The protective effect of prostacyclin on adriamycin-induced apoptosis in rat renal tubular cells

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摘要

Abstract

Adriamycin-induced nephrosis in rats is a commonly used experimental model for pharmacological studies of human chronic renal diseases. Adriamycin-induced apoptosis of renal tubular cells has been reported in adriamycin-treated rats. In addition, prostacyclin (PGI2) is known to have various protective effects on many kinds of cells. To investigate the protective effect of PGI2 on cells undergoing adriamycin-induced apoptosis, this study selectively augmented PGI2 production via adenovirus-mediated transfer of genes for cyclooxygenase-1 (COX-I) and prostacyclin synthase (PGIS) (two key enzymes of PGI2 synthesis) to renal tubular cells. This PGI2 overexpression protected rat renal tubular cells from adriamycin-induced apoptosis. Ad-COX-1/PGIS transfection was found to reduce the adriamycin-stimulated activities of caspase-3 and caspase-9, inhibit adriamycin-induced release of cytochrome c, elevate the expression of Bcl-xL, and suppress the activation and translocation of nuclear factor-kappaB (NF-κB) in adriamycin-treated renal tubular cells. Our results reveal that selective augmentation of PGI2 production can protect rat renal tubular cells from adriamycin-induced apoptosis via the NF-κB signaling pathway. This implies the therapeutic potential of combined COX-1 and PGIS gene transfer in gene therapy for chronic renal diseases.