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Adenosine A_{2A} receptor antagonist (SCH 58261) attenuates AngII-induced ROS production and preserved endothelial function in mouse aortas

Junjie Du, Susanna Hourani, Jian-Mei Li. Faculty of Health and Medical Sciences, University of Surrey, Guildford, Surrey GU2 7XH, United Kingdom.

The endothelium expresses abundantly an adenosine A_{2A} receptor ($A_{2A}R$) which plays important roles in the regulation of vascular function. The endothelium expresses also an NADPH oxidase which by generating reactive oxygen species (ROS) participates in normal endothelial redox-signalling, and is involved in the pathogenesis of endothelial dysfunction. However little is known about the role of $A_{2A}R$ in AngII-induced endothelial ROS production. In this study, we investigated the effect of $A_{2A}R$ blockade on AngII-induced ROS production and endothelium function using freshly isolated aortas from CD1 mice at 10-12 weeks of age. Comparison between 2 groups was made using student t-test. Significance was accepted at $P < 0.05$. All data are presented as mean ± SEM. Compared to vessels treated with vehicle, acute AngII (200 nM for 45 min) treatment significantly increased the ROS production in the vessel wall as detected by DHE (Fluorescence intensity: 28±1.3 vs 55±4.2). These AngII effects were inhibited back to the control levels in the presence of a specific $A_{2A}R$ antagonist, SCH58261 (100 nM). Compared to control vessels, treatment with AngII severely compromised the endothelium-dependent vessel relaxation to acetylcholine as assessed by an organ bath (Emax: 89±2.5% vs 71±3.2%). Addition of SCH58261 (100 nM) or tiron (20 mM, a specific cell membrane permeable superoxide scavenger) during AngII stimulation protected the endothelium from AngII damage and preserved endothelium-dependent vessel relaxation to acetylcholine (Emax: 88±3.0%). The endothelium-dependence of the relaxation to acetylcholine was confirmed by mechanical denudation of the endothelium. In conclusion, blockade of $A_{2A}R$ protects the endothelium from acute AngII-induced oxidative stress and endothelium dysfunction. $A_{2A}R$ antagonist may have a potential therapeutic application in treating endothelial oxidative stress-related diseases.