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Endothelium and Nitric Oxide: Therapy-Related Mechanisms

Abstract 413: Different Effects Of Organic Nitrates On Endothelial Progenitor Cell Mobilisation And Endothelial Function In Patients With Established Coronary Artery Disease

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Endothelial progenitor cells (EPC) contribute to vascular homeostasis and are in part regulated by nitric oxide (NO). Reduced levels and impaired function of EPC contribute to vascular dysfunction and progression of atherosclerotic lesions. Organic nitrates such as pentaerythritol-tetranitrate (PETN) or isosorbiddinitrate (ISDN) are potent NO donors. ISDN but not PETN stimulates formation of reactive oxygen species. In patients with coronary artery disease (CAD), we investigated the effects of PETN and ISDN on endothelial function and mobilization and functional properties of EPCs. We randomized patients with angiographically-proven CAD to treatment with either PETN (80 mg twice daily, n=18) or ISDN (40mg twice daily, n=15). Baseline characteristics were similar among the groups. Before and after 14 days of treatment we measured EPC number by flow cytometric determination of CD34+/VEGFR2+ and CD34+/CD133+/VEGFR2+ cells and EPC function by a standardized colony forming unit as well as a transwell migration assay. Endothelial function (reactive hyperemia index, RHI) and arterial stiffness (augmentation index) were determined by an established plethysmographic method (EndoPAT2000 device). In patients treated with PETN circulating EPCs were substantially increased (+65% , p<0.05), whereas no effects were observed in patients treated with ISDN (-5% , p=0.84). Functionally, there were no significant changes in EPC migratory capacity in the two treatment groups. In contrast, proliferative capacity of EPC was enhanced 1,8-fold in patients treated with PETN, whereas no changes were observed in ISDN-treated patients. There were no significant changes in endothelial function or arterial stiffness in the PETN-group, whereas a trend towards endothelial dysfunction was observed in patients treated with ISDN (RHI -12,3%). Treatment with organic nitrates causes different effects towards endogenous circulating EPC in patients with CAD. PETN increased number and function of EPC, whereas ISDN had no effects, but impaired endothelial function within 14 days of treatment. Organic nitrates which increase number and function of EPC may confer long-term athero-protective effects in patients with CAD.