Metabolic Effects of Omega 3 PUFA in Dietary Obese Mice

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Complex etiology of obesity-associated diseases implies the need of treatments, which are based on multiple mechanisms of action. Development of type 2 diabetes, dyslipidemia and cardiovascular disease could be delayed by lifestyle modifications, while both dietary and pharmacological interventions are required for the therapy. Naturally occurring *n*-3 long-chain PUFA, namely eicosapentaenoic and docosahexaenoic acids (Omega-3), act as hypolipidaemics, reduce cardiac events and may decrease the progression of atherosclerosis. In animals, Omega-3 prevent the development of obesity, hepatic steatosis and dyslipidaemia, as well as impaired glucose tolerance, while exerting pronounced anti-inflammatory effects. However, Omega-3 fail to improve glycaemic control in diabetic patients.

Experiments in mice fed high-fat diet revealed that (i) liver, adipose tissue and muscle represent important targets for Omega-3, and (ii) Omega-3 effects include changes in fatty acid composition of phospholipids, in formation of Omega-3-derived lipid mediators, in gene expression, and in activity of adiponectin-AMPK axis and endocannabinoid system. Omega-3 administered as phospholipids prevented glucose intolerance and tended to reduce obesity better than triacylglycerols. The better efficacy of the phospholipid form correlated with changes of the endocannabinoid metabolome, and anti-inflammatory lipid levels in both adipose tissue and plasma. Importantly, Omega-3 augment beneficial effects of other treatments. Thus, (i) a combination treatment using Omega-3 and a mild calorie restriction efficiently reduced body fat accumulation, while inducing a metabolic switch toward lipid catabolism in adipose tissue; and (ii) a combination with anti-diabetic drugs thiazolidinediones exerted additive effects in the amelioration of dyslipidaemia and insulin resistance, while preserving muscle insulin sensitivity and metabolic flexibility, and reverting insulin resistance. Both combination treatments strongly suppressed low-grade inflammation of adipose tissue. Combination treatment using Omega-3 and a low dose of rosiglitazone reduced obesity. These results are relevant for prevention and treatment of obesity and its comorbidities.