T Tetramethylpyrazine protects rat renal tubular cell apoptosis induced by gentamicin

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摘要

Abstract

BACKGROUND: Gentamicin, a widely used antibiotic for the treatment of bacterial infection, can cause nephrotoxicity. Tetramethylpyrazine (TMP) is a compound purified from the rhizome of Ligusticum wallichi (Chuanxiong) and has been found to protect against ischaemia-reperfusion injury, nephritis and alcohol-induced toxicity in rat kidneys. METHODS: We used rat renal tubular cells (RTCs), NRK-52E, in this study. The cytotoxicity of gentamicin was checked with transferase-mediated deoxyuridine triphosphate nick end-labeling (TUNEL) staining, and the generation of reactive oxygen species was measured using the fluorescent probe 2,7-dichlorofluorescein. We evaluated several apoptotic parameters: cleaved caspase levels, tumour necrosis factor (TNF-alpha) excretion and nuclear factor Kappa B (NF-kappaB) activity. We also examined the TMP protective effect on gentamicin-induced apoptosis in rat kidneys. RESULTS: The results of this study showed that gentamicin was found to markedly induce apoptosis in NRK-52E cells in a dose-dependent manner; that TMP expressed a dose-dependent protective effect against gentamicin-induced apoptosis; that pre-treatment of the cells with 50 or 100 microM of TMP effectively decreased the reactive oxygen species formation induced by gentamicin; that TMP was found to inactivate the gentamicin-stimulated activities of caspase-3, caspase-8 and caspase-9, to inhibit gentamicin-induced release of cytochrome c, as well as to raise the expression of Bcl-x(L); that TMP inhibited the gentamicin-induced TNF-alpha excretion, and inactivated the transcription factor NF-kappaB; and that the TMP treatment significantly reduced apoptotic injury in rat RTCs. CONCLUSIONS: Based on the results of this study, we suggest that TMP can attenuate gentamicin-induced oxidative stress and apoptotic injury in rat RTCs, and that its character may have therapeutic potential for patients with renal diseases.

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