placebo 1.25 gram capsules containing sunflower-seed oil with high monounsaturated fatty acid . PGE2 was done by competitive enzymatic immunoassay method, IGF-1 was analyzed by IRMA method supported the sandwich method and ALK-P of bone. Before and after intervention the questionnaires about general information and medical record were filled. Nutrition calculation with 24-hour greatest questionnaire about three day's diet was done. The results were analyzed using SPSS version 18 software.

Biochemical analysis Blood sample collection: A sample of 15 ml blood was obtained from each patient before the trial and at the top of it. The patients were fast for 12–14 h. Ethylene diamine tetra ethanoic acid as anticoagulant was used for plasma isolation.

Plasma α-tocopherol was measured by high-performance liquid chromatography (Cuesta–Sanz method) with a C15 column and ultraviolet–visible detector.

Measurement of plasma inflammatory and immunity reactants: Plasma cytokines were done by ELISA method and by human high sensitivity ELISA kits from eBioscience Company [USA] (sensitivities for interleukin-2 (IL-2), IL-4, IL-1, tumor necrosis factor-α (TNF-α) were 0.4, 0.1, 0.05, 0.13 pg/ml, respectively). Matrix metalloproteinase 3 (MMP-3) was measured by human ELISA Platinum kits from Ebioscience Company; sensitivity was 0.008 ng/ml. Citrullinated antibody (CPP-A) was measured by ELISA method for IgG Antibody

Aryaeian Naheed
Tehran University of Medical Sciences, Iran

citrullinated protein and kits produced by Genesis (England) company, and clinical sensitivity was 80%.Hematological values were determined by an automatic blood counter (Beckman Coulter, Miami, USA).

Nutrients intakes were estimated using 24 h dietary recall questionnaire before and at the top of the trial for 3 days analyzed by Nutrition IV(San Bruno, CA, USA, Firsty Data Bank) software. the themes were asked to not change their usual diets and physical activities throughout the study, and any changes in their medications were avoided if possible.

Compliance with the supplement intake was assessed by counting number of the capsules used and determining changes within the plasma α-tocopherol.

Statistics methods:

Differences between the four groups were determined by ANOVA (one-way analysis of variance) for continuous data and therefore the Chi-square test for group data. Log transformation was wont to normalize the abnormal distributions. Differences between before and after data in each group were determined with paired-sample t-test. If the distribution of a variable wasn't normal, Mann–Whitney U-test was wont to compare the differences between two groups and Wilcoxon signed-rank test was performed for every group to match mean values before and after intervention. ANOCVA were wont to adjust the effect of confounding factors. Correlation decided by Pearson test. $P < 0.05$ was considered as statistically significant. (Version 18; SPSS Inc., Chicago, Il, USA) was used for data analysis. Quantitative values are reported as mean ± variance.

Findings: Totally 102 subjects entered to the study, and 87 of them completed the study. Fifteen patients were excluded from the study thanks to either incomplete consumption of prescription drugs (6 patients: 1 in each groups C [CLA] and CE [CLA + Vitamin E], 2 in each groups E [Vitamin E] and P [Placebo]), changing the dose of their antiinflammatory drugs (8 patients: 2 in each groups), or side-effects (1 patient in group C).

There were no significant differences among the four groups at the start of the study regarding age, sex, BMI, daily intake of vitamin E , disease duration and diseases activity score ($P > 0.05$). Also, the differences between drugs intake (NSAIDS, glucocorticoid and other disease-modifying antirheumatic drugs) weren't significant between groups ($P > 0.05$). The Plasma level of α-tocopherol increased significantly in groups E and CE in contrast to the placebo group ($P \leq 0.017$, $P < 0.023$ respectively).

There were no significant differences between groups at the baseline in cytokines IL-2, IL-4, TNF-α, IL-1β, IL-2/IL-4 and citrullinated antibody variables also as white blood corpuscle (WBC). during this study, significant changes weren't seen in neutrophils, lymphocyte, monocytes, eosinophil numbers and BMI after treatment between groups. Decrease in WBC count was significant in group CLA plus vitamin E , and therefore the lymphocytes increased in group P ($P \leq 0.05$).

Although TNF-α was reduced during the study altogether groups, this reduction was significant only in group CE ($P < 0.05$). IL1β increased significantly in group P and E but decreased in group CE ($P > 0.05$). the rise in IL-1β in group E was less than Placebo. The IL-4 decreased in groups C, E, CE ($P = 0.03$, $P = 0.07$ and $P = 0.003$ respectively), but didn't changed significantly in group P. No significant changes were seen within the plasma IL-2 levels altogether groups, although increased in group P and decreased in other groups ($P > 0.05$). IL-2/IL-4 increased altogether groups with $P = 0.005$, $P = 0.016$, $P = 0.005$, $P = 0.006$ for group P, CLAs, E and CE respectively, but differences between groups wasn't significant. CCP-A increased in group P and decreased in group CE significantly ($P \leq 0.05$). the rise in CCP-A in group E was less than Placebo. MMP-3 increased in group P and decreased in group CE ($P \leq 0.05$), and therefore the differences between group P and group CE was significant ($P = 0.018$). The difference between groups for all data apart from CCP-A and MMP-3 wasn't significant.

No significant side effects were observed. There are three reports of flatulence (2 in group C and 1 in group CE). It had been relieved in two patients by prescribing tablets during meals instead of before meals, but one patient in group C was needed to exclude.

Conclusion: there's a possible benefit effect of CLAs on bone markers in patients with atrophic arthritis. Therefore, so as to

Aryaeian Naheed
Tehran University of Medical Sciences, Iran

review the effect of CLAs on decrease bone density reduction in patients with RA also as all patients with autoimmune and bone diseases, more studies are required with longer duration alongside the evaluation of bone density.

Aryaeian Naheed
Tehran University of Medical Sciences, Iran