Assessment of nephrotoxicity in mice of herbal medicine containing aristolochic acid

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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.