

Acute nephrotoxicity of aristolochic acid in mice

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Abstract

Aristolochic acids (AA), present in Aristolochia plants, are the toxin responsible for Chinese herbs nephropathy (CHN), a rapidly progressive tubulointerstitial nephritis (TIN). To clarify the mechanisms of the development of CHN, we tried to induce TIN in mice using AA. Three strains of inbred mice, BALB/c, C3H/He and C57BL/6, received 2.5 mg kg⁻¹ of AA or AA sodium salt (AANA) daily by intraperitoneal or oral administration, 5 days a week for 2 weeks. Serum and renal tissue were obtained at sacrifice. Twelve-hour urine samples were individually collected in a metabolic cage at one-week intervals. In the AA-injected groups, severe tubular injury, with the appearance of acute tubular necrosis, and rare cell infiltration into the interstitium, were seen in BALB/c mice. C3H/He mice also developed TIN with prominent cell infiltration into the interstitium and interstitial fibrosis. In C57BL/6 mice, only mild and focal tubulointerstitial changes were seen. Serum creatinine and blood urea nitrogen increased in BALB/c and C3H/He mice. Immunofluorescent study revealed no deposition of immune components in kidneys. In the AANA-treated groups, TIN was also seen in all groups, but even more severe tubulointerstitial changes were induced by intraperitoneal injection. Further examination using purified AAI, AAI, AAIv and aristolactam I (ALI) revealed that AAI induced strong nephrotoxicity in mice, and that AAI resulted in mild nephrotoxicity. However, AAIv and ALI caused no nephrotoxicity in this experimental system. There are strain differences in mice in their susceptibility to AA nephropathy. AAI exerted the strongest nephrotoxic effect in mice.