The role of Akt-eNOS-NO pathway in the inhibitory effect of propofol on Ang II-induced cardiac fibroblast proliferation

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Objectives: Propofol used as an anesthetic agent for more than twenty years, but the mechanism of its cardiovascular effect appears to be complicated and is only partially understood. Experimental results revealed that propofol exerted hypotensive and antioxidative effects. However, the intracellular mechanism of propofol remains to be delineated. The aims of this study were to identify the signaling pathways involved in the protective effect of propofol on Ang II–induced cardiac fibroblast proliferation (in vitro).

Methods: Cultured cardiac fibroblasts were exposed to Ang II in the presence of propofol, Activation of cardiac fibroblast nitric oxide synthase (NOS), and Akt were assessed by Western blot analysis. Nitric oxide (NO) analyzer (Seivers 270B NOA; Seivers Instruments Inc., Boulder, CO, U.S.A.) were used for the detection of NO of medium samples. The p value less than 0.05 were considered significant(ANOVA).

Results: To identify the signaling pathways involved in the effect of propofol, L-NAME (a NOS inhibitor), and short interfering RNA (siRNA) transfection for Akt and eNOS were applied in cardiac fibroblasts. The Akt and eNOS protein levels were markedly reduced by Akt and eNOS siRNA transfection, respectively. The inhibitory effect of propofol on the Ang II-induced cell proliferation was partially reversed by L-NAME, Akt and eNOS siRNA transfection. Similarly, the inhibitory effect of propofol on Ang II-increased BrdU (5-bromo-2'-deoxyuridine) incorporation was also reduced by L-NAME, Akt and eNOS siRNA transfection. These results reveal the involvement of Akt-eNOS-NO signaling pathway in propofol's effect on Ang II-induced cardiac fibroblast proliferation.

Conclusion: we demonstrate for the first time that propofol prevents cardiac fibroblast proliferation by the activation of the Akt-eNOS-NO 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.