Monoamine oxidase inhibition corrects endothelial dysfunction in experimental diabetes

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Monoamine oxidases (MAOs) are mitochondrial dehydrogenases with two isoforms, A and B, that catalyze the electron transfer from biogenic amines to molecular oxygen, with the constant generation of hydrogen peroxide (H2O2) as by-product. The resent study was aimed to assess whether MAO-derived H2O2 contributes to the aggravation of oxidative stress-related endothelial dysfunction. We hypothesized that MAO inhibition improves endothelial-dependent relaxation in experimental diabetes, a condition widely recognized as being associated with increased oxidative stress as happens in diseased vessels.

Methods. Segments from aorta, carotid and femoral arteries with intact and denuded endothelium (using CHAPS solution) were harvested from Zucker obese diabetic rats and streptozotocin-induced diabetic rats and studied in an organ-bath system. The contractile response was assessed using phenylephrine (0.01-1 microM) in the presence vs. absence of a MAO-A inhibitor, clorgyline (10 microM). H2O2 production was measured by a spectrophotometric method (Feric Oxidation Xylenol Orange assay). The effect of hyperglycemia on MAO gene expression was tested by quantitative RT-PCR technique. Results. MAO inhibition reduced the diabetic-induced aortic H2O2 generation by 30% and partially normalized the contractility of diseased vascular segments. Conclusion. MAO inhibition might be useful in restoring endothelial-dependent relaxation in conditions associated with increased vascular oxidative stress and endothelial dysfunction, including diabetes. Further investigations aimed at characterizing the mechanisms underlying MAO-dependent H2O2 formation are warranted. Research supported by the PII-C2-TC-2014 project (ARTERIO-MAO-DIAB).