Organic nitrates differentially modulate endothelial function and circulating angiogenic cells in patients with symptomatic coronary artery disease

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BACKGROUND AND AIM

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 isosorbidinitrate (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.

STUDY DESIGN AND METHODS

We randomized patients with angiographically-proven CAD to treatment with either PETN (80 mg twice daily, n=18) or ISDN (40 mg twice daily, n=18), clinical trial number: NCT01030367. 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 assay. Endothelial function (reactive hyperemia index, RHI) was determined by an established plethysmographic method (EndoPAT2000 device, Itamar).

RESULTS

1.) Short-term PETN treatment increases formation of endothelial colony forming units in patients with CAD, but has no effects on EPC migration.

2.) Short-term PETN treatment increases early and late EPC.

3.) ISDN, but not PETN treatment impairs endothelial function in CAD patients.

CONCLUSION

Treatment of symptomatic CAD patients with PETN for fourteen days significantly increased levels of circulating EPC and improved markers for EPC function, whereas ISDN was without effects on EPCs and worsened endothelial function.