ACC.15
TCT@ACC-i2 | innovation in intervention

A2139
JACC March 17, 2015
Volume 65, Issue 10S

Vascular Medicine

EICOSAPENTAENOIC ACID REDUCES SMALL DENSE LOW DENSITY LIPOPROTEIN OXIDATION AND IMPROVES ENDOTHELIAL FUNCTION IN VITRO AS COMPARED TO OTHER TRIGLYCERIDE-LOWERING AGENTS

Poster Contributions
Poster Hall B1
Monday, March 16, 2015, 9:45 a.m.-10:30 a.m.

Session Title: Vascular Medicine Potpourri
Abstract Category: 43. Vascular Medicine: Basic
Presentation Number: 1259-342

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Background: The omega-3 fatty acid, eicosapentaenoic acid (EPA), has been shown to reduce oxidized low-density lipoprotein (oxLDL) and small dense LDL (sdLDL) levels in hypertriglyceridemic patients. EPA may produce these effects through a potent antioxidant mechanism leading to increased LDL clearance and improved endothelial function. We hypothesize that these benefits are unique to EPA as compared to other TG-lowering agents.

Methods: sdLDL was isolated from human plasma by isopycnic centrifugation, separated into test samples of 200 μg/mL, and incubated at 37°C for 30 min in the absence (vehicle) or presence of EPA, fenofibrate, niacin, or gemfibrozil, each at 10.0 μM. All samples, with the exception of non-oxidized sdLDL controls, were subjected to copper-induced oxidation for 1 hr. Human umbilical vein endothelial cells (HUVECs) were incubated with the various sdLDL samples, stimulated with calcium, and monitored for nitric oxide (NO) and peroxynitrite (ONOO–) release using nanosensor technology.

Results: EPA treatment reduced sdLDL oxidation by >90% ($p<0.001$) as compared to vehicle treatment alone. When applied directly to HUVECs, vehicle-treated, oxidized sdLDL reduced NO release by 20% as compared to non-oxidized sdLDL (from 758 ± 40 to 610 ± 43 nM). Following exposure to EPA-treated, oxidized sdLDL, however, HUVEC NO release (931 ± 59 nM) increased by 53% and 23% as compared to oxidized LDL and non-oxidized sdLDL treatments, respectively. All of the other TG-lowering agents failed to inhibit sdLDL oxidation, resulting in reduced NO release. In HUVECs challenged with oxidized sdLDL, pretreated with fenofibrate, niacin, or gemfibrozil, NO release was reduced by 21%, 45%, and 33%, respectively, as compared to effects observed with vehicle-treated, oxidized sdLDL ($p<0.05$).

Conclusion: EPA pretreatment reduced sdLDL oxidation and improved endothelial function as compared to other TG-lowering agents. These changes may be attributed to the unique antioxidant activity of EPA and its putative effects on NO synthase function. These results indicate distinct antioxidant and endothelial benefits of EPA that merit further study.