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Assessment of nephrotoxicity in mice of herbal medicine containing aristolochic acid

YI QUAN, Long Jin, Kang Luo, Sun Woo Lim, Yoo Jin Shin, Eun Jeong Ko, Byung Ha Chung, Chul Woo Yang

Department of Internal Medicine-Nephrology, The Catholic University of Korea, Seoul St. Mary's Hospital, Korea, Republic of

Objectives: It is undetermined if herbal medicines (HM) containing aristolochic acid (AA)-containing have similar nephrotoxicity to AA itself.

Methods: We administered HM containing a high concentration (5mg/kg) of AA for 5 days (short-term study) or a low concentration (0.073mg/kg bid) of AA for 30 days (long-term study) to C57BL/6 mice; for comparison, same dose of AA compound was used as controls.

Results: The nephrotoxicity in the HM- and AA-treated mice was compared in terms of renal function, histopathology, oxidative stress, apoptotic cell death, and mitochondrial damage. Short-term HM treatment resulted in acute kidney injury (AKI, marked renal dysfunction, acute tubular necrosis [Injury score- VH: 0 ± 0 vs. AA: 2.9 ± 0.2 , HM: 1.8 ± 0.4 ; $P < 0.05$], and N-GAL expression[VH: 0.8 ± 0.02 vs. AA: 15.5 ± 1 , HM: 14 ± 2 ; $P < 0.05$]) in which the severity of renal dysfunction and histopathology was comparable with that induced by the administration of AA alone. Long-term HM treatment resulted in features of chronic kidney disease (CKD, mild renal dysfunction and tubular atrophy and dilatation [1.9 ± 0.2 vs. 3.3 ± 0.4 $P > 0.05$]). No significant differences in these parameters were observed between the HM- and AA-treated mice. HM-induced oxidative stress (8-OHdG and MnSOD expression) and apoptotic cell death (TUNEL-positive cells and active caspase-3 expression) were similar in HM- and AA-treated mice in the short-term and long-term studies. Mitochondrial injury, evaluated by electron microscopy, was also similar in HM- and AA-treated mice in the short-term and long-term studies.

Conclusions: The nephrotoxic potential of HM containing AA was similar to that of AA itself.