P25: VASORELAXATION EFFECT OF METFORMIN IN RAT THORACIC AORTA

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ABSTRACT

Metformin is an oral antihyperglycemic agent used in the management of type 2 diabetes mellitus. Metformin appears to provide cardiovascular protection with intrinsic antihypertensive property. This study was to investigate the role of endothelium in metformin-induced vasorelaxation, using rat thoracic aorta isolated from adult male wistar rats (250-300 g). The aortic segments were cut helically and incubated in 15-ml organ chambers containing Krebs-Henseleit solution (KHS), pH 7.4. The medium was maintained at 37 °C and gased continuously with 95 % O_2 and 5 % CO_2. Each tissue was placed under an initial resting tension of 1 g and allowed to equilibrate for 60 min prior to the experimental protocol.

To determine the metformin-mediated relaxation in both endothelium-intact and endothelium-denuded aortic strips, the contraction was induced by the submaximal concentration of norepinephrine (NE, 10^{-7} M), and then followed by cumulatively addition of metformin (10^{-7}-$1.5x10^{-3}$ M). To probe the mechanism involve in the relaxation effect of metformin, several compounds including methylene blue (10^{-5} M, an inhibitor of soluble guanylyl cyclase inhibitor), indomethacin (10^{-5} M, an inhibitor of cyclooxygenase), tetraethylammonium (TEA, 10^{-3} M, an inhibitor of calcium-sensitive potassium channels) and glibenclamide (10^{-5} M, an inhibitor of ATP-sensitive potassium channels) were preincubated 15 minutes prior to precontraction with NE. The relaxation response was calculated as the percentage of NE-induced contraction.

In this study, we found that metformin caused significant vasodilation ($p< 0.05$), in comparison with the control group. The percentage of maximal relaxation in endothelium-intact (32.96±2.84, n = 16) was significantly higher than that of endothelium-denuded (14.93±3.07, n = 7) ($p< 0.05$). Moreover, Methylene blue significantly inhibited the relaxation effect of metformin in endothelium-intact segment ($p< 0.05$), but not in endothelium-denuded segment. However, the metformin-mediated relaxation was not affected by indomethacin, TEA, and glibenclamide.

In conclusion, metformin caused vasorelaxation of rat thoracic aorta both in endothelium dependent and endothelium independent manner. In endothelium-dependent relaxation, metformin may, at least in part, exert its effect through the cyclic GMP pathway.

Key words : Metformin, Thoracic aorta, Endothelium, vasodilation,