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Endothelium and Nitric Oxide: Therapy-Related Mechanisms

Abstract 412: Pentaerithryltetranitrate Does Not Deteriorate Endothelial Dysfunction In Patients With Coronary Artery Disease. A Prospective, Randomized, Double-blind, Placebo-controlled, Monocentric Clinical Trial (PENTA)

Robert Schiewe¹; Boris Schnorbus¹; Mir Abolfazl Ostad¹; Christoph Medler²; Philip Wenzel³; Andreas Daiber³; Thomas Münzel³; Ascan Warnholtz³

¹ Univ of Mainz Hosp, Mainz, Germany

² Coordination Cntr of clinical trials (KKS), Mainz, Germany

³ Univ of Mainz Hosp, Mainz, Germany

Purpose: Chronic nitrate therapy remains controversial in patients with coronary artery disease (CAD) due to induction of tolerance and deterioration of endothelial dysfunction. Pentaerithryl-tetranitrate (PETN) differs from other organic nitrates by the lack of tolerance induction and by antioxidative properties. We hypothesized that treatment with PETN improves endothelial dysfunction in patients with CAD.

Methods: In a prospective, double-blind trial, we randomly assigned 80 patients to double-blind treatment for 8 weeks with oral PETN 80mg t.i.d. (PETN) or placebo (C), respectively. The primary endpoint was the absolute change in flow-mediated dilation of the brachial artery (FMD) from baseline to follow-up. Secondary endpoints were the changes in nitroglycerin-mediated dilation (NMD), peripheral arterial tonometry (EndoPAT2000) index as a marker of endothelial function of small arteries, the augmentation index (AI) as a marker of arterial stiffness and the activity of the PETN bioactivating enzyme aldehydedehydrogenase-2 (ALDH-2) in monocytes from baseline to follow-up. Raw data entry, data monitoring and statistic analysis were independently performed by the coordination centre of clinical trials (KKS), Mainz. The trial was registered as ISRCTN 14741768.

Results: Both treatment groups were comparable regarding age, gender, distribution of cardiovascular risk factors and concomitant medication. There was no difference in the mean (\pm SD) change in FMD between the two treatment groups (PETN: $+1.6\pm 3.3\%$ vs. C: $+1.4\pm 4.1\%$ $p=0.7$). NMD significantly rose after treatment with PETN compared to C (PETN: $+3.8\pm 5.5\%$ vs. C: $+0.6\pm 4.2\%$ $p=0.0036$). Mean PAT-Index, AI and ALDH-2 activity remained unchanged in both treatment groups.

Conclusions: The three main findings of our trial are: In contrast to other organic nitrates PETN does not deteriorate endothelial dysfunction (1), does not impair ALDH-2 activity (2) and does not induce cross tolerance to nitroglycerin (3). We conclude that chronic PETN therapy in patients with CAD may be established for symptomatic treatment without adverse effects on endothelial function.