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Journal of Obesity & Body Weight

Commentary

Unsaturated Fatty Acid for Preventive Cardiovascular Disease

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Abstract

Obesity and metabolic syndrome have lipids intake problems including Monounsaturated Fatty Acid (MUFA) and Polyunsaturated Fatty Acid (PUFA). For decreasing the Atherosclerotic Cardiovascular Disease (ASCVD) risk, to replace of Saturated Fatty Acid (SFA) with PUFA and/or MUFA would be adequate. Finn Study including 2200 cases showed that Odd Ratio (OR) for obesity was SFAs: 1.28, MUFAs: 1.38, PUFAs: 0.70, Linoleic Acid (LA): 0.67 and DHA: 0.75. In Norwegian study with 3706 cases, higher LA levels were significantly associated with lower values of LDL-C, triglycerides, blood glucose, body mass index, blood pressure and eGFR. These current data are useful for practice.

Keywords: Atherosclerotic cardiovascular disease (ASCVD); Monounsaturated fatty acid (MUFA); Nonalcoholic fatty liver disease (NAFLD); Polyunstaturated fatty acid (PUFA); ω-3 Fatty acids (FA)

Medical and social problems about obesity and metabolic syndrome have been found in lots of countries for decades. Recent topics concerning lipids would be introduced in this article. American Diabetes Association (ADA) has proposed a new guideline in January, 2021 [1]. Among them, lipid management has been the important matters. Concerning the lifestyle intervention, it recommends the reduction of Saturated Fat Acid (SFA) and trans fat, increase of dietary ω-3 fatty acids, viscous fiber, and plant stanols/sterols intake. For the primary prevention, to use high-intensity statin therapy would be reasonable in diabetic patients at high risk. It is especially necessary for patients with aged 50-70 years or multiple Atherosclerotic Cardiovascular Disease (ASCVD) risk factors.

The standard nutritional recommendations are currently introduced from American College of Cardiology (ACC), American Heart Association (AHA) and National Lipid Association (NLA) [2]. These matters include fundamental impact on prevention of ASCVD. Several recommendations are in the following: i) to limit the intake of SFA to 5-6% of total calorie intake, ii) to avoid the intake of trans fat as possible by reading the labels carefully, iii) to decrease sodium intake to 2.4g a day for healthy people and 1.5g a day for higher risk people, and there is an evidence that decreased sodium intake can lower BP and prevent hypertension, iv) to combine DASH pattern with lowering sodium intake, and a strong evidence is found for better blood pressure decrease, v) to make referral to physician and/or Registered Dietician-Nutritionist (RDN) who can advise personalized nutrition therapy [2].

For decreasing the Cardiovascular Disease (CVD) risk, to replace of SFA with cis Polyunsaturated Fatty Acid (PUFA) and/or cis Monounsaturated Fatty Acid (MUFA) would be adequate [3]. When replacing of SFA with carbohydrate, it leads to no decrease or even increasing CVD risk. In previous most studies, the efficacy of food on CVD risk were evaluated by LDL-C and/or total Cholesterol as the biomarker of the risk. Dairy products contain various kinds of lipids. There has been formerly no clear evidence of increased CVD risk from large doses of dairy products.

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Received Date: March 09, 2021

Accepted Date: March 24, 2021

Published Date: March 30, 2021

Citation: Bando H, Bando M (2021) Unsaturated Fatty Acid for Preventive Cardiovascular Disease. J Obes Bod Weig 2: 007.

The reason may be that even if a large amount of fat is taken, some factors would be involved in weakening the direct influence of the lipid. For example, food matrix effects on fat bioavailability, the influence of several proteins, and the efficacy of lipids and proteins on blood pressure, blood glucose, and lipids are present. To clarify these, several various biomarkers are required related to blood pressure, blood glucose and lipids. Although it has been beneficial to replace some of the SFA in milk fat with cis-MUFA, it is not clear whether this method consistently reduces the risk of CVD [3]. According to some Randomized Controlled Trials (RCTs), risk biomarkers such as LDL-C and/or TC may provide useful indicators in relation to clinical cardiovascular events.

Various reports were found on MUFA and PUFA. The beneficial efficacy of MUFA/PUFA includes improving lipids profile and extending lifespan [4]. In a recent study, MUFA (olive oil, OO) was provided to Senescence-Accelerated Mouse-Prone 8 (SAMP8), and the aging index was suppressed [5]. In the United States, there has been well-known study, National Health and Nutrition Examination Survey (NHANES). NHANES has enormous data such as VO2max, CRP, intake of various fatty acids and so on. Using these, significant negative interactions were found between VO2max and ω-3 PUFAs, but not found for saturated, MUFA, or ω-6 PUFAs [6]. This result suggests that ω-3 PUFA may show anti-inflammatory benefits from increasing activity of cardiovascular fitness.

The discussion has been continued concerning the relationship between lipid and CVD for long. In the Finn Study, the associations between fatty acid ratio and cardiometabolic outcomes were investigated [7]. The subjects included 2200 cases, who were aged 24-39 yo for 10 years prospective data from the Young Finns Study. Markers were obesity, insulin resistance, elevated Blood Pressure (BP) and incident Nonalcoholic Fatty Liver Disease (NAFLD). There were impressive results. As to adjusted models for obesity, Odd Ratio (OR)

were SFAs: 1.28, MUFAs: 1.38, palmitoleic: 1.39 and oleic acids: 1.37. Further, inverse relation with obesity were PUFAs: 0.70, linoleic: 0.67 and DHA: 0.75, while positive relation was γ-linolenic acid: 1.32. For age/sex-adjusted models for HOMA-IR, OR were MUFAs: 1.26, oleic acid: 1.25, PUFAs: 0.81, linoleic acid: 0.78. Similar data was found for elevated BP, with palmitic acid: 1.22, MUFAs: 1.28, oleic acid: 1.28, whereas PUFAs: 0.77, ω-6 PUFAs: 0.79, and linoleic acid: 0.77. Regarding adjusted models for fatty liver, OR were palmitic: 1.61 and linoleic acid: 0.63. From these results, we can predict unfavorable cardiometabolic outcomes in higher ratio of total SFAs/MUFAs, lower PUFAs and certain FAs in Finnish adults [7].

Fish contains much ω-3 PUFAs, and such diet has been evaluated to decrease the risk for CVD. The beneficial effect of PUFA and fish oil is thought to be mediated by epigenetic state of some genes related with lipid metabolism and inflammatory situation. In a recent study, DNA methylation levels were investigated for 298 adults who did not have CVD or cancer [8]. The research theme was whether intake of fish and fatty acid may influence DNA methylation levels or not in the leukocyte ATP-Binding Cassette transporter A1 (ABCA1) DNA methylation levels. The results showed that methylation levels were significantly lower in the subject group of highest fish consume in comparison with the lowest group (p=0.004), and that higher intake of ω-3 PUFAs and ω-3 highly unsaturated fatty acid was correlated with lower levels of methylation (P=0.001 and 0.005). These results may raise potential perspectives for biological mechanisms related to protective function of ω-3 PUFA on CVD [8].

Intake of ω-3 PUFA is reported to present favorable health efficacy on various biological mechanism including improved cognition, increasing immunity and optimized neuromuscular function. There are some studies showing beneficial effects of ω-3 PUFA on skeletal muscles [9]. Furthermore, it may prevent the loss of lean body mass by administration of ω-3 PUFA in the case of patients with cancer cachexia. What is the mechanism of positive impact skeletal muscle mass by ω-3 fatty acids? It has been known that the primary means would be via incorporation of EPA; 20:5n-3 and DHA; 22:6n-3 into the membrane phospholipids of intracellular organelles and the sarcolemma [9].

Omega-3 have been PUFAs with anti-inflammatory properties, which include three well-known forms, Linoleic Acid (LA), EPA and DHA. According to recent studies for younger and elder people, ω-3 will possibly increase muscle mass and improve physical function [10]. From several clinical studies and meta-analyses for LA, it showed relationship between higher dietary intakes or tissue levels of LA, and the improvement of CV risks [11].

As the major dietary PUFA, higher intake of LA has been associated with decreased Cardiovascular (CV) morbidity and mortality. A cross-sectional study was conducted including 3706 cases who were all born in 1950 [12]. The associations between blood LA levels and CV risk factors were investigated. Norwegian people show characteristic points of relative lower LA and higher marine ω-3 PUFA intake. The results showed that higher LA levels were significantly associated with lower biomarkers, such as LDL-C (p=0.02), triglycerides (p<0.001), fasting blood glucose (p<0.001), body mass index (p<0.001), systolic BP (p=0.03), diastolic BP (p=0.02), estimated glomerular filtration rate (eGFR) (p<0.001). In contrast, there were no relationships between LA levels and HDL-C, HbA1c, C-reactive protein and carotid intima-media thickness [12].

In summary, adequate intake of MUFA and PUFA would be beneficial. Consequently, recent lipids research will contribute the development of health promotion in clinical practice.

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