Propofol Attenuates Angiotensin II-Induced Prolifer Ation of Cardiac Fibroblasts: Role of Nadph Oxidase Inhibition and Decreased Reactive Oxygen Species Generation

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Aims:. Propofol may have protective effects on the prevention of angiotensin II (Ang II)-induced cardiac fibroblast proliferation via its anti-oxidative properties. The aim of this study was designed to examine whether propofol may alter Ang II-induced cell proliferation and to identify the anti-oxidative effect and underlying signaling pathways in rat cardiac fibroblasts.

Methods: The effect of propofol on Ang II-induced NADPH oxidase activity, reactive oxygen species (ROS) formation, ERK1/2 phosphorylation, and activator protein-1 (AP-1)-mediated reporter activity in cultured cardiac fibroblast were examined. In addition, the effect of propofol on nitric oxide (NO) production, protein kinase B (Akt) and eNOS phosphorylations were also tested to elucidate the intracellular mechanism of propofol in proliferation. The p value less than 0.05 were considered significant(ANOVA).

Results: Ang II (100 nM) increased cell proliferation and ET-1 expression which were partially inhibited by propofol (10 ,30 μM). Propofol also inhibited Ang II-increased NADPH oxidase activity, ROS formation, ERK phosphorylation, and AP-1-mediated reporter activity. In addition, propofol also increased the nitric oxide generation, Akt and eNOS phosphorylations. L-NAME, an inhibitor of NO synthase, and the short interfering RNA transfection for Akt or eNOS markedly attenuated the inhibitory effect of propofol on Ang II-induced cell proliferation.

Conclusions: we demonstrate for the first time that propofol prevents cardiac fibroblast proliferation by interfering with the generation of ROS and involves the activation of the Akt-eNOS- nitric oxide pathway. Thus, this study delivers important new insight in the molecular pathways that may contribute to the proposed protective effects of propofol in the cardiovascular system.

*(*Acknowledgement: This study was accepted by "Anesthesiology " for publication at July, 2009; Funded by: National Science Council of Taiwan no. 96-2320-B-039-009-MY3. Parts of the result had presented at the 2009 Annual Meeting of the European Society of Anaesthesiology, Milan, Italy, Jun/6-9, 2009)*