MONOAMINE OXIDASE CONTRIBUTION TO VALVULAR HEART DISEASE: MORE THAN MEETS THE EYE

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A growing body of research showed that oxidative stress has an important causative role in the pathophysiology of valvular heart disease complicated with fibrocalcification. The identified local enzymatic sources of reactive oxygen species (ROS) are: NADPH isoform 2 (NOX2) and uncoupled NOS. Monoamine oxidases (MAOs) with 2 isoforms, A and B, are flavoenzymes located at the outer mitochondrial membrane which constantly generate hydrogen peroxide (H_2O_2) as a by-product of their activity of oxidative deamination of biogenic amines and neurotransmitters. Whether MAOs are mediators in oxidative stress in the pathogenesis of valvular disease it is not known and was investigated here in patients with severe mitral regurgitation (due to valve degeneration and chordae rupture). Samples of mitral valve (n = 30) were harvested during the valvular replacement procedures and used for ROS assessment (immune-fluorescence, spectrophotometry/FOX assay) and MAO-A and B gene and protein expression measurement (qPCR and immune-fluorescence). We report here that human mitral valve contain both MAO isoforms involved in catecholamine degradation. Ex vivo incubation of the mitral valve samples with AII (100 nM, 12 h) induced MAO-A and B expression and resulted in increased H_2O_2 formation. MAO-related oxidative stress was mitigated by MAO inhibition with the MAO-A inhibitor, clorgyline (10 microM) and the MAO-B inhibitor, selegyline (10 microM) and also by the AII receptor type 1 antagonist, irbersartan (10 microM). In conclusion, MAO is expressed in human mitral valves, can be induced by AII stimulation and thus may contribute via H_2O_2 generation to the pathophysiology of valvular heart disease.

Keywords*:* valvular heart disease, oxidative stress, monoamine oxidase, angiotensin 2