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Klotho와 S100A8/A9는 신전성과 내인성 급성 신손상의 감별 마커 이다

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김애진, 노한, 장제현, 이현희, 정우경, 정지용

Klotho and S100A8/A9 as Descriminative Markers between Pre-renal and Intrinsic Acute Kidney Injury

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Background: Acute kidney injury (AKI) still has a high morbidity and mortality rate. Early detection and accurate differentiation of the cause of AKI may improve the prognosis of the patient. However, to date there is few reliable biomarkers for the discrimination of prerenal and intrinsic AKI. The purpose of this study was to determine whether AKI is associated with an altered level of Klotho and S100A8/A9 (an endogenous toll-like receptor 4 ligand) protein that may contribute to discriminate between pre-renal and intrinsic AKI.

Method: Volume depleted pre-renal AKI model was induced by Male Sprague-Dawley rat were fed a low-salt diet (0.03%) without water 96hr before two times at 24hr intervals intraperitoneal (IP) injection of furosemide (20 mg/kg). In contrast, cisplatin-induced intrinsic AKI model were given by a single IP injection of cisplatin (5 mg/kg). All animals were euthanized 72hr after first IP injection. Serum and urinary klotho, NGAL, and S100A8/A9 were measured using an ELISA. We also performed a proof of concept cross-sectional study to measure serum and urinary biomarkers in 77 hospitalized patients with established AKI.

Results: Both AKI groups induced somewhat similar increased serum creatinine level than control group. Compared with intrinsic AKI group, pre-renalAKI group caused a marked depression of urinary Klotho level (13.21±17.32 vs. 72.97±17.96 pg/mL; p=0.002). In addition, intrinsic AKI group caused a marked elevation of S100A8/A9 level than those of pre-renal AKI group (2,629.97±598.05 ng/mL vs. 685.09±111.65 ng/mL; p=0.002 in serum; 3,361.11±250.86 ng/mL vs. 741.72±101.96 ng/mL; p=0.003 in urine). The proof of concept study with hospitalized AKI patients also demonstrated decreased urinary klotho in prerenal AKI patients and increased urinary S100A8/A9 concentrations in intrinsic AKI patients.

Conclusion: The attenuation of urinary Klotho and increment of urinary S100A8/A9 may contribute to discriminate the pre-renal AKI and intrinsic AKI.

Key Words: 급성 신손상
Klotho, S100A8/A9, Acute kidney injury