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THE ANTI-OXIDATIVE EFFECT OF PROPOFOL ON ANGIOTENSIN-II INDUCED APOPTOSIS IN NEONATAL RAT CARDIOMYOCYTES

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Propofol (2,6-diisopropylphenol), an intravenous sedative¡Vhypnotic agent popular for sedation, has been found to be effective in protecting against pathological states characterized by an increase in basal rate of reactive oxygen species (ROS) production in hearts, but the cardioprotective mechanism is not well established. Angiotensin-II (Ang-II), an important neurohormonal factor during heart failure, can induce cardiomyocyte apoptosis which has an important role in the transition from compensatory cardiac remodeling to heart failure. In the present study, we evaluated the effects of propofol on Ang-II-mediated cardiomyocyte apoptosis. Cultured cardiomyocytes from neonatal rats were stimulated with Ang-II. Apoptosis was evaluated by measuring caspase 3 activity and by TdT-mediated dUTP nick-end labeling (TUNEL) method. It was found that incubation with Ang-II (0.1 micromolar) for 48 h increased cardiomyocyte apoptosis. Administration of propofol (3-10 micromolar) significantly decreased this Ang-II-induced apoptosis. To further investigate the underlying mechanisms, the quantity of cleaved caspase-3, cytosol cytochrome c release, BcL-xL expression, and ROS generation were examined. These results suggest that propofol abates cardiomyocytes from Ang II-induced apoptosis possibly via reduced the quantity of cleaved caspase-3, and cytosol cytochrome c, and increased BcL-xL expression, and inhibiting the increased ROS generation. In addition, propofol was found to increase the Akt phosphorylation in cardiomyocytes. The siRNA transfection for Akt significantly reduced propofol-induced Akt phosphorylation and propofol¡¦s protective effect. Our data provide the first evidence that propofol prevents Ang-II-induced apoptosis, suggesting that propofol may provide a new therapeutic target for the prevention of the cardiac remodeling process.