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MEETING ABSTRACT

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Effect of the potassium channel opener pinacidil on isolated human internal mammary artery grafts from patients with type-2 diabetes mellitus

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Background: Arterial grafts used for coronary artery bypass grafting (CABG) surgery have a tendency to develop vasospasm. Diabetes melllitus increases cardiovascular risk, induces endothelial dysfunction and alters basal vascular tone in blood vessels through different mechanisms. Potassium channel openers (PCOs) have the ability to inhibit vasospasm. Little is known about the effects of PCOs on human arteries that are used as CABGs obtained from patients with diabetes. Thus, the aim of this study was to investigate the involvement of smooth muscle K^+ channels in the effect of the PCO, pinacidil, on vasorelaxation of human internal mammary arteries (HIMA) obtained from patients with type-2 diabetes mellitus.

Methods: Segments of HIMA were obtained from patients undergoing coronary bypass surgery. Rings of HIMA without endothelium were mounted in an organ bath system and isometric tension was recorded. The experiments followed a multiple curve design. Pinacidil was used as PCO for vasorelaxation of HIMA precontracted with 5-hydroxytryptamine (100 µM).

Results: Pinacidil (0.01–100 µM) produced a concentration-dependent vasorelaxation of HIMA ($pD_2 = 5.9 \pm 0.3$, $n = 16$). Glibenclamide (GLB, 10 µM, $n = 6$), a highly selective blocker of ATP-sensitive K^+ (K_{ATP}) channels, 4-aminopyridine (4-AP, 1 mM, $n = 6$), a nonselective blocker of voltage-gated K^+ (K_V) channels, and tetraethylammonium (TEA, 1 mM, $n = 6$), a nonselective blocker of calcium-dependent K^+ (K_{Ca}) channels, induced a shift to the right of the concentration-response curves for pinacidil. There was no difference between the maximal vasorelaxation effects (E_{max}), produced by 0.1 mM of pinacidil in the absence and presence of K^+ channel blockers.

Discussion: Pinacidil induced endothelium-independent vasorelaxation of HIMA from diabetic patients. It seems that different potassium channels, located in the vascular smooth muscle, are partly involved in vasodilatation of HIMA induced by pinacidil. This study demonstrates that the mechanism of pinacidil includes potassium-channel-dependent and potassium-channel-independent effects.

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