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VASCULAR DISEASE

PREVENTIVE EFFECT OF EXENATIDE TO ENDOTHELIAL DYSFUNCTION INDUCED BY ISCHEMIA-REPERFUSION INJURY VIA ADP K CHANNELS

ACC Poster Contributions
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Background_Animal studies have demonstrated that administration of exenatide can limit myocardial damage induced by prolonged ischemia, an effect that appears to be mediated by opening of adenosine triphosphate-sensitive potassium(KATP) channels. No study has investigated whether exenatide can also prevent the impairment in endothelium-dependent vasodilatation induced by ischemia-reperfusion (IR) in humans.

Methods and Results_In a double-blind, placebo-controlled, crossover design, 20 healthy volunteers (25 to 40 yearsold) were randomized to subcutaneous exenatide (10 μg) or placebo. 30 minutes later, endothelium-dependent, flow-mediated dilatation (FMD) of the radial artery was measured before and after IR (15 minutes of ischemia at the level of the brachial artery followed by 15 minutes of reperfusion). Seven days later, subjects received the other treatment (ie,placebo or exenatide) and underwent the same protocol. Pre-IR radial artery diameter and FMD, as well as baseline radial artery diameter after IR, were similar between visits (P=NS). After placebo administration, IR significantly blunted FMD (before IR: 12%; after IR: 4.57%, P =0.02). Importantly, exenatide limited this impairment in endothelium-dependent vasodilatation (before IR: 15%; after IR: 15%, P=NS; P <0.001 compared with placebo). In a separate protocol, this protective effect was completely prevented by previous administration of the sulfonylurea glibenclamide (glyburide, 5 mg), a blocker of KATP channels (n=7; FMD before IR: 12.02 %; after IR: 3.17%, P<0.001).

Conclusions_In humans, subcutaneous exenatide induces potent protection against IR-induced endothelial dysfunction through opening of KATP channels. Further studies are needed to test the potential clinical implications of this finding.