Poster

[P25-5] P25-5: Anti-infective drugs (5)

Chair: Paula Schaiquevich, Argentina

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[P25-5-3] Vancomycin-induced nephrotoxicity in mice

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Keywords: apoptosis, CD10, kidney, nephrotoxicity, vancomycin

Background

Vancomycin hydrochloride (VCM) is a glycopeptide antibiotic that is commonly used against methicillin-resistant, Gram-positive cocci despite the nephrotoxic side effects. The aim of this study was to clarify time-dependent alterations of VCM-induced nephrotoxicity in mice.

Methods

Animal experiments were carried out in accordance with the animal care and use protocol approved by the Institutional Animal Care and Use Committee of Tokyo Metropolitan Institute of Gerontology (TMIG) and in accordance with Guidelines for the Care and Use of Laboratory Animals of TMIG. VCM was injected intraperitoneally into mice at a dose of 400 mg/kg body weight at 24-h intervals for 3, 5, 7, and 14 days. At 24 h after the last injection, we examined histopathological alterations of the kidney as well as blood biochemistry.

Results

VCM administration resulted in a decrease of body weight and increase of kidney weight. Histological examination revealed renal damage such as dilated proximal tubules with occasional casts and interstitial fibrosis in VCM-treated mice. Furthermore, immunohistochemical staining with anti-CD10 and anti-single-stranded DNA antibodies highlighted damaged renal proximal tubules with marked dilatation as well as numerous apoptotic cells as early as day 4 of VCM-treatment. The severity of symptoms progressed until day 15.

Conclusions

Renal failure caused by VCM administration in mice was observed early in the treatment process and progressed thereafter. Moreover, histological and immunohistochemical analyses revealed specific sites of renal damage such as dilated renal proximal tubules with occasional casts and interstitial fibrosis. These results are consistent with those derived from clinical and pathological studies in humans. Moreover, this model in mice is exceedingly useful for clarifying the little known mechanism of VCM-induced nephrotoxicity.