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Effects of Hypolipidemic Agents in Aminoglycoside-Induced Experimental Nephrotoxicity in Rats: Biochemical and Histopathological Evidence

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Abstract : The study examined the pretreatment and post-treatment effects of low-doses of fenofibrate and rosuvastatin in gentamicin-induced acute nephrotoxicity in rats. Gentamicin (100 mg/kg/day, i.p.) was administered to rats for 8 days. In the pretreatment protocol, low-dose fenofibrate (30 mg/kg/day, p.o.) or low-dose rosuvastatin (2 mg/kg/day, p.o.) treatments were started a day before the administration of gentamicin and continued for 8 days. In the post-treatment protocol, rats administered gentamicin were treated with low-dose fenofibrate (30 mg/kg/day, p.o.) or low-dose rosuvastatin (2 mg/kg/day, p.o.) for 6 days after the completion of 8 days protocol of gentamicin administration. Gentamicin-associated acute nephrotoxicity in rats was assessed in terms of biochemical analysis and renal histopathological studies. Gentamicin-administered rats showed marked renal functional changes as assessed in terms of a significant increase in serum creatinine and urea levels as compared to normal rats. The renal dysfunction noted in gentamicin administered rats was accompanied with elevated serum uric acid level as compared to normal rats while there was no significant change in lipid profile. Low-dose fenofibrate pretreatment in gentamicin-administered rats afforded a significant renal functional improvements and renoprotection while its post-treatment showed no significant renoprotection. On the other hand, pretreatment with low-dose rosuvastatin partially reduced gentamicin-induced increase in serum creatinine level, but its post-treatment did not afford renal functional improvements in gentamicin-administered rats. However, all pre and post-treatments with low-doses of fenofibrate or rosuvastatin significantly reduced the elevated serum uric acid concentration in gentamicin-administered rats. Renal histopathological analysis showed a discernible incidence of acute tubular necrosis in gentamicin-administered rats which were markedly reduced by low-dose fenofibrate or low-dose rosuvastatin pretreatments; but, not by their post-treatments. In conclusion, low-dose fenofibrate pretreatment considerably prevented gentamicin-induced acute tubular necrosis and renal functional abnormalities in rats while its post-treatment resulted in no significant renoprotective action. In spite of effective prevention of gentamicin-induced acute tubular necrosis, the pretreatment with low-dose rosuvastatin had only a partial and fractional protection on renal functional abnormalities. The post-treatment with low-dose rosuvastatin was ineffective in affording a renoprotection in gentamicin-administered rats.

Keywords : gentamicin-nephrotoxicity, low-dose fenofibrate, low-dose rosuvastatin, renoprotection
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