Aristolochic acid-containing herbal medicine enhances the kidney oxidative stress and apoptosis in mice.

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Objectives: This study was performed to define a causal relationship between herbal medicine (HM) and aristolochic acid nephropathy (AAN) in mice.

Methods: We obtained remained herbal medicine in a patient with AAN and tested the nephrotoxic potential of HM by comparing aristolochic acid (AA) itself. Two experiments were done separately in C57BL/6 mice. Short-term study was performed to evaluate nephrotoxic potential of HM by treating HM or AA to mice intraperitoneally for five days, and long-term study was made based on prescribed dose of HM or AA for days, similar to patients. We measured a number of death, body weights, renal function, oxidative stress and apoptosis in mice, and compared these parameters with AA itself.

Results: Short-term treatment of HM significantly decreased body weight. Serum creatinine and blood urea nitrogen levels were considerably increased in both of AA and HM groups compared with control group, and acute tubular necrosis, N-GAL expression, and macrophage infiltration were markedly increased in both AA and HM groups. Oxidative stress measured with 8-OHdG was also increased in blood and urine, and antioxidant MnSOD2 expression was decreased in AA and HM group. Apoptotic cell death and active caspase-3 were increased in both HM and AA groups. Long-term treatment of HM showed similar result but severity was less than those of short-term treatment of HM. Electron microscopic finding revealed decreased number of mitochondria in both HM and AA in short and long-term treatment.

Conclusions: Our experiment demonstrates that HM containing AA is causally related with AAN.