EICOSAPENTAENOIC ACID (EPA) INCREASES HEME OXYGENASE-1 EXPRESSION IN ENDOTHELIAL CELLS UNDER CONDITIONS OF INFLAMMATION UNLIKE DOCOSAHEXAENOIC ACID (DHA)

Poster Contributions
Sunday, May 16, 2021, 1:15 p.m.-2:00 p.m.

Session Title: Vascular Medicine: Basic and Translational Science 2
Abstract Category: 50. Vascular Medicine: Basic and Translational Science

Authors: R. Preston Mason, Samuel C. R. Sherratt, Hazem Dawoud, Tadeusz Malinski, Deepak Bhatt, Brigham & Women’s Hospital, Boston, MA, USA

Background: Inducible heme oxygenase-1 (HO-1) catalyzes the degradation of heme into biliverdin, carbon monoxide and ferrous iron. These HO-1 products have potent antioxidant, vasodilatory and anti-inflammatory actions. Expression of HO-1 has been linked to nitric oxide (NO) bioavailability, a process influenced by the omega-3 fatty acid (ω-3) eicosapentaenoic acid (EPA). Unlike trials using mixed ω-3 formulations containing docosahexaenoic acid (DHA), EPA only treatment (icosapent ethyl) was associated with reduced cardiovascular (CV) events in REDUCE-IT.

Methods: Human umbilical vein endothelial cells (HUVECs) were pretreated with EPA or DHA at equimolar levels (10 µM) for 2 h, then challenged with IL-6 at 12 ng/ml for 24 h. Proteomic analysis was performed using LC/MS to measure relative expression levels of >1,000 proteins. Only significant (p<0.05) changes in expression between treatment groups >1-fold were analyzed. Cells were stimulated with calcium ionophore to measure NO release using a porphyrinic nanosensor.

Results: Cells pretreated with EPA and DHA significantly down/up-regulated expression of 195/132 and 103/76 proteins, respectively, compared with IL-6 alone. Only EPA upregulated inducible HO-1 by 150% (p = 0.02). Finally, only EPA significantly increased NO release by 13% (p = 0.04) from these cells.

Conclusion: EPA significantly increased expression of HO-1 and NO release under conditions of inflammation. These beneficial effects of EPA were not reproduced by DHA and may contribute to preserved vascular EC function and reduced CV risk as demonstrated in large outcome trials.