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Inflammatory gene expression in whole blood cells after EPA *vs.* DHA supplementation: Results from the ComparED study

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ABSTRACT

Background and aims: Whether EPA and DHA exert similar anti-inflammatory effects through modulation of gene expression in immune cells remains unclear. The aim of the study was to compare the impact of EPA and DHA supplementation on inflammatory gene expression in subjects at risk for cardiometabolic diseases.

Methods: In this randomized double-blind crossover trial, 154 men and women with abdominal obesity and low-grade inflammation were subjected to three 10-wk supplementation phases: 1) EPA (2.7 g/d); 2) DHA (2.7 g/d); 3) corn oil (3 g/d), separated by a 9-wk washout. Pro- and anti-inflammatory gene expression was assessed in whole blood cells by RT-qPCR after each treatment in a representative sample of 44 participants.

Results: No significant difference was observed between EPA and DHA in the expression of any of the genes investigated. Compared with control, EPA enhanced *TRAF3* and *PPARA* expression and lowered *CD14* expression ($p < 0.01$) whereas DHA increased expression of *PPARA* and *TNFA* and decreased *CD14* expression ($p < 0.05$). Variations in gene expression after EPA and after DHA were strongly correlated for *PPARA* ($r = 0.73$, $p < 0.0001$) and *TRAF3* ($r = 0.66$, $p < 0.0001$) and less for *TNFA* ($r = 0.46$, $p < 0.005$) and *CD14* ($r = 0.16$, $p = 0.30$).

Conclusions: High-dose supplementation with either EPA or DHA has similar effects on the expression of many inflammation-related genes in immune cells of men and women at risk for cardiometabolic diseases. The effects of EPA and of DHA on anti-inflammatory gene expression may be more consistent than their effects on expression of pro-inflammatory genes in whole blood cells.

1. Introduction

Low-grade systemic inflammation is an etiological feature of many chronic conditions, including metabolic syndrome (MetS), type 2 diabetes mellitus (T2DM) and cardiovascular diseases (CVD) [1]. There is a substantial amount of evidence to suggest that many foods and nutrients, and in particular marine omega-3 fatty acids, modulate the chronic inflammatory state observed in cardiometabolic diseases [2,3]. Consumption of eicosapentaenoic acid (EPA, 20:5n-3) and docosahexaenoic acid (DHA, 22:6n-3), both long-chain omega-3 fatty acids (LCn-3PUFA) present in significant amounts in oily fish, may attenuate the low-grade inflammation profile associated with obesity and MetS [4]. Studies suggest that EPA and DHA may exert anti-inflammatory effects in part by altering properties and cellular function of immune cells through changes in gene expression [5]. Indeed, EPA and DHA are strong natural ligands for specific nuclear receptors called the peroxisome proliferator activated receptors (PPAR) involved in the down-regulation of inflammatory gene expression and of the pro-inflammatory nuclear factor κB (NFKB) [6,7]. A whole-genome analysis demonstrated that supplementation with a combination of EPA and DHA (1.8 g/d) for 26 weeks regulated 1040 genes involved in inflammatory- and atherogenic-related pathways in peripheral blood mononuclear cells (PBMC) [8]. However, almost all of the available evidence on the putative anti-inflammatory

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