The exogenous natural phospholipids, EPA-PC and EPA-PE, contributes to ameliorate lipid accumulation and inflammation via activation of PPARα/γ

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Abstract

Background and Purpose: PPARα/γ play an important role in glucose homeostasis and lipid metabolism making it an attractive anti-diabetic target. Focusing on the development of PPARα/γ dual agonists, we evaluated the activity of phosphatidylcholine (EPA-PC) and phosphatidylethanolamine (EPA-PE) on PPARα/γ. Moreover, we investigated the long-term effects of EPA-PC and EPA-PE on insulin resistance. Experimental Approach: The activities of EPA-PC/PE with respect PPARα/γ transcription were tested using a luciferase reporter gene assay, lipid binding assay and a Protein-Lipid overlay assay. Moreover, the agonistic effects of EPA-PC/PE on PPARα/γ were evaluated in HepG2 and 3T3L1. respectively. In a 3T3L1/Raw264.7 transwell system, the effect of EPA-PC/PE on macrophages polarization and inflammation were studied. In mice, we sought to determine if insulin resistance and lipid accumulation induced by high-fat high-sucrose diet, was attenuated by EPA-PC or EPA-PE diet (0.3% of diet). Key Results: EPA-PC/PE are potent PPARα/γ dual agonists, which promoted hepatic PPARα-mediated fatty acid oxidatio, and promoted the preadipocytes differentiation and PPARγ target genes expression in adipocytes. In mice on the HFSD, EPA-PC/PE significantly suppressed body weight gain and ameliorated insulin resistance as well as abnormal glucose and lipid metabolism. EPA-PC/PE could regulate PPARγ-responsive genes and slightly inhibited the phosphorylation of PPARγ at Ser273, resulted in adipose tissue remodeling. Finally, we found that EPA-PC/PE promoted macrophages polarization and attenuated inflammation in vitro and in vivo. Conclusion and Implications: These data indicate that the exogenous natural phospholipids, EPA-PC or EPA-PE, activate PPARα/γ, may be useful for the treatment of insulin resistance.

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