EFFECTS OF WY14643 AND FENOFIBRATE ON ACETYLCHOLINE-INDUCED CONTRACTIONS IN AORTIC RINGS FROM SPONTANEOUSLY HYPERTENSIVE RATS

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INTRODUCTION AND OBJECTIVE: Oxidative stress is implicated in the release of endothelium-derived contracting factors, the release of which is associated with endothelial dysfunction. Peroxisome proliferator-activated receptor (PPAR) –alpha agonists, Wy14643 (WY) and fenofibrate (FF) have been found improving endothelial function in cardiovascular diseases. The present study was designed to examine whether or not WY and FF inhibit endothelium-dependent contractions through reduction of free radicals in aortae of spontaneously hypertensive rats (SHR). METHOD: Male SHRs of 40-44 weeks old were used. Thoracic aortic rings with and without endothelium were suspended in organ chambers for isometric tension recording. RESULTS: Acetylcholine caused contractions in aortic rings with endothelium in the presence of Nω-nitro-L-arginine methyl ester (an inhibitor of nitric oxide synthase). Tiron (a scavenger of intracellular superoxide anion) plus DETCA (an inhibitor of superoxide dismutase) significantly reduced the responses, suggesting that oxygen-derived free radicals are involved in the contractions. Both WY and FF significantly decreased the acetylcholineinduced contractions, suggesting that they may inhibit the production of hydrogen peroxide or its downstream signaling mediators. Exogenous hydrogen peroxide evoked contractions in aortic rings with and without endothelium. Both WY and FF partially inhibited the contractions in rings with endothelium, but not in rings without endothelium, indicating that WY and FF act on the endothelium to produce their inhibitory effects. CONCLUSION: Both WY and FF reduce contractions evoked by acetylcholine in aortic rings of SHR, which may result from their effects on decreasing the production of reactive oxygen species.